

Infections in people with diabetes

Fiona J Cooke

Abstract

People with diabetes mellitus are at an increased risk of many common infections, such as urinary tract infections, lower respiratory tract infections and skin/soft tissue infections. This is caused by a combination of systemic and local host factors, and also specific organism characteristics. People with diabetes mellitus also tend to acquire more complex infections, such as emphysematous cholecystitis and emphysematous pyelonephritis. Some conditions, such as malignant otitis externa and rhinocerebral mucormycosis, occur almost exclusively in people with diabetes. Despite greater susceptibility to infections and worse outcomes, there is little guidance regarding prevention and treatment measures for infections in people with diabetes. Comprehensive longitudinal studies are needed to further investigate the complex relationship between glycaemic control and infections.

Keywords Diabetic foot; emphysematous cholecystitis; emphysematous pyelonephritis; infections; malignant otitis externa; MRCP; osteomyelitis; rhinocerebral mucormycosis; urinary tract infections

Introduction

The relationship between diabetes mellitus and infections is complex,^{1–3} and the suggestion that infection may be a contributory cause or precipitant of diabetes mellitus is somewhat controversial (Figure 1). Infections can cause metabolic complications such as diabetic ketoacidosis and hypoglycaemia. Infections, and the antibiotics used to treat them, can complicate glycaemic control, and HIV antiretroviral agents can cause insulin resistance. In addition to the specific infections listed below, there are associations with other bacterial infections, tuberculosis and viral infections. People with diabetes can respond less promptly to appropriate antibiotics, for example from a reduced concentration of antibiotics at the site of infection as a consequence of diabetic vasculopathy.

In addition to patient education about reducing the risk of infection (e.g. good glycaemic control),⁴ people with diabetes should be offered vaccination against influenza and pneumococcal disease to prevent infection. In terms of infection management, sending appropriate samples to the microbiology laboratory and seeking expert advice early are recommended. Infections caused by multidrug-resistant organisms are increasing. The latest ‘superbugs’ are carbapenemase-producing

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Key points

- People with diabetes mellitus are at increased risk of many common infections because of a combination of systemic and local host factors, and specific organism characteristics
- Individuals with diabetes often have different disease courses once the infection has been established, which is reflected by increased rates of hospital admission, length of stay and complications
- Some rare infections (sometimes called ‘signal infections’ – emphysematous cholecystitis; emphysematous pyelonephritis, malignant otitis externa, rhinocerebral mucormycosis) are pathognomonic of a patient having diabetes

Enterobacteriaceae, which were initially seen in the UK in patients returning from overseas and in certain hospitals in London and the North-West of England, but are now becoming more widespread.

Urinary tract infections (UTIs)

People with diabetes are at increased risk of asymptomatic bacteriuria, which is a relatively benign condition that does not require antimicrobial therapy. If symptomatic (uncomplicated cystitis/lower UTI), people with diabetes usually require a longer course of antibiotic treatment (7 days) than do patients without diabetes. Diabetic neuropathy can lead to a neurogenic bladder, which predisposes to UTIs as a result of poor bladder emptying. These patients should be referred for a urological opinion.

Upper UTIs (pyelonephritis) in people with diabetes are more likely to result in complications, such as renal abscesses, renal papillary necrosis, overwhelming Gram-negative sepsis and emphysematous pyelonephritis. The latter is a rare, necrotizing infection, usually caused by *Escherichia coli* or *Klebsiella pneumoniae*. Imaging reveals the presence of gas, and urgent surgery may be required. Overall, managing upper UTIs in people with diabetes should follow the same principles as for those without diabetes, but they may need hospital admission for optimal glycaemic control and adequate hydration.⁵

Skin and soft tissue infections

Peripheral neuropathy, hyperglycaemia and atherosclerosis of peripheral vessels predispose people with diabetes to skin and soft tissue infections. Prolonged antibiotic therapy for mild soft tissue infections is not beneficial, and can be harmful in selecting for resistant organisms. Superficial infections such as erysipelas, cellulitis and follicular skin infection (commonly caused by *Staphylococcus aureus*) can progress more rapidly in people with diabetes. Bullosis diabeticorum is spontaneous blistering of the sacral skin, seen only in people with diabetes. It usually resolves spontaneously in 2–6 weeks, but antibiotics may be required for secondary bacterial infection.

Deeper, necrotizing infections are more common in diabetes, and can complicate foot ulcers and other wounds. These are often polymicrobial, with organisms such as *Streptococcus pyogenes*, *Enterococcus* spp., *Staph. aureus*, *Enterobacteriaceae* and

The increased susceptibility to infection in people with diabetes is due to a number of host and organism factors. The magnitude of the effect of diabetes on the risk of infection, and whether hyperglycaemia is an independent risk factor for infection, remain unclear.

