Diabetic foot

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The size of the problem:

- 18.6 M people worldwide are affected by a DFU each year
- 50% to 60% of ulcers become infected, and about 20% of moderate to severe infections lead to lower extremity amputations
- The 5-year mortality rate for individuals with a DFU is approximately 30%, exceeding 70% for those with a major amputation.

- *Diabetic foot Ulcer. A Review.. JAMA 2023*
- *International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Belgium; 2021. https://www.diabetesatlas.org*

7% of all DM develop foot gangrene after 15 yrs leading to the fact that 15-45 X as many diabetics have amputations as do nondiabetics of the same age and the rate of contralat amputation & mortality is depressingly high.

DM prevalence: IDF estimated that 537 M adults (20 and 79 years) worldwide were living with diabetes in 2021 , JORDAN 14.8 %

Pathophysiology of DF

- Neuropathy
- Ischemia
- Infection

Contribute to the onset of ulceration , necrosis and gangrene

Pathogenetic types of the Diabetic Foot:

- NEUROPATHIC
  INFECTED TYPE
  INCIDENCE : 45 -60%

- PURELY ANGIOPATHIC
  ISCHAEMIC TYPE
  INCIDENCE : 10 – 25%

- MIXED TYPE NEURO-
  ISCHEAMIC
  INCIDENCE: 25 -45 %

Diabetic Neuropathy:

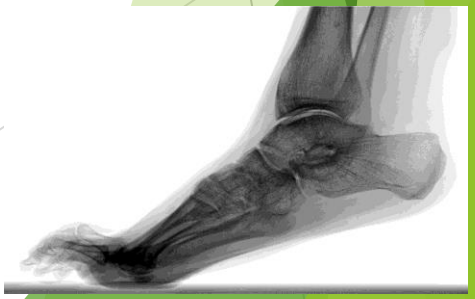
- Microvascular disease leading to nerve hypoxia
- Direct effect of hyperglycemia on neuronal metabolism.
- Abnormalities in nitric oxide metabolism resulting in perineural vasoconstriction & nerve damage.

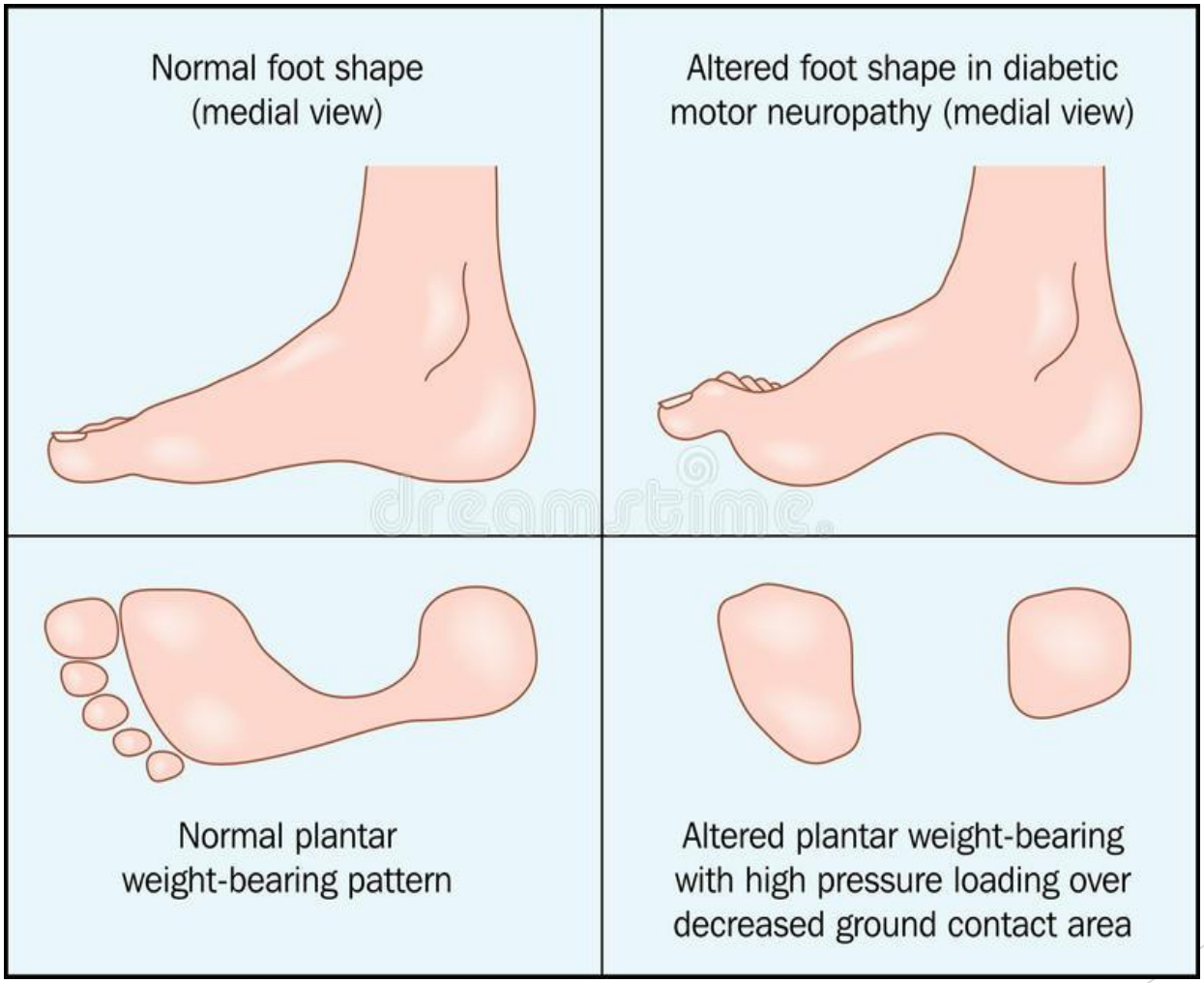
A)Sensory Neuropathy

- Painless
- Stocking distribution
- Reduced light touch & temperature
- Impaired propioception.

B)Motor neuropathy

- Muscle imbalance: altered flexor – extensor balance at MTP joints
- Alter foot shape resulting in clawed toes & prominent metatarsal heads
- Equinus ankle

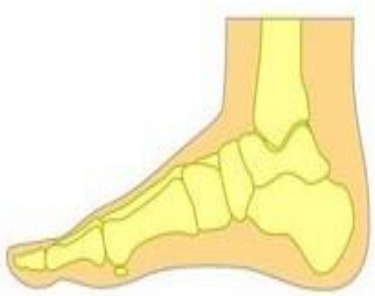


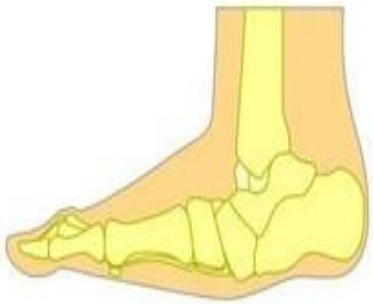

Normal foot shape
(medial view)
Altered foot shape in diabetic
motor neuropathy (medial view)
Normal plantar
weight-bearing pattern
Altered plantar weight-bearing
with high pressure loading over
decreased ground contact area

