

# Fungi and diabetes

Rowan Hillson

Fungi include single-celled yeasts, and multicellular filamentous organisms which may form fleshy fruiting bodies – mushrooms or toadstools. Some are edible, some poisonous. Fungi can cause distress and danger for people with diabetes.

## Magic mushrooms

'I prefer being sugar high on shrooms than thinking that you might die with low sugars on shrooms. It's actually a really scary feeling, specially if you are up in the woods and might not have any sugar stuff available. I always carry candy when i do that stuff too.'<sup>1</sup>

Psilocybin or magic mushrooms – hallucinogenic 'shrooms' – are used recreationally. They are illegal in some countries. Hypoglycaemia is among many serious risks.

## Candida Symptoms

'If any one thing causes me to try and keep my blood glucose under control, it's to avoid yeast infections... I itched. I burned. I wriggled and scratched. I wished sandpaper was absorbent and came in a roll. I treated and treated... with over-the-counter creams... It wasn't until I switched to a female doctor that I finally got somebody who really understood what I was going through. It was a time when Diflucan (fluconazole) was new and the general wisdom was that you need only take one pill, and voila!

'Not with diabetes, you don't. Yeast loves sugar, and I was very sweet in those days. The doc prescribed two pills and a prescription vaginal cream. It took two courses...for the yeast infection to go away.

'And stop snickering, guys: You can get diabetes-related yeast infections, too. In fact, I know of one man who was diagnosed with diabetes when his "little friend," as he called it, got a red, itchy rash that wouldn't go away.'<sup>2</sup>

## Frequency

Vaginal candidiasis (thrush) is more common in women with diabetes than in those without diabetes – 46% versus 23% in an Indian study.<sup>3</sup> The diabetes group had *Candida glabrata* (39%), *C. albicans* (26%) and *C. tropicalis* (17%) while non-diabetic people had 30% each of *C. albicans*, *C. glabrata* and *C. haemulonii*.

'Among the diabetic group, subjects with vulvovaginal candidiasis had significantly higher mean HbA<sub>1c</sub> when compared to those who had no such infection (12.8+/-2.6% versus 9.7+/-1.7% respectively).<sup>3</sup> The link between candidiasis and hyperglycaemia is not always clear.

*Candida* species were found in 28.7% of US women with diabetes – *C. albicans* (41.4%) and *C. glabrata* (37.9%). Women with type 1 diabetes were more likely to have *Candida* (OR 2.6; 95% CI: 0.99–6.98) than those with type 2 diabetes (T2DM).<sup>4</sup>

## Sodium-glucose transport protein inhibitors

SGLT2 inhibitors lower glucose via glycosuria. These drugs increase the risk of genital tract infections: for example, dapagliflozin 10mg (9.5%) versus placebo (2.6%), (RR 3.45; 2.19–5.33); canagliflozin 3.1–7.8% versus placebo or sitagliptin 1.5%.<sup>5</sup>

Among women with negative vaginal swabs initially, 31% converted to a positive *Candida* swab on canagliflozin versus 14% in the pooled placebo and sitagliptin treatment groups.<sup>6</sup>

## Treating thrush

Most patients with vulvovaginal thrush do not seek medical help. In the UK, antifungal creams and single-dose fluconazole are available over the counter. Does this work in people with diabetes? Often not.

A group of women with proven yeast infection, with and without diabetes, took a single dose of fluconazole. After two weeks, *Candida* persisted in 67.1% of patients with diabetes and in 47.3% of controls. Persistent *C. glabrata* was found in 54.1% of women with diabetes versus 22.6% in controls. Most patients with *C. glabrata* (83.1% with diabetes, 78.6% of controls) did not respond to fluconazole. *C. albicans* persisted in 45.4% of diabetic women and in 21.5% of controls.<sup>7</sup>

An Indian study of women with diabetes and vulvovaginal candidiasis found *C. glabrata* in 61.3%, *C. albicans* in 28.8%, and *C. tropicalis* in 3.6%. Patients were randomly allocated to fluconazole 150mg orally or boric acid vaginal pessaries (600mg daily). Cure rates for women with *C. glabrata* were 63.6% with boric acid versus 28.6% on fluconazole; for *C. albicans* 61.1% versus 85.7%.<sup>8</sup> Boric acid is not listed in the *British National Formulary*.

