

# Can probiotics reduce *Candida* infection?



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## Vaginal Microflora

The microbial species that inhabit the female urogenital system play an important part in maintenance of health and prevention of infection. In particular, *Lactobacillus* species are considered essential to the maintenance of a healthy vaginal microbiota. Lactobacilli effectively modulate the vaginal flora to protect against pathogens by producing antimicrobials such as hydrogen peroxide, bacteriocins, and weak organic acids like acetic and lactic acid<sup>1</sup>. They have been shown to have direct inhibitory effects on common vaginal pathogens.

In comparison to the intestinal microbiota, which can have up to a thousand microbial species inhabiting it, the vaginal microflora is less diverse with approximately 50 species present, dominated by *Lactobacillus* species. The reason for this lower diversity is still unclear, but may involve poor receptivity of the vagina, different nutrient availability compared to the gut, and competition with resident bacteria<sup>2</sup>. While studies have shown that a vaginal tract dominated by Lactobacilli appears to protect the host against some vaginal infections, it does not fully prevent colonisation by other species. Pathogens are still able to coexist with commensal organisms and there is still potential for infection during periods of overgrowth of pathogens. Infections causing urinary tract infections, vaginitis and candidiasis are the most common seen worldwide.

## *Candida* in the microflora

At least one-third of healthy individuals carry the *Candida* fungus; in the mouth, the intestine or the vagina<sup>3-6</sup>. This prevalence, without symptoms, means that *Candida* can be considered a member of the normal microflora of human beings<sup>7</sup>. The microflora is the population of microscopic organisms that inhabit and live in a symbiotic relationship with the human body. This includes the bacterial populations that reside in the human gastrointestinal tract, an important mechanism in the defence against infections.

Under certain circumstances, however, *Candida* fungus can cause infectious disease, occasionally very serious disease. How can a microorganism be a member of our microflora and also cause disease?

The answer to this question is not yet known for certain, but it could be that *Candida* provides benefits to the host and is therefore accepted. Alternatively, *Candida* could be a pathogen that is very tricky to eradicate, but is controlled by the normal microflora. As no benefits from *Candida* have yet been identified, the second explanation seems more likely. Whilst it is considered part of the normal microflora it is a pathogenic organism that can cause infection with serious implications in terms of morbidity and mortality if the balance between colonisation and the host is temporarily disturbed.

In most people, the risk from *Candida* is low, because the fungus constitutes a very small proportion of the overall microfloral population. Several studies have found that only about 3-4,000 *Candida* cells are present in 1 gram of content of the large intestine. This is a tiny number compared with the billions of bacteria found in the same amount of colonic content<sup>4,5,6,8</sup>.

Despite the relatively low risk from *Candida* in the microflora, and the development of new anti-fungal drugs, the incidence of *Candida* infections continues to rise, especially among hospital patients<sup>9</sup>. For example, over a 13-year period (1980-1992) there was a 5-fold increase in bloodstream infections caused by *Candida* in US hospitals.

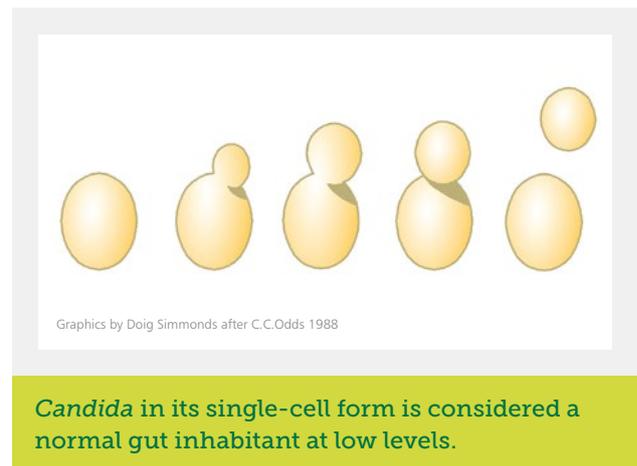


**Contrary to belief, men are at just as much risk form *Candida* infections as women.**

To understand why this is happening, it is necessary to look at *Candida* fungus in greater detail.

