Diabetic Foot Infection
How I do it?

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Center of Excellence for Diabetic foot care (TU-CDC)

Thammasat University Hospital
Center of Excellence for Diabetic foot care

TU-CDC Committee (Multidisciplinary team)

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**APN**
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- Arpaporn Kuthongkul
Diabetes mellitus (DM)

• Global registry (International diabetes federation, IDF)¹
  • 2015: 415 Million DM patients
  • 2050: 643 Million DM patients

• Thailand registry²
  • 2014: 5 Million DM patients

¹ International Diabetes Federation. DF Diabetes Atlas 2015
² Aekplakorn W. Thai National Health Examination. Survey (NHES V), National Health Examination Survey Office, Health System Research Institute 2016
Diabetic foot ulcer (DFU)

- **DFU**
  - 1 in 4 of DM (25%) \(^1\)

- **DFU vs non-DFU**
  - 3 years Mortality rate: 31.9% VS 12.0% \(^2\)
    - Most common cause of death: Coronary artery disease (CAD)
    - Ankle brachial index (ABI): correlate negatively with the severity of CAD \(^3\)

- **DFU with amputation**
  - 5 years Mortality rate: 46% \(^4\)
  - one amputation every 7 min could be directly attributed to diabetes \(^5\)

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Etiologies of DFU

• Peripheral arterial disease (PAD) – Atherosclerosis$^{1,2}$
• Peripheral neuropathy$^{1,2}$

  • Foot deformity $\rightarrow$ Repetitive trauma $\rightarrow$ Chronic ulcer
  • Poor vascular supply $\rightarrow$ Delay wound healing $\rightarrow$ Chronic ulcer
  • Hyperglycemia $\rightarrow$ Oxidative stress $\rightarrow$ Chronic ulcer

Etiologies of Diabetic foot infection (DFI)

- Peripheral arterial disease (PAD) – Atherosclerosis
- Peripheral neuropathy

- Poor vascular supply (Poor capillary flow)
  \[ \rightarrow \text{Poor local wound immune system} \rightarrow \text{DFI}^{1,2} \]

- Hyperglycemia
  \[ \rightarrow \text{Poor systemic immune system} \rightarrow \text{DFI}^{1,2} \]

Peripheral arterial disease (PAD)

- PAD: closed associated with DFU
  - DM = major atherosclerotic risk factor - increases risk of symptomatic PAD \(^1-^2\)
- Prevalence of PAD in DM: 10.9 - 31.5\%\(^3\)
- 1\% increase in Hb\(_{A1c}\) = increased 28\% risk of PAD in DM\(^4\)
- DM + PAD = increased risk of DFI + high morbidity/mortality\(^5\)
- Poor control of atherosclerotic risk factor in Thai DM population\(^6\)

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2. Tendera M, European heart journal. 2011
3. Rhee SY, Diabetes research and clinical practice. 2007
6. Orrapin S, AVD 2015

Hb\(_{A1c}\): glycated hemoglobin
DM + PAD (Neuroischemic ulcer)
DM foot

• Diabetic foot infection (DFI): soft tissue or bone infection below the malleoli \(^1,2\)

Definition of DFI

• Infection of soft tissue or bone at below malleoli in DFU patients\(^1\)
  1. Soft tissue infection
  2. Osteomyelitis

• Presence of local +/- systemic signs and symptoms of inflammation\(^2\)

• DFI - 60% of all cause of lower extremity amputation\(^3\)

1. Novoung A, Rutherford's Vascular surgery 2014
2. Lipsky BA, Diabetes/metabolism research and reviews. 2016
DFI

Local sign

• ≥2 of the following:\(^1\)
  1. Local swelling or induration
  2. Erythema >0.5 cm around the wound
  3. Local tenderness or pain
  4. Local warmth
  5. Purulent discharge

Excluded: other causes of skin inflammation
- gout, fracture, trauma, venous thrombosis, etc.

