

**Review Article****DIFFERENTIAL DIAGNOSIS OF REDNESS OF EYE: A REVIEW**

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**ABSTRACT**

Most cases of "red eye" seen in general practice are likely to be conjunctivitis or a superficial corneal injury, however, red eye can also indicate a serious eye condition such as acute angle glaucoma, iritis, keratitis or scleritis. Features such as significant pain, photophobia, reduced visual acuity and a unilateral presentation are "red flags" that a sight-threatening condition may be present. In the absence of specialised eye examination equipment, such as a slit lamp, General Practitioners must rely on identifying these key features to know which patients require referral to an Ophthalmologist for further assessment. Typically orbital cellulitis is not associated with drop of vision unless the eye globe is involved. Fever and leukocytosis are usually present in children, but they may be absent in adults. Toxic conjunctivitis is not allergic in nature, but it is frequently confused with allergic ocular disease. It implies direct damage to ocular tissues from an offending agent, usually a preservative or medication. Many techniques were available for diagnosis like Fluorescein angiography allows a doctor to clearly see the blood vessels at the back of the eye. The eye can be examined by ultrasonography. A probe is placed gently against the closed eyelid and painlessly bounces sound waves off the eyeball. The reflected sound waves produce a two-dimensional image of the inside of the eye. Optical coherence tomography (OCT) provides high-resolution images of structures at the back of the eye, such as the optic nerve, retina, choroid, and vitreous humor

**Key words:** Red eye, Conjunctivitis, Scleritis, Sclera, Orbital Cellulitis, OCT.

**1. INTRODUCTION:**

Conjunctivitis, also known as pink eye, is inflammation of the outermost layer of the white part of the eye and the inner surface of the eyelid.<sup>3</sup> It makes the eye appear pink or reddish.<sup>1</sup> There may also be pain, burning, scratchiness, or itchiness.<sup>1</sup> The affected eye may have increased tears or be "stuck shut" in the morning.<sup>1</sup> Swelling of the white part of the eye may also occur.<sup>1</sup> Itching of the eye is more common in cases due to allergies.<sup>2</sup> Conjunctivitis can affect one or both eyes.<sup>1</sup>

The most common infectious causes are viral followed by bacterial.<sup>2</sup> The viral infection may occur along with other symptoms of a common cold.<sup>1</sup> Viral and bacterial cases are easily spread between people.<sup>1</sup> Allergies

to pollen or animal hair is also a common cause.<sup>2</sup> Diagnosis is often based on signs and symptoms.<sup>1</sup> Occasionally a sample of the discharge is sent for culture.<sup>1</sup>

Most general practice clinics will not have access to specialised equipment for eye examination, e.g. a slit lamp and tonometer for measuring intraocular pressure, and some conditions can only be diagnosed using these tools.<sup>4</sup> Therefore primary care management relies on noting key features such as pain, photophobia and reduced visual acuity, to identify which patients require referral for ophthalmological assessment. In general, a patient with a unilateral presentation of a red eye suggests a more serious cause than a bilateral presentation.<sup>5</sup>

## 2. CAUSES OF RED EYE:

- Acute angle closure glaucoma occurs when there is an obstruction to drainage of aqueous humour from the eye, rapidly causing increased intraocular pressure. This condition typically occurs in middle-aged to elderly, hypermetropic (long-sighted) females,<sup>2</sup> however, it can occur in any patient.<sup>6</sup>
- Keratitis is inflammation of the corneal epithelium caused by infection (e.g. herpes simplex virus, bacteria, fungi or protozoa) or auto-immune processes (e.g. collagen vascular diseases).<sup>7</sup>
- Microbial keratitis is usually precipitated by a change to normal corneal epithelial health, caused by a factor such as trauma, contact lens use or tear film and/or eyelid pathology.<sup>5</sup> Iritis is inflammation of the iris that can be associated with other inflammatory disorders, e.g. ankylosing spondylitis, or occur as an isolated idiopathic condition. Iritis is also known as anterior uveitis; posterior uveitis is inflammation of the choroid (choroiditis). Complications include glaucoma, cataract and macular oedema.<sup>8</sup>
- Scleritis is inflammation of the sclera. This is a very rare presentation, usually associated with autoimmune disease, e.g. rheumatoid arthritis.<sup>9</sup>
- Penetrating eye injury or embedded foreign body; red eye is not always a feature.<sup>10</sup>
- Acid or alkali burn to the eye.<sup>6</sup>

