CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com *Research Article*

# CAUSES AND MANAGEMENT OF VIRAL EYE INFECTION

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**Abstract:**

***Introduction:*** *The eye is a fascinating organ for several reasons. It is not only have a composite structure, however it is considered an immune-privileged organ. The anatomy of the eye is composed of the anterior and posterior parts, the line of division is posterior to the lens. The anterior chamber lies within the anterior segment and is an immuneprivileged anatomical location, this is due to the fact that the T-cell response in this area is suppressed This protects the eye from potentially destructive immune attacks however it also makes defence against infectious agents challenging, particularly where T-cell responses are critical for immunological defence. Viruses could get into the eye by direct inoculation, or through haematogenous or neuronal spread. The diagnoses of viral eye infections are usually clinical one, helped by taking a thorough history and performing ophthalmic examination. But in challenging cases the lab tests are essential. In this review, we will discuss the most recent evidence regarding Causes and management of viral eye infection*

***Aim of work:*** *In this review, we will discuss the most recent evidence regarding Causes and management of viral eye infection*

***Methodology:*** *We did a systematic search for Causes and management of viral eye infection using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.*

***Conclusions:*** *A wide range of of viruses can affect the eye and cause viral eye infections, either as a primary infection or reactivation. Some affect the eye directly while the others indirectly but may still manifest with eye disease. One virus may affect several parts of the eye, while different viruses may cause the same eye disease. This could complicate the clinical diagnosis of viral eye disease, but the lab tests like PCR and antibody tests could assist in challenging cases where there may be diagnostic dilemma.*

*The HIV epidemic has had an huge impact on ophthalmology clinics, this is because the virus can cause different eye diseases, and the associated decrease in cell-mediated immunity makes the person highly susceptible to opportunistic viral eye infections, sometimes with severe morbidity. There could be other viruses that may affect the eye that we did not discuss.*

**Key words:** *Causes, management, viral eye infection.*

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*Please cite this article in press Anas Hassan Saeed Alzahrani et al.,* ***Causes and Management Of Viral Eye Infection.,*** *Indo Am. J. P. Sci, 2018; 05(12).*

## INTRODUCTION:

The eye is a fascinating organ for several reasons. It is not only have a composite structure, however it is considered an immune-privileged organ. The anatomy of the eye is composed of the anterior and posterior parts, the line of division is posterior to the lens. The anterior chamber lies within the anterior segment and is an immuneprivileged anatomical location, this is due to the fact that the T-cell response in this area is suppressed [1]. This protects the eye from potentially destructive immune attacks however it also makes defence against infectious agents challenging, particularly where T-cell responses are critical for immunological defence. Viruses could get into the eye by direct inoculation, or through haematogenous or neuronal spread. The diagnoses of viral eye infections are usually clinical one, helped by taking a thorough history and performing ophthalmic examination. But in challenging cases the lab tests are essential. In this review, we will discuss the most recent evidence regarding Causes and management of viral eye infection

## METHODOLOGY:

We did a systematic search for Causes and management of viral eye infection using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Causes, management, viral eye infection.

### HIV and The Eye

HIV is considered a Retroviridae. It is now spread globally, especially in the sub-Saharan Africa. The transmission often happens after unprotected sex or from mother-to-child. The virus causes immune suppression eventually if not treated, which makes the patient vulnerable to a widespread range of infections, this can affect any part of the body,
as well as the eye. It is projected that about seventy percent of adult AIDS patients will develop an ocular complication during their lifetime [2]. Typically, the main groups of ophthalmic manifestations include but not limited to: microvasculopathy, opportunistic infections, neoplasms and neuroophthalmic illnesses [3]. Microvasculopathy could affect the conjunctiva or retina, also known as HIV retinopathy, and could present on fundoscopy as cotton wool spots, intraretinal haemorrhages and retinal microaneurysms [4]. It is suggested that the pathological reason behind conjunctival and retinal microvasculopathy is potentially alike and could involve increased plasma viscosity, circulating immune complexes and infectious damage of the vasculature.

Orbital and adnexal presentations of HIV are rare, with Kaposi sarcoma, conjunctival microvasculopathy and opportunistic viral infections are the most
common. The likely opportunistic viral infections that could infect the eye involve CMV, HSV, VZV, Molluscum contagiosum and many others, though the bacterial and fungal infections are also critical [5]. Additionally, infectious complications, HIV could
cause optic neuropathies by different mechanisms, including but not limited to compression of the optic nerve by cancers, and vaso-occlusion.

In pediatric population, eye manifestations of HIV are less often than in adults. The reasons are not so clear, with the most common eye manifestation of HIV in kids is keratoconjunctivitis sicca or dry eyes [6].