Systemic sign (SIRS)

• ≥ 2 of the following:\(^1\)
  1. Temperature > 38 °C or < 36 °C
  2. Heart rate > 90 beats/min
  3. Respiratory rate >20 breaths/min or PaCO\(_2\) < 32 mmHg
  4. WBC >12 000/mm\(^3\) or < 4000/mm\(^3\), or >10% immature (band) forms

SIRS: systemic inflammatory response syndrome, WBC: white blood cell count

DFU

- Callus formation
- Foot deformities
DFI

- Erythema
- Purulent discharge
- Local swelling
# The classification systems: Presence and Severity of DFI

*by IDSA with PEDIS classification (Infection part) by IWGDF*¹,²

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IWGDF; International Working Group on the Diabetic Foot

IDSA; Infectious Diseases Society of America

1. Schaper NC. Diabetes Metab Res Rev 2004
2. Lipsky BA. Clin Infect Dis 2012
IWGDF/IDSA classification

- High IWGDF/IDSA $^{1,2}$
  - Long hospital stay
  - Poor prognosis – Amputation prediction

1. Wukich DK, Diabetes care. 2013
Other classification

1. Meggitt-Wegner Ulcer Classification Score\(^1\)
2. The University of Texas Health Science Center San Antonio Diabetic Wound Classification System\(^2\)
3. Etc.

2. Lavery LA, J Foot Ankle Surg 1996
# Meggitt-Wegner Ulcer Classification Score\(^1\)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Lesion</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Superficial diabetic ulcer (partial or full thickness)</td>
</tr>
<tr>
<td>2</td>
<td>Ulcer extension to ligament, tendon, joint capsule, or deep fascia</td>
</tr>
<tr>
<td>3</td>
<td>Deep ulcer with <strong>abscess, osteomyelitis, or joint sepsis</strong></td>
</tr>
<tr>
<td>4</td>
<td>Gangrene localized to portion of forefoot or heel</td>
</tr>
<tr>
<td>5</td>
<td>Extensive gangrenous involvement of the entire foot</td>
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The University of Texas Health Science Center San Antonio Diabetic Wound Classification System

<table>
<thead>
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<th>Grade</th>
<th>0</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Pre- or post ulcerative lesion completely epithelialized</td>
<td>Superficial wound, not involving tendon, capsule, capsule or bone</td>
<td>Wound penetrating to tendon or capsule</td>
<td>Wound penetrating to bone</td>
</tr>
<tr>
<td>B</td>
<td>Pre- or post ulcerative lesion, completely epithelialized with infection</td>
<td>Superficial wound, not involving tendon, capsule, or bone with infection</td>
<td>Wound penetrating to tendon or capsule with infection</td>
<td>Wound penetrating to bone or joint with infection</td>
</tr>
<tr>
<td>C</td>
<td>Pre- or post ulcerative lesion, completely epithelialized with ischemia</td>
<td>Superficial wound. not involving tendon, capsule, or bone with ischemia</td>
<td>Wound penetrating to tendon or capsule with ischemia</td>
<td>Wound penetrating to bone or joint with ischemia</td>
</tr>
<tr>
<td>D</td>
<td>Pre- or post ulcerative lesion, completely epithelialized with infection and ischemia</td>
<td>Superficial wound, not involving tendon, capsule, or bone with infection and ischemia</td>
<td>Wound penetrating to tendon or capsule with infection and ischemia</td>
<td>Wound penetrating to bone or joint with infection and ischemia</td>
</tr>
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1. Lavery LA, J Foot Ankle Surg 1996
Diabetic Wound Classification System

- Outcomes deteriorated with increasing grade and stage of wounds\(^1\)

- **Combination tools** with additional **clinical information**: accurate interpretations\(^2\)

- Need of **further studies** assessing reliability and accuracy of all systems\(^3\)

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1. Armstrong DG, Diabetes Care. 1998
Osteomyelitis (OM)

- High risk OM wound
  1. Ulcer lies over a bony prominence
  2. Sausage toe (indurated and redness toes)
  3. Large ulcers (area >2 cm²)
  4. Unresponsive to adequate treatment


Bony prominence  Sausage toe  Large ulcers
Osteomyelitis (OM)

• **Probe-to-bone test**¹
  - Blunt sterile metal probe inserted through bone
  - Hard and Gritty
  - 7.2 time of OM

• For all infected open wound:¹
  - Probe-to-bone test
    - Low risk OM: negative test → rules out diagnosis
    - High risk OM: positive test → largely diagnostic

• Erythrocyte sedimentation rate (ESR): suggest of OM in suspected patients¹,²,³
  - > 70 mm/h (*77% sensitivity and 77% specificity*)

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¹. Lipsky BA. Diabetes Metab Res Rev 2016
². Uzun G.The Tohoku journal of experimental medicine. 2007
³. Papanas, Int J Low Extrem Wounds 2013
Osteomyelitis (OM)

• **Definite diagnosis:**
  • **Bone sample:** positive results on histological (microbiological) examinations
    • Equivocal diagnosis or
    • Determining causative pathogen’s antibiotic susceptibility: for unresponsive for ordinary treatment (Empirical antibiotic)

