

Summary of New Diabetic Foot Infection Guidelines (2015/2016 IWGDF)



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A diabetic patient with fever-chill, hypotension



A diabetic man with fever and foot pain



Epidemiology of Diabetic Foot Infection

Develop a foot wound: ~25%



Wound infected at presentation: ~55%



Mild: 35+%



Moderate: 30-60%



Severe: 5-25%



DFO: $\leq 20\%$



DFO: ~30-40%



DFO: ~50-80%

2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections^a

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IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes

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Recommendations

Classification/diagnosis

1. Diabetic foot infection must be diagnosed clinically, based on the presence of local or systemic signs or symptoms of inflammation (strong; low).
2. Assess the severity of any diabetic foot infection using the Infectious Diseases Society of America/International Working Group on the Diabetic Foot classification scheme (strong; moderate).

Osteomyelitis

3. For an infected open wound, perform a probe-to-bone test; in a patient at low risk for osteomyelitis, a negative test largely rules out the diagnosis, while in a high-risk patient, a positive test is largely diagnostic (strong; high).
4. Markedly elevated serum inflammatory markers, especially erythrocyte sedimentation rate, are suggestive of osteomyelitis in suspected cases (weak; moderate).
5. A definite diagnosis of bone infection usually requires positive results on microbiological (and, optimally, histological) examinations of an aseptically obtained bone sample, but this is usually required only when the diagnosis is in doubt or determining the causative pathogen's antibiotic susceptibility is crucial (strong; moderate).
6. A probable diagnosis of bone infection is reasonable if there are positive results on a combination of diagnostic tests, such as probe-to-bone, serum inflammatory markers, plain X-ray, magnetic resonance imaging (MRI) or

The New IWGDF Guidelines: What's New?

- ▶ Updated all sections with *new references* (2010-2014)
- ▶ *Added recommendations* for each section
- ▶ **GRADE system** to rank evidence*:
 - Strength of recommendation: *Strong or Weak*
 - Quality of evidence: *High, Moderate, Low, Very Low*

Revised *management algorithm*

Added new *figures & tables*

Added section on management in *low-income* areas

Added section on *“key controversies”*

IWGDF: Recommendations (1)

- ▶ Total of 26 recommendations
- ▶ Key recommendations (GRADE) by topics
 - Classification/Diagnosis
 - *Diagnosis* diabetic foot infections *clinically*, based on presence of local or systemic signs or symptoms of inflammation (Strong; Low)
 - Assess the *severity of any diabetic foot infection* using the IDSA/IWGDF (PEDIS) classification scheme (Strong; Moderate)

Table 2. Infectious Diseases Society of America and International Working Group on the Diabetic Foot Classifications of Diabetic Foot Infection

Clinical Manifestation of Infection	PEDIS Grade	IDSA Infection Severity
No symptoms or signs of infection	1	Uninfected
Infection present, as defined by the presence of at least 2 of the following items:		
<ul style="list-style-type: none"> • Local swelling or induration • Erythema • Local tenderness or pain • Local warmth • Purulent discharge (thick, opaque to white or sanguineous secretion) 		
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be >0.5 cm to ≤2 cm around the ulcer.	2	Mild
Exclude other causes of an inflammatory response of the skin (eg, trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis).		
Local infection (as described above) with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, fasciitis), and	3	Moderate
No systemic inflammatory response signs (as described below)		
Local infection (as described above) with the signs of SIRS, as manifested by ≥2 of the following:	4	Severe ^a
<ul style="list-style-type: none"> • Temperature >38°C or <36°C • Heart rate >90 beats/min • Respiratory rate >20 breaths/min or PaCO₂ <32 mm Hg • White blood cell count >12 000 or <4000 cells/μL or ≥10% immature (band) forms 		

Abbreviations: IDSA, Infectious Diseases Society of America; PaCO₂, partial pressure of arterial carbon dioxide; PEDIS, perfusion, extent/size, depth/tissue loss, infection, and sensation; SIRS, systemic inflammatory response syndrome.

