Diabetic Foot Infection
How I do it?

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- *Dr. Pimjai Anthanon*

Dermatologist

- *Dr. Patcha Pongjareon*

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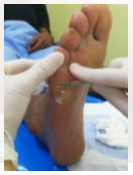
Orthopedic Surgeon and Podologist

- *Dr. Chayanin Angthong*
- *Dr. Marut Arunakul*

APN

- *Phunyada Napunnaphat*
- *Saowaluck Triwiroj*
- *Arpaporn Kuthongkul*



Diabetes mellitus (DM)

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

- Thailand registry[2]
  - 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]

1.Boulton AJ, Diabetes care. 2008.
2. Junrungsee S. Diabetic Medicine. 2011.
3. Benyakorn T. Int J Low Extrem Wounds. 2012.
4. Nouvong A, Rutherford's Vascular surgery. 2014
5. Carinci F, Acta Diabetol. 2016

Etiologies of DFU

- Peripheral arterial disease (PAD) – Atherosclerosis[1,2]
- Peripheral neuropathy[1,2]

  - Foot deformity → Repetitive trauma → Chronic ulcer
  - Poor vascular supply → Delay wound healing → Chronic ulcer
  - Hyperglycemia → Oxidative stress → Chronic ulcer

1. . Dosluoglu HH., Rutherford's Vascular surgery. 2014
2. Orrapin S et al. Applied Vascular Surgery Vol 4: Clinical practice in Vascular surgery 2017
3. Armstrong DG, N Engl J Med 2017

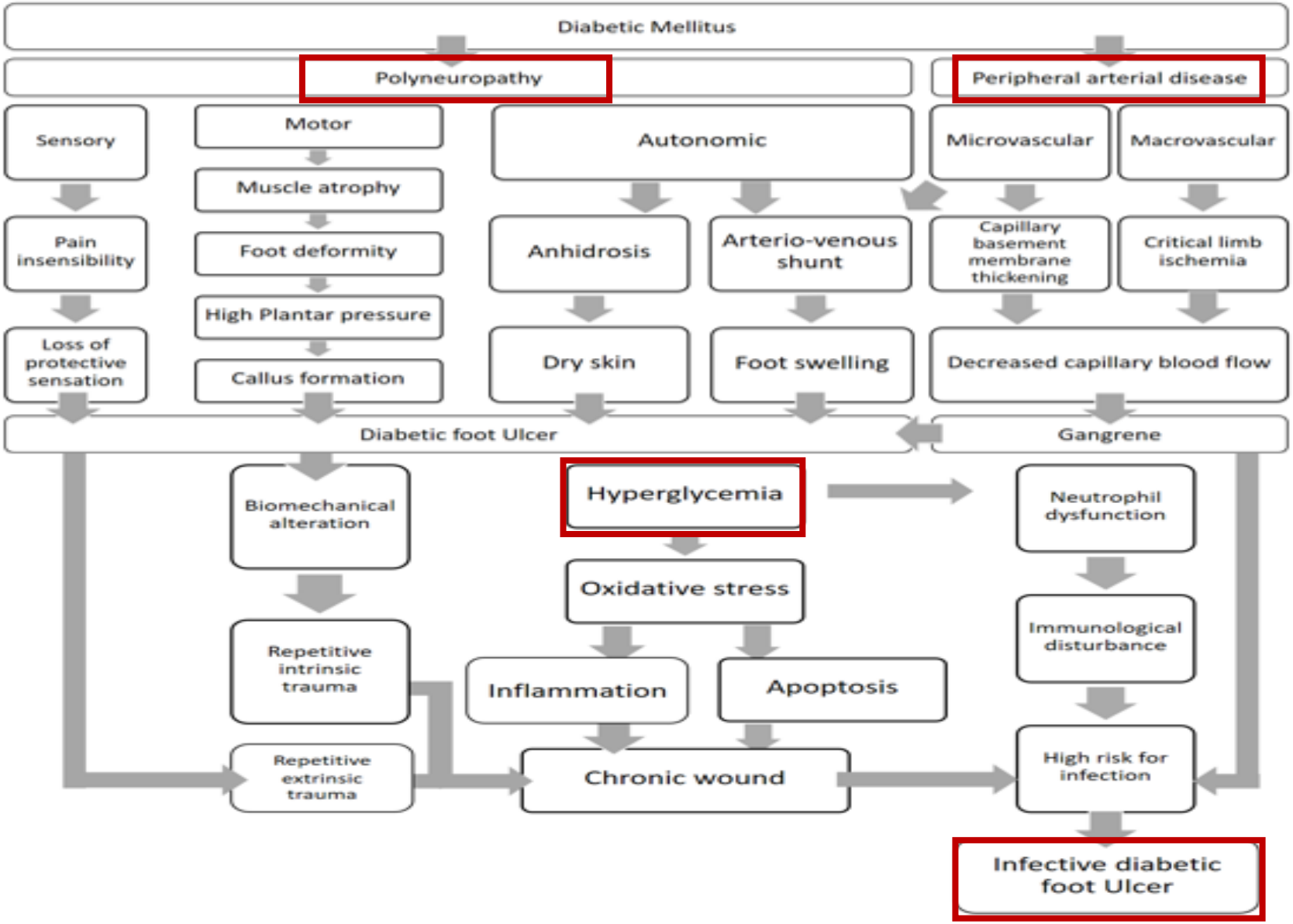
Etiologies of Diabetic foot infection (DFI)

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

  - Poor vascular supply (Poor capillary flow)
    → Poor *local* wound immune system → DFI[1,2]

  - Hyperglycemia
    → Poor *systemic* immune system → DFI[1,2]

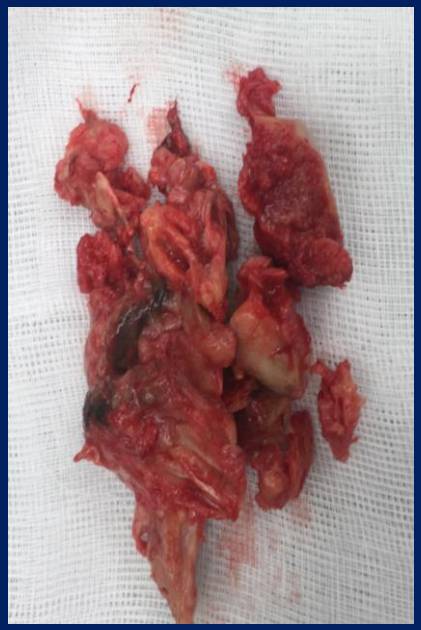
1. . Nouvong A, Rutherford's Vascular surgery. 2014
2. Orrapin S et al. *Applied Vascular Surgery Vol 4: Clinical practice in Vascular surgery 2017*
3. Armstrong DG, N Engl J Med 2017

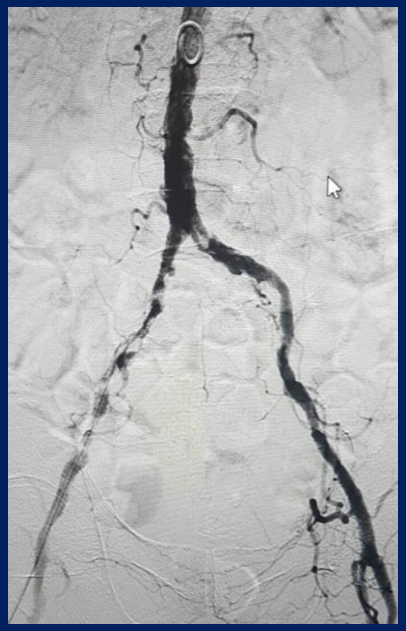


Orrapin S et al. *Applied Vascular Surgery Vol 4: Clinical practice in Vascular surgery 2017.*

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]