The immune-recovery uveitis is a syndrome that has been known as the advent of highly active antiretroviral therapy (HAART). It involves paradoxical worsening of intraocular inflammation, which could be caused by an immune response to CMV and other infectious agents present in the eye, and is characterised by an increase in
CD4+ cell count to above one hundred cells/mm3.

### The Herpesviruses

Herpesviridae family viruses are large; they are double-stranded DNA viruses, which form a large and very important group of infective agents. In humans, they can cause a wide range of syndromes, ranging from the mild to severe.

### Herpes simplex viruses

The transmission of HSV-1 and 2 are through close contact. HSV-1 can get into the host through the oropharyngeal mucosa, that lets the initial replication, but could also be transmitted through sexual intercourse. This is can be followed by latency in the trigeminal or sacral ganglia. The Initial HSV-2 replication is often in the genital mucosa, with latency in the sacral ganglia, and could be linked to congenital HSV-2 infection, which might have ocular manifestations, such as cataract [7]. HSV-1 and 2 have a similar clinical presentations and can cause a wide spectrum of illnesses. HSV-1, but prevails with

regard to eye infections compared with its type two counterpart.
HSV-1 Infection can cause keratitis, which is the single most common cause of infectious blindness in developed countries [8] and herpetic infections have the same exact characteristics of HSV disease elsewhere in the body. The primary infection could be followed by intermittent reactivation [9]

The reactivation episodes could be responses to different stimuli, including fever, stress, cold and others, and are maybe due to the viruses' capability to remain latent in the sensory ganglia of the first division of the trigeminal nerve.

The pathological manifestations of HSV-1 include but not limited to blepharitis, conjunctivitis, infectious epithelial keratitis, neurotrophic keratopathy, necrotizing stromal keratitis, immune stromal keratitis and endotheliitis. Dendritic ulcer caused by HSV-1 is a form of infectious epithelial keratitis and occurs due to active viral replication. Other eye manifestations are iridocyclitis, panuveitis and acute retinal
necrosis (ARN) [10].

HSV keratitis is often a clinical diagnosis. But sometimes especially in difficult cases the specific diagnostic tests are vital. The detection of viral DNA by PCR is sensitive and better than virus isolation or antigen detection. The intraocular infection could be found by PCR of anterior chamber or vitreous fluids. The locally produced antibody could also be detected, and by comparing with total IgG, one can determine intraorbital antibody production.

The antiviral medications are the mainstay of treatment in HSV infections. The decision on whether depends on the location, severity of infection and immune status of the patient. There are several topical medications include acyclovir and trifluridine, with acyclovir being the most widely used. The systemic antiviral medications, other than acyclovir, are valaciclovir and famciclovir. The topical antivirals are used to treat HSV blepharitis, conjunctivitis, infectious epithelial keratitis and used as prophylaxis to cover corticosteroid treatment of certain forms of keratitis. Oral medications are used in some cases of endotheliitis, severe cases of uveitis, in immunocompromised patients, paediatric patients not responding to topical treatment or as prophylaxis. Intravenous therapy is ususally preserved for patients with posterior site involvement, such as necrotising herpetic retinitis (NHR).

Corticosteroids use for inflammation in HSV ocular disease are controversial as it may cause increased severity of the HSV infection by inhibiting the host immune response, however in some cases can be helpful in reducing scarring and neovascularisation.

**Cytomegalovirus**

The first time CMV was isolated was in 1956 after cell culture technology was developed. The name is derived from the cytopathic effect seen in cell culture, i.e. 'cytomegaly' [11]. The virus could be transmitted vertically or horizontally and is shed frommultiple sites. Risk factors for severe disease involve primary infection, high viral load and immune suppression [12].

Although CMV mainly causes retinitis, other eye presentations include anterior uveitis and corneal endotheliitis [13]. There are as well reports of ARN being caused by CMV [14]. CMV retinitis often happens in advanced HIV disease, alone, with disseminated CMV disease or with immune reconstitution after initiation of HAART [15].

The diagnosis of CMV retinitis is often a clinical one, however more lab tests might help in the diagnosis and involve serum antibody testing, viral isolation and PCR of blood or ocular fluids looking for CMV DNA [16].

The management of CMV retinitis involves beginning with an antiviral medication, which can be given systemically, as an intravitreal injection or as a long-acting intravitreal implant, in addition to HAART. The systemic antiviral medications involve the nucleoside analogue ganciclovir and its prodrug valganciclovir. There are as well Ganciclovir-resistant mutants and are often the result of a mutation in the unique long ninety seven region of the genome [17].

Intravitreal cidofovir may precipitate hypotony and so is generally avoided. Ganciclovir intravitreal implants have been shown to provide effective treatment of CMV retinitis.

