Diabetic Foot Syndrome

EMPIRIC THERAPY OF DIABETIC FOOT INFECTIONS

Culture results (if any) and clinical assessment determine the choice and duration of therapy.

Antibiotic dose is adjusted to renal function, if necessary.

<table>
<thead>
<tr>
<th>Antibiotic*</th>
<th>Dosage</th>
<th>Approximate cost per day†</th>
<th>Antibiotic*</th>
<th>Dosage</th>
<th>Approximate cost per day†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line therapy</strong></td>
<td></td>
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<td><strong>Second-line therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin (Primaxin®)</td>
<td>500 mg-1 g</td>
<td>$71 IV q8h</td>
<td>Vancomycin†§</td>
<td>1 g-2 g IV q6h</td>
<td>$89</td>
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<td>AND</td>
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<tr>
<td>Metronidazole (Flagyl®)</td>
<td>500 mg-1 g</td>
<td>$43 IV q8h</td>
<td>Ceftazidime (Fortaz®)</td>
<td>1 g-2 g IV q8h</td>
<td>$57</td>
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<td>Cefoxitin (Mefoxin®)</td>
<td>2 g IV q6h</td>
<td>$80</td>
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<tr>
<td>Ceftriaxone (Rocephin®)</td>
<td>1 g IV q24h</td>
<td>$60</td>
<td>Piperacillin/tazobactam (Tazocin®)</td>
<td>4/0.5 g</td>
<td>$64 IV q6h</td>
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<tr>
<td>Aztreonam (Azactam®)</td>
<td>1 g IV q8h</td>
<td>$56</td>
<td>Imipenem/cilastatin (Primaxin®)</td>
<td>500 mg IV q6h</td>
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<td>30-60 mg</td>
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<td>Ciprofloxacin (Cipro®)</td>
<td>400 mg PO BID</td>
<td>$5</td>
<td>Cefepime (Maxipime®)</td>
<td>1 g IV q8h</td>
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† Approximate cost based on price listed in the Liste de médicaments published by the Régie de l’assurance maladie du Québec (RAMQ) (February 2005).
‡† Follow-up of trough plasma concentrations is recommended, with a goal of 5-10 µg/mL. Certain authors suggest maintaining trough levels of 10-15 µg/mL in presence of bone involvement.
¶ Third generation cephalosporins: Ceftriaxone 2 g IV q24h, Cefotaxime 2 g IV q8h, Ceftriaxone 2 g IV q6h if P. aeruginosa is suspected.
¶¶ Vancomycin 1-2 g IV q8h (or q12h if renal impairment) if a P. aeruginosa is isolated.
§ First generation cephalosporins: Cefazolin 2 g IV q4h, Cefoxitin 2 g IV q8h, Cefadroxil 2 g IV q12h (if P. aeruginosa is suspected).
** Second course: 7-10 days of antibiotics if no infection is detected on second week of antibiotic therapy.
††† First course: 7-10 days of antibiotics if no infection is detected on second week of antibiotic therapy.
§§ Contraindication for multi-resistant nonfermentative bacteria (MRNFB, Pseudomonas) on the basis of local resistance patterns, in a patient with a history of hospitalization or with recent antibiotic therapy and in a diabetic patient. In these circumstances, consider adjunction vancomycin or another antibiotic against Pseudomonas (e.g. rifampicin, amoxicillin-clavulanate).
TREATMENT GUIDELINES

GENERAL

Treat the infection:

- Combined medical, surgical and multidisciplinary approach depending on the clinical situation;
- Assess indication for drainage, aggressive surgical debridement (avoid amputation if possible);
- Determine if presence of associated ischemia and the need for revascularization:
  - Ischemia is involved in 60% of non-healing ulcers and in 45% of amputations.
  - Assess ischemic component once the infection seems adequately controlled and the acute infectious state is resolved (use revascularization procedure offering the most lasting effect and having the lowest procedure-related risk)
- Reduce pressure on ulcer (off-loading);
- Enhance wound care;
- Control glyceria;
- Prevent relapse once wound has healed

ADJUNCTIVE DIAGNOSTIC TESTING

Biological

- CBC/dimensions/C-reactive protein - low sensitivity but may be useful for follow-up
- Blood glucose
- Other testing depending on the clinic

Imagery

Mainly to assess the presence of ostitis or deep infection or for follow-up:
- Plain radiograph (cortical erosion, periosteal reaction, gas formation) (sensitivity 25-90%; specificity 50-90%);
- Scintigraphy (sensitivity and specificity depending on particular testing);
- CAT or MRI (MRI is standard reference when indicated and available);
- Blood glucose
- CBC/sedimentation/C-reactive protein - low sensitivity but may be useful for follow-up

Blood cultures

Routine cultures in presence of systemic signs or symptoms

Sample collection for bacteriologic cultures

- Indicated only if ulcer appears infected, Routine test for aerobes and anaerobes.
- Superficial wound swabs are questionable (30-60% correlation with peroperative sampling).
- Sampling after careful curettage of the ulcer (post debridement/post cleansing) is usually more accessible.
- Peroperative sampling, if necessary (+ histopathology) (+ bone biopsy, if indicated).

