

## Development of *Candida parapsilosis* Complex Species

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### Opinion

Ashford isolated *Candida parapsilosis* (as a species of *Monilia* incapable of fermenting maltose) from the stool of a diarrhoea patient. To distinguish it from the more common isolate, *Monilia psilosis*, better known today as *Candida albicans*, the species was named *Monilia parapsilosis*. Despite being initially thought to be nonpathogenic, *Candida parapsilosis* was identified in 1940 as the causative agent of a fatal case of endocarditis in an intravenous drug user. Even at this early stage, investigators linked infection to *Candida parapsilosis* exogenous introduction, which foreshadowed the link between *Candida parapsilosis* and invasive medical instrumentation and hyperalimentation.

*Candida parapsilosis* was classified into three groups: I, II, and III. However, further genetic studies revealed enough differences to separate the groups into three closely related, distinct species: *Candida parapsilosis*, *Candida orthopsilosis*, and *Candida metapsilosis*. Nonetheless, *Candida parapsilosis* is responsible for the vast majority of clinical disease, and few medical microbiology laboratories distinguish between these species, especially since commercial systems are insufficient.

Cells of *Candida parapsilosis* have oval, round, or cylindrical shapes. *Candida parapsilosis* colonies are white, creamy, shiny, smooth or wrinkled when grown on Sabouraud dextrose agar. *Candida parapsilosis*, unlike *Candida albicans* and *Candida tropicalis*, does not form true hyphae and instead exists in either a yeast phase or a pseudohyphal form. Light microscopy has been used to identify pseudohyphae found on cornmeal agar. Recent evidence suggests that the formation of *Candida parapsilosis* pseudohyphae is linked to a specific set of amino acids, particularly citrulline, which cause significant changes in cellular and colony morphology. The form of *Candida parapsilosis* also influences colony phenotypes: yeast colonies have smooth or crater phenotypes, whereas pseudohyphae have crepe or concentric phenotypes.

*Candida parapsilosis* is usually a skin commensal, and its pathogenicity is limited by intact integument. *Candida parapsilosis* is well-known for its ability to grow in total parenteral nutrition and form biofilms on catheters and other implanted devices, as well as for nosocomial spread via hand carriage and persistence in the hospital environment. *Candida parapsilosis* is especially dangerous in critically ill neonates, accounting for more than one-quarter of all invasive fungal infections in low-birth-weight infants in the UK and up to one-third of neonatal *Candida* bloodstream

infections in North America. Furthermore, it is the most common fungal organism isolated in many neonatal intensive care units (NICUs), where it is frequently linked to neonatal mortality.

Since the 1980s, there has been a significant increase in bloodstream infections caused by *Candida* species other than *Candida albicans*, particularly *Candida glabrata* in the United States and *Candida parapsilosis* and *Candida tropicalis* in Europe, Canada, and Latin America. Although *Candida parapsilosis* is often thought to be less virulent than *Candida albicans*, it is the *Candida* species with the greatest increase in prevalence since 1990. Invertebrate models have become increasingly useful in the study of fungal pathogenesis over the last decade. Several factors, including ethical concerns, costs, and physiological simplicity, prompted the development of these models. Furthermore, the evolutionary conservation of invertebrate and mammalian innate immune mechanisms provides insight into common virulence factors involved in fungal pathogenesis of different types of hosts.

*Caenorhabditis elegans*, in particular, has been successfully used as a candidiasis infection model, with its utility demonstrated in the assessment of fungal virulence traits and the identification of new anti-fungal compounds. Nematodes eat fungal pathogens instead of the standard laboratory diet of *Escherichia coli*. Ingested fungi cause an infection within the worm gut, which is characterised by yeast accumulation and intestine distention. Infected nematodes can be studied using either solid or liquid media assay conditions. Yeast forms hyphae that protrude through the worm cuticle in liquid medium assays. *Candida albicans* and *Candida non-albicans* species have both been found to cause lethal infections in *Candida elegans*.

Although *Candida elegans* has proven to be a valuable host for the study of *Candida albicans* and a limited number of non-albicans

species, there have been few evaluations of *Candida parapsilosis* species complex infections.

*Candida parapsilosis* can cause endocarditis in patients who have prosthetic valves (57.4 percent), intravenous drugs (20 percent), or intravenous parenteral nutrition (6.9 percent), abdominal surgery (6.9 percent), immunosuppression (6.4 percent), broad-spectrum antibiotic treatment (5.6 percent), and previous valvular

disease (4.8 percent). Despite the fact that the mortality rate ranges from 41.7 to 61 percent, the treatment is still unknown. *Candida parapsilosis* ocular infection has been linked to cataract surgery and the use of corticosteroid eye drops. Infection of the skin and gastrointestinal tract by *Candida parapsilosis* can occur, and the production of pseudohyphae is associated with the elicitation of an inflammatory response. *Candida parapsilosis* is a rare occurrence in onychomycosis.