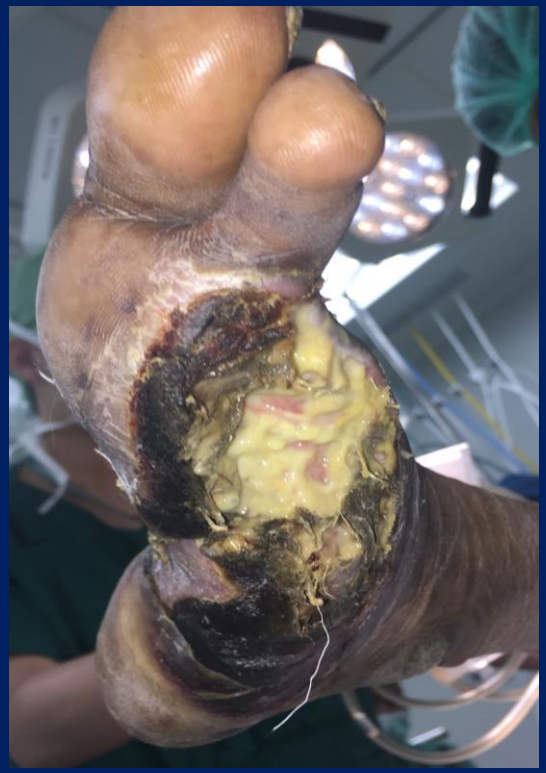


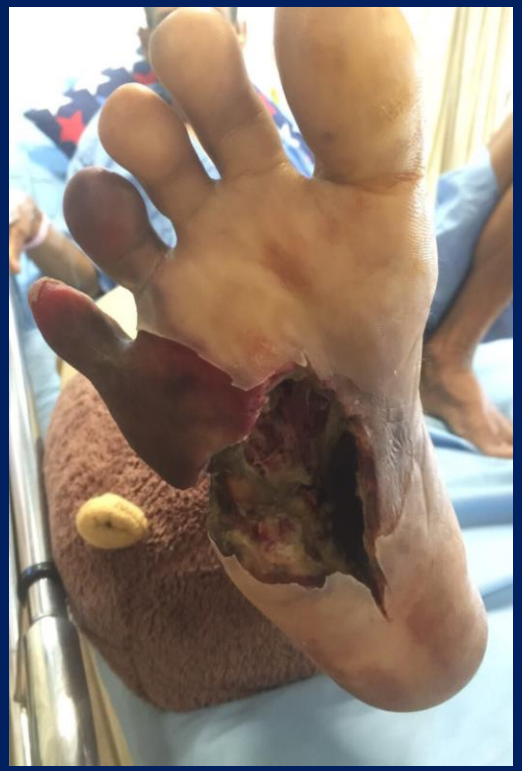


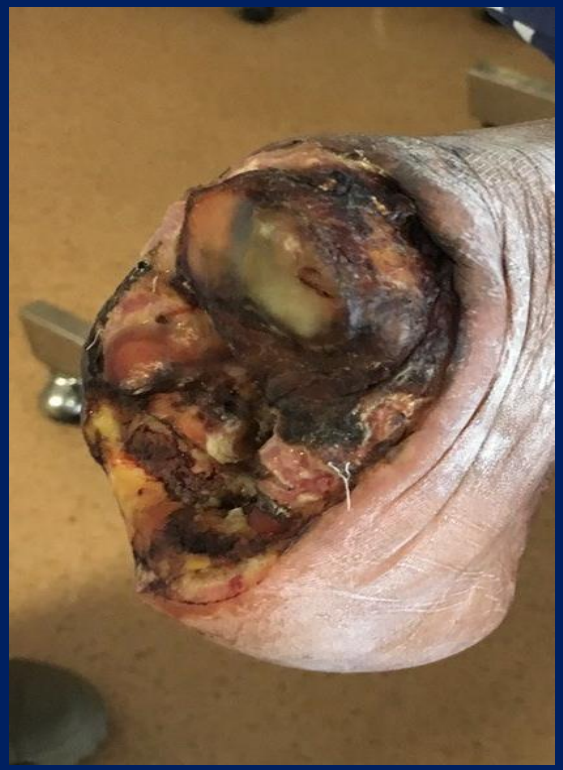
1. Norgren L, *J Vasc Surg*. 2007
2. Tendera M, *European heart journal*. 2011
3. Rhee SY, *Diabetes research and clinical practice*. 2007
4. Dosluoglu HH, Rutherford's Vascular surgery. Philadelphia: Elsevier; 2014
5. Britton KA, *Vascular medicine (London, England)*. 2012
6. Orrapin S, AVD 2015

Hb_{A1c}: glycated hemoglobin

DM + PAD *(Neuroischemic ulcer)*







DM foot

DIABETES/METABOLISM RESEARCH AND REVIEWS
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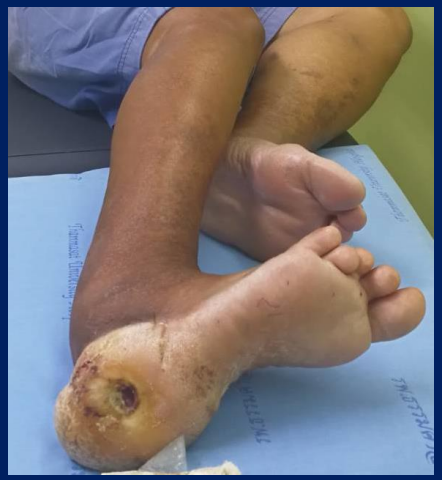
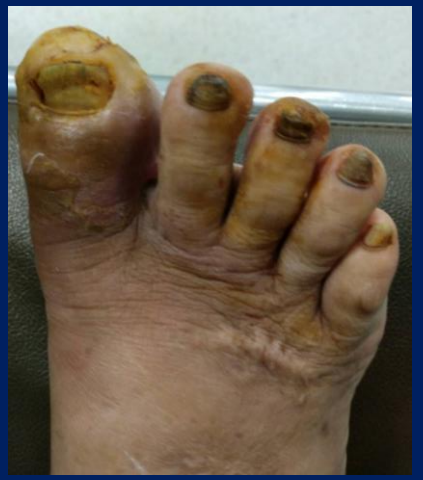
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/dmrr.2699

SUPPLEMENT ARTICLE

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

- **Diabetic foot infection (DFI):** *soft tissue or bone infection below the malleoli* [1,2]





1. Fassil W et al. *Am Fam Physician* 2013.
2. Lipsky BA et al. *Diabetes Metab Res Rev* 2016.

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. Nouvong A, Rutherford's Vascular surgery 2014
2. Lipsky BA, Diabetes/metabolism research and reviews. 2016
3. Peters EJ, Medical Clinics of North America. 2013

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

Systemic sign (SIRS)

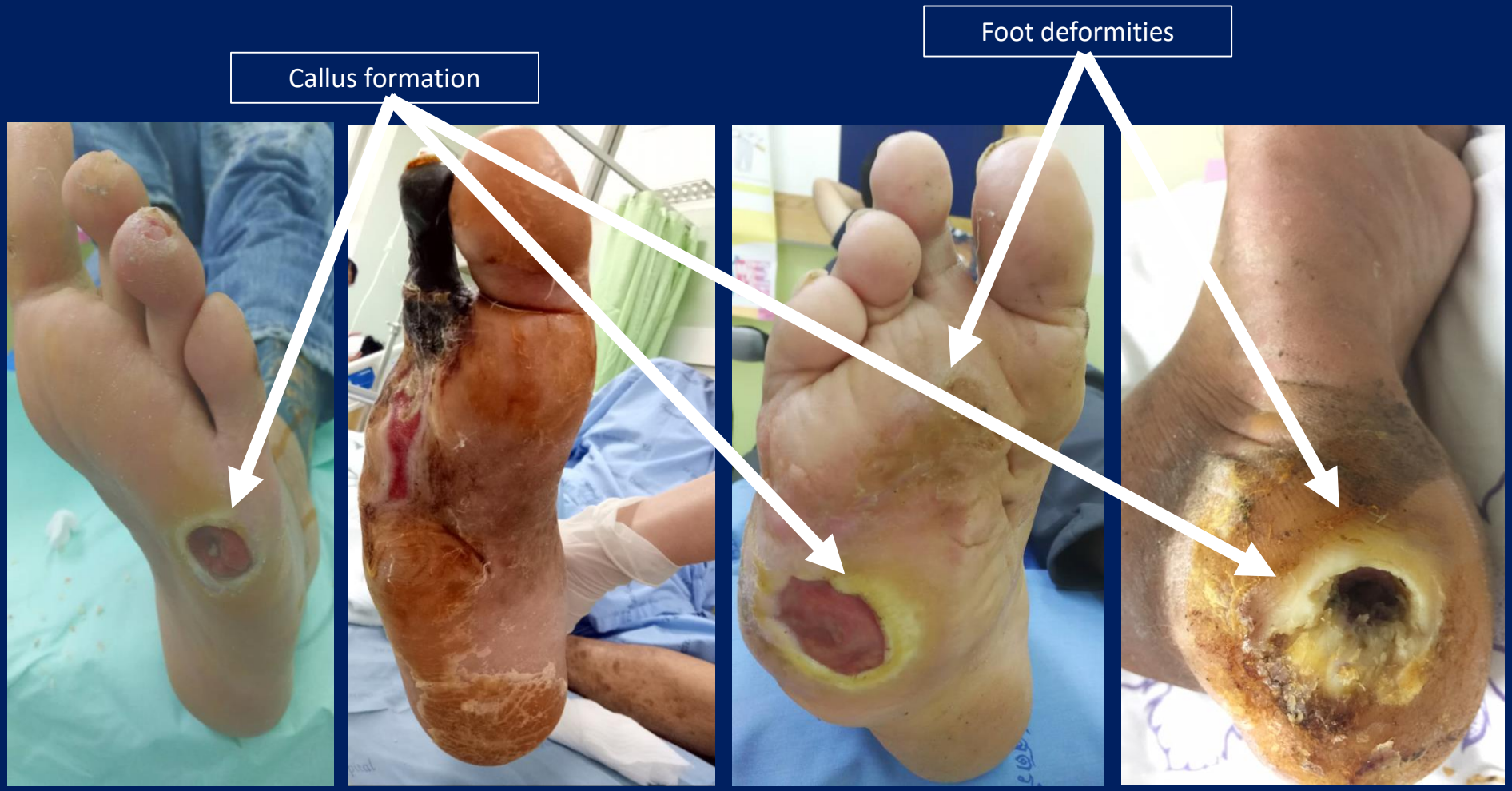
- ≥ 2 of the following:[1]
  1. Temperature > 38 °C or < 36 °C
  2. Heart rate > 90 beats/min
  3. Respiratory rate >20 breaths/min or $PaCO_2$ < 32 mmHg
  4. WBC >12 000/mm^3 or < 4000/mm^3, or >10% immature (band) forms