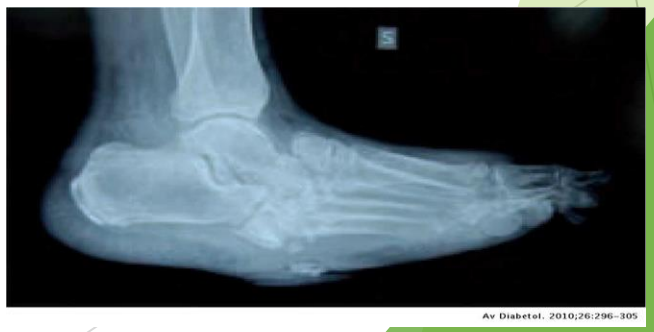
C) Autonomic neuropathy

(skin / vessels /bone)

- Reduced sweating ~ dry skin ,cracking ,fissures (ports for infection)
- Abnormal autoregulation of microcirculation
- Vasodilatation & Shunting →Auto sympathectomy
- Loss of bone minerals (washout)
- Development of Charcot's foot







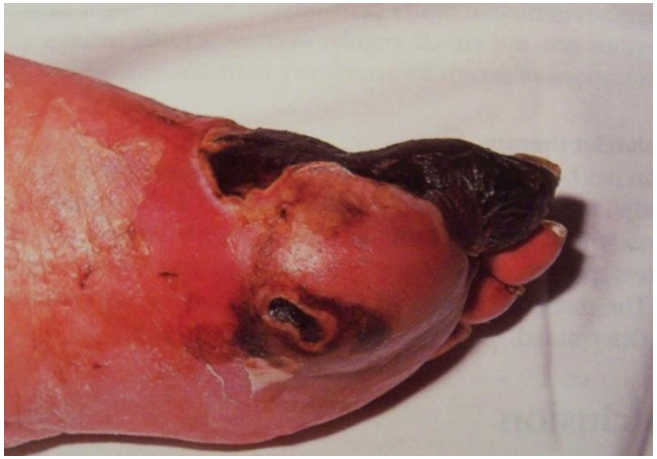
Diabetic Angiopathy:

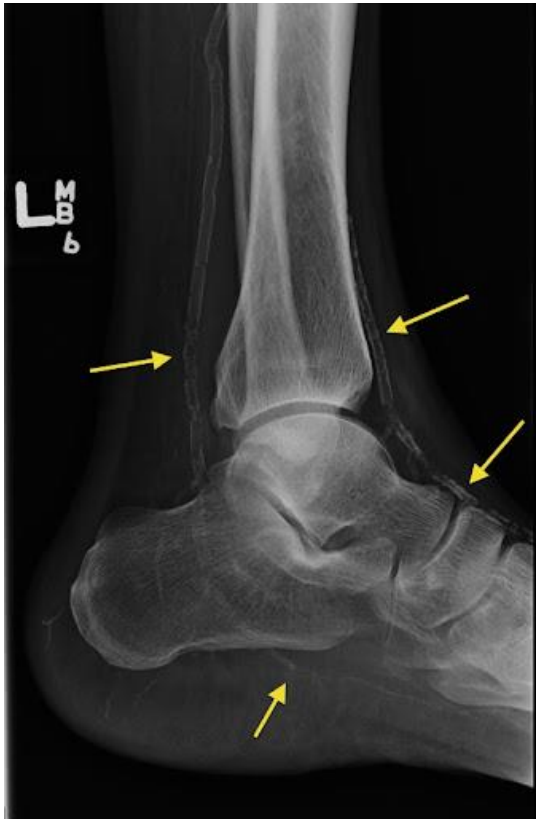
- **Diffuse atherosclerosis** in all pts with long duration DM showing similar pathophysiology as in non D.M. & characterized by endothelial damage , plt aggregation, lipid deposition & smooth muscles proliferation with plaque formation.

- Non occlusive **capillary basement membrane thickening** with impaired leukocytes migration.
- Diminished maximal **hyperemic response** following injury & inflammation.

- Pattern & location: affection of **infrageniculate arterial tree** with sparing of fem-pop & foot arteries .PA is the last to occlude.

- **Medial** arterial non obstructive **calcinosis** resulting in non compressible arteries (lead pipe calcification).

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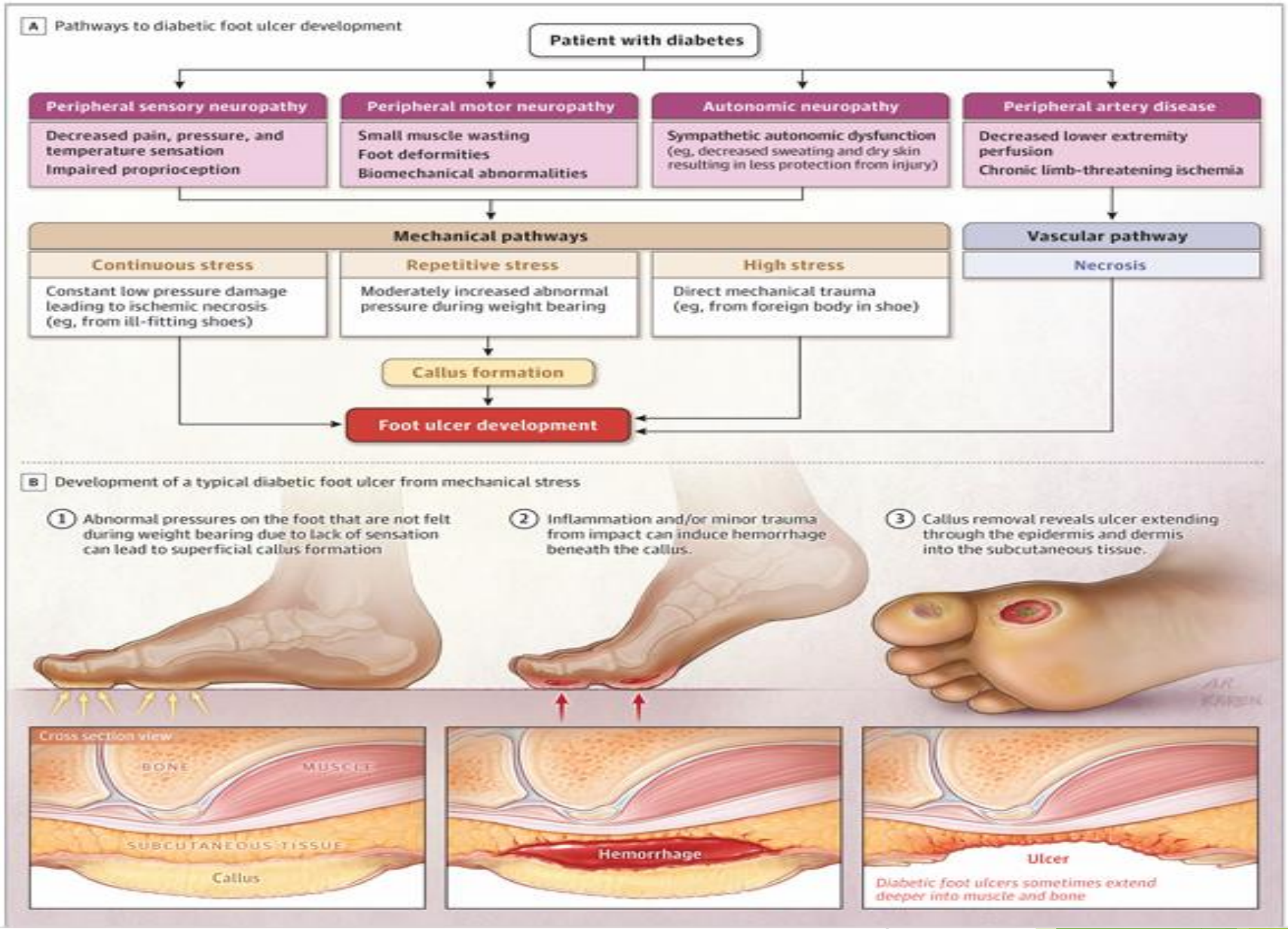


Diabetic foot Ulcer. A Review.. JAMA 2023

VASCULAR EVALUATION :

- **(1) History & Examination:**

~ D.M patients may develop **intermittent claudication & rest pain** but often these are absent due to immobility & neuropathy & the first presentation may be **ischemic** foot **ulcers**.