Many doctors would treat vulvovaginitis with oral fluconazole with antifungal cream without investigation. This treatment is unlikely to cure many women, especially if they have diabetes. Send a high vaginal swab initially. With your microbiology or genitourinary medicine service, develop local protocols for managing thrush in women with diabetes.

## Non-genital Candida

Oral *Candida* especially affects patients with dentures and/or stomatitis. *Candida* is also found under breasts or in groins (intertrigo).

## Invasive Candida infections

Invasive infection is rare but can occur in people with diabetes; for example, liver and perinephric abscesses,<sup>9</sup> and foot abscess.<sup>10</sup>

*C. parapsilosis*, a normal skin commensal, grows biofilms on catheters and implanted devices. Diabetes is a risk factor for parapsilosis candidaemia, for example in 9% of cases in a Spanish study.<sup>11</sup>

*Candida* may be fatal. In French intensive care units, 45.9% of patients with invasive *Candida* (67.9%

candidaemia) died. Diabetes increased the risk of death (OR 4.51; 1.72–11.79).<sup>12</sup> Candidaemia is a rare cause of diabetic ketoacidosis – seek this in puzzling cases.

## Fungal foot infections

Fungal skin diseases like athlete's foot (tinea pedis) and nail infections (onychomycosis) are common, especially in people with diabetes. In onychomycosis the nail becomes thickened, discoloured, and brittle. Fungal foot infections are irritant and unsightly, risking bacterial entry via damaged skin.

Among patients with type 1 diabetes attending a conference, 84.6% had proven fungal foot infections. *Trichophyton rubrum* (the most common cause of athlete's foot) was found in 69.2%. 'Marked mycoses on the soles of the feet were often considered to be dry skin by the patients.' In a second group, 35.5% of type 1 patients, 53.1% of T2DM, and 37.9% of non-diabetic family members had fungal foot infections. Impaired sweating (61.5% of all subjects) correlated with fungal infection in T2DM as did higher glycosylated haemoglobin.<sup>13</sup>

Among US patients with maceration between toes, 42.5% of those with diabetes and 37.5% without had tinea pedis. Antifungal treatment for diabetic patients with interdigital maceration was advised.<sup>14</sup>

A review suggested 'that oral terbinafine is as safe and effective as oral itraconazole therapy for the treatment of onychomycosis in people with diabetes. However, efficacy results were found to be poor.' There was no evidence for optimal treatment of tinea pedis in diabetes.<sup>15</sup>

## Aspergillosis

Aspergilli are filamentous fungi often found in homes. Rarely, *Aspergillus* forms balls in cavities, for example lungs or sinuses, or becomes invasive. People with diabetes are vulnerable. A 23-year-old with uncontrolled diabetes and headaches had *Aspergillus* in his sinus treated successfully.<sup>16</sup>

## Zygomycosis/mucormycosis

Zygomycosis includes infection by Mucorales and similar fungi found on soil and decaying plants. A literature review from 1885 to 2005 found 929 cases – 36% had diabetes of whom 66% had sinus disease and 33% had rhinocerebral disease. Among those with diabetes 44% died.<sup>17</sup>

## Alternative medicine

*Ganoderma lucidum* (Lingzhi or Reishi) was viewed as sacred. This big mushroom is dark, shiny and woody, and has been used for over 2000 years. It is believed to help diabetes.<sup>18</sup> *Ganoderma lucidum* extracts appear to lower glucose in animals<sup>19</sup> but safety and efficacy in man have not been demonstrated.<sup>20</sup>

## Summary

People with diabetes often have fungal infections. *Candida* species cause distressing symptoms, especially vulvovaginitis which is more likely in patients taking SGLT2 inhibitors. *C. glabrata* is common in women with diabetes so fluconazole treatment often fails. Agree local

protocols for testing and treating diabetic women with thrush. Do not leave patients to suffer for months.

Fungal foot infections are frequent in people with diabetes, often unrecognised. Macerated cracks between toes should be treated with antifungals, as should onychomycosis. 'Dry' skin may also reflect fungal infection. Treat fungal foot infections before bacterial invasion causes 'the diabetic foot'.

Invasive fungal infections (*Candida*, *Aspergillus*, mucormycosis and others) are uncommon and often missed. Consider fungi in ill patients with diabetes who are not recovering despite antibacterial treatment, especially if indwelling medical devices are present. Such infections have a high mortality rate in people with diabetes.

Don't forget fungi!

**Dr Rowan Hillson, MBE**, National Clinical Director for Diabetes, England 2008–2013

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