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

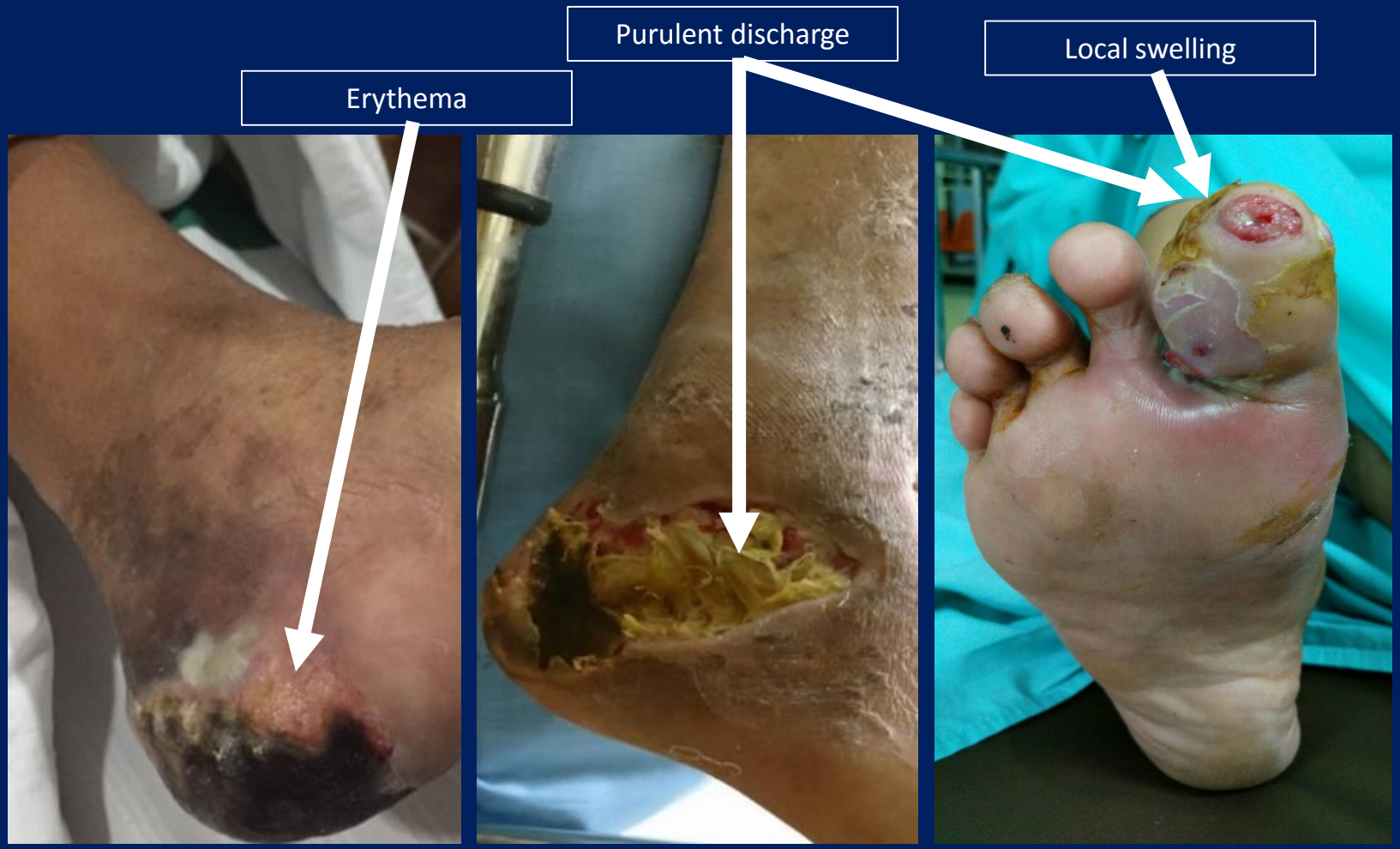
SIRS: systemic inflammatory response syndrome, WBC; white blood cell count

1. Lipsky BA. Diabetes Metab Res Rev 2016

DFU



DFI



The classification systems: Presence and Severity of DFI

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

Infective Clinical classification	IWGDF/IDSA classification
No local and systemic signs of infection	1 (uninfected)
Skin or subcutaneous tissue infection - Erythema extends > 0.5 , <2 cm around rim of wound	2 (mild infection) - Superficial Soft tissue infection
Deep structure than skin and subcutaneous tissues (Bone, Joint, Tendon or Muscle) or Erythema extending ≥2 cm from the wound margin	3 (moderate infection) - Deep Soft tissue infection (Myositis) - Osteomyelitis
Local sign + SIRS (≥ 2 sign of systemic inflammation)	4 (severe infection)

IDSA; Infectious Diseases Society of America
IWGDF; International Working Group on the Diabetic Foot

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
2. Lipsky BA. Diabetes Metab Res Rev 2016

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.

1. Wagner FW Jr. The diabetic foot. Orthopedics 1987
2. Lavery LA, J Foot Ankle Surg 1996

Meggitt-Wegner Ulcer Classification Score[1]

Grade	Lesion
1	Superficial diabetic ulcer (partial or full thickness)
2	Ulcer extension to ligament, tendon, joint capsule, or deep fascia
3	Deep ulcer with abscess, osteomyelitis, or joint sepsis
4	Gangrene localized to portion of forefoot or heel
5	Extensive gangrenous involvement of the entire foot

1. Wagner FW Jr. The diabetic foot. Orthopedics 1987

The University of Texas Health Science Center San Antonio Diabetic Wound Classification System[1]

Grade	0	I	II	III
A	Pre- or post ulcerative lesion completely epithelialized	Superficial wound, not involving tendon, capsule, capsule or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone
B	Pre- or post ulcerative lesion, completely epithelialized with infection	Superficial wound, not involving tendon, capsule, or bone with infection	Wound penetrating to tendon or capsule with infection	Wound penetrating to bone or joint with infection
C	Pre- or post ulcerative lesion, completely epithelialized with ischemia	Superficial wound. not involving tendon, capsule, or bone with ischemia	Wound penetrating to tendon or capsule with ischemia	Wound penetrating to bone or joint with ischemia
D	Pre- or post ulcerative lesion, completely epithelialized with infection and ischemia	Superficial wound, not involving tendon, capsule, or bone with infection and ischemia	Wound penetrating to tendon or capsule with infection and ischemia	Wound penetrating to bone or joint with infection and ischemia