## 3. LOCATION ON EYE:

- Eyelids vs eyelid margin
- Eyelid vs palpebral conjunctiva
- Palpebral vs bulbar conjunctiva
- Sectoral vs limbal injection
- Scleral vs episcleral<sup>11,12</sup>

Acute red eye can be due to a rather simple disorder. It can be caused by a subconjunctival hemorrhage which does not usually require any

treatment, or it may be due to a mild infectious conjunctivitis that can be treated easily by the primary care provider, and in some cases, might even resolve spontaneously. However, the red eye could be much more serious possibly leading to loss of sight or indicating an underlying systemic disease which must be attended to.<sup>11</sup>

Numerous conditions may be associated with acute red eye. These include subconjunctival hemorrhage, conjunctivitis, keratitis, acute congestive glaucoma, episcleritis, scleritis, iritis, endophthalmitis, panophthalmitis, orbital cellulitis, and cavernous sinus infection.<sup>12</sup>

## 4. CONJUNCTIVITIS:

Conjunctivitis is inflammation of the bulbar and/or palpebral conjunctiva. It can be caused by an infectious agent such as bacteria, viruses and chlamydia, It can be also caused by an allergic situation such as phlyctenular conjunctivitis or vernal conjunctivitis (spring catarrh).<sup>13</sup>

### 4.1 Acute Allergic conjunctivitis:

Allergic conjunctivitis is an eye inflammation caused by an allergic reaction to an exogenous antigen like pollen, dust mites, contact lens solution or medicated eye drops. It often occurs in people with a strong personal or family history of allergies. When the eyes are exposed to an inciting substance, the response is release of histamine and other active mediators by mast cells, which stimulate dilation of blood vessels, irritation of nerve endings, and increased secretion of tears (Type I hypersensitivity).<sup>14</sup>

## 5. DIAGNOSIS:

### 5.1 Non-infectious (Idiopathic):

Diagnosis Routine extensive laboratory work up is NOT required in many cases of uveitis since: 1) Idiopathic cases are the majority and 2) Most causes or associations can be diagnosed or suspected on clinical grounds only. The Lab work, if needed, must be targeted towards the suspected clinically diagnosed etiology. A

nonspecific workup may be requested only if the history and the physical examination findings are unremarkable, in the presence of uveitis that is granulomatous, or recurrent.<sup>15</sup>

The following tests may be of help:

- Complete blood cell (CBC) count
- Erythrocyte sedimentation rate (ESR)
- Antinuclear antibody (ANA)
- Venereal disease research laboratory (VDRL) and Rapid plasma reagin test (RPR)
- Purified protein derivative (PPD)
- Lyme antibody titre
- HLA ( such as B27 and B5) testing
- Chest radiography (to assess for sarcoidosis or tuberculosis)
- Infectious workup (eg, HIV, toxoplasmosis), depending on the presentation.<sup>14</sup>

### 5.2 Endophthalmitis:

Endophthalmitis is a clinical diagnosis, supported by culture of intra-ocular fluids, although a negative culture occurs in more than 30% of cases. The patient complains of decreased vision, red eye, and eye pain. Patients feel otherwise well and are usually afebrile.<sup>16</sup>

### 5.3 Orbital Cellulitis:

Inflammation of the soft tissue posterior to the orbital septum. Patients may have proptosis, decreased ocular mobility, ocular pain, and tenderness on eye movement. Typically orbital cellulitis is not associated with drop of vision unless the eye globe is involved. Fever and leukocytosis are usually present in children, but they may be absent in adults.