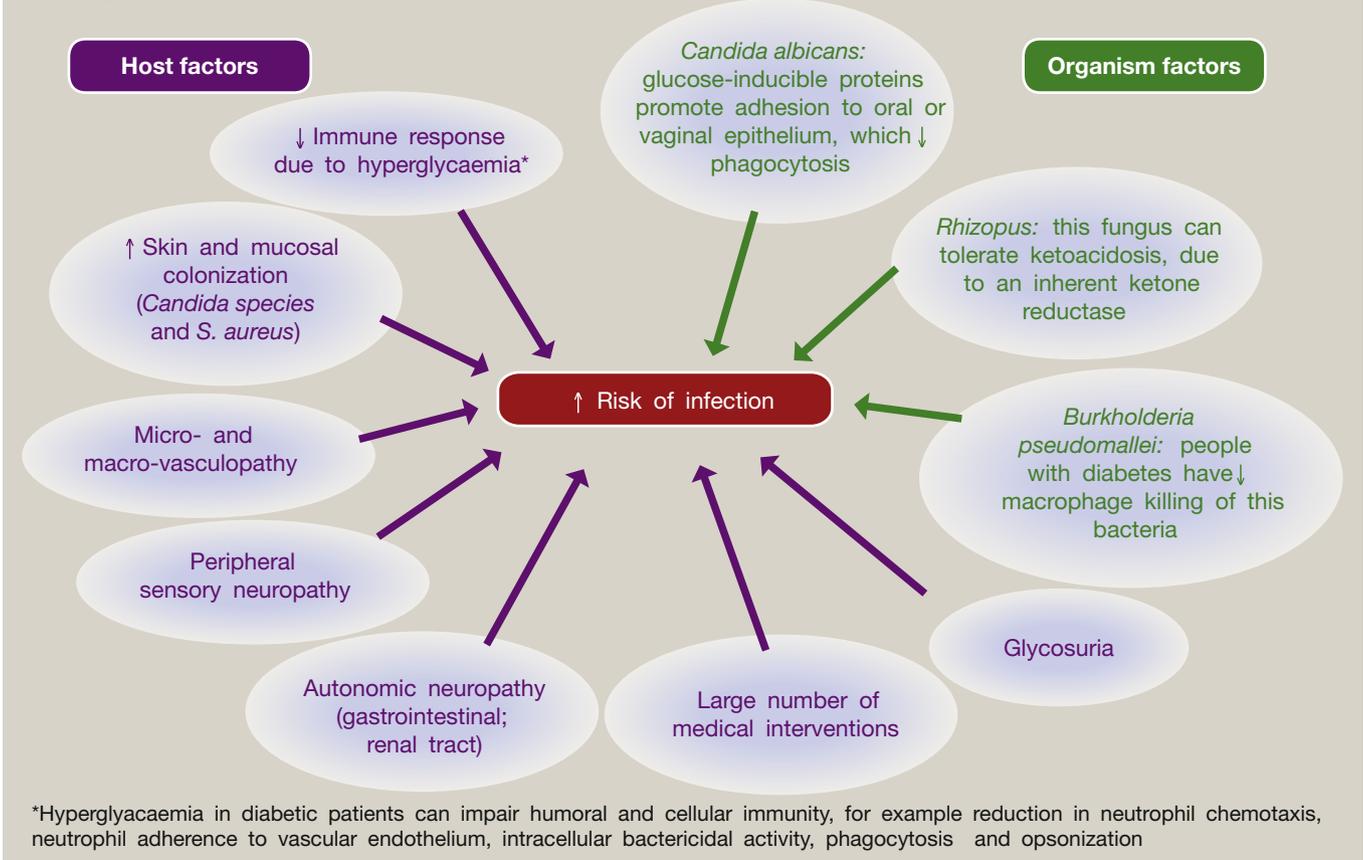


Figure 1

anaerobes. Imaging for the presence of gas is important, and management involves surgery and broad-spectrum antibiotics. The results of superficial swabs can be misleading, so deep tissue samples should be submitted to the microbiology laboratory. Diabetes also predisposes to pyomyositis, which is a primary bacterial infection of skeletal muscle with intramuscular abscesses, usually arising from haematogenous spread.

Osteomyelitis

Osteomyelitis (Figure 2) is more common in people with diabetes, and occurs as a result of contiguous spread from a chronic ulcer to neighbouring bone. Chronic osteomyelitis complicates >50% of serious soft tissue infections in diabetic feet, and is more likely if:

- the ulcer has been present for >2 weeks
- the ulcer is larger than 2 cm × 2 cm
- bone is visible or can be probed
- the erythrocyte sedimentation rate is >70 mm in the first hour.

Infections are usually mixed, commonly with *S. aureus*, *Streptococcus* spp., *Enterobacteriaceae*, *Pseudomonas* spp. or anaerobes. Meticillin-resistant *Staph. aureus* (MRSA), enterococci and coagulase-negative staphylococci are occasionally isolated,

usually after treatment with multiple courses of antibiotics. Deep aspiration or bone biopsies are recommended. Management, including debridement or excision of infected bone, is best directed by the multidisciplinary foot-care team.