1. Lavery LA, J Foot Ankle Surg 1996

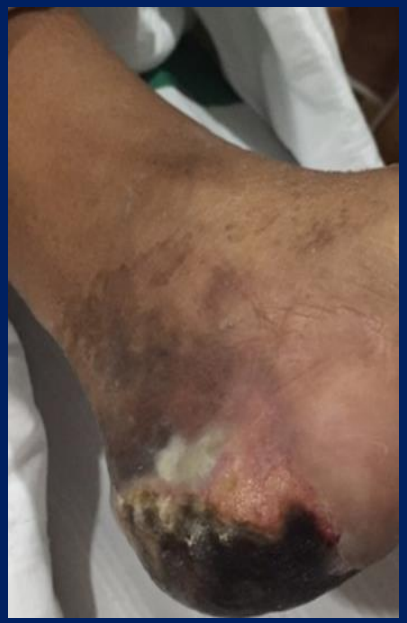
Diabetic Wound Classification System

- 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]

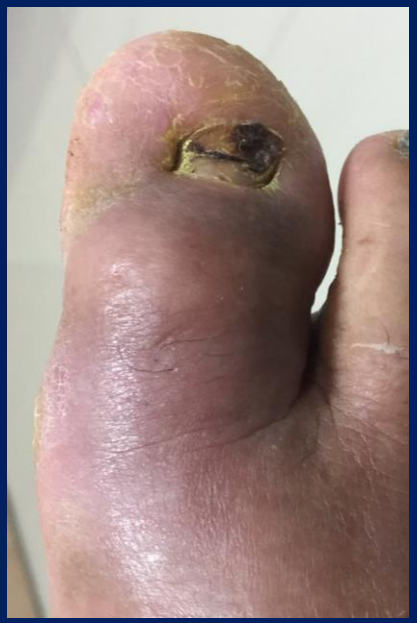
1. Armstrong DG, Diabetes Care. 1998
2. Santema, Int Wound J 2016
3. Monteiro-Soares M, Diabetes Metab Res Rev 2014

Osteomyelitis (OM)

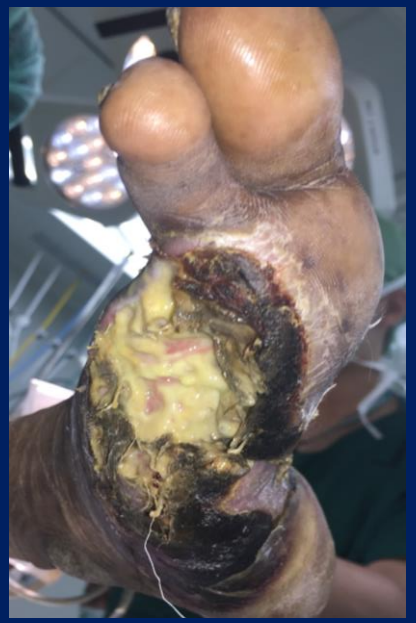
- High risk OM wound
  1. Ulcer lies over a bony prominence
  2. Sausage toe (indurated and redness toes)
  3. Large ulcers (area >2 cm^2)
  4. Unresponsive to adequate treatment



Bony prominence



Sausage toe

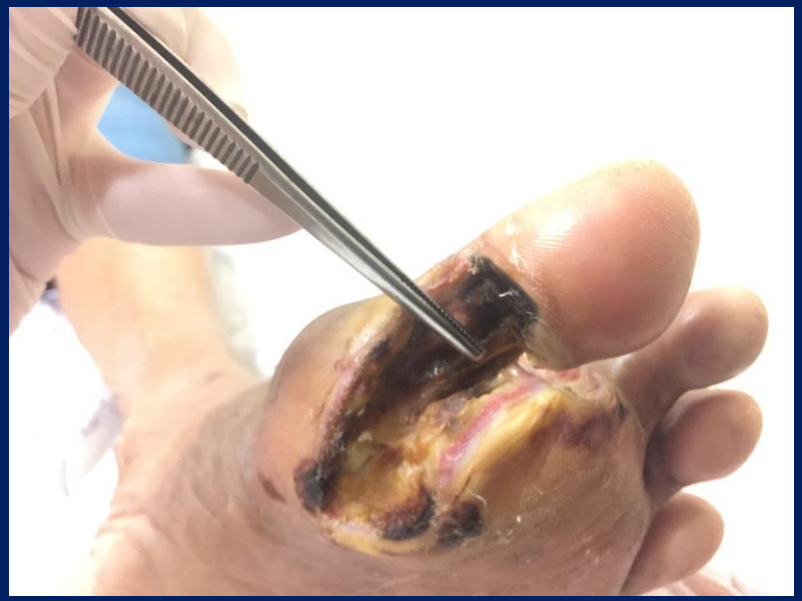


Large ulcers

1. Lipsky BA. Diabetes Metab Res Rev 2016

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 patients[1,2,3]
  - > 70 mm/h *(77% sensitivity and 77%specificity)*

1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Uzun GThe Tohoku journal of experimental medicine. 2007
3. Papanas, Int J Low Extrem *Wounds* 2013

Osteomyelitis (OM)

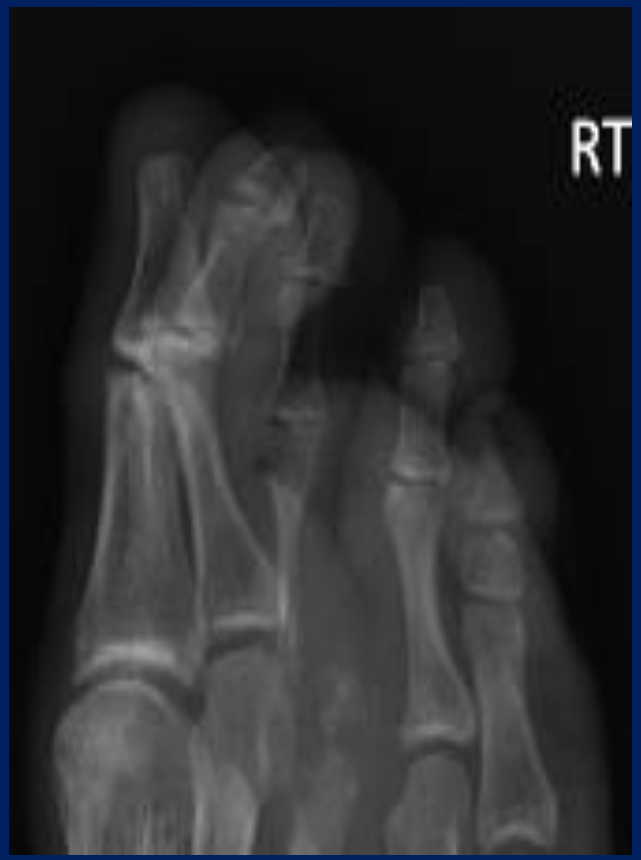
- **Definite diagnosis:**
  - **Bone sample:** positive results on histological (microbiological) examinations
    - Equivocal diagnosis or
    - Determining causative pathogen's antibiotic susceptibility: for unresponsive for ordinary treatment (Empirical antibiotic)

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

1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Armstrong DG, N Engl J Med 2017

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



1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Hingorani A, Journal of vascular surgery. 2016

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

1. Dinh T, Int J Low Extreme. 2010
2. Lipsky BA. Diabetes Metab Res Rev 2016
3. Hingorani A, Journal of vascular surgery. 2016

Assessing severity

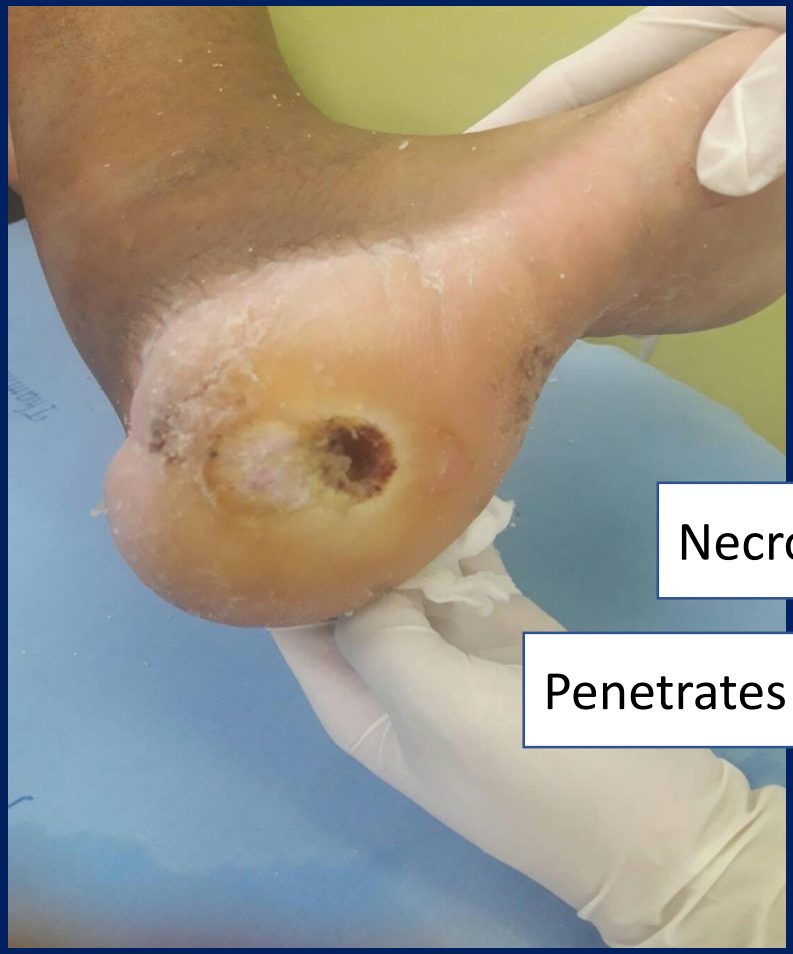
- Vital signs and Physical examination
- Basic blood tests
- Debride wound
- Probe assess depth and extent of infection
- Assess arterial perfusion → further vascular assessment (ABI, TBI, TCOM) → Angiogram → Revascularization

