

# Investigating immune cell trafficking on the ocular surface and its correlation to disease stage and treatment outcomes

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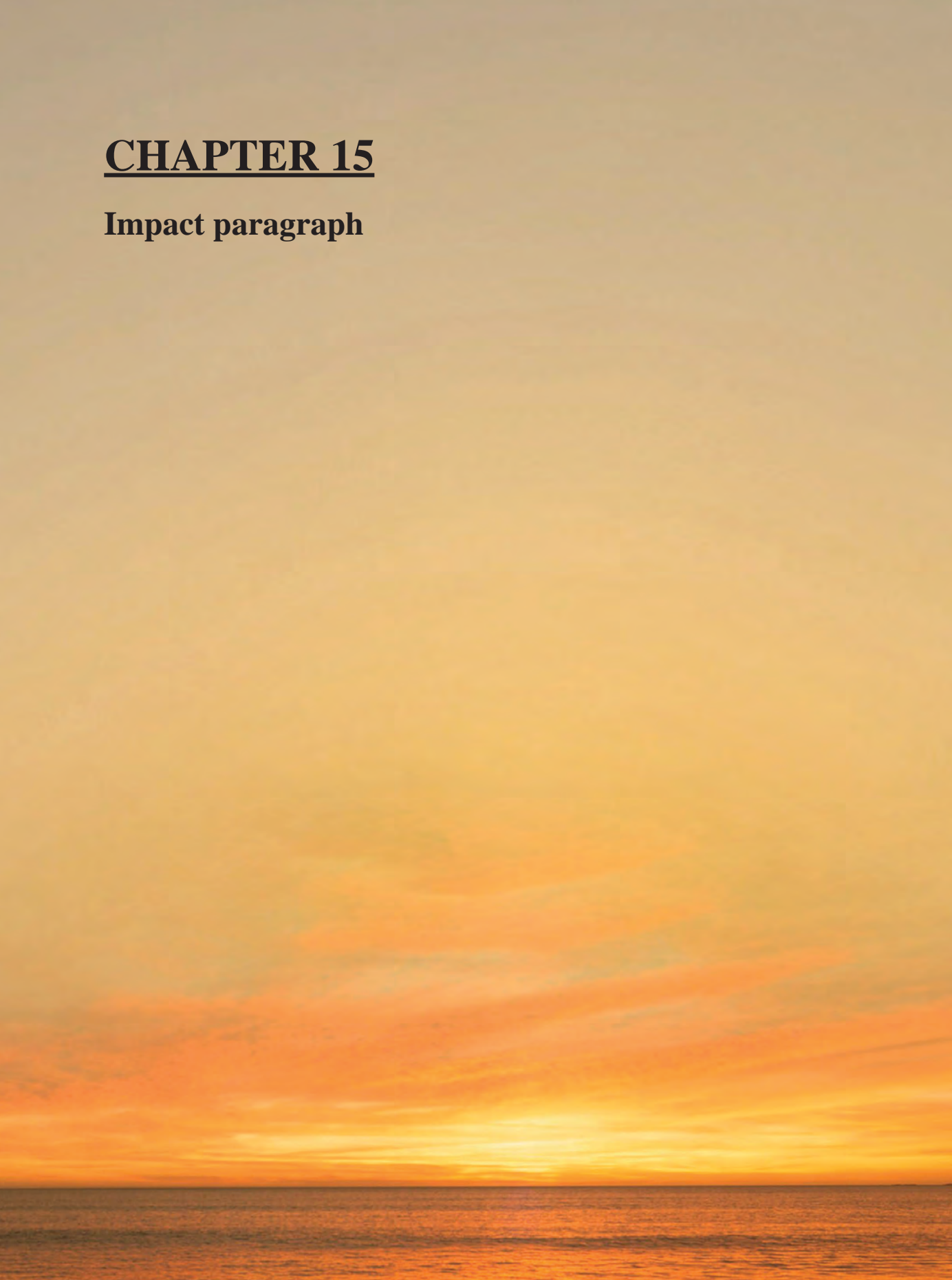
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# **CHAPTER 15**

