**Bacterial Infections in Diabetic Foot Ulcer**

**Overview of the Endocrine System**

Endocrine systems, also referred to as hormone systems, are found in all mammals, birds, fish, and many other species. The endocrine system consists of:

* Glands located throughout the body.
* Hormones made by the glands and released into the bloodstream or the fluid surrounding cells.
* Receptors in various organs and tissues that recognize and respond to the hormones.

The endocrine system, made up of all the body's different hormones, regulates all biological processes in the body from conception through adulthood and into old age, including the development of the brain and nervous system, the growth and function of the reproductive system, as well as the metabolism and blood sugar levels. The female ovaries, male testes, and pituitary, thyroid, and adrenal glands are major constituents of the endocrine system.

**Where are Endocrine Glands Located in the Human Body?**



**Diabetes mellitus** (**DM**) is one of the most common endocrine diseases affecting millions of people worldwide. Its prevalence is increasing rapidly. Diabetes mellitus is the leading cause of kidney dysfunction, blindness, strokes, lower limb amputation, and heart attacks. Common symptoms of DM are frequent urination, increased thirst, hunger, fatigue, blurred vision, and numbness and tingling in the hands and feet. Broadly, DM is divided into two categories, type 1 DM and type 2 DM.

Insulin is an anabolic hormone produced by the islets of Langerhans in the pancreas. It helps in regulating blood sugar in the body by increasing the uptake of glucose by various cells. The glucose taken by cells is either stored in glycogen by the liver or used for energy expenditure by cells. Therefore, deficiency or resistance to insulin causes increased glucose in the blood.

Persistently high levels of blood sugar cause damage to blood vessels, nerves, and various cell types in the body. Complications associated with DM are diabetic retinopathy, neuropathy, and nephropathy. DM also impairs the ability of the human body to fight infections by weakening cellular immunity. It also increases the time frame of recovery from an infection or injury. Common factors which help in preventing and delaying the onset of DM are regular physical activity, eating healthy, and maintaining average body weight. Routine screening, proper diet, participating in physical activity, and medications help treat and prevent DM complications.

In general, people with diabetes have an increased risk of infection, and worse outcomes are known to be diabetes foot infection, urinary tract infection (especially *E. coli* infection), *streptococcus pneumonia*, Candida and mucor invasive fungal infection, cellulitis (the common cause of streptococcal species) and frequent skin infections.

**Bacterial Infection of Endocrine System**

The incidence of bacterial infections of endocrine glands is low when compared to that in other organs of the body. The endocrine glands that may be affected by bacterial infections are: **Pituitary**, **Thyroid**, **Adrenals** and **Gonads**. Bacterial infection of parathyroid glands is extremely rare.

In general, bacteria may be classified as gram positive, gram negative, and miscellaneous. Among all the bacteria, *Mycobacterium tuberculosis* remains the most common agent involving the endocrine glands. *Mycobacterium tuberculosis* is a weakly gram positive highly aerobic bacterium that can cause tuberculosis in any organ of the body. This organism can affect the adrenal glands and lead to primary adrenal insufficiency. In developing countries, tuberculosis remains the most common cause of primary adrenal insufficiency. Tuberculosis can also affect pituitary, thyroid, and gonads.

The other common bacteria that may affect the endocrine system are *Staphylococcus* *aureus*, *Streptococcus pneumoniae*, *Neisseria meningitides*, *Escherichia coli*, *Chlamydia trachomatis*, *Pseudomonas aeruginosa, Klebsiella pneumoniae*, *Treponema pallidum*, and *Yersinia enterocolitica*.

Bacterial Infections in Diabetic Patients

Due to weakened defenses and disease complications, people with diabetes are susceptible to new infections and recurrences. Uncommon life-threatening infections are more frequent in people with diabetes than in people without diabetes such as necrotizing soft tissue infection, emphysematous pyelonephritis, emphysematous cholecystitis, malignant otitis, and perioperative infection.

Diabetes is associated with the risk of blood flow infections and sepsis obtained in communities and hospitals. Causing the change of congenital immune response and acquired immune response, increasing immune function disorder, chronic inflammation, and microbial persistence.

**Common infectious events in people with diabetes**

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| **Common infectious events in people with diabetes.** |
| **Body site** | **infection** | **Etiologic agent(s)** |
| Head and neck | Periodontal disease |  *Treponema denticola, Rhizopus*spp.*, Mucor*spp*., E. coli, K. pneumoniae, P. aeruginosa, Aspergillus*spp. |
| Mucormycosis  |
| Endophthalmitis |
| Malignant otitis externa |
| Respiratory tract | Pneumonia and bronchopneumonia　 | *S. pneumoniae, S.aureus, K.pneumoniae.* |
| *Legionella*spp. |
| *Influenza virus* |
| Tuberculosis | *M. Tuberculosis*. |
| Urinary tract　　　　 | Urinary tract infection: cystitis, urethritis, pyelonephritis, complications　 | *E. coli, Klebsiella* spp*.,*and other*enterobacteria.* |
| *Acinetobacter*spp. |
| *P. aeruginosa.* |
| *S. agalactiae.* |
| *Candida albicans*, other yeasts. |
| Intra-abdominal compartment　　 | Hepatic and intra-abdominal abscesses | *K. pneumoniae* |
| Cholecystitis　 | *Enterobacteriaceae: E. coli*. |
| Obligate anaerobic bacteria*: Bacteroides fragilis, Clostridium perfringens.* |
| Skin and subcutaneous tissues　　　 | Intertrigo | *Candida*spp*.* |
| Cellulitis　 | *S. aureus.* |
| *S. pyogenes.* |
| Superficial mycoses and onychomycosis | Dermatophytes. |
| Soft tissue, bones, joints　　　　　　 | Necrotizing fasciitis　　　　 | *S. pyogenes; S. aureus, Enterobacteriaceae.* |
|  *Bacteroides*spp*., Clostridium perfringens.* |
| *Vibrio*spp*.* |
| *Salmonella* spp*.* |
| *Enterococcus*spp*.* |
| Diabetic foot | *S. pyogenes, S. aureus,*Gram-negative bacilli*,*anaerobic bacteria*,*fungi. |
| Osteomyelitis, septic arthritis | *S. aureus, M. tuberculosis*complex. |
| Bacteremia andsepsis | Community-acquired and hospital-acquired | *E. coli, S. aureus, Streptococcus pneumoniae, Enterobacteriaceae, enterococci, Pseudomonas aeruginosa, Candida albicans,*other agents. |