1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Armstrong DG, N Engl J Med 2017

Characteristics suggesting a more serious diabetic foot infection

Wound	
Wound	Penetrates to subcutaneous tissues (e.g. fascia, tendon, muscle, joint and bone)
Cellulitis	Extensive (>2 cm), distant from ulceration or rapidly progressive
Local signs	Severe inflammation or induration, crepitus, bullae, discoloration, necrosis or gangrene, ecchymoses or petechiae and new anaesthesia

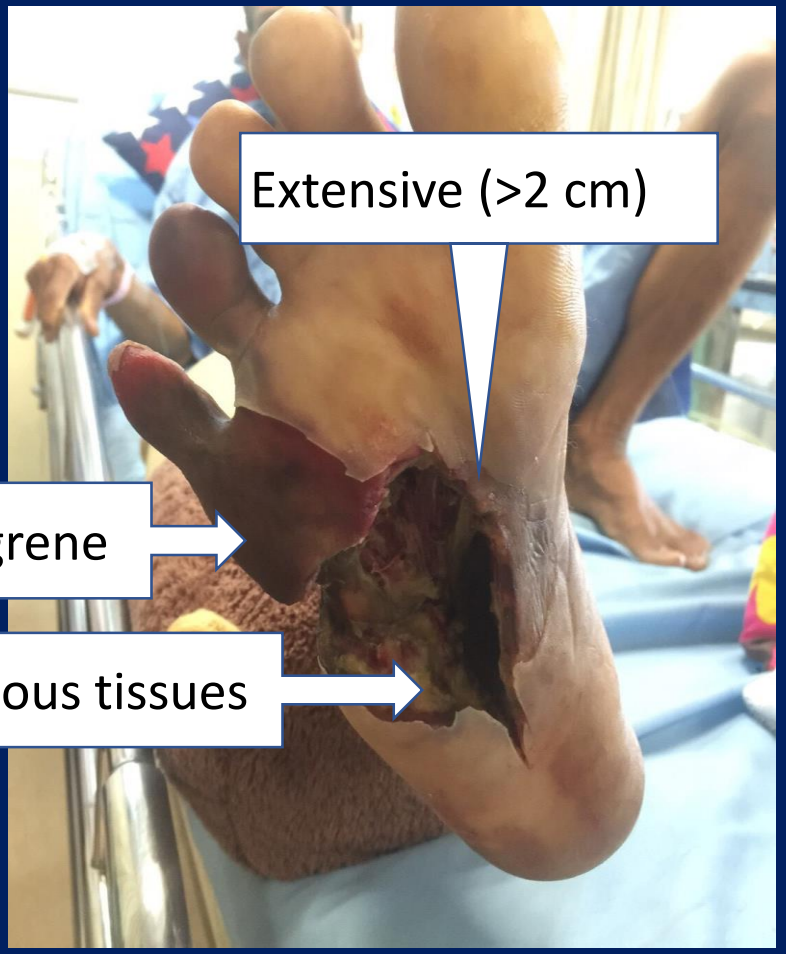
1. Lipsky BA. Diabetes Metab Res Rev 2016



VS

Necrosis or gangrene

Penetrates subcutaneous tissues



Characteristics suggesting a more serious diabetic foot infection

Systemic (hospitalization)	
Presentation	Acute onset/worsening or rapidly progressive
Systemic signs	Fever, chills, hypotension, confusion and volume depletion
Laboratory tests	Leukocytosis, very high CRP/ESR, severe/worsening hyperglycemia, acidosis, AKI and electrolyte abnormalities
Complicating features	Presence of a foreign body (accidentally or surgically implanted), puncture wound, deep abscess, arterial or venous insufficiency, lymphedema, immunosuppressive illness or treatment
Current treatment	Progression on appropriate antibiotic and supportive therapy

1. Lipsky BA. Diabetes Metab Res Rev 2016

Microbiological considerations

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

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

1. Lipsky BA. Diabetes Metab Res Rev 2016

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

1. Lipsky BA. Diabetes Metab Res Rev 2016

Empiric antibiotic regimen

Severity	Factors	Pathogen	Empirical antibiotic regimen
Mild	No complicating features	GPC	Pen, 1st Ceph
	ß-lactam allergy or intolerance	GPC	Clindamycin; FQ; T/S; macrolide; doxy
	Recent antibiotic exposure	GPC + GNR	ß-L-ase-1; T/S; FQ
	High risk for MRSA[a]	MRSA	Linezolid; T/S; doxy; macrolide; FQ

[a] high local prevalence of MRSA, recent stay in healthcare institution, recent antibiotic therapy or known MRSA colonization

[b] high local prevalence of Pseudomonas infections, warm climate or frequent exposure of the foot to water.

Severity	Factors	Pathogen	Empirical antibiotic regimen
Moderate and severe	No complicating features	GPC + GNR	ß-L-ase 1; second/third gen ceph
	Recent antibiotics	GPC + GNR	ß-L-ase 2; third gen ceph, group 1 carbapenem (depends on prior therapy; seek advice)
	Macerated ulcer and warm climate	GNR + Pseudomonas	ß-L-ase 2; S-S pen+ceftazidime, S-S pen+cipro, group 2 carbapenem
	Ischemic limb/necrosis/gas forming	GPC + GNR + Anaerobes	ß-L-ase 1 or 2; group 1 or 2 carbapenem; second/ third gen ceph+clindamycin or metronidazole
	MRSA risk factors[a]	MRSA	Consider addition of, or substituting with, glycopeptides; linezolid; daptomycin; fusidic acid; T/S (±rif)*; doxycycline; FQ
	Risk factors for resistant GNR[b]	ESBL	Carbapenems, FQ, aminoglycoside and colistin

[a] high local prevalence of MRSA, recent stay in healthcare institution, recent antibiotic therapy or known MRSA colonization

[b] high local prevalence of Pseudomonas infections, warm climate or frequent exposure of the foot to water.

Management

- Consult surgical specialist
  - Moderate DFI
  - Severe DFI

The classification systems: Presence and Severity of DFI

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

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IDSA; Infectious Diseases Society of America
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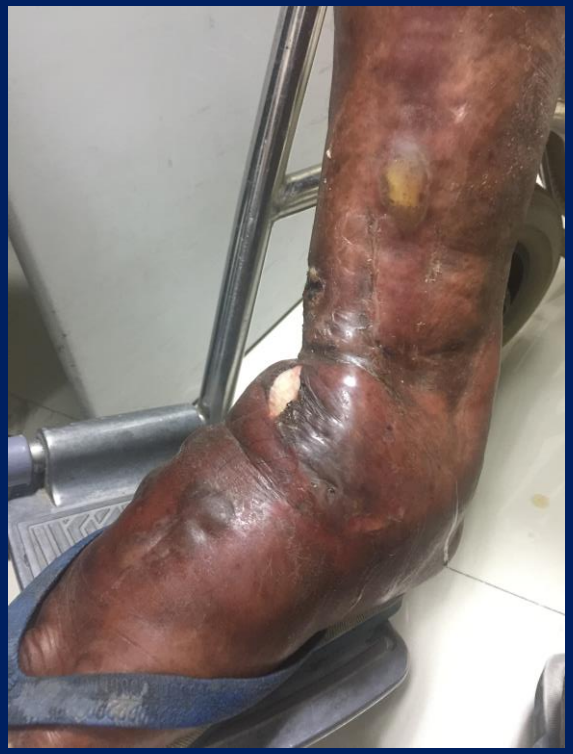
1. Schaper NC. Diabetes Metab Res Rev 2004
2. Lipsky BA. Clin Infect Dis 2012