### **Why is *Candida* such a troublesome opportunistic pathogen?**

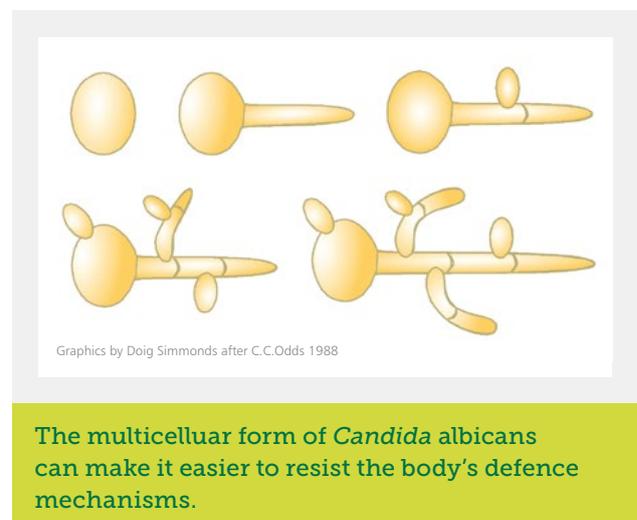
As a fungus, *Candida* is unlike the vast majority of microbes in the human flora, which are bacteria. A bacterium is a prokaryote (containing no nucleus or other organelles), while a fungus is a eukaryote, which is a more complex type of cell, closer in evolutionary terms to a human cell. Such greater complexity makes *Candida* a troublesome microbe when it switches into pathogenic mode.



***Candida* in its single-cell form is considered a normal gut inhabitant at low levels.**

*Candida albicans* is the species responsible for the majority of infections, but other species such as *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis* are also pathogenic in humans<sup>10</sup>.

One of the reasons why *Candida albicans* is such a persistent pathogen is that it can take two forms. Most of the time it exists as a single-celled yeast, but sometimes it converts to a mycelium (a network of fine filaments). The yeast-form can flow more easily in fluid and the mycelium-form can move more easily between the cells of human tissues by the insertion of growing tubes (hyphae). There is also a third and intermediate form, known as pseudohyphae, which are strings of elongated yeast cells, and these structures also appear to have invasive ability<sup>11</sup>. These different forms of the fungus may all coexist together. The ability to change form, which can occur quickly, makes it easier for *C. albicans* to resist the body's various defence mechanisms<sup>12</sup>.



**The multicellular form of *Candida albicans* can make it easier to resist the body's defence mechanisms.**

*Candida* infection (candidiasis) causes two main types of disease: superficial and systemic. Superficial infection, known as 'thrush', may occur in the mouth or vagina, with the production of a white itchy surface layer, and also discharge from the vagina<sup>7</sup>. Superficial candidiasis may also occur on the skin, especially at moist folds and creases.

Systemic candidiasis involves the passage of *Candida* cells into the bloodstream, where they may form colonies in almost any part of the body. Such entry through the skin or mucosal surfaces usually only occurs if there is damage to these surfaces. Systemic candidiasis can be life-threatening and is especially difficult to treat.

The increase in incidence of *Candida* infections is probably due, in part, to the greater use of broad-spectrum antibiotics that disturb the microflora. *In vitro* studies have shown that colonic microflora reduces *Candida* numbers, and *in vivo* studies have shown that the use of broad-spectrum antibiotics increases the risk of *Candida* infection<sup>6,8,13,14</sup>. Antibiotics kill or inhibit bacteria, but leave fungi unaffected. With the bacteria of the gut microflora disturbed, there is opportunity for *Candida* numbers to increase substantially.

Another factor in the increased incidence of *Candida* infection is the greater use of corticosteroids and other immunosuppressive agents that alter the functioning of the immune system<sup>15</sup>. The relevance of a weakened immune system is reflected in the fact that leukaemia patients carry higher levels of *Candida*, and patients with HIV virus are much more likely to develop candidiasis<sup>16</sup>.

