# **General Internal Medicine and Clinical Innovations**

# **Review Article**

# Ocular Inflammation

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# Abstract

Ocular inflammation can be caused by a number of different etiological mechanisms. These include allergens, contact lens wear, trauma and dietary or lifestyle changes. While there are different "triggers" of ocular inflammation, they produce similar symptoms because all induce essentially the same immunological cascades. The "irritation" produced is caused by the induction of the interleukin system, immune cell recruitment and complement activation. Additionally, the available treatment options for these variously induced syndromes are similar. These options range from passive approaches such as the application of either hot or cold treatment to the affected area to more aggressive actions such as the treatment of antibiotic or steroid drops and in more rare cases surgery. The industry that surrounds the treatment of ocular disorders is massive with billions of dollars generated in over the counter and prescription product sales every year all over the world.

# Introduction

Inflammation of the eye and surrounding tissues have a variety of causes, but have similar symptoms. Inflammation manifests itself to the sufferers as redness, swelling, itching, exudate formation and often involvement of the fellow eye [1]. While the overt signs and symptoms are similar regardless of the etiological agent, the causes are varied. Allergens from the environment, contact lens wear, microbial colonization, animal dander and reactions to drugs can all cause ocular inflammation [2]. Inflammation occurs by the activation of the cytokine system, complement activation, and initially cellular infiltration into the sclera or cornea [3-5]. Cellular infiltration of the avascular cornea is a serious condition as immune cells are not usually found there. Should they lyse, corneal tissue can be damaged.

## The Eye

The eye may be considered to be in essence a sterile external organ. It is the one animal organ that is free from microbial contamination (on the outside), yet directly exposed to the external environment, unlike the internal organs. This is due to the combination of lysozyme presence, constant blinking and the presence of IgA. It is constantly exposed to stimuli such as environmental factors like pollen or air pollutants, or other environmental microbes. The eye allows humans (and other animals) to see by collecting light from an individual's surroundings, with the intensity of the light regulated through a diaphragm and then an image is formed. This image is converted into a series of electrical signals which are transmitted to the brain. Different types of disease affect the eye and thus vision in different ways.

## Contact lens wear

Ever since the introduction of contact lens wear, there have been issues related to inflammation in the ocular environment as the result of wear. These range from minor redness and "foreign body sensation" to more severe bacterial infections associated with either insertion of a contaminated contact lens or use of contaminated contact lens solutions, or both [5]. Most commonly there is redness, swelling and irritation associated with the use of the lens as the body sees the plastic as a foreign body and attempts to cope with what it determines as an "invader" [6]. The induction of cellular infiltrates such as neutrophils into the non-vascular cornea is of particular concern as these may coalesce, lyse, ulcerate or cause wounds in the cornea. Key to this is the induction of the cytokine system and the recruitment of immune cells to a given area [3,7]. The immune cells that are recruited first are neutrophils and eosinophils. These cells have the ability to induce cytokine production in the form of tumor necrosis factor (TNF), interleukin 1 (IL-1), interleukin 2 (IL-2) and interleukin 6 (IL-6) [3,7]. The eye initially detects the contact lens as an invader, and soon after cellular activation (minutes) the cytokine system is activated. Different types of contact lens materials can lead to greater or lesser severity of symptoms including "red eye" which is non-specific inflammation [6,8]. Clinical fit is also critical to avoiding this condition. Improper fit or torn or dry contact lenses can lead to prolonged rubbing of the eye with a potential for abrasion. This is referred to as foreign body sensation.

# Allergens

Allergens are complex environmental compounds that affect most individuals' immune system to greater or lesser degree, depending on an individual's previous exposure and genetics [9]. Allergens function in the body by activating certain cellular and non-cellular aspects of the immune system. Allergens are capable of initiating a Type-1 Hypersensitivity reaction through IgE stimulation. Allergens work by interaction with IgE antibody which are a part of the immune system. IgE binds to an allergen and then onto an effector cell such as a basophil or mast cell. Following this complex binding histamine is released by these cells. This action may occur in a matter of minutes. IgE can be stimulated against parasitic infections and in those affected by environmental antigens as well. There are many different types of allergens, but as with much in terms of overt symptomology, they express the same reactions, redness, swelling, itching, pain and perhaps photophobia. These symptoms are expressed by cells and cellular by-

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products in the form of cytokines and by the activation and action of complement.