**Impact paragraph**



Every day in the outpatient clinic, we are faced with a myriad clinical challenges. Our aim as doctors is to treat each patient to the best of our ability, making the accurate diagnosis, managing the disease such that we can slow progression or reverse potential sight threatening status, if any. However, sometimes we may be stumped by clinical conundrums where the existing clinical and scientific knowledge is unsuccessful in achieving this goal. Be it the middle aged lady with severe dry eye disease unable to do her daily activities in spite of maximum therapy, the child with keratoconus who progressed aggressively to advanced stage requiring a corneal transplant or the one with Stevens-Johnson syndrome who, after an idiosyncratic reaction, is relegated to a lifetime of suboptimal vision and eye pain; there are situations where we wish we had more to offer.

The term ocular surface disease encompasses a large group of conditions including dry eye, Stevens Johnson syndrome, chronic cicatrizing conjunctivitis, corneal graft rejection, allergy and keratoconus. These diseases can have varied presentations and clinical features. However, a common denominator is that patients can develop severe visual loss and discomfort due to inflammation and in severe cases, damage to the ocular surface. Being able to treat these conditions effectively before the onset of permanent irreversible ocular changes would go a long way in reducing the prevalence of blindness in the world. The prevalence of ocular surface disease can vary across the world and is influenced by environment, ethnicities and regions. The different conditions grouped under this broad umbrella, also have different incidence and prevalence. In India, the prevalence of DED ranges from 5-35% and 29 % of these have severe forms of sight threatening disease with similar numbers from around the world. Keratoconus is more prevalent in the younger age groups and has been shown to be strongly associated with allergy and eye rubbing. Many of these conditions affect children and young adults and therefore have an impact on their schooling and working capacity. This in turn results in deterioration of their quality of life and a socioeconomic burden on the system. Often the visual deterioration is so significant that the patient is

unable to manage even their activities of daily living independently. Thus, there are far reaching implications to these diseases.

The immune cells in the body have important protective functions in modulating the inflammatory response to various external stimuli and pathogens. This is manifested on the ocular surface as it acts as a sentinel on the eye. The variety of immune cells are also interlinked to the structural tissues on the cornea and ocular surface by the molecular factors released into the corneal environment. These interactions result in alterations in the normal balance and can trigger structural changes including scarring, loss of clarity of the cornea and ocular surface and deterioration of vision. A lot of the work done and knowledge available in this field has been established through animal experiments and laboratory based experiments. It is important to study this immune response in the human subjects to get as accurate an understanding as possible.

We now have various medical and surgical means to treat these conditions. Unfortunately, there are situations where the patient presents very late in the disease process after irreversible damage or in some cases the disease may worsen despite maximum therapy. Although significant advances have been made in understanding and treatment of these conditions, ocular surface disease remains inadequately understood. Such situations make us feel at a loss as clinicians and thus warrants a deeper understanding of the underlying pathology. There are also cases in which the diagnosis is missed or the case is sub-optimally managed due to overlapping symptomatology, all of which can result in high degree of visual morbidity. Most of the therapies available to us at present are aimed at treating the existing condition and severity at presentation, but we need to discover means of preventive and prophylactic medicine. Understanding the immunology takes us a step closer to understanding the disease at depth. Our work has improved the understanding of the etiopathogenesis and immune basis of different ocular surface conditions opening the possibility to explore novel targets for therapy. In addition, we hope to raise awareness about these disease conditions which will prompt people to seek treatment early before it reaches the end stage disease. The improvement in quality of life in a patient with well-controlled

disease is very gratifying. The ultimate goal is to create an evidence-based comprehensive approach to management from prevention to early diagnosis and effective, tailored treatment for each type of ocular surface disease. Our work provides the first compilation of the changes to the immune profile of a number of conditions; DED, Keratoconus, SJS as well as ocular surface pain/discomfort. Our data opens the field to develop management protocols specific to each disease in the near future, potentially furthering personalized, effective therapy in the context of the ocular surface. These discoveries thus may impact the way ocular surface diseases are managed in the clinic by allowing the treating physician to precisely stratify the patient's condition using their immune profile and truly understand the root cause.