

***Lichtheimia* species exhibit differences in virulence potential.**

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Abstract

Although the number of mucormycosis cases has increased during the last decades, little is known about the pathogenic potential of most mucoralean fungi. *Lichtheimia* species represent the second and third most common cause of mucormycosis in Europe and worldwide, respectively. To date only three of the five species of the genus have been found to be involved in mucormycosis, namely *L. corymbifera*, *L. ramosa* and *L. ornata*. However, it is not clear whether the clinical situation reflects differences in virulence between the species of *Lichtheimia* or whether other factors are responsible. In this study the virulence of 46 strains of all five species of *Lichtheimia* was investigated in chicken embryos. Additionally, strains of the closest-related genus *Dichotomocladium* were tested. Full virulence was restricted to the clinically relevant species while all strains of *L. hyalospora*, *L. sphaerocystis* and *Dichotomocladium* species were attenuated. Although virulence differences were present in the clinically relevant species, no connection between origin (environmental vs clinical) or phylogenetic position within the species was observed. Physiological studies revealed no clear connection of stress resistance and carbon source utilization with the virulence of the strains. Slower growth at 37°C might explain low

virulence of *L. hyalospora*, *L. spaherocystis* and *Dichotomocladium*; however, similarly slow growing strains of *L. ornata* were fully virulent. Thus, additional factors or a complex interplay of factors determines the virulence of strains. Our data suggest that the clinical situation in fact reflects different virulence potentials in the Lichtheimiaceae.

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