Allergen related reactions are often seasonal or occur as a result of exposure to a specific allergic toxin. Allergens can be found and attributed to a variety of sources including foods, insect stings or bites, and drugs such as penicillin.

Treatments include medications designed to alleviate the symptoms caused by histamine release (mentioned above). These are steroids and anti-histamines which interfere with the process of binding. In severe reactions epinephrine is recommended for relief from anaphylaxis.

### Complement

Complement is one of the most important and most complicated processes that exist in mammals [10]. Once activated the complement cascade leads to blood clotting. But as important as that end result is the development of soluble by products which may be thought of almost as "waste" are produced as a result of the induction of the cascade. Chief among these are components C3a and C5a, which stimulate non-specific inflammatory responses systemically [4]. Sohn and colleagues demonstrated that if component C3 were not activated that complement mediated inflammation would not ensue [4,11]. But this positive feature has another side. Should complement for whatever reason not be active, resistance to bacterial infections would be limited. Conversely, uncontrolled and unregulated activation can cause damage to the cornea. In order to prevent this, CRegs are expressed at the surface of the cornea [11]. This regulatory system is critical as the cornea and the greater environment of the eye are constantly challenged by bacteria which secrete components CRegs from the ocular surface. Should this happen tissue damage by activated complement may ensue.

#### The Cytokine System

The cytokine system has several functions but at the core it is a communications network [9]. Cytokines are soluble molecules that are released by cells in response to stimuli. They are considered small molecules of 5-20 kDa molecular weight. The induction of cytokines may be of a general nature in that their response is non-specific (in contrast to antibody) but their action is somewhat more specific. Cytokines have the ability to stimulate responses between cell types. They function by interacting with receptors on the cell membrane of effector cells such as neutrophils and macrophages. In some cases, they may serve duel functions of both communication and effector molecule, such as tumor necrosis factor (TNF) [3]. TNF may be necrotic to tissue in addition to stimulating other cell types to activate and either carry the same signal or induce other cells to carry another signal for a related function.

### **Microbial Agents**

The presence of microbes whether they be bacteria or virus on the surface of a compromised eye can be cause for a medical emergency [12]. A compromised eye in this case is one where there has been a break at the cellular level unlike the skin surface which has several layers. The ocular environment is in essence not as "deep". Should bacteria or virus colonize the cornea or sclera, the infections that result develop rapidly in the nutrient rich environment. In extreme cases amputation of the eye may be the end result. Initial symptoms of a bacterial infection are pain, irritation, redness and then development of exudate and photophobia. As long as the surface of the eye remains intact-like the surface of the skin, bacteria tend to be repelled. The surface lysozymes

that are present, blinking and tear flow, tend to keep the eye "sterile" in that while bacteria may be present, they do not colonize the eye surface. These microbes are simply not on site long enough to elicit any sort of response or colonize. Some of the more common types of microbial agents are Pseudomonas sps, and Staphylococcus sps. Acanthamoeba infections are more serious as are some viral infections [13]. Acanthamoeba have the ability to compromise an eye and gain entry via a direct route.

Bacterial infections usually occur due to breaks in the skin, for the eye this means the cornea or sclera. Once compromised, bacteria will grow rapidly as the eye is a rich source of nutrients. In a majority of cases the bacteria are water bourn, meaning that they come from some water source or perhaps a contact lens case that has not been properly sterilized [14,15]. As mentioned once colonization occurs, the cells tend to grow and reproduce rapidly. Only quick intervention will often save the organ in extreme cases.

#### Treatments

Treatment options for ocular inflammation may be passive, such as ice packs or heat, or they may be more aggressive such as the use of antibiotic or steroid drops or oral antibiotics, or a combination. In severe allergic reaction cases, epinephrine may be given [8,12].

### Conclusion

Ocular inflammation is not a fatal condition. However, it can lead to a reduced quality of life in both the short and long term. The variety of conditions be leigh the relative conserved number of symptoms associated with those conditions. There is pain, redness, exudate in some cases, foreign body sensation and itching. There are a variety of over the counter drugs that are used to treat these symptoms of these conditions, which garner companies around the world billions of dollars in sales every year.

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