1. Lipsky BA. Diabetes Metab Res Rev 2016

Management

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

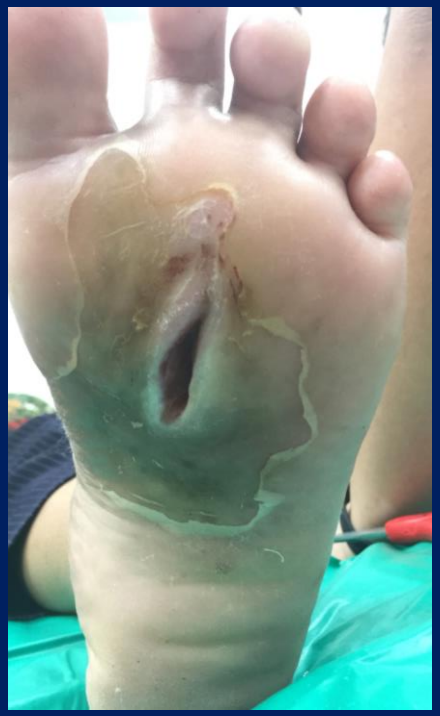
- Procedure: minor debridement or drainage to extensive resections, major amputation.

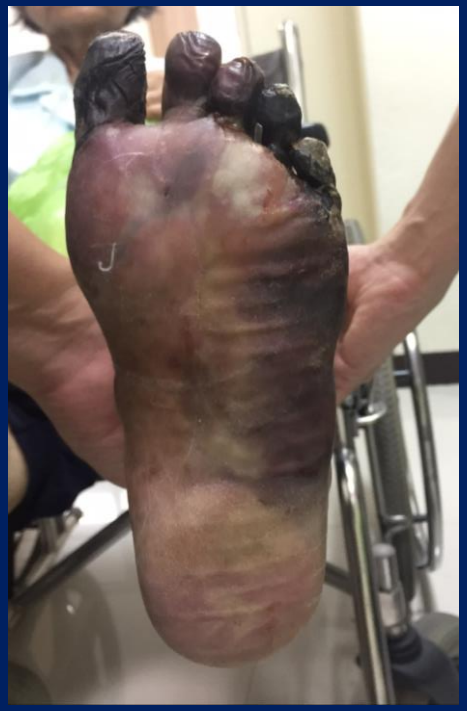


1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Armstrong DG, N Engl J Med 2017

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





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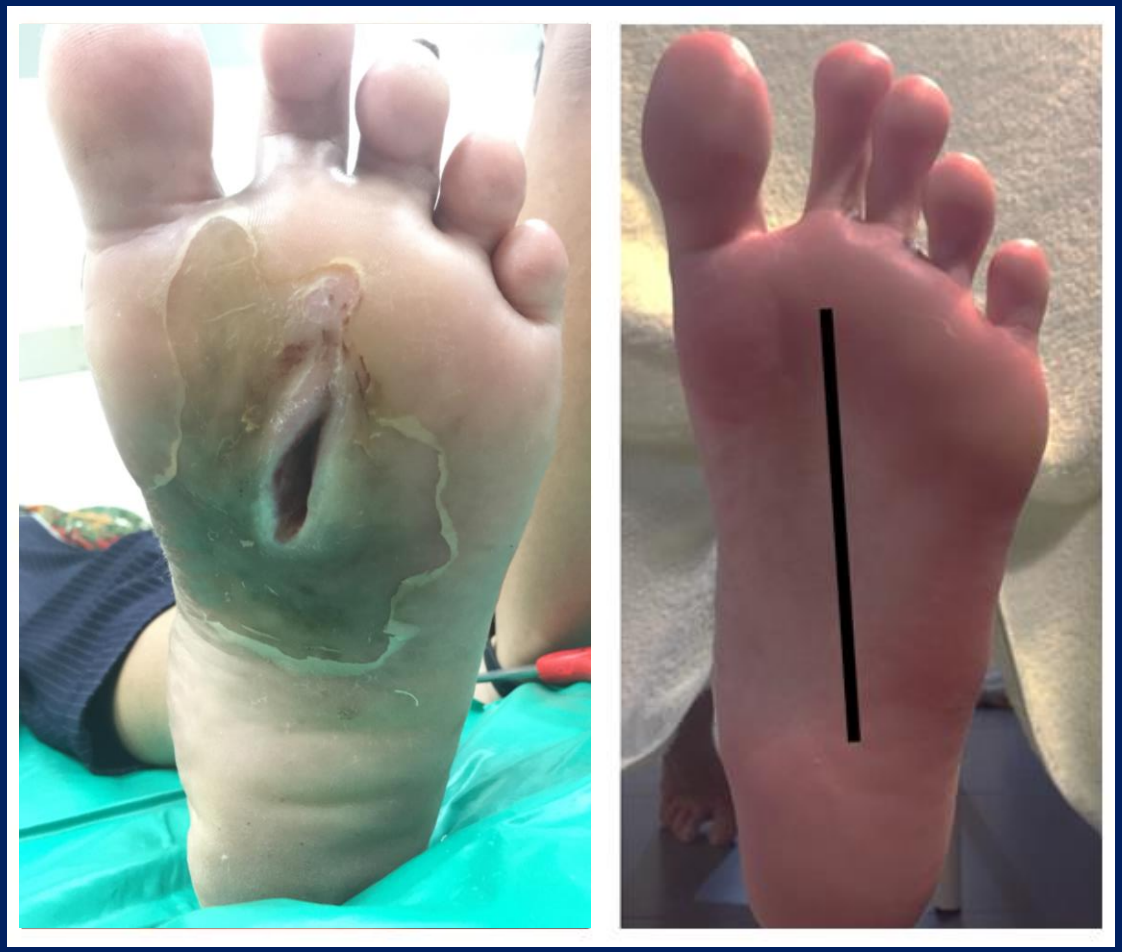


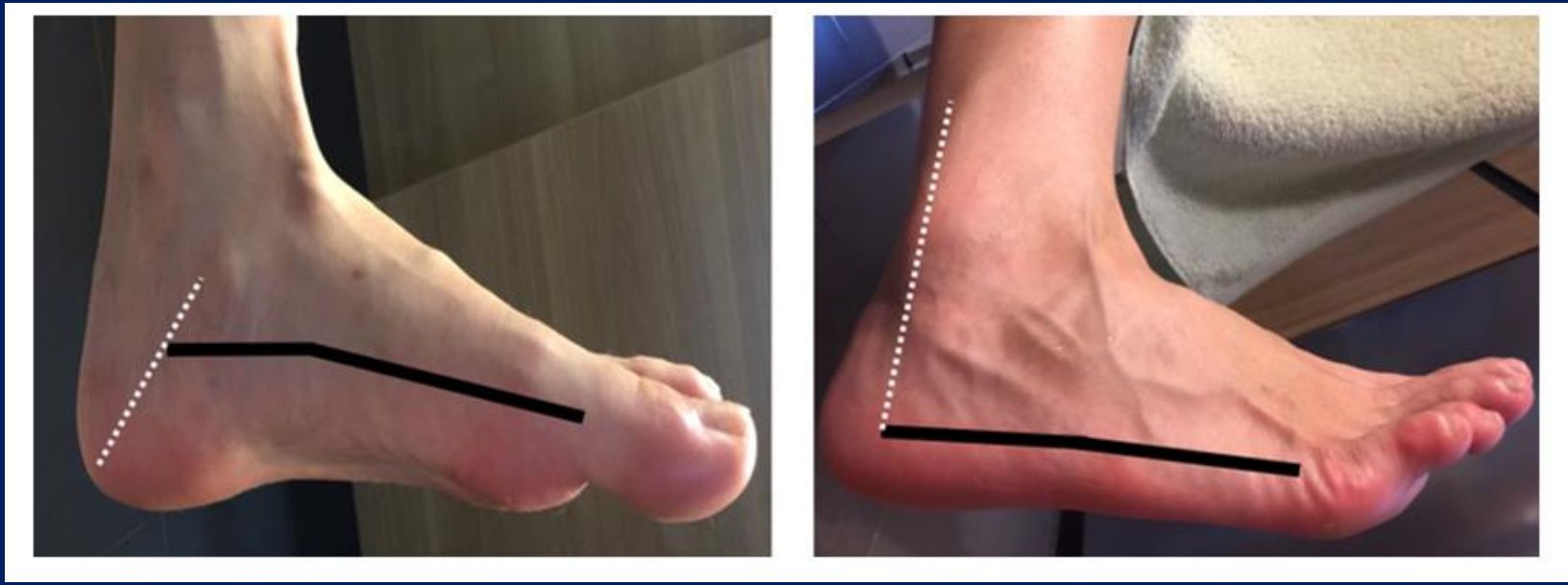
Dorsum incision

- 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

1. Rerkasem K, Vascular Surgery 2008
2. Orrapin S, Prevention and Management of The Diabetic foot 2009
3. Orrapin S et al. *Applied Vascular Surgery Vol 4: Clinical practice in Vascular surgery 2017*