Diabetic Foot Infection

###### Pathophysiology

Patients with diabetes are particularly susceptible to foot infection primarily because of **neuropathy**, **vascular insufficiency**, and **diminished neutrophil function**.

Peripheral neuropathy has a central role in the development of a foot infection and it occurs in about 30 to 50 percent of patients with diabetes. Patients with diabetes lose the protective sensations for temperature and pain, impairing awareness of trauma such as abrasions, blistering, or penetrating foreign body. Motor neuropathy can result in foot deformities, making skin ulceration even more likely. Once the skin is broken (typically on the plantar surface), the underlying tissues are exposed to colonization by pathogenic organisms. The resulting wound infection may begin superficially, but with delay in treatment and impaired body defense mechanisms caused by neutrophil dysfunction and vascular insufficiency, it can spread to the contiguous subcutaneous tissues and to even deeper structures.

##  Pathogens:

\*Most Diabetic Foot Infections (DFIs) are polymicrobial.

\*Frequent pathogens: based on deep wound or bone cultures.

* + Initially, wounds usually have Gram-positive flora from the skin; as it becomes more chronic, it tilts toward Gram negatives. Following broad-spectrum abx, flora may evolve to [MRSA](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540518/all/Staphylococcus_aureus), [VRE](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540203/all/Enterococcus) (Vancomycin-Resistant Enterococcus) and more resistant Gram negatives.

**a)** Aerobic Gram positive:
[*Staphylococcus aureus*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540518/all/Staphylococcus_aureus)

 [Streptococcal spp.](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540525/all/Streptococcus_species)

 [*Enterococcus* spp.](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540203/all/Enterococcus)

1. Aerobic Gram negatives

[*Enterobacteriaceae*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540201/all/Enterobacter_species)

[*Pseudomonas aeruginosa*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540457/all/Pseudomonas_aeruginosa)

1. Anaerobes, facultative anaerobes: usually when ulcers are deep, chronic and/or necrotic tissue is present.
[*Bacteroides. fragilis*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540052/all/Bacteroides_fragilis_Group)

[*Clostridia* spp](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540135/all/Clostridium_species).

[*Peptococcus* and *Peptostreptococcus*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540426/all/Peptostreptococcus_spp___and_Finegoldia_magna_).

\*Superficial, early infections ([cellulitis](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540106/all/Cellulitis), [cellulitis](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540106/all/Cellulitis) involving blisters and shallow ulcers) are typically caused by [*S. aureus*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540518/all/Staphylococcus_aureus) or beta-hemolytic streptococci.

\*Infections of ulcers that are chronic or previously treated with antibiotics may be caused by aerobic Gram-negative bacilli, [*S. aureus*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540518/all/Staphylococcus_aureus) or Streptococci.

\*Deep soft tissue infections, [osteomyelitis](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540405/all/Osteomyelitis__Chronic), and gangrene are more often polymicrobial, including aerobic Gram-negative bacilli and anaerobes (anaerobic streptococci, *[Bacteroides fragilis](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540052/all/Bacteroides_fragilis_Group)* group, [*Clostridium* species](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540135/all/Clostridium_species)), but [*Staphylococcus aureus*](https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540518/all/Staphylococcus_aureus) is also common as a single pathogen.

**The Diagnosis**

The clinical diagnosis of foot infection is based on the presence of purulent discharge from an ulcer or the classic signs of inflammation (i.e., erythema, pain, tenderness, warmth, or induration). Other suggestive features of infection include foul odor, the presence of necrosis, and failure of wound healing despite optimal management. Local inflammatory findings may be less prominent or absent in some diabetic foot infections. For example, pain and tenderness may be reduced or absent in patients who have neuropathy, whereas erythema may be absent in those with vascular disease.

**Treatment**

Effective management of diabetic foot infection requires appropriate antibiotic therapy, surgical drainage, debridement and resection of dead tissue, appropriate wound care, and correction of metabolic abnormalities.

**Antibiotic therapy**

The selection of antibiotic therapy for diabetic foot infection involves decisions about choice of empiric and definitive antibiotic agent, route of administration, and duration of treatment. Initial empiric antibiotic therapy should be based on the severity of the infection, history of recent antibiotic treatment, previous infection with resistant organisms, recent culture results, current Gram stain findings, and patient factors (e.g., drug allergy). A Gram-stained smear of an appropriate wound specimen may help guide therapy. The empiric antibiotic regimen for diabetic foot infection should always include an agent active against *S. aureus*, including MRSA if necessary, and streptococci. The patient should be reassessed 24 to 72 hours after initiating empiric antibiotic therapy to evaluate the response and to modify the antibiotic regimen, if indicated by early culture results.

Several antibiotics have been shown to be effective. Antibiotic therapy should not be used for foot ulcers without signs of infection because it does not enhance wound healing or prevent infection. Clinical failure of appropriate antibiotic therapy might be because of patient nonadherence, antibiotic resistance, superinfection, undiagnosed deep abscess or osteomyelitis.