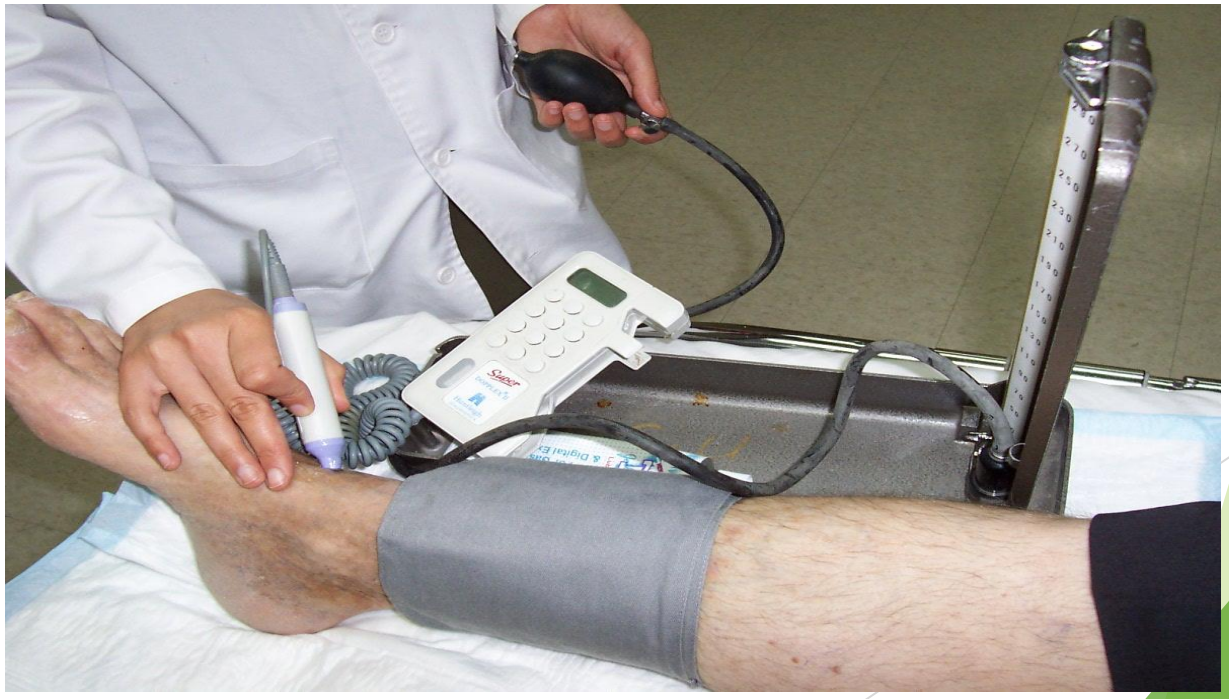
~Foot **pulse status** is the most important aspect of physical exam .

~**Neuropathic pain** burning, tingling/ front of shin relieved by exercise worse at night .

(2) Ankle brachial pressure index:

Falsely elevated due to medial calcification & resultant incompressibility

but loss of the normal triphasic Doppler wave form indicates vascular disease. Ankle syst pr < 80mmHg denotes poor healing in D.M.