- 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

1. Rerkasem K, Vascular Surgery 2008
2. Orrapin S, Prevention and Management of The Diabetic foot 2009
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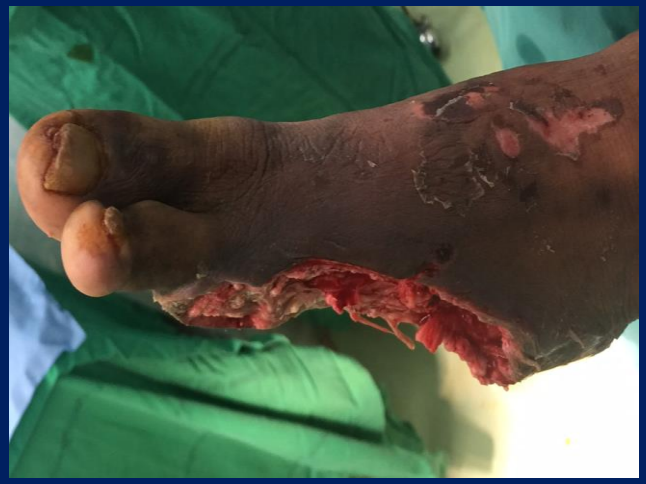
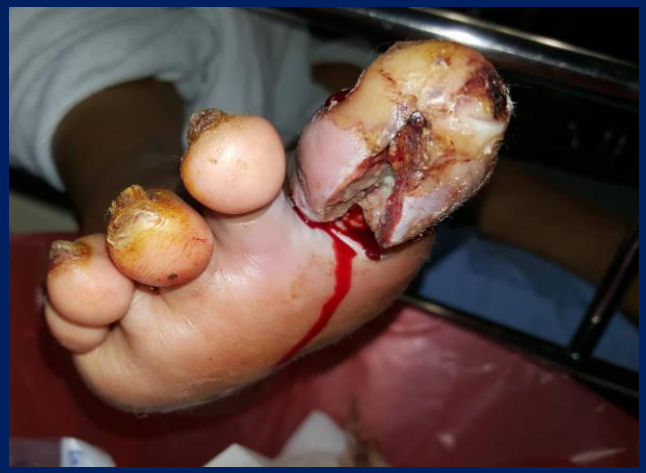
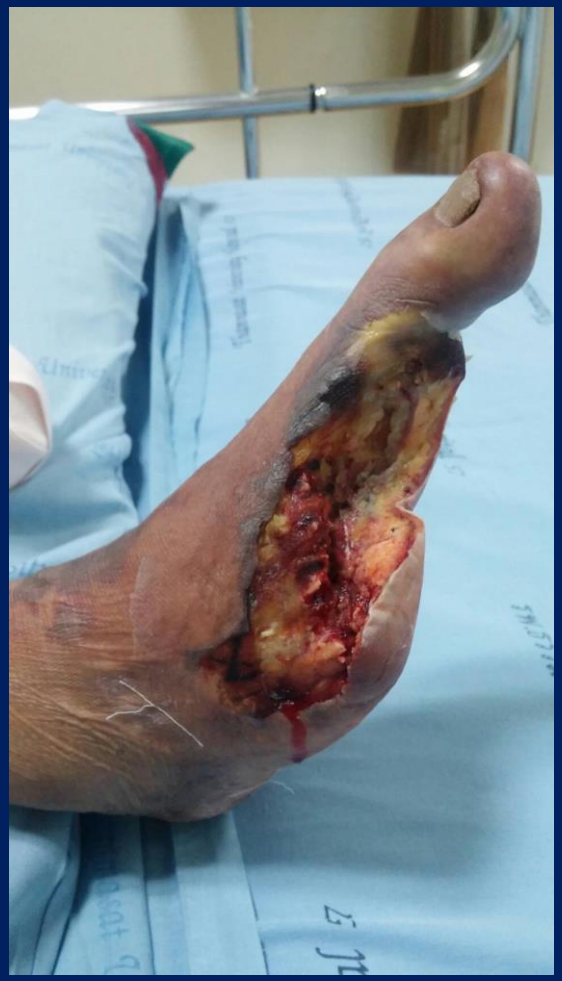
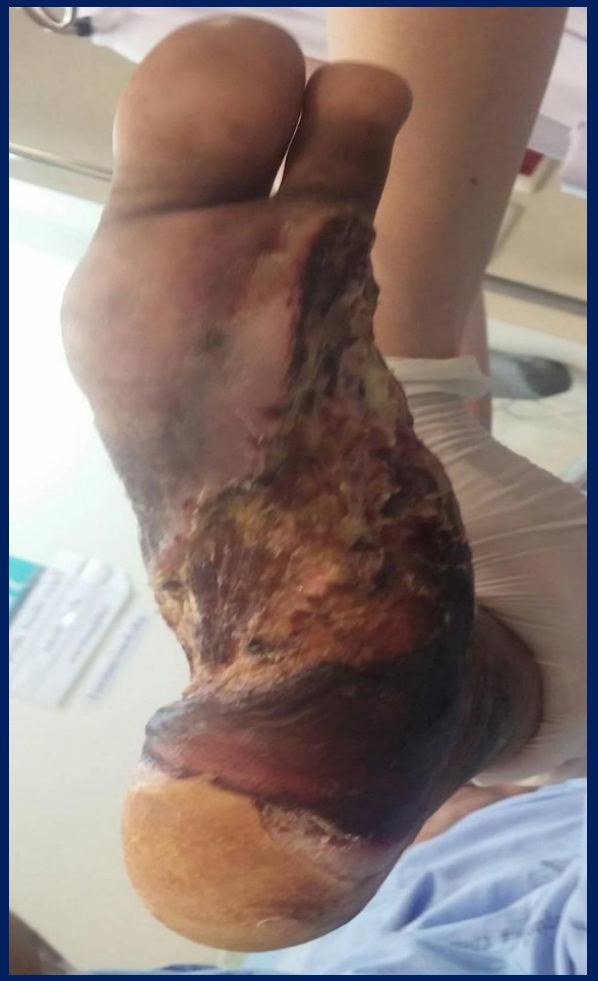