TREATMENT GUIDELINES

DIAGNOSIS

CLINICAL DIAGNOSIS (Favor specific signs over sensitive signs)

1. Evaluate the presence of the following local signs:
   - Local inflammatory syndrome
   - Open wound and discharge
   - Nature of ulceration (depth/wall)
     - Wagner Ulcer Classification System (June 2004)
   - Foul odor (suggests the presence of anaerobes but is not specific)
   - Crepitation

2. Identify the presence of systemic signs (fever, chills, etc.):
   - Are often absent
   - Indicate a more serious impairment (abscess, gangrene, bacteremia (≤ 35%))

3. Assess concomitant vascular impairment:
   - Gangrene/Ischemia
   - Palpation of peripheral pulses

4. Assess the presence of neuropathy (e.g. test with nylon monofilament)

FOLLOW-UP AND PROGRESS

- Assess clinical state daily or more frequently at first.
- Adjust antibiotic therapy (broaden or narrow spectrum) as needed, based on clinical response and microbiologic results.
- Determine treatment efficacy.
- To prevent relapse, assess healing and complete tissue repair before terminating follow-up
- Enhance wound care
- Reduce pressure on ulcer (off-loading)
- Control glycemia

REFERENCES

Lipsky BA. Diagnosis and treating diabetic foot infections. Diabetes Care 2004; 27 suppl 1: S156-S164.
Lipsky BA. A report from the international consensus on diagnosing and treating the infected diabetic foot. Diabetes Care 2004; 27 suppl 1: S156-S164.
**DIAGNOSIS**

**CLINICAL DIAGNOSIS (Favor specific signs over sensitive signs)**

1. Evaluate the presence of the following local signs:
   1. Local inflammatory syndrome
   2. Open wound and discharge
   3. Nature of ulceration (depth/extent)
   4. Wound odor (suggests the presence of anaerobes but is not specific)
   5. Crepitation
   6. Visible bone and/or signs of osteitis:
      - probe-to-bone test (with stainless steel probe) without encountering soft tissue (highly predictive of osteitis)

   Infection is the usual precipitating factor of local digital gangrene (neutrophilic vasculitis).

2. Identify the presence of systemic signs (fever, chills, etc.):
   - Are often absent
   - Indicate a more serious impairment [abscess, gangrene, bacteremia (≤35%)]

3. Assess concomitant vascular impairment:
   - Gangrene/Ischemia
   - Palpation of peripheral pulses

4. Assess the presence of neuropathy (e.g., test with nylon monofilament)

5. Nature of ulceration (depth/extent)
   - Open wound and discharge
   - Ulcer + surrounding cellulitis
   - Fever
   - Nauseating discharge
   - Ulcer + surrounding cellulitis

   Mainly to assess the presence of osteitis or deep infection or for follow-up:
   - Plain radiograph (cortical erosion, periosteal reaction, gas formation) (sensitivity 25-90%; specificity 50-90%)
   - Scintigraphy (sensitivity and specificity depending on particular testing)
   - CAT or MRI (MRI is standard reference when indicated and available)
   - Blood glucose
   - CBC/sedimentation/C-reactive protein - low sensitivity but may be useful for follow-up

   According to availability and clinical relevance

**ADJUNCTIVE DIAGNOSTIC TESTING**

**Biological**
- CBC/differential/C-reactive protein - low sensitivity but may be useful for follow-up
- Blood glucose
- Other testing depending on the clinical situation

**Imagery**
- Mainly to assess the presence of osteitis or deep infection or for follow-up:
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- Plain radiograph (cortical erosion, periosteal reaction, gas formation) (sensitivity 25-90%; specificity 50-90%)
- Scintigraphy (sensitivity and specificity depending on particular testing)
- CAT or MRI (MRI is standard reference when indicated and available)

**Blood cultures**
- Routine cultures in presence of systemic signs or symptoms

**Sample collection for bacteriologic cultures**
- Indicated only if ulcer appears infected, Routine test for aerobes and anaerobes
- Superficial wound swabs are questionable (30-60% correlation with peroperative sampling)
- Sampling after careful curettage of the ulcer (post debridement/post cleansing) is usually more accessible
- Peroperative sampling, if necessary (+ histopathology) (+ bone biopsy, if indicated)

