Schistosomiasis is a severe and chronic disease caused by the parasitic trematode Schistosoma mansoni after deposition of eggs in the liver and intestines. The immune response to S. mansoni eggs is characterized by increased Th2 cells, eosinophilia, and high serum IgE levels. Granulomas are formed around the eggs to protect the organs against tissue damage caused by toxic products that are secreted from the eggs. Egg-derived components have further been shown to activate the IgE-mediated release of IL-4 and IL-13 from basophils, suggesting that basophils could be involved in protection against a fatal course of infection. Using T cell-specific IL-4/IL-13-deficient mice and basophil-deficient Mcpt8Cre mice, we determined the contribution of Th2 cells and basophils for protective immunity against S. mansoni egg-induced pathology during the patent stage of infection. Our results demonstrate that T cell-derived IL-4/IL-13 was essential for granuloma formation, IgE production, basophilia, differentiation of alternatively activated macrophages, and protection against fatal infection. Although basophils were recruited into liver granulomas, they appeared to be dispensable as a source of IL-4/IL-13 both for differentiation of Th2 cells and for prevention of weight loss and mortality.