Differential diagnosis of bacterial orbital cellulitis includes malignancy, invasive fungal disease (mucormycosis) and orbital pseudotumor (an idiopathic cause of painful ophthalmoplegia with inflammatory proptosis).<sup>17</sup>

### 5.4 Cavernous Sinus Thrombosis:

A rare condition in which clotting occurs inside the cavernous sinus. Usually occurs due to spread of infection from sinusitis and orbital or preseptal cellulitis.

Investigations required include MRI and MRV to confirm the diagnosis. Differential diagnosis includes Orbital cellulitis and Carotido-Cavernous fistula. Treatment consists of antibiotics, anticoagulants and rarely surgical intervention<sup>18</sup>

### 5.5 Subconjunctival hemorrhage:

A subconjunctival hemorrhage is an accumulation of blood in the potential space between the conjunctiva and the sclera. It is often spontaneous without an apparent cause. It may occur due to some Valsalva's phenomenon (increase in venous pressure due to straining). It may infrequently indicate hypertension or blood coagulation defect.<sup>19</sup>

### 5.6 Chronic Red Eye:

Keratoconjunctivitis Sicca (KCS) Vernal Keratoconjunctivitis (VKC) Trachoma Pterygium Toxic conjunctivitis TED, Keratoconjunctivitis sicca Keratoconjunctivitis sicca, commonly called dry eye, is a disorder resulting from tear deficiency or dysfunction. It causes ocular redness with discomfort, burning sensation, sense of dryness and in later stages it may cause blurred vision, light sensitivity (photophobia).<sup>20</sup>

### 5.7 Trachomatous Conjunctivitis:

Trachomatous conjunctivitis is a chronic inflammatory condition. Trachoma is the world's leading cause of preventable blindness of infectious origin. It is endemic in Egypt. Among children under 5, prevalence of active trachoma infections can be 60 percent or more.<sup>21</sup>

### 5.8 Pterygium Pterygium:

is an abnormal wedge-shaped growth of degenerated fibrovascular conjunctiva that extends progressively over the cornea, usually

from the nasal side. Usually occurs in patients living in hot climates with excessive exposure to ultraviolet rays from the sun and to dust.<sup>22</sup>

### **5.9 Toxic Conjunctivitis (Conjunctivitis Medicamentosa):**

Toxic conjunctivitis is not allergic in nature, but it is frequently confused with allergic ocular disease. It implies direct damage to ocular tissues from an offending agent, usually a preservative or medication. It occurs in patients on long-term therapy with multiple preservative-containing topical ocular medications, such as those for glaucoma. Conjunctival hyperemia predominantly involving the inferior fornix is the most common manifestation. The eyelids and cornea may also be involved (eyelid hyperemia and /or corneal superficial punctate keratitis). Commonly, the original eye condition improves upon initial treatment, but the eye symptoms worsened with continued use. Treatment involves discontinuing the suspected offending agent(s) and switching to preservative-free topical therapies or oral medications when possible if continued therapy is required.<sup>23</sup>

### **5.10 Thyroid eye disease (Grave's Disease):**

Patients with Graves' disease have ophthalmopathy. It is characterized by inflammation of the extraocular muscles, orbital fat and connective tissue resulting in proptosis (exophthalmos), impairment of eye-muscle function, and periorbital and conjunctival edema. Ophthalmopathy is more common in patients who smoke cigarettes.

Diagnosis Done By CT scan showing enlargement of extraocular muscles in Thyroid Eye Disease.<sup>24</sup>

A variety of tests can be done to confirm a problem or to determine the extent or severity of a disorder. Each eye is tested separately.

### **6. ANGIOGRAPHY:**

In general, angiography involves injecting dye into blood vessels to make them more visible on

imaging tests. Angiography of the eye, however, uses dye to make blood vessels more visible when doctors directly examine or photograph them.<sup>25</sup>

### **7. FLUORESCEIN ANGIOGRAPHY:**

Allows a doctor to clearly see the blood vessels at the back of the eye. A fluorescent dye, which is visible in blue light, is injected into a vein in the person's arm. The dye circulates through the person's bloodstream, including the blood vessels in the retina. Shortly after the dye is injected, a rapid sequence of photographs is taken of the retina, choroid, optic disk, iris, or a combination. The dye inside the blood vessels fluoresces, making the vessels stand out. Fluorescein angiography is particularly useful in the diagnosis of macular degeneration, blocked retinal blood vessels, and diabetic retinopathy. This type of angiography is also used to assess people who may need laser procedures done on the retina.<sup>26</sup>