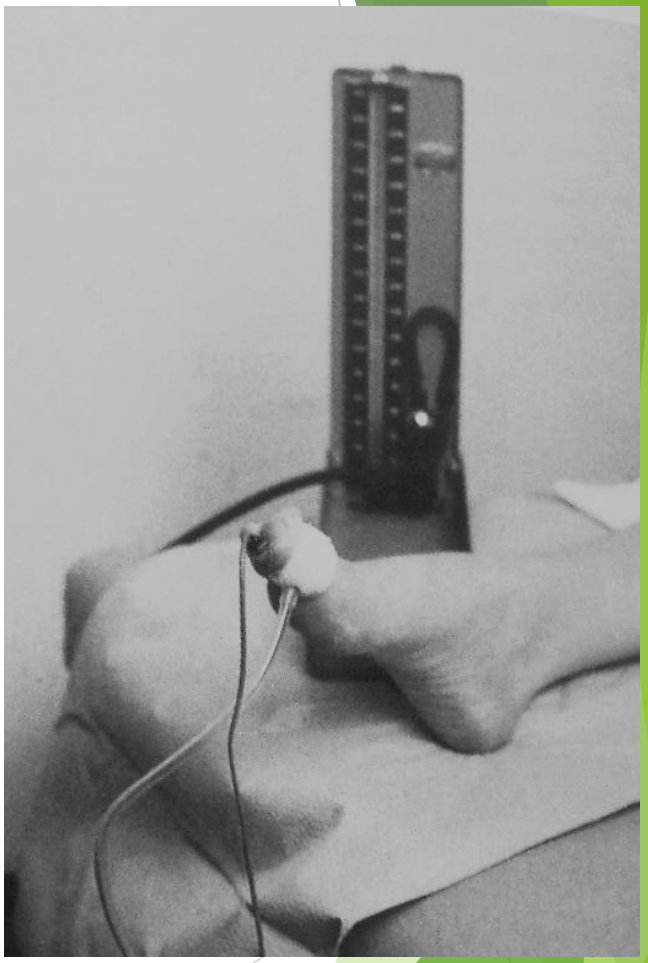


- **(3) Toe pressures measurement & TBI:**

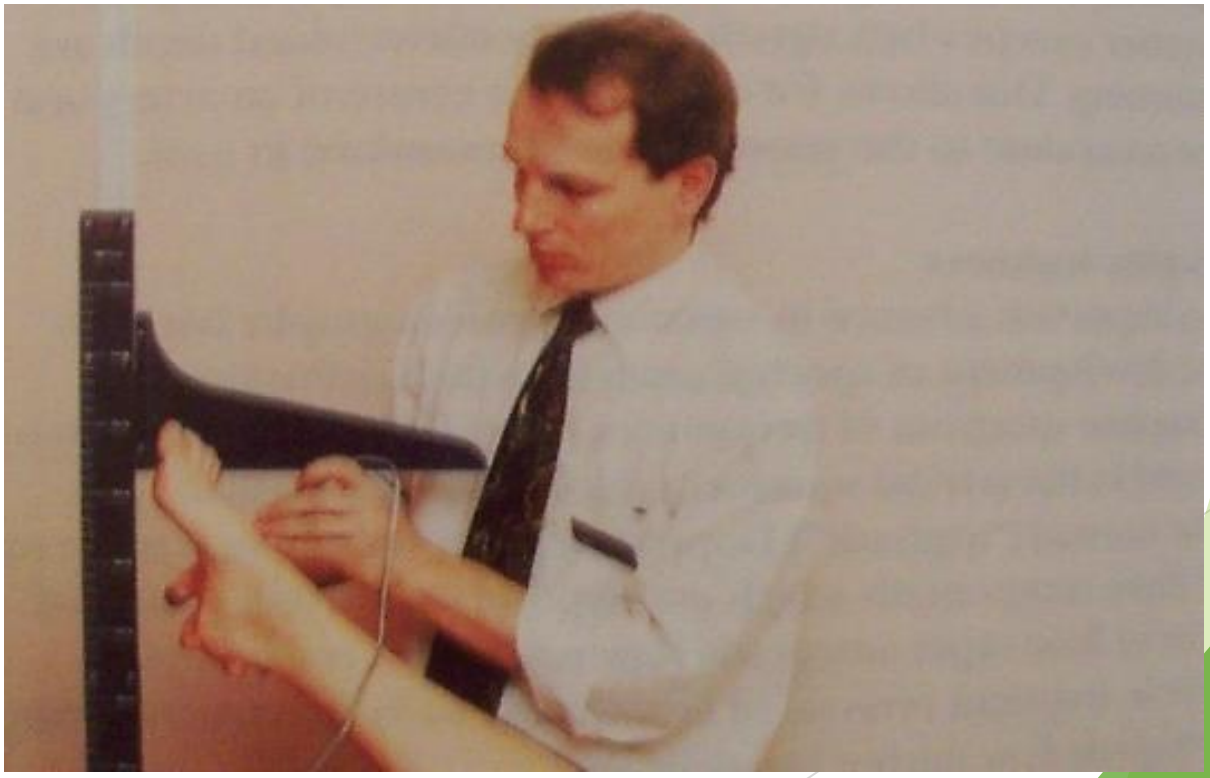
~ Normal toe syst pressure ranges 90 – 100 mmHg equivalent to 80-90% of brachial Pr &

TBI of 0.8 – 0.9 .

~ **Toe syst Pr < 30 mmHg** indicates critical ischemia & poor healing .



- **(4) Pole test :** listening to pedal pulse by Doppler while leg is raised alongside a pole calibrated in mmHg till signal disappears.



(5) Transcutaneous oxygen tension(TcO2):

Reflects skin oxygenation & used to determine :

1* severity of ischemia.

2* likely hood that an ulcer will heal

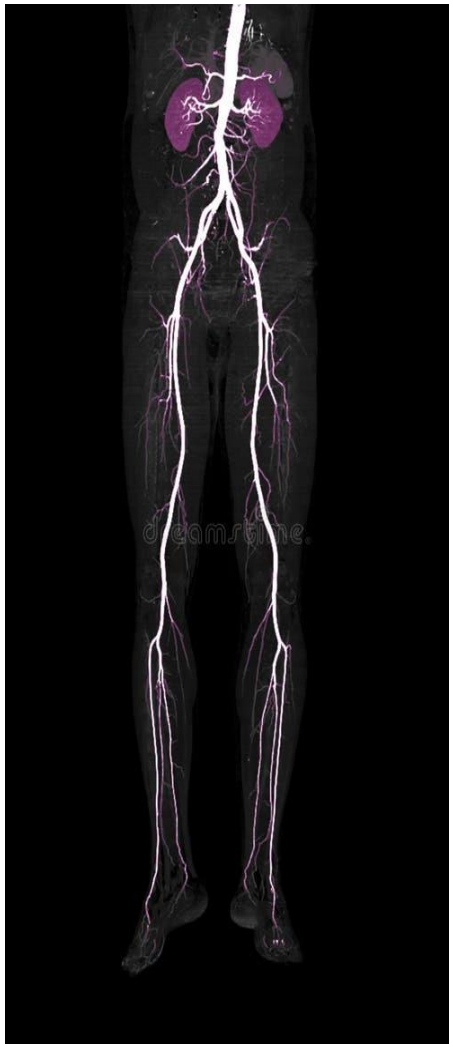
3* An appropriate level of amputation.

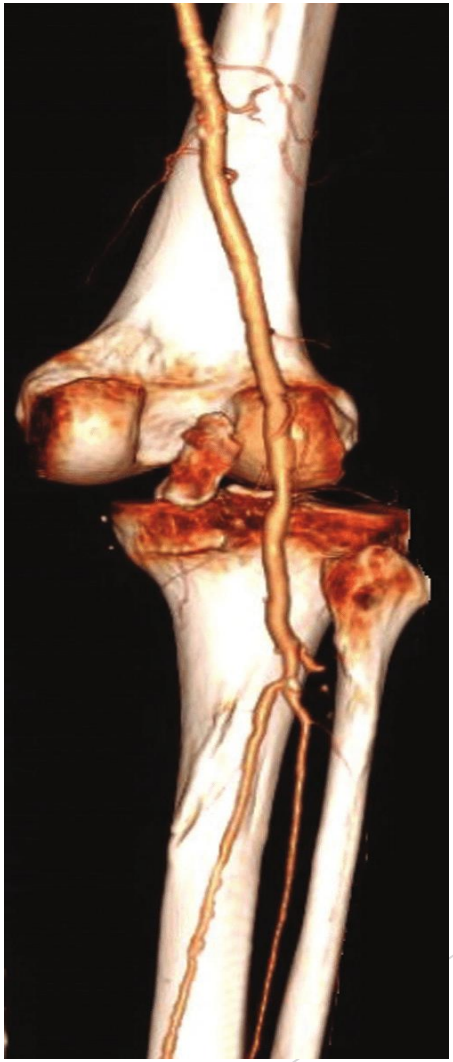
(6) Color Duplex Scanning:

1. Involves tracing the vessels in both real time & color. Normal peripheral waveforms are pulsatile with a distinct reverse flow component during diastole.

2. Detection of echogenic areas & comparison of peak systolic velocity & waveforms at different levels of a vessel determine stenotic & occluded segments .