Diagnosis and classification

- ▶ IDSA and the IWGDF (the 'infection' part of the PEDIS classification) describe how to define both the presence and severity of infection
- ▶ to predict the need for hospitalization or lower extremity amputation

In one study, patients with grade 4 infections VS grade 3 infections

→ 7.1-fold higher risk of major amputation

→ 4-day longer mean hospital stay

IWGDF Recommendation (2)

- ▶ Key recommendations (GRADE) by topics

Osteomyelitis

- ▶ **Definite diagnosis** of bone infection
 - usually requires **positive results on microbiological (& optimally, histological) examinations of aseptically obtained bone**
 - but, usually required only when diagnosis in doubt or crucial to determine the pathogens' antibiotic sensitivity (Strong; Moderate)
- ▶ **Probable diagnosis** of bone infection is **reasonable** if positive results on **combination of clinical and diagnostic tests**, eg, probe-to-bone, serum inflammatory markers, plain X-ray, MRI or radionuclide scanning (Strong; Weak)



Film of osteomyelitis



Typical features of diabetic foot osteomyelitis on plain X-rays

- ▶ Periosteal reaction or elevation
- ▶ Loss of bone cortex with bony erosion
- ▶ Focal loss of cortical trabecular pattern or marrow radiolucency
- ▶ Bone sclerosis, with or without erosion
- ▶ Presence of sequestrum: devitalized bone with radiodense appearance that has become separated from normal bone
- ▶ Presence of involucrum: a layer of new bone growth outside previously existing bone resulting from stripping off of the periosteum and new bone growing from the periosteum
- ▶ Presence of cloacae: opening in the involucrum or cortex through which sequestrate or granulation tissue may discharge
- ▶ Presence of evidence of a sinus tract from the bone to the soft tissue

IWGDF Recommendations (3)

► Key recommendations (GRADE) by topics

Osteomyelitis

- *Avoid using cultures of soft tissue/sinus tract* for selecting antibiotic therapy for osteomyelitis (Strong; Moderate)
- *Obtain plain X-rays of foot in all cases of non superficial diabetic foot infection* (Strong; Low)
- *Use MRI when an advanced imaging test is needed* for diagnosing diabetic foot osteomyelitis (Strong; Moderate)

ผู้ป่วยชายไทยอายุ 50 ปี known cases DM เข้าซา มีแผล
เรื้อรังที่ 1st Rt toe. Pedal pulse +2



Probe to bone test +
positive predictive value 85%
negative predictive value 98%



Plain film: negative what next?

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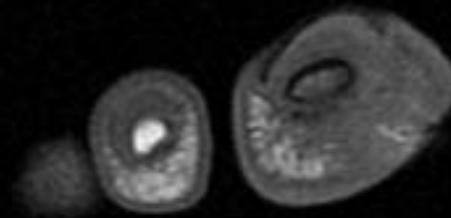
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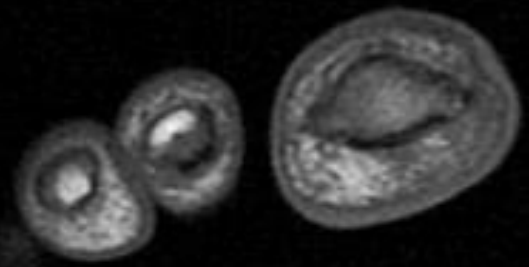


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IWGDF Recommendations (4)

- ▶ Key recommendations (GRADE) by topics
 - Assessing severity
 - ▶ **At initial evaluation of infected foot:** obtain *vital signs*; order appropriate *blood tests*; *debride* the wound; *probe* and assess the *depth & extent* of infection to establish its *severity* (Strong; Moderate)
 - ▶ **Assess arterial perfusion** of foot; determine the necessity for vascular W/U (Strong; Low)

IWGDF Recommendations (5)

- ▶ Key recommendations (GRADE) by topics
- Microbiological considerations
 - ▶ Obtain cultures, preferably of a *tissue specimen*, to determine causative pathogens & antibiotic sensitivity (Strong; High)
- Surgical treatment
 - ▶ Perform *urgent* surgical interventions for deep abscesses, compartment syndrome, necrotizing soft tissue infection (Strong; Low)
- Antimicrobial therapy
 - ▶ Provide for clinically infected, but *not* clinically uninfected, wounds (Strong; Low)

IWGDF Recommendations (6)

- Key recommendations (GRADE) by topics
 - Antimicrobial therapy
 - 1-2 Week duration adequate for most mild & moderate soft tissue infections (Strong; High)
 - For osteomyelitis suggest 6 weeks of therapy if no resection of infected bone and ≤ 1 week of therapy if all infected bone is resected (Strong; Moderate)
 - Suggest not using any adjunctive treatments specifically for treating infection (Weak; Low)

Osteomyelitis

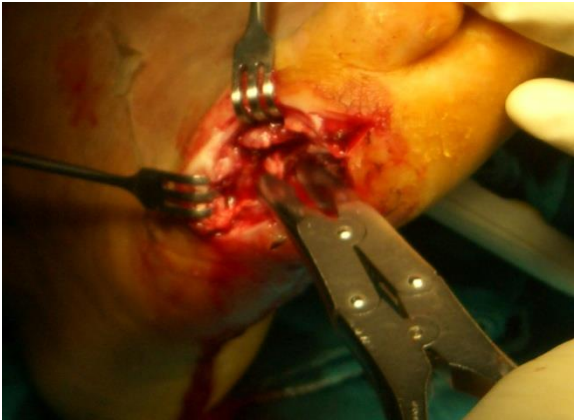


Table 7. Factors potentially favoring selecting either primarily antibiotic or surgical resection for diabetic foot osteomyelitis

