

## Abstract

Invasion of the mammalian skin by cercariae of avian schistosomes of the genus *Trichobilharzia* is associated with the skin pathology called cercarial dermatitis (CD). Although the manifestation of CD, characterized by the presence of maculo-papular rash and pruritus, is believed to be linked with the previous sensitization, the role of the infection dose and the specific causative agent is rarely considered. Therefore the skin immune response in mouse pinnae infected by 100, 1000 or 4x100 (repeated infections) cercariae of two *Trichobilharzia* species – *T. regenti* and *T. szidati* – was examined in this work. To compare the effect of these factors (the infection dose and species), a complex approach was ensured by employing both *in vivo* and *in vitro* methods. Firstly, histopathological changes in the pinnae were examined by classical histology and infiltrated leukocytes were characterized by flow cytometry. Sera of mice were used to detect the systemic production of cytokines and parasite-specific antibodies. *In vitro* cultivation of mouse pinnae was used to detect the local production of cytokines. The most remarkable observation was that the infection dose largely impacted the course of the immune response, both locally and systematically. In primary infected mouse pinnae, 100 cercariae of both species evoked only a mild reaction which was almost undetectable. On the other hand, 1000 cercariae caused extensive skin pathology, induced rapid cellular influx, and triggered antibody production. Furthermore, penetration of *T. regenti* led to the increased local production of both pro-inflammatory and regulatory cytokines. The production of pro-inflammatory cytokines, including alarmin TSLP, seemed to be less pronounced during reinfections. Generally, in contrast to the primary-infected mice (100 cercariae), exposures to 4x100 cercariae led to a detectable immune response. While cercariae of *T. szidati* caused similar (histo)pathological changes as *T. regenti*, the flow cytometry and cytokine production analysis revealed a much weaker immune response against the former species, regardless of the infection dose, indicating the higher immunopathogenic potential of *T. regenti* during early phases of mammalian invasion. Altogether, the data indicate that the course of CD reflects not only the number of exposures but also infection dose and the specific causative agent.

**Key words:** avian schistosome, cercarial dermatitis, immune response, infection dose, pathology, skin, *Trichobilharzia*.