INTRODUCTION

Approximately 200 million individuals are infected with filarial helminths, the parasitic helminths that cause lymphatic filariasis and onchocerciasis (river blindness). Filariae are thread-like nematodes that are transmitted by the bite of blood-sucking arthropods (mosquitoes transmit lymphatic filariae and black flies transmit onchocerciasis). Adult males and females are viviparous, and the early first stage larvae, termed microfilariae, are present in either the blood (lymphatic filariae) or the skin (onchocerciasis).

This review will focus on two animal models of disease caused by microfilariae in which eosinophils are prominent, and will examine the differential outcomes of IL-5 deficiency and recombinant IL-12 treatment. The murine models are of Tropical Pulmonary Eosinophilia (TPE), caused by *Brugia malayi* and *Wuchereria bancrofti* (reviewed in Ottesen and Nutman, 1992), and *Onchocerca volvulus*: mediated corneal disease, which is a major cause of river blindness (reviewed in Ottesen, 1995; Hall and Pearlman, 1999).

**Tropical Pulmonary Eosinophilia**

Much of the pathology associated with the lymphatic filariasis is attributed to the presence of adult worms causing blockage of the lymphatics. First stage...
larvae (microfilariae), which are present in the blood, generally do not induce pathological sequelae. However, in many individuals, the presence of microfilariae in the lungs is associated with a severe asthmatic response. This reaction, termed Tropical Pulmonary Eosinophilia (TPE), can be distinguished from allergic asthma by the effectiveness of anthelminthics in relieving clinical symptoms (Ottesen and Nutman, 1992). Patients with acute TPE have a pronounced eosinophilic alveolitis and elevated blood eosinophilia (>3,000/µl) and serum IgE (>2,000 ng/ml) (Ottesen and Nutman, 1992; Pinkston et al., 1987). Ultrastructural analysis of eosinophils from these patients show that these cells are activated, based on their highly vacuolated appearance and loss of granule content (Pinkston et al., 1987). In that study, the number of eosinophils recovered from the lungs of patients with acute TPE was 20-fold greater than in a group of asthmatics (Pinkston et al., 1987). TPE patients also demonstrate increased airway hyper responsiveness to inhalation of cholinergic agonists (Chhabra and Gaur, 1988; Ottesen and Nutman, 1992).

**Onchocerca volvulus- mediated corneal disease (river blindness)**

In contrast to lymphatic filariasis, adult male and female *O. volvulus* are found in subcutaneous host-derived nodules. The adults cause no pathology, although blood eosinophilia and serum IgE are elevated (Ottesen, 1995). Microfilariae are present throughout the dermis, and migrate through the conjunctiva into the cornea. So long as the parasites remain alive, they elicit little or no inflammatory response, and motile worms can be detected in the cornea by slit lamp examination (Abiose, 1998; Hall and Pearlman, 1999). However, when the microfilariae die, parasite antigens are released into the microenvironment of the corneal stroma and trigger a local inflammatory response. In individuals who have been sensitised by chronic exposure to the parasites, the immediate inflammatory response is characterized by discrete areas of corneal inflammation (seen as opaque areas in the otherwise transparent cornea) termed punctate keratitis (Abiose, 1998; Hall and Pearlman, 1999). Histological examination of punctate keratitis shows local edema with infiltrating lymphocytes and eosinophils (WHO 1987; Abiose, 1998). These lesions resolve spontaneously with minimal visual impairment. In contrast, in heavily infected individuals where there is prolonged invasion of the cornea, the inflammatory response progresses through a stage of bilateral corneal opacification to stromal keratitis, where much of the cornea is opaque and vascularized. These individuals develop severe visual impairment and eventually become completely blind (WHO 1987; Abiose, 1998).