Medical

- Patient is too medically unstable for surgery
- Poor postoperative mechanics of foot likely (e.g. with midfoot or hind foot infection)
- No other surgical procedures on foot are needed
- Infection is confined to small, forefoot lesion
- No adequately skilled surgeon is available
- Surgery costs are prohibitive for the patient
- Patient has a strong preference to avoid surgery

Surgical

- Foot infection is associated with substantial bone necrosis or exposed joint
- Foot appears to be functionally nonsalvageable
- Patient is already nonambulatory
- Patient is at particularly high risk for antibiotic-related problem
- Infecting pathogen is resistant to available antibiotics
- Limb has uncorrectable ischaemia (precluding systemic antibiotic delivery)
- Patient has a strong preference for surgical treatment

Modified from Lipsky, 2014, diabetes Care[234].

Factors Influencing Antibiotic Rx DFI (IWGDF)

Infection related

- Clinical severity of infection
- Antibiotic therapy w/n 3 mos
- Presence of bone infection

Patient related

- Allergy to any antibiotics
- Impaired immunological status
- Patient treatment preferences
- patient adherence to therapy
- Renal or hepatic insufficiency
- Impaired GI absorption
- Peripheral arterial disease
- Hi risk MDROs, unusual bugs

Pathogen related

- Likelihood of non-GPC
- H/O MDRO
colonization/infxn
- Local abx resistance rates

Drug related

- Safety profile (freq., severity)
- Drug interactions potential
- Frequency of dosing
- Formulary avail^{ability} /restrict^{ions}
- cost (acquisi^{tion}, adminis^{tration})
- Approval for indication
- ↑ risk C. diff or abx resis^{tance}
- Published efficacy data

Table 6. Selecting Empiric Antibiotic Regimen for DFI

Infection severity	Additional Factors	Pathogens	Potential Regimens
Mild	No complicating features	GPC	S-S penicillin; 1 st gen. ceph
	β - lactam allergy or intolerance	GPC	Clindamycin ;FQ; T/S; macrolide; doxy
	Recent antibiotic exposure	GPC + GNR	β-L-ase-1;T/S; FQ
	High risk for MRSA	MRSA	Linezolid; T/S ; doxy ; macrolide; FQ
Moderate and severe ^b	No complication features	GPC± GNR	β- L-ase 1; 2nd/3rd gen ceph
	Recent antibiotics	GPC± GNR	β- L-ase 2; 3 gen ceph, group1 carbapenem
	Macerated ulcer and warm climate	GNR (Pseudomonas)	β- L-ase-2; S-S pen+ceftazidime, S-S pen + cipro, group 2 carbapenem
	Ischemia limb/ necrosis/gas forming	GPC± GNR± anaerobes	β- L-ase 1 or 2: group 1 or 2 carbanenem; 2/3 gen ceph clindamycin or metronidazole
	MRSA risk factors	MRSA	Consider addition of, or substituting with glycopeptides; linezolid; daptomycin fusidic acid ; T/S (± rifampin)*; doxycycline; FQ
	Risk factors for resistant GNR	ESBL	Carbapenems, FQ, aminoglycoside and colistin

GPC, Gram-positive cocci (staphylococci and streptococci); GNR, Gram-negative rod; MRSA, methicillin-resistant Staphylococcus aureus; ESBL, extended-spectrum β-lactamase-producing organism; S-S pen, semisynthetic penicillinase-resistant penicillin; β-L-ase, β-lactam, β-lactamase inhibitor; β-L-ase 1, amoxicillin/clavulanate, ampicillin/sulbactam; β-L-ase 2, ticarcillin/clavulanate, piperacillin/tazobactam; doxy, doxycycline; group 1 carbapenem, ertapenem; group 2 carbapenem, imipenem, meropenem, doripenem; ceph, cephalosporin; gen generation; Pip/tazo, piperacillin/tazobactam; FQ, fluoroquinolone with good activity against aerobic Gram-positive cocci (e.g.levofloxacin or moxifloxacin); Cipro, antipseudomonal fluoroquinolone, for example, ciprofloxacin; T/S, trimethoprim/sulfamethoxazole; T/S (±rif), trimethoprim/sulfamethoxazole with or without rifampin.