• **Probable diagnosis**
  • Combination of diagnostic tests:
    • Probe-to-bone
    • Serum inflammatory markers
    • Plain X-ray: all case of Non-superficial DFI
    • MRI
    • Radionuclide scanning

Osteomyelitis (OM)

- **Plain X-ray:** all Non-superficial DFI
  - 54% sensitivity and 68% specificity

- Typical feature of OM in DFI
  - Loss of bone cortex with bony erosion
  - *Trabecular bone destruction* or marrow radiolucency
  - Bone sclerosis, Periosteal reaction or elevation
  - Presence of sequestrum: devitalized bone
  - Presence of involucrum: bone growth outside previously existing bone
  - Presence of cloacae: opening in the involucrum or cortex
  - Presence of evidence of a sinus tract from the bone to the soft tissue

Osteomyelitis (OM)

- MRI: best imaging for OM diagnosis
  - 90% sensitivity and 85% specificity

- MRI is not available or contraindicated
  - white blood cell-labelled radionuclide scan,
  - single-photon emission computed tomography and computed tomography (SPECT/CT)
  - fluorine-18-fluorodeoxyglucose positron emission tomography (PET) scans

References:
1. Dinh T, Int J Low Extreme. 2010
Assessing severity

• Vital signs and Physical examination
• Basic blood tests
• Debride wound
• Probe assess depth and extent of infection
• Assess arterial perfusion → further vascular assessment (ABI, TBI, TCOM) → Angiogram → Revascularization

Characteristics suggesting a more serious diabetic foot infection

<p>| | |</p>
<table>
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<tbody>
<tr>
<td><strong>Wound</strong></td>
<td>Penetrates to subcutaneous tissues (e.g. fascia, tendon, muscle, joint and bone)</td>
</tr>
<tr>
<td><strong>Cellulitis</strong></td>
<td>Extensive (&gt;2 cm), distant from ulceration or rapidly progressive</td>
</tr>
<tr>
<td><strong>Local signs</strong></td>
<td>Severe inflammation or induration, crepitus, bullae, discoloration, necrosis or gangrene, ecchymoses or petechiae and new anaesthesia</td>
</tr>
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</table>

VS

Necrosis or gangrene

Penetrates subcutaneous tissues

Extensive (>2 cm)
Characteristics suggesting a more serious diabetic foot infection

<table>
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<tr>
<td><strong>Presentation</strong></td>
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<tr>
<td><strong>Systemic signs</strong></td>
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<tr>
<td><strong>Laboratory tests</strong></td>
</tr>
<tr>
<td><strong>Complicating features</strong></td>
</tr>
<tr>
<td><strong>Current treatment</strong></td>
</tr>
</tbody>
</table>

Microbiological considerations

• Tissue specimen:
  • For Causative microorganisms + antibiotic sensitivity
• Do not swab culture

• Send collected specimens to microbiology laboratory promptly + sterile transport containers

Management

• Select specific antibiotic agents for 1-2 weeks for treatment
• Based on
  • causative pathogens
  • antibiotic susceptibilities
  • clinical severity
  • efficacy and costs

• Moderated and Severe infection: Parenteral therapy initially
• Switch to oral therapy when infection responding

## Empiric antibiotic regimen

<table>
<thead>
<tr>
<th>Severity</th>
<th>Factors</th>
<th>Pathogen</th>
<th>Empirical antibiotic regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>No complicating features</td>
<td>GPC</td>
<td>Pen, 1\textsuperscript{st} Ceph</td>
</tr>
<tr>
<td></td>
<td>ß-lactam allergy or intolerance</td>
<td>GPC</td>
<td>Clindamycin; FQ; T/S; macrolide; doxy</td>
</tr>
<tr>
<td>Recent antibiotic exposure</td>
<td>GPC + GNR</td>
<td>GPC</td>
<td>ß-L-ase-1; T/S; FQ</td>
</tr>
<tr>
<td>High risk for MRSA\textsuperscript{a}</td>
<td>MRSA</td>
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<td>Linezolid; T/S; doxy; macrolide; FQ</td>
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\textsuperscript{a} high local prevalence of MRSA, recent stay in healthcare institution, recent antibiotic therapy or known MRSA colonization