Empirical broad-spectrum antibiotics (e.g. intravenous co-amoxiclav or piperacillin–tazobactam) should be started in theatre as soon as specimens have been taken. If the patient is MRSA-positive, or has previously had *Pseudomonas* or multi-resistant organisms isolated, treatment should be discussed with an infection specialist. Subsequent antibiotic choice depends on the culture results of pre-debridement operative specimens, while their duration is dictated by culture results of post-debridement specimens (2 weeks if culture-negative, 6 weeks if culture-positive).

Fungal infections

People with diabetes are more likely to suffer from superficial fungal infections such as oral or genital candida, onychomycosis and intertrigo. They are also at risk of systemic fungal infections, such as cryptococcosis and coccidioidomycosis.

Rhinocerebral mucormycosis is a potentially fatal systemic infection involving septic necrosis and infarction of the nasopharynx and orbital tissues that is seen almost exclusively in



Figure 2

people with diabetes. It is caused by the Mucorales pin-moulds from the Zygomycetes family (*Mucor*, *Rhizopus*, *Absidia*). The patient can present with facial pain, headache and fever, and later develop orbital cellulitis or cranial nerve involvement. The characteristic bloody or black nasal discharge and black crusty material on the nasopharynx or palate are the result of tissue necrosis. Non-septate branching hyphae may be seen on biopsy. Complications include cerebral abscess, retinal artery thrombosis, cavernous sinus thrombosis and internal carotid artery thrombosis.

A successful outcome depends on early diagnosis, high-dose antifungals (e.g. amphotericin) with surgical debridement and correction of metabolic abnormalities. In practice, broad-spectrum antibiotics are given until the diagnosis is confirmed. After apparently successful therapy, close monitoring is recommended as mucormycosis can recur.

Emphysematous cholecystitis

People with diabetes have a similar risk of cholecystitis to the normal population, but severe infection with gas-forming organisms (emphysematous cholecystitis) is more common. This is

usually polymicrobial, involving *Clostridium* spp. in >50% of cases. Clinical presentation is indistinguishable from acute cholecystitis, but the presence of gas in the gallbladder wall or surrounding tissue is diagnostic. Perforation is common, and requires immediate surgery. Mortality is high, and early diagnosis is critical.

Ear, nose, throat

Malignant otitis externa, also called necrotizing otitis externa, is caused by *Pseudomonas aeruginosa*, and encompasses severe otitis externa, perichondritis and temporal bone osteomyelitis. Patients usually present with severe pain and tenderness around the ear, and ear discharge. The infection can progress rapidly to affect the lower cranial nerves. If the skull base, sigmoid sinus or meninges are involved, the condition becomes life-threatening. Antipseudomonal antibiotics (such as piperacillin–tazobactam or meropenem) should be prescribed immediately, followed by urgent imaging and a surgical opinion to assess tissue damage. The use of corticosteroids should be considered. Note that, for severe otitis externa without invasion, close observation and treatment with oral ciprofloxacin and antibiotic ear drops may suffice.

Tuberculosis

There is growing evidence that diabetes is an important risk factor for tuberculosis and can affect disease presentation and treatment response. In addition, tuberculosis can induce glucose intolerance and worsen glycaemic control in people with diabetes.

Melioidosis

Diabetes is the most significant risk factor for developing this tropical disease, which is caused by the Gram-negative rod *Burkholderia pseudomallei* and is endemic in South-East Asia and northern Australia. Acute melioidosis presents with fever, pneumonia and abscesses, while chronic infection mimics tuberculosis. The bacterium is resistant to many antibiotics, so expert advice regarding treatment should be sought. ◆

TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

Question 1

A 78-year-old woman presented with a 3-day history of increased frequency and dysuria, and a 1-day history of loin pain. She had had type 2 diabetes for 15 years. A dipstick test was positive for leucocytes, nitrites and blood.

Investigations

- Renal tract imaging showed gas and necrosis
- Blood cultures were flagged positive
- Gram staining showed Gram-negative rods

Which organism is most likely to be identified?

- A *Clostridium perfringens*
- B *Escherichia coli*
- C *Morganella morganii*
- D *Pseudomonas aeruginosa*
- E *Streptococcus pyogenes*

Question 2

A 23-year-old man presented with headache and fever, and swelling and redness around his eye. He was found to have been diagnosed with type 1 diabetes 10 years previously. On clinical examination, he was developing a facial nerve palsy, and a bloody discharge from his nose was seen. He became

KEY REFERENCES

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increasingly unwell, and black crusty material was seen on examination of the nasopharynx.

Which of the following fungi would most likely be seen on tissue biopsy?

- A *Aspergillus niger*
- B *Candida albicans*
- C *Candida tropicalis*
- D Mucoraceous mould
- E *Sporothrix shenckii*

Question 3

A 67-year-old man presented with severe ear pain. Twelve years previously, he had been found to have type 2 diabetes. On clinical examination, there was tenderness around the ear and a purulent discharge, and he was developing a facial nerve palsy. He had had oral ciprofloxacin from his GP in the recent past.

Which antibiotic should be started empirically?

- A Ceftriaxone
- B Vancomycin
- C Meropenem
- D Ertapenem
- E Linezolid