**Varicella zoster virus**

VZV is transmitted through respiratory pathway and is very contagious. After the primary infection, the virus stays latent in one or more posterior root ganglia, often the trigeminal or thoracic nerves. The ophthalmic branch of the trigeminal nerve is the most commonly affected is its three divisions. About ten to twenty percentof all herpes zoster manifests as herpes

zoster ophthalmicus [18].

During times of low immunity, the virus could reactivate and spread from the ganglia down the peripheral nerves to the skin, to cause the typical lesions of herpes zoster. Acute retinal necrosis is also reported in older patients, The management of VZV infection is usually aimed to manage the symptoms, till the recovery and avoid complications. In addition to analgesia, good hydration and adequate personal hygiene to avoid secondary bacterial infection, there are 3 antiviral medications used in VZV infection.

**Epstein–Barr virus**

Primary infection generally happens after contact with the saliva [19]. EBV usually infects the B-cells however it can also infect some types of squamous epithelial cells.
Some studies concluded wide range of manifestations of corneal epithelial and stromal infections associated with EBV, however the most frequent eye presentations of acute mononucleosis include periorbital oedema and follicular conjunctivitis [20].

**Other Herpesviruses**

The other less common Herpesviruses causing eye disease are HHV-6 and HHV-8, with the latter also known as Kaposi sarcoma-associated Herpesvirus. HHV-6 seldom causes optic neuritis and could cause conjunctivitis. HHV-8 might cause conjunctival Kaposi's sarcoma and possibly uveitis.

**Adenovirus**

Adenoviruses are part of the Adenoviridae family and are a wide range of double-stranded DNA viruses, that can cause a wide variety of diseases. These variety from upper and lower respiratory tract infections, to viral conjunctivitis, to gastroenteritis and others. These viruses are non-enveloped and thus are particularly resistant to inactivation and can survive in the environment for prolonged periods.
Eye manifestations of adenoviral infection are categorized into four syndromes: pharyngoconjunctival fever (PCF), epidemic keratoconjunctivitis (EKC), acute nonspecific follicular conjunctivitis (NFC) and chronic keratoconjunctivitis (CKC) [21].
In addition, adenovirus might be the cause of acute haemorrhagic conjunctivitis.
Pharyngoconjunctival fever is most frequently found in children and is generally due to serotype 3, but serotypes 1, 4, 5, 6, 7 and 14 have also been identified.

Epidemic keratoconjunctivitis is most frequently associated with serotypes eight and nineteen, although it has also been reported with serotypes 2, 3, 4, 7 to 11, 14, 16 and 29. The condition is very contagious and is most frequently in fall and winter. Acute nonspecific follicular conjunctivitis produces a mild conjunctivitis and is usually self-limiting.

Management of keratitis and uveitis secondary to severe adenoviral conjunctivitis is managed with topical steroids but must be supervised.

**Enteroviruses**

Enteroviruses are members of the Picornaviridae family of single-stranded RNA viruses, that replicate in the intestinal tract and cause asymptomatic infection or mild symptoms. However in some cases the virus might travel to other organs, causing severe disease. These include ocular diseases such as conjunctivitis, keratoconjunctivitis and uveitis [22].

Topical steroids must not be used, that is due to the risk of corneal perforation.
Parechovirus, which previously was under the human enteroviruses, has been isolated from ocular fluids in patients with uveitis [23].

**Rubella**

Rubella (German measles) was first described as a distinct disease in the late 19th century. In general rubella virus causes a mild exanthematous disease that affects all ages [24]. Damage to fetal endothelial cells in early pregnancy is the result of viral replication, because the immune system has not developed by this time. The virus can also induces retardation of mitosis in infected cells.

The goal of treatment of congenital rubella is at managing the complications, like cataract surgery and management of secondary glaucoma. If acquired following labor, which is generally in the form of conjunctivitis or keratitis, symptomatic treatment might be necessary, however the condition is usually self-limiting.

**Measles**

Measles viruses are a member of the Paramyxoviridae family of single-stranded RNA viruses, which spreads through the respiratory route and is very contagious [25]. After an incubation period of eight to twelve days, the symptoms of fever, cough, coryza and conjunctivitis begin. The

typical measles rash lasts for three to seven days.

Measles is the most critical cause of blindness in pediatric population in developing countries. Acute MV infection decreases the serum retinol concentration, which could present as xerophthalmia and finally result in blindness. Blindness could also result from cortical damage from measles encephalitis.

## CONCLUSION:

A wide range of of viruses can affect the eye and cause viral eye infections, either as a primary infection or reactivation. Some affect the eye directly while the others indirectly but may still manifest with eye disease. One virus may affect several parts of the eye, while different viruses may cause the same eye disease. This could complicate the clinical diagnosis of viral eye disease, but the lab tests like PCR and antibody tests could assist in challenging cases where there may be diagnostic dilemma.

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