**TREATMENT GUIDELINES**

**GENERAL**

- Treat the infection:
  - Combined medical, surgical and multidisciplinary approach depending on the clinical situation
  - Assess indication for drainage, aggressive surgical debridement (avoid amputation if possible)
  - Determine if presence of associated ischemia and the need for revascularization:
    - Ischemia is involved in 60% of non-healing ulcers and in 45% of amputations
    - Assess ischemic component once the infection seems adequately controlled and the acute infectious state is resolved
    - Use revascularization procedure offering the most lasting effect and having the lowest procedure-related risk
  - Reduce pressure on ulcer (off-loading)
  - Enhance wound care
  - Control glycemia
  - Prevent relapse once wound has healed

**OTHER TREATMENT MODALITIES**
- More costly and advanced technologies: Aligraf™, Dermagraft™, Regranex™ (bepicameline). Consider these when there is no response to standard care and after consulting a medical specialist. These procedures increase the percentage of wound closure and reduce the healing time.
- Hyperbaric therapy/G-CSF and others: for particular cases only since their role is unclear.

**FOLLOW-UP AND PROGRESS**

- Assess clinical state daily or more frequently at first
- Adjust antibiotic therapy (broader or narrower spectrum) as needed, based on clinical response and microbiologic results
- Determine treatment efficacy
- To prevent relapse, assess healing and complete tissue repair before terminating follow-up
- For particular cases only since their role is unclear.

**REFERENCES**
Diabetic Foot Syndrome

translated from the original French version published November 2005

This guide is provided for information purposes and is not a substitute for clinical judgment.

Foot Infection is a major cause of hospitalization, of nontraumatic amputation and peri- and postoperative mortality in diabetics.

• Annual incidence of new foot ulcerations in diabetics = 2-3%
• Infections ulcers requiring surgical bone resection = 15-25% of cases

Prevention

• Adequate follow-up of diabetes and glycaemia
• Treatment of Tinea pedis when present
• Use of appropriate footwear
• Adequate follow-up of diabetes and glycemia
• Regular examination of feet and meticulous foot care

Pathophysiology

• Adequate correction of callus and deformities,
• Treatment of Tinea pedis when present
• Use of appropriate footwear
• Adequate follow-up of diabetes and glycemia
• Regular examination of feet and meticulous foot care

Associated Pathogens

• Immunopathy also contributes to the occurrence of infection.

Pathogenotypes

• Monomicrobial infections (45-50%)
• Polymicrobial infections (aerobes and anaerobes)

Severe or deep infections

• Infections extending over skin and subcutaneous tissues (abcess, fascia, tendon, bone, etc.)
• CTX-M-15 extended-spectrum beta-lactamase
• Initial parenteral antibiotic therapy
• Adjunctive vancomycin ± another antibiotic against Pseudomonas (e.g. ciprofloxacin, aminoglycosides)

Antibiotic Therapy

First-line therapy

<table>
<thead>
<tr>
<th>Antibiotic*</th>
<th>Dosage</th>
<th>Approximate cost per day</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>Amoxicillin/Clavulanate potassium (Augmentin®)</td>
<td>1 g PO BD</td>
<td>$4</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>Ceftriaxone (Rocephin®)</td>
<td>1 g IV q12h</td>
<td>$8</td>
<td>2-3 weeks</td>
</tr>
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</table>

Second-line therapy

<table>
<thead>
<tr>
<th>Antibiotic*</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Vancomycin††</td>
<td>1 g IV q6h or more**</td>
<td>$89</td>
<td>2-4 weeks</td>
</tr>
<tr>
<td>Ceftazidime (Fortaz®)</td>
<td>1-2 g IV q8h</td>
<td>$100</td>
<td>1-2 weeks</td>
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† Approximate cost based on price listed in the Guide de médicaments published by the Régie de l’Assurance maladie du Québec (RAMQ) (February 2005).
‡ First generation cephalosporin: Cefuroxime 2 g IV q4h, Cefoxitin 2 g IV q6h. Quinolones 2 g IV q12h if renal insufficiency is suspected.
§ Third generation cephalosporins: Ceftriaxone 2 g IV q4h, Cefotaxime 2 g IV q6h. Quinolones 2 g IV q12h if renal insufficiency is suspected.
¶ A minimum of 4-6 weeks therapy overall (if a P. aeruginosa is isolated)
|| Follow-up of trough plasma concentrations is recommended, with a goal of 5-10 µg/mL. Certain authors suggest maintaining trough levels of 10-15 µg/mL.
** In presence of bone involvement.
†† Consider coverage of multi-resistant nosocomial bacteria (MRSA Enterococci, Pseudomonas) on the basis of local resistance patterns, in a patient with a history of hospitalization or with recent antibiotic therapy and in a diabetic patient.

This guide was developed in collaboration with professional corporations (CMQ, OPQ), the federations (FMOQ, FMSQ) and Québec associations of pharmacists and physicians.