\textsuperscript{b} high local prevalence of Pseudomonas infections, warm climate or frequent exposure of the foot to water.
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<tr>
<td>Moderate and severe</td>
<td>No complicating features</td>
<td>GPC + GNR</td>
<td>β-L-ase 1; second/third gen ceph</td>
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<tr>
<td></td>
<td>Recent antibiotics</td>
<td>GPC + GNR</td>
<td>β-L-ase 2; third gen ceph, group 1 carbapenem (depends on prior therapy; seek advice)</td>
</tr>
<tr>
<td></td>
<td>Macerated ulcer and warm climate</td>
<td>GNR + Pseudomonas</td>
<td>β-L-ase 2; S-S pen+ceftazidime, S-S pen+cipro, group 2 carbapenem</td>
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<td>Ischemic limb/necrosis/gas forming</td>
<td>GPC + GNR + Anaerobes</td>
<td>β-L-ase 1 or 2; group 1 or 2 carbapenem; second/third gen ceph+clindamycin or metronidazole</td>
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<td>MRSA risk factors&lt;sup&gt;a&lt;/sup&gt;</td>
<td>MRSA</td>
<td>Consider addition of, or substituting with, glycopeptides; linezolid; daptomycin; fusidic acid; T/S (±rif)*; doxycycline; FQ</td>
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<tr>
<td></td>
<td>Risk factors for resistant GNR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>ESBL</td>
<td>Carbapenems, FQ, aminoglycoside and colistin</td>
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<sup>a</sup> high local prevalence of MRSA, recent stay in healthcare institution, recent antibiotic therapy or known MRSA colonization

<sup>b</sup> high local prevalence of Pseudomonas infections, warm climate or frequent exposure of the foot to water.
Management

- Consult surgical specialist
  - Moderate DFI
  - Severe DFI

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1. Schaper NC, Diabetes Metab Res Rev 2004
2. Lipsky BA, Clin Infect Dis 2012

Management

• Urgent surgical intervention
  • Deep abscesses
  • Compartment syndrome
  • Necrotizing soft tissue infections

• Procedure: minor debridement or drainage to extensive resections, major amputation.

Management

• Non-urgent infections
  • Initial surgical intervention: limited to incision and drainage
  • If non responding - further resection

• Major amputation
  1. Non-viable limb
  2. Potentially life-threatening infection
  3. Functionally useless

Dorsum incision

- Metatarsal head to base at
  - Medial border of 2nd metatarsal bone
  - Lateral border of 4th metatarsal bone
  - Skin bridge (full-thickness skin bridge) > 2 cm

Plantar incision

- Imaginary line from 2nd toe to mid calcaneal bone
- Avoid weight-bearing surface

2. Orrapin S, Prevention and Management of The Diabetic foot 2009
• **Medial incision:**
  • first metatarsal head - navicular tuberosity – mid imaginary line from plantar heel to medial malleolus

• **Lateral incision:**
  • fifth metatarsal base - Achilles tendon and fibula

2. Orrapin S, Prevention and Management of The Diabetic foot 2009
Management

• OM
  • Considering orthopedic surgical intervention
    1. Spreading soft tissue infection
    2. Destroyed soft tissue envelope
    3. Progressive bone destruction on X-ray
    4. Bone protruding through the ulcer

• For resection OM:
  • no more than 1 week of antibiotic therapy

• For non-resection OM:
  • 6 weeks of antibiotic

Surgical treatment VS Antibiotic treatment

• Nonsurgical approach with antibiotic therapy can be successful in selected cases.¹
  1. No ischemia (CLI)²
  2. No necrotizing soft tissue infections²

• Similar outcomes: healing rates, time to healing, and short-term complications²

¹ José Luis Lázaro-Martínez, Diabetes Care. 2014
² Mesut Mutluoğlu, Lancet Diabetes Endocrinol. 2017
Management

• **PAD**
  - Revascularization $^{1,2}$
    - Endovascular VS Open bypass
  - Critical limb ischemia (Severe PAD)$^{2,3}$
    - Resting Ankle pressure $< 50-70$ mmHg
    - Toe pressure $< 50$ mmHg
    - TCOM $<30$ mmHg
    - PVR: flat or barely pulsatile

Take home message

1. Diagnosis of **soft tissue infection VS osteomyelitis**
2. Control blood sugar and co-morbid condition (esp. Cardiac disease)
3. **Assessing severity** and **Eradicated infection**
   - Antibiotic
   - Limited debridement and amputation
4. **Microbiologic consideration**
   - tissue specimen culture
5. Evaluation **vascular supply** and revascularization as indicated
6. **Off-loading technique**
   - Total Contact Cast (TCC) or other instrument
   - Surgery
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IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes

The NEW ENGLAND JOURNAL of MEDICINE

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