The increase in *Candida* infections may also be due to the 'hygiene' effect. The hygiene hypothesis blames the increase in diseases of the malfunctioning immune system (e.g. asthma, eczema, autoimmune diseases) on the absence of appropriate microbial stimulation at an early age. The latest version of the hygiene hypothesis proposes that the gut microflora is missing certain microbes, such as helminthic worms, that are important in an evolutionary context to the proper development of our immune systems. If infants do not have their gut lymphoid tissues suitably provoked by the gut flora, their immune system may not function efficiently in later life.

Given these potential factors behind *Candida* infection, it is no surprise that a number of experts have concluded that the most important aspect of avoiding *Candida* infection is having a balanced microbial flora and a healthy immune system<sup>5,15</sup>. This has led people to consider the use of probiotics, because these beneficial microbes are good at restoring disturbed microflora and improving immune function.

## Evidence of probiotic benefits

There have been a number of clinical studies examining the effects of probiotics on vaginal candidiasis. A group of women with recurrent vaginal candidiasis consumed yoghurt containing *Lactobacillus acidophilus* for six months, and there was a three-fold lower level of infections compared with the control group<sup>17</sup>.

In a more recent randomised controlled trial (RCT), an oral probiotic consisting of two *Lactobacillus* species (a *Lactobacillus rhamnosus* and a *Lactobacillus reuteri*) significantly improved the effectiveness of an anti-fungal drug. Vaginal discharge was reduced, as were *Candida* cell numbers<sup>18</sup>.

There have also been two studies in which the probiotics were administered vaginally. One used an *L. rhamnosus* and the other used an *L. acidophilus*. Both showed benefit, including a halving of the risk of developing candidiasis in the latter study<sup>19</sup>.

An RCT has also been undertaken with 80 premature infants, with a view to preventing *Candida* infection. *Candida* can be a major threat to the lives of such infants with their underdeveloped immune systems. The group of infants receiving *L. rhamnosus* for six weeks were significantly less likely to have their intestine colonised by *Candida* (23% compared with 49% in the control group)<sup>20</sup>.

Other studies have looked at the way in which probiotics are able to influence and modulate the vaginal microflora in patients with candidiasis, reducing the ability of *Candida albicans* to translocate to and colonise the vagina. One such study conducted by Reid *et al* demonstrated the ability of probiotic *Lactobacilli* to reduce numbers of vaginal *Candida* which in turn reduces the risk of developing infection<sup>21</sup>.

## Different species

A number of different probiotic species were used in the above studies, so how important is the type of species used in a probiotic product? By definition, species of bacteria have different characteristics. In fact, even within a species, some strains behave slightly differently. Therefore it can be expected that some probiotic bacteria will be more effective against *Candida* than others.

Furthermore, the mechanisms of benefit from probiotic bacteria are wide-ranging. This should not be surprising, because we are dealing with a living organism (the bacterium) interacting with cells of another organism (human being). Their complicated metabolisms and surface structures are bound to offer a range of potential influences.

The importance of species used was demonstrated in one study of mice using four different probiotic species. Two of the species (*Bifidobacterium animalis* and *L. acidophilus*) were superior to the other two (*L. reuteri* and *Lactobacillus casei*) in controlling *Candida*<sup>22</sup>.

Unfortunately, good quality studies on the use of probiotics against *Candida* are still relatively uncommon, and a clear picture of the most desirable characteristics of a probiotic species has not yet been obtained. Pending more research, it may be that a good quality, multi-species probiotic is currently the best choice.

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Peter Cartwright has 17 years experience of working for patient and self-help associations, as Assistant Director of the National Association for Colitis and Crohn's Disease, Director of the British Stammering Association and National Development Officer of the Self-Help Alliance. Peter has an MSc in Microbiology, BSc in Biomedicine and an MA in Sociology. He is the author of four books for the general public on intestinal health, including *Probiotic Allies* and *Probiotics for Crohn's and Colitis* and has given over 50 lectures on probiotics to doctors in 14 countries.

Probiotics International Ltd is one of the largest manufacturers and suppliers of probiotics for the healthcare, veterinary and animal health industry. Products are marketed under the brand name of Protexin.

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