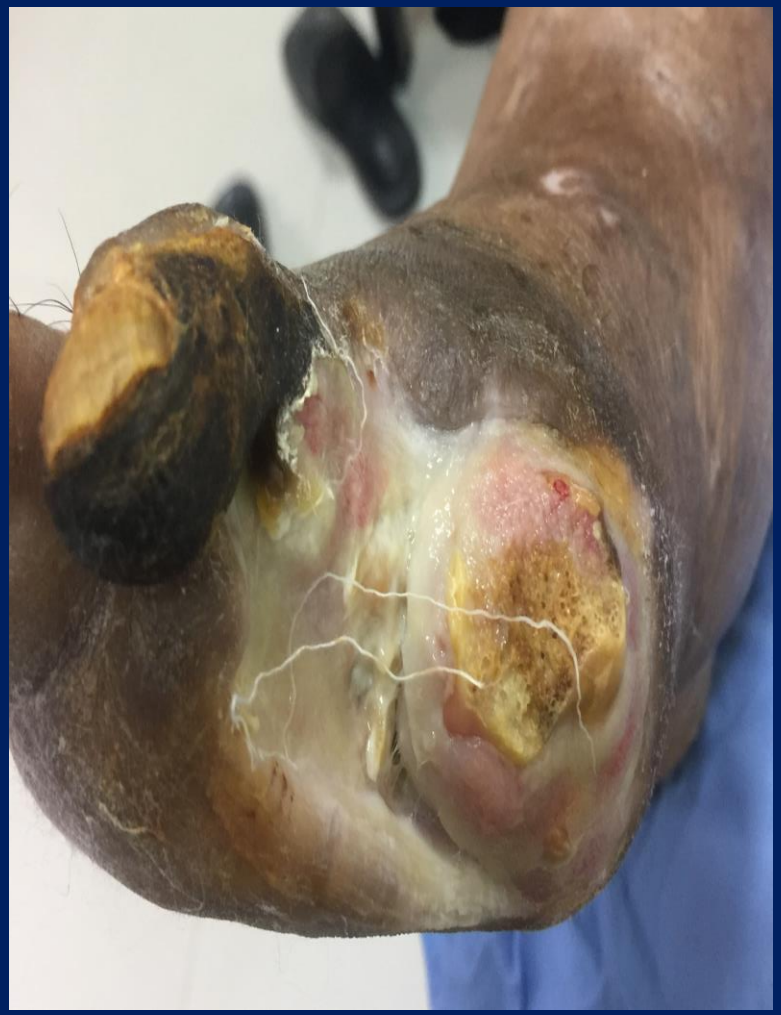






Management

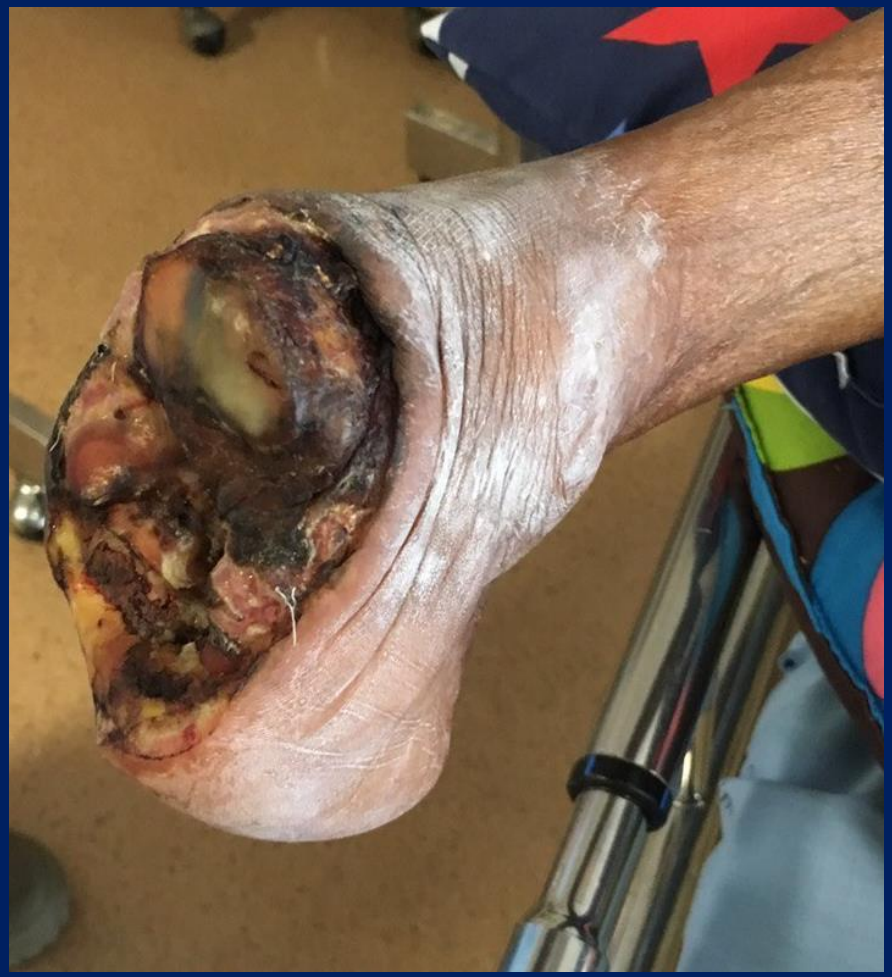
- **OM**
  - Considering orthopedic surgical intervention
    1. Spreading soft tissue infection
    2. Destroyed soft tissue envelope
    3. Progressive bone destruction on X-ray
    4. Bone protruding through the ulcer
  - For resection OM:
    - no more than 1 week of antibiotic therapy
  - For non-resection OM:
    - 6 weeks of antibiotic



1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Armstrong DG, N Engl J Med 2017

Surgical treatment VS Antibiotic treatment

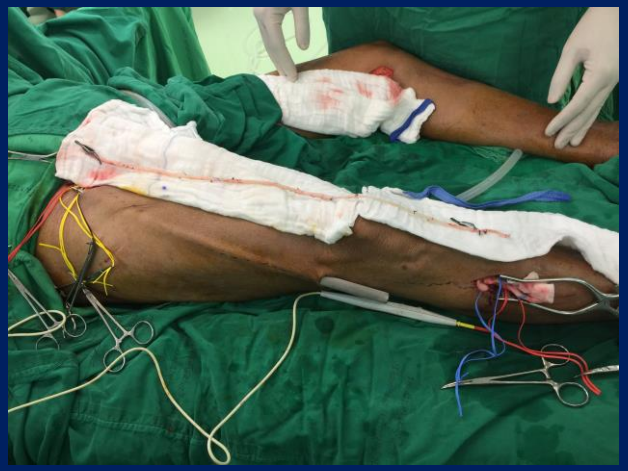
- Nonsurgical approach with antibiotic therapy can be successful in selected cases.[1]
  1. No ischemia (CLI)[2]
  2. No necrotizing soft tissue infections[2]
- Similar outcomes: healing rates, time to healing, and short-term complications[2]

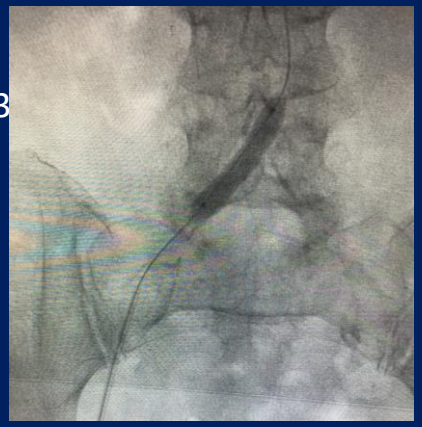


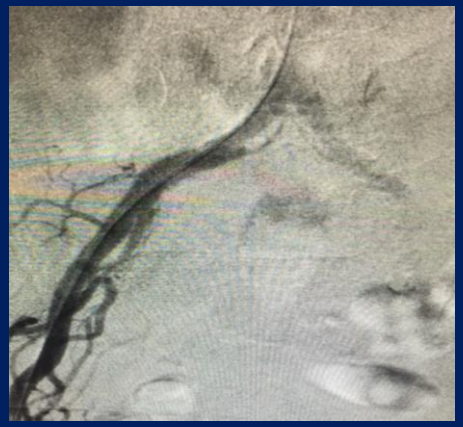
1. José Luis Lázaro-Martínez, Diabetes Care. 2014
2. Mesut Mutluoglu, Lancet Diabetes Endocrinol. 2017

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







1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Bianchi C, Rutherford's Vascular surgery 2014
3. Hopf, Wound Rep Reg 2006

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

Center of Excellence for Diabetic foot care

TU-CDC Committee (Multidisciplinary team)

Endocrinologist

- *Dr. Thipaporn Tarawanich*
- *Dr. Pimjai Anthanon*

Dermatologist

- *Dr. Patcha Pongjareon*

Physical Medicine and Rehabilitation

- *Dr. Natetaya Nimpitak*
- *Dr. Sirunya Parjareon*

Vascular Surgeon

- Dr. Boonying Siribumrungwong
- Dr. *Theotphum Benyakorn*
- *Dr. Kanoklada Srikua*
- *Dr. Saritphat Orrapin*

Orthopedic Surgeon and Podologist

- *Dr. Chayanin Angthong*
- *Dr. Marut Arunakul*

APN

- *Phunyada Napunnaphat*
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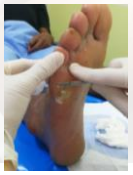

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SUPPLEMENT ARTICLE

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

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Julie R. Ingelfinger, M.D., *Editor*

Diabetic Foot Ulcers and Their Recurrence

David G. Armstrong, D.P.M., M.D., Ph.D., Andrew J.M. Boulton, M.D., and Sicco A. Bus, Ph.D.

1. Lipsky BA. Diabetes Metab Res Rev 2016
2. Armstrong DG, N Engl J Med 2017