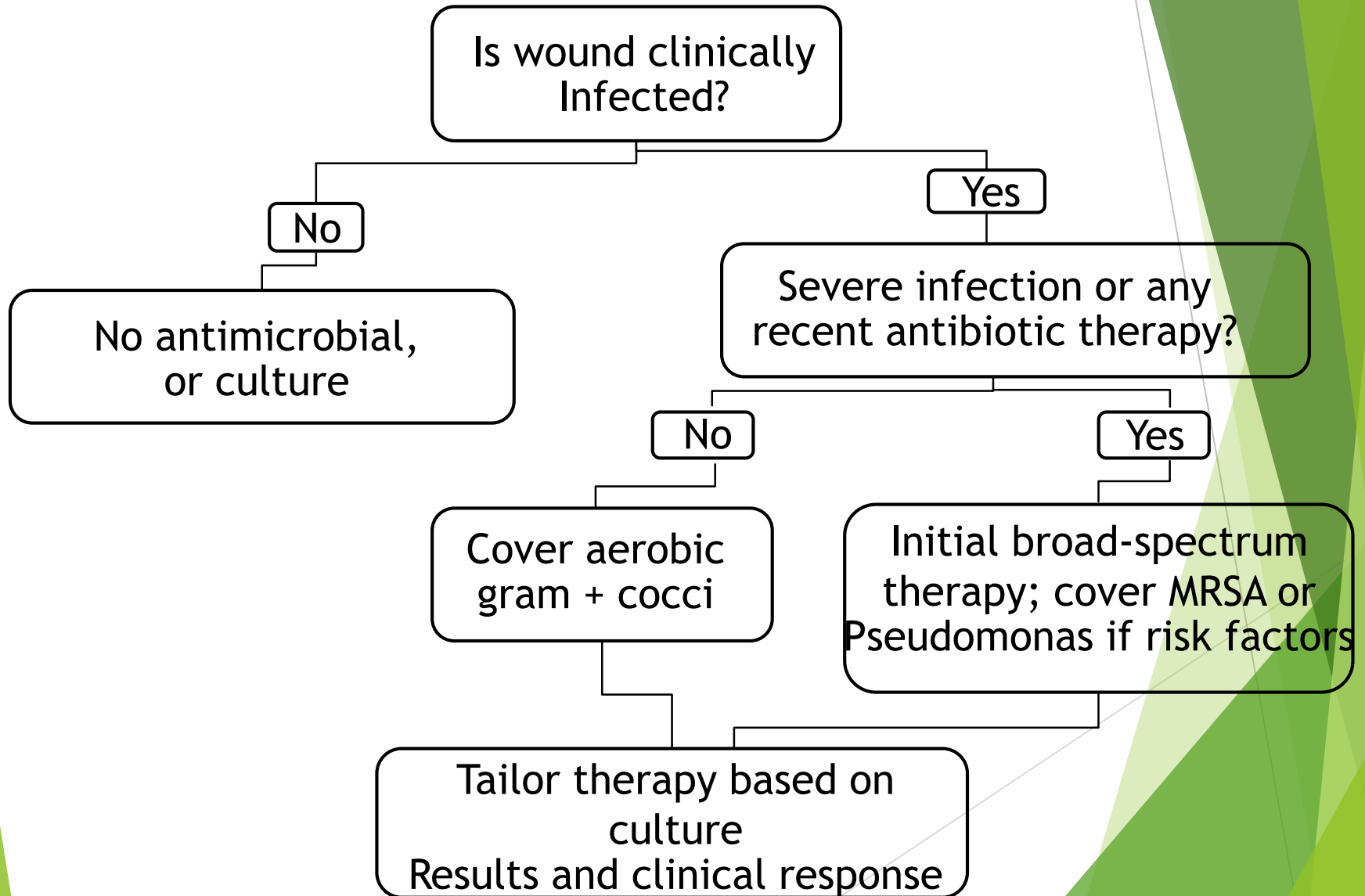
*Rifampin [270] (for now, we think that rifampin) should only be used for osteomyelitis).

^a Given at usual recommended doses for serious infections. Modify doses or agents selected for azotaemia, liver dysfunction and so on.

Recommendations based upon theoretical considerations and available clinical trials.

^bOral antibiotic agents should generally not be used for severe infections, except as follow-on (switch) after initial parenteral therapy.

Approach to Antibiotic Therapy for DFI



Diabetic Foot Infection Guidelines: Summary

- Most used guidelines: IDSA & IWGDF
- Classification: based on severity (\pm ischemia)
- Antibiotic therapy: choosing empiric, definitive
- Surgery often needed: debridement, I&D; \pm revascularization
- Osteomyelitis: approach to diagnosis & treatment
- Adjunctive measures generally not proven helpful
- Interdisciplinary teams improve outcomes
- How do we improve in your setting?: implement, audit, study