### **8. INDOCYANINE GREEN ANGIOGRAPHY:**

Doctors to see the blood vessels of the retina and choroid. As in fluorescein angiography, a fluorescent dye is injected into a vein. This type of angiography gives doctors more detail of the blood vessels of the choroid than fluorescein angiography. Indocyanine green angiography is used to show macular degeneration and detect the development of new blood vessels in the eye.<sup>27</sup>

### **9. ELECTRORETINOGRAPHY:**

Electroretinography allows a doctor to examine the function of the light-sensing cells (photoreceptors) in the retina by measuring the response of the retina to flashes of light. Eye drops numb the eye and dilate the pupil. A recording electrode in the form of a contact lens is then placed on the cornea, and another electrode is placed on the skin of the face nearby. The eyes are then propped open. The room is darkened, and the person stares at a flashing light. The electrical activity generated by the retina in response to the flashes of light is recorded by the electrodes.

Electroretinography is particularly useful for evaluating diseases, such as retinitis pigmentosa, in which the photoreceptors are affected.<sup>28</sup>

#### 10. ULTRASONOGRAPHY:

The eye can be examined by ultrasonography. A probe is placed gently against the closed eyelid and painlessly bounces sound waves off the eyeball. The reflected sound waves produce a two-dimensional image of the inside of the eye. Ultrasonography is useful when an ophthalmoscope or slit lamp cannot view the retina because the inside of the eye is cloudy or something is blocking the line of sight. Ultrasonography can be used to determine the nature of abnormal structures, such as a tumor, inside the eye, or retinal detachment. Ultrasonography can also be used to examine blood vessels supplying the eye (Doppler ultrasonography) and to determine the thickness of the cornea<sup>29</sup>

#### 11. PACHYMETRY:

Pachymetry (measuring the thickness of the cornea) is very important in refractive eye surgery, such as laser in situ keratomileusis (LASIK). Pachymetry is usually done by using ultrasonography. For ultrasound pachymetry, the eye is numbed with drops, and an ultrasound probe is placed gently onto the surface of the cornea. Optical pachymetry does not require numbing eye drops because the instruments do not touch the eye.<sup>30</sup>

#### 12. OPTICAL COHERENCE TOMOGRAPHY:

Optical coherence tomography (OCT) provides high-resolution images of structures at the back of the eye, such as the optic nerve, retina, choroid, and vitreous humor. OCT can be used to identify swelling of the retina. OCT is similar to ultrasonography but uses light instead of sound. Doctors use OCT to view disorders of the retina, including macular degeneration, disorders that can cause new blood vessels to develop in the eye, and glaucoma.<sup>31</sup>

#### 13. COMPUTED TOMOGRAPHY (CT) AND MAGNETIC RESONANCE IMAGING (MRI):

Computed tomography and magnetic resonance imaging can be used to provide detailed information about the structures inside the eye and the bony structure that surrounds the eye (the orbit). These techniques are used to evaluate eye injuries, particularly if doctors suspect a foreign object is in the eye, tumors of the orbit and optic nerve, and optic neuritis.<sup>32</sup>

#### 14. CONCLUSION:

Many techniques were available for diagnosis like Fluorescein angiography allows a doctor to clearly see the blood vessels at the back of the eye. The eye can be examined by ultrasonography. A probe is placed gently against the closed eyelid and painlessly bounces sound waves off the eyeball. The reflected sound waves produce a two-dimensional image of the inside of the eye. Optical coherence tomography (OCT) provides high-resolution images of structures at the back of the eye, such as the optic nerve, retina, choroid, and vitreous humor, Most general practice clinics will not have access to specialised equipment for eye examination, e.g. a slit lamp and tonometer for measuring intraocular pressure, and some conditions can only be diagnosed using these tools.

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