7) CTA





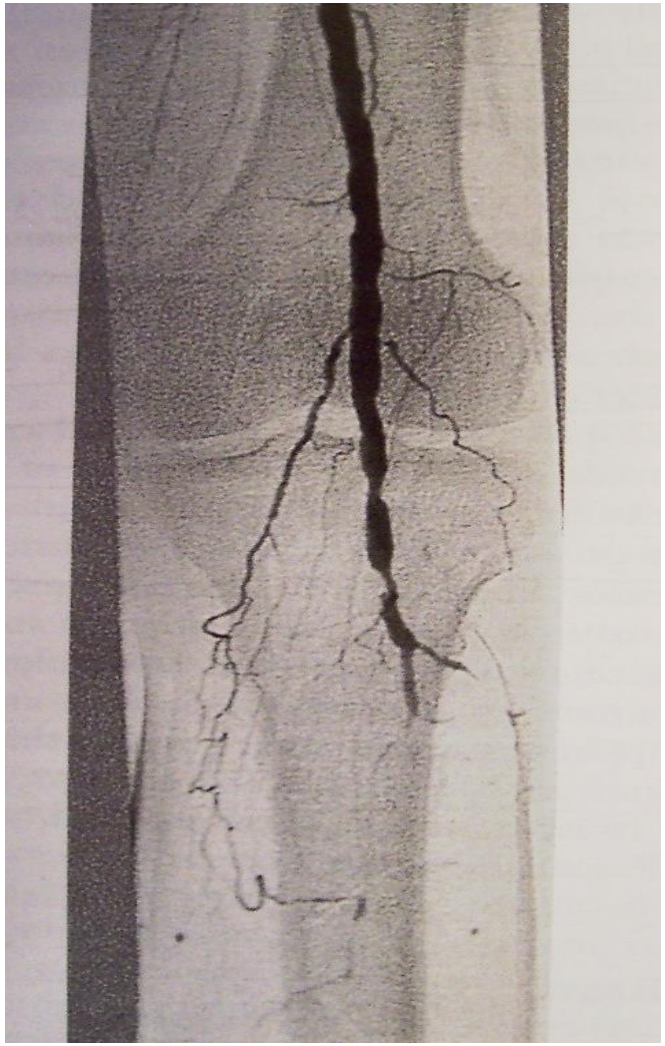
- **(8) Arteriograpghy:**

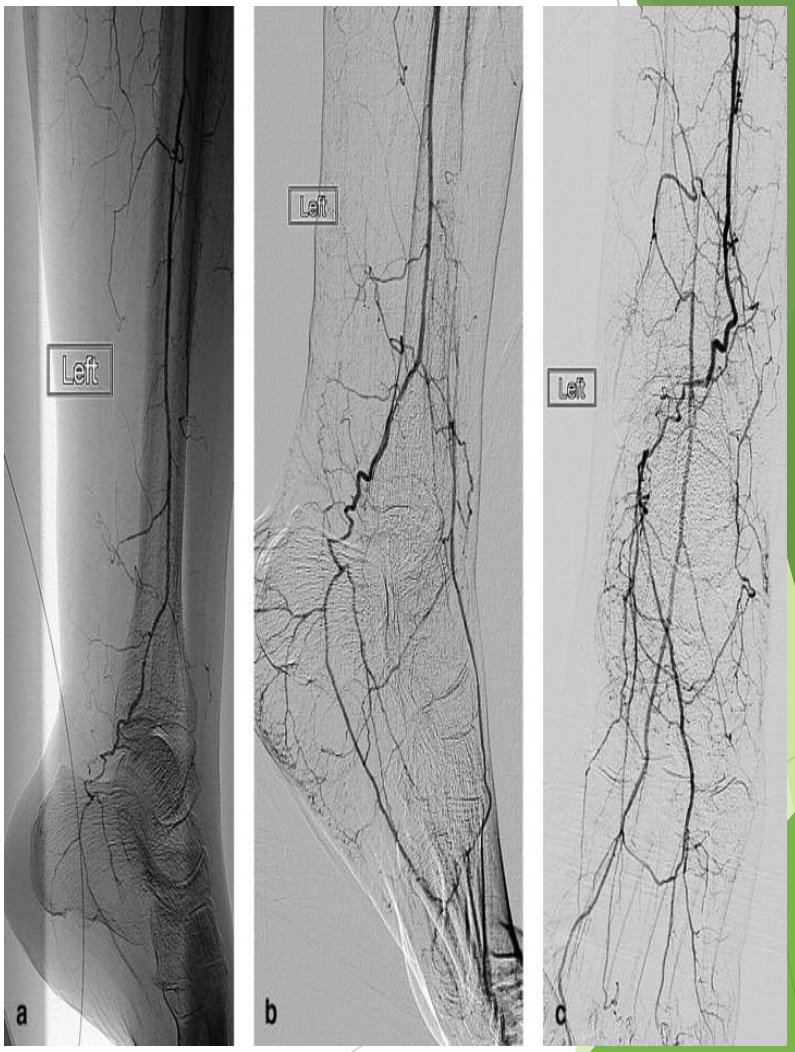
~ Remains the **Gold Standard** both for diagnosis & treatment of vascular disease .

~ Facilitates choosing an outflow that will restore foot pulses.

~ Complete infra popliteal circulation including the foot vessels should be incorporated .

~ Care for contrast media in patients with renal impairment.

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REVASCULARISATION:

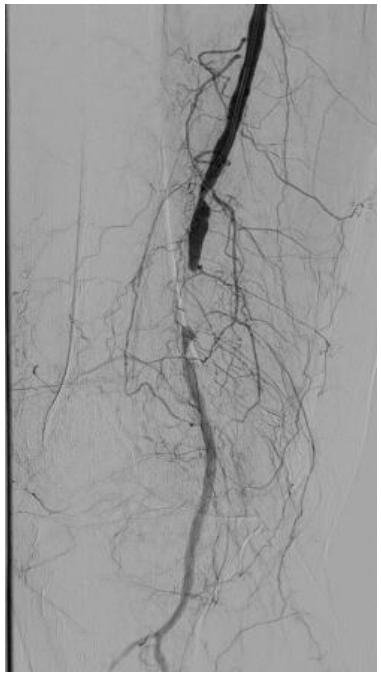
- It is the **gold standard** treatment of limb salvage in Diabetic foot .
- It requires a **good inflow** to be bypassed to a **patent** non resistant **outflow** artery that is in direct continuity with the foot to restore normal arterial pressure to the target area.
- It should precede local surgical measures such as debridment & micro amputation due to poor healing .

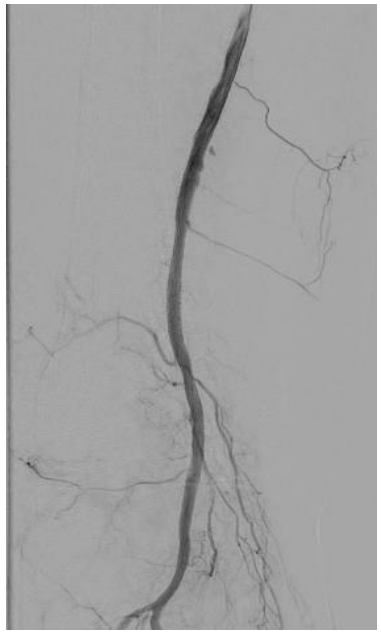
TECHNIQUES of REVASCULARISATION:

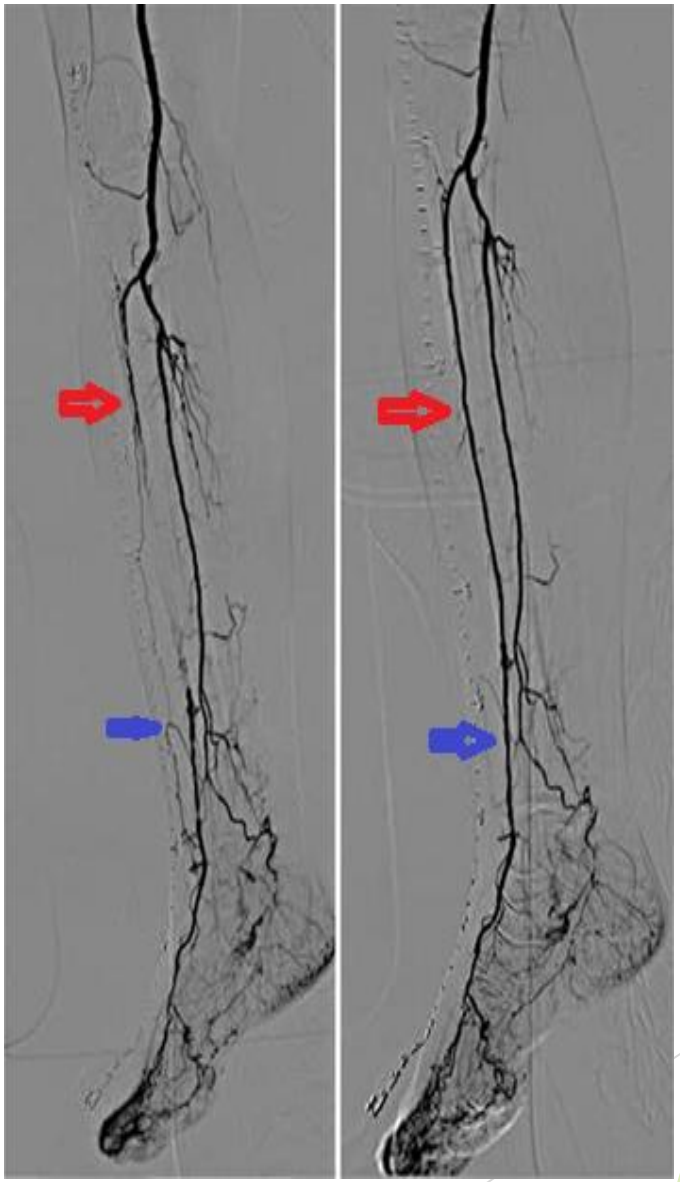
- **ENDOVASCULAR INTERVENTION**
- **OPEN SURGICAL PROCEDURES**
- **COMBINED TECHNIQUE**

ENDOVASCULAR INTERVENTION:

- Balloon Angioplasty +/- stenting is appropriate in pts with **focal disease** especially stenosis of larger proximal vessels or **short occlusions** of the iliac or SFA.
- In pts with longer occlusions , the technique of subintimal angioplasty may be used.
- Pre or per-op angioplasty can improve graft inflow or runoff thus decreasing the length of bypass.

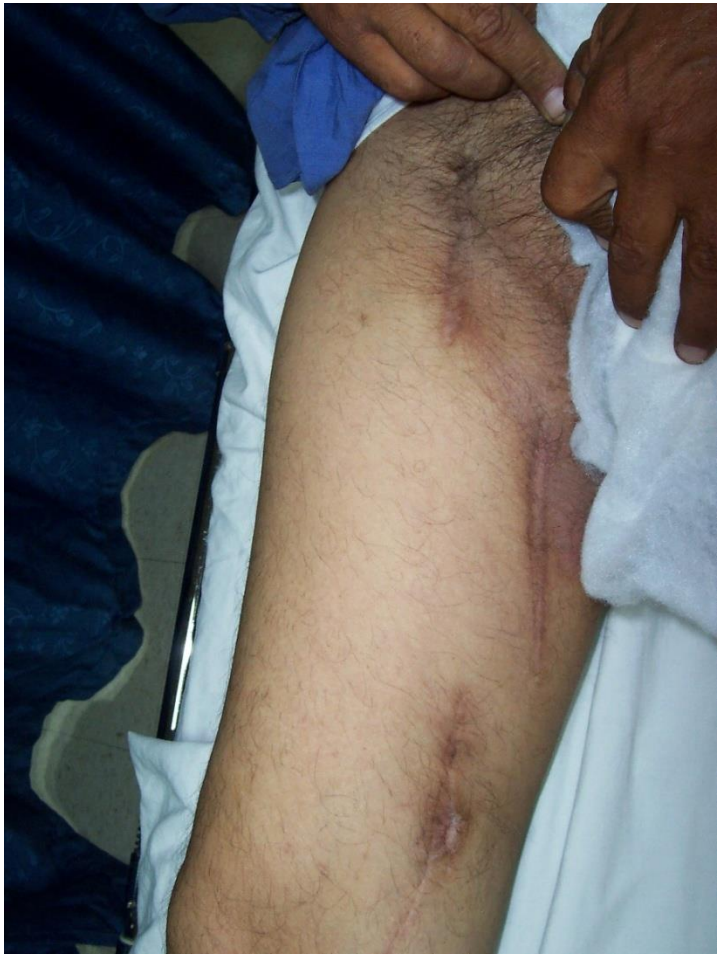


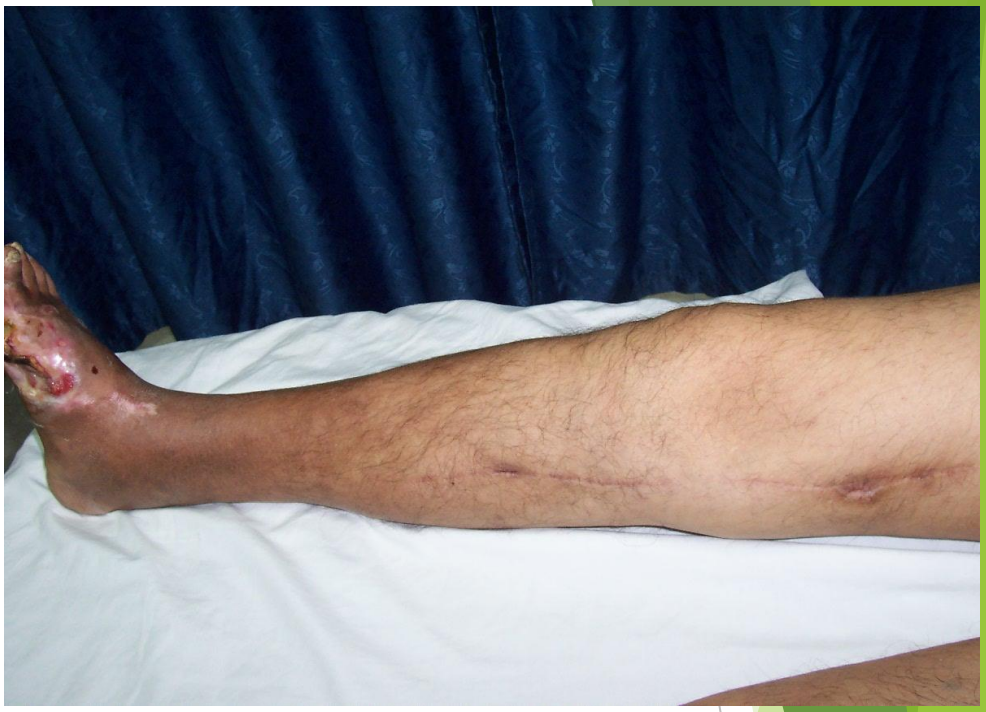


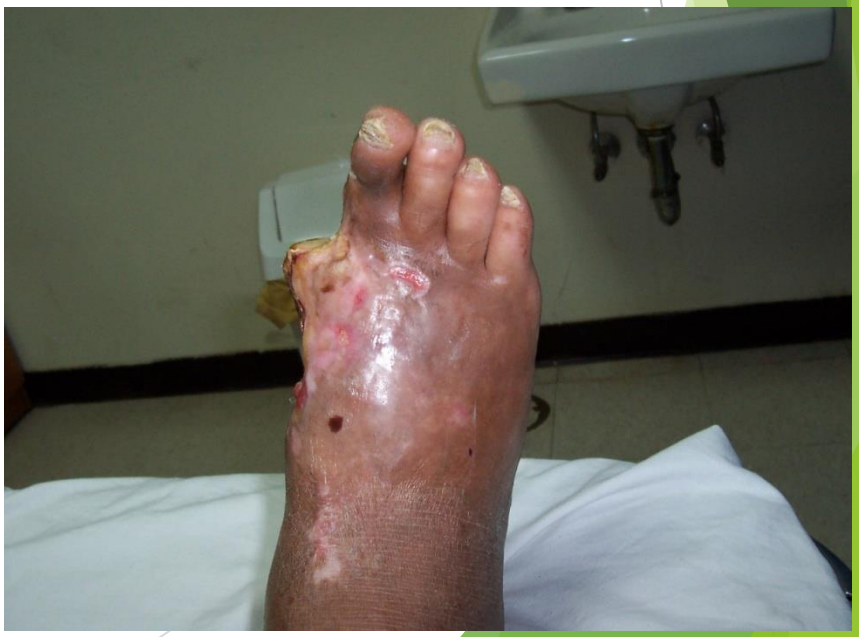


SURGICAL REVASCULARIZATION:

- Infra-POP disease in D.M pts mandates **distal bypass** with graft anastomosed to the distal tibial or planter arteries.
- **Autogenous vein graft** should be used : better patency & infection resistance.
- Pre-op Duplex venous mapping identify suitable sized non diseased veins .
- Ipsilateral LSV is preferred, else SSV , arm veins or deep leg veins are harvested.
- Vein graft can be prepared as : **InSitu , Reversed & NonReversed .**





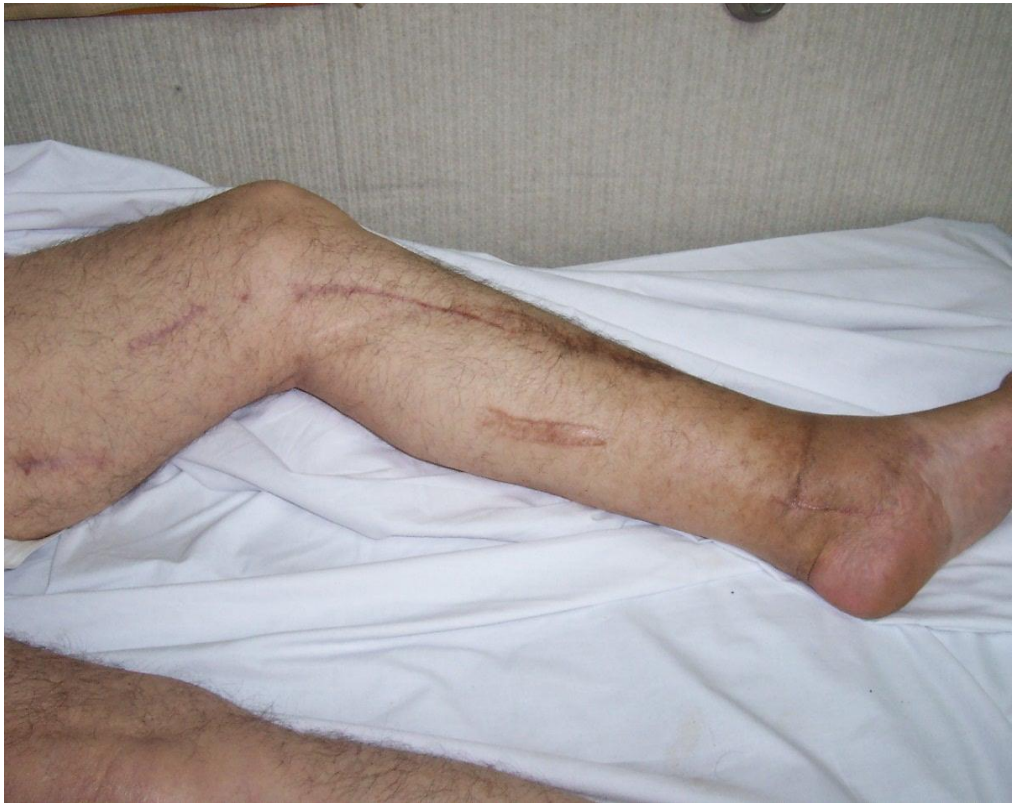


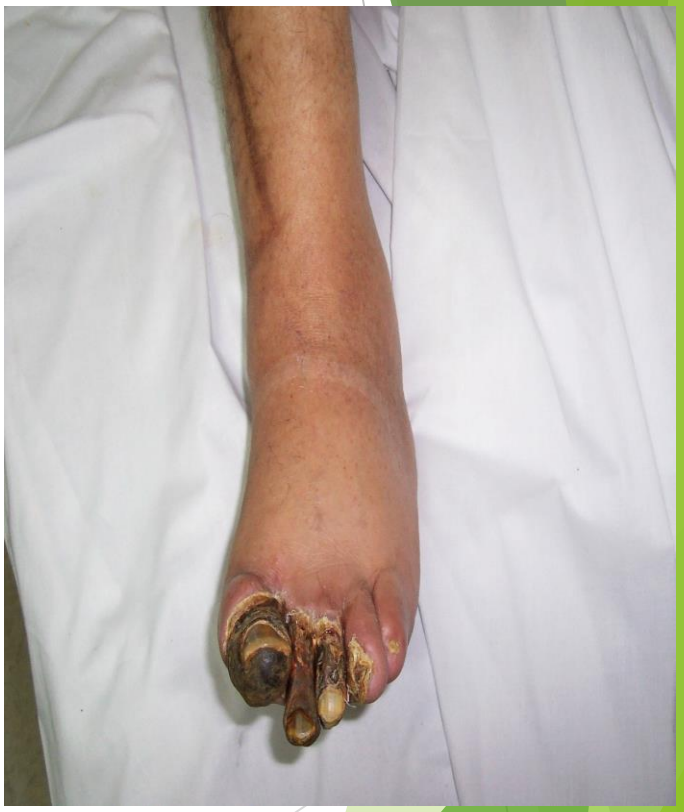
- Vein graft patency depends on :

1. The quality of inflow.
2. Status of the Runoff.
3. Vein quality & length.
4. Surgeon experience.

- Late Revascularization failure:

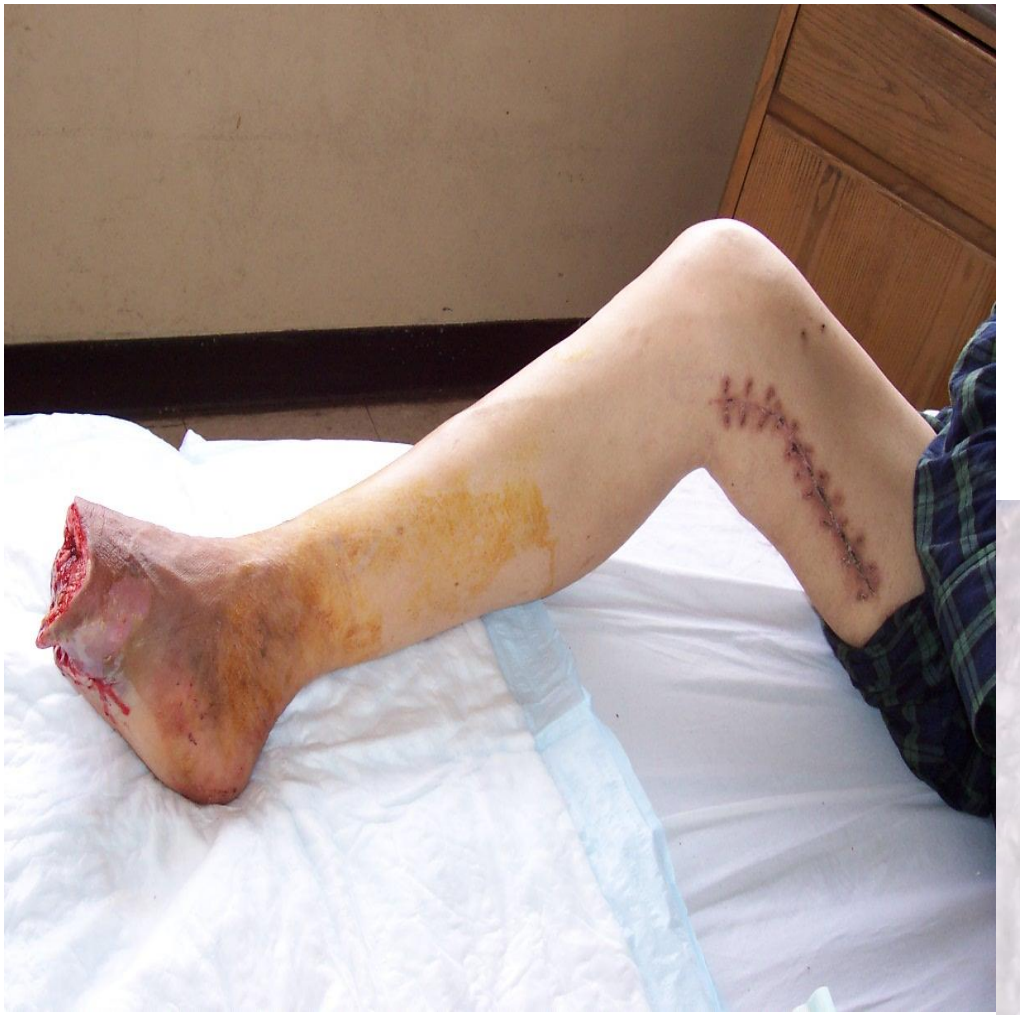
1. Intimal hyperplasia at sites of anastomoses,valves & angioplasty.
2. Progression of the disease.

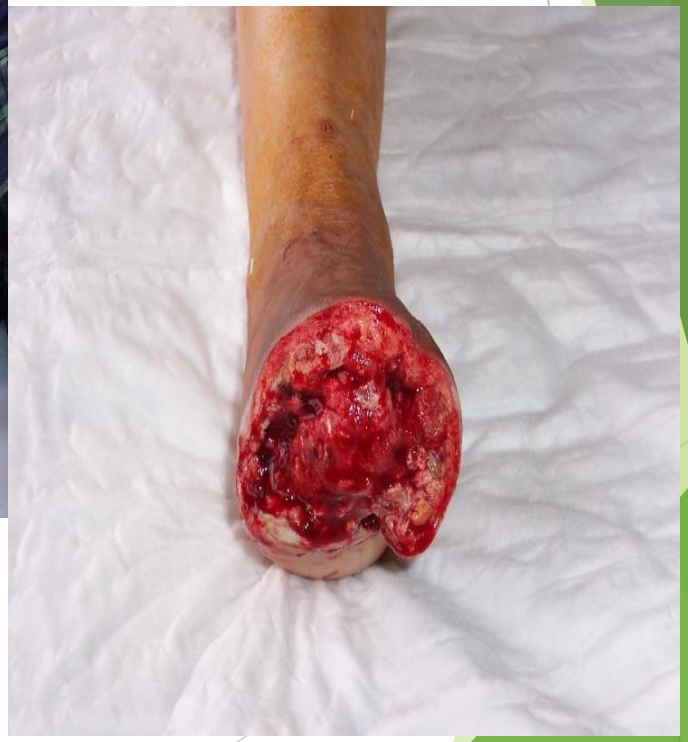




- After successful revascularization ,**Secondary Procedures** may be performed for foot salvage including :

1. Debridment ~ inside – out , probing
2. Partial ostectomy of prominent bone.
3. Local or free flaps in extensive tissue loss cases.





Why Diabetic Foot Ulcers are at Risk of Infection?

- In DFUs, the normal wound healing process consisting of inflammation, angiogenesis, and extracellular matrix (ECM) remodeling is dysregulated
- In DFUs, the excess unregulated MMP-9 is detrimental, destroying the ECM and preventing the wound from healing
- DFUs are typically infected with biofilm-producing bacteria that are resistant to antibiotics --- Infection increases the time for wound healing and the likelihood for a lower-limb amputation.

Strategy for Treatment of Infected Diabetic Foot Ulcers. Acc Chem Res

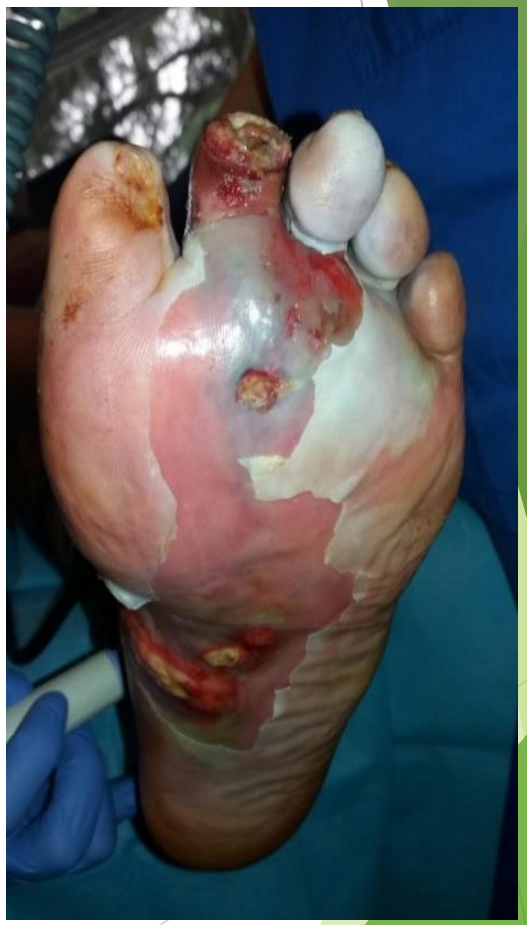
2021 March

- Deep, long-standing, recurrent wound , or of traumatic aetiology predispose inf
- Presence of DM-related immunological alarms ex neutrophil dysfunction
- Concomitant CRF
- Foot anatomy, which is divided into several separate but inter communicating compartments, fosters the proximal spread of infection
- Inflammatory response for inf cause compartmental pressure > capillary pressure = ischaemic necrosis
- Bacterial virulence factors

Infection is the most serious complication in diabetic foot

SIGNS OF ALERT : CLINICAL PICTURES TO CONSIDER EARLY REFERRAL TO SPECIALIZED DIABETIC FOOT SERVICES)

- Superimposed infection (onset of hyperemia around the wound, cellulitis, pus secretion, new area of wet gangrene, oedema, pain, fever)
- Superimposed ischemia or ischemia evolution (new areas of necrosis or gangrene, rest pain, hyperemia of the foot)
- Worsening of target wound (extension of ulcer size, involvement of soft tissues/bone, signs of ischemia or infection as above)



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The Wound, Ischemia, and Foot Infection (WIfI) classification system consists of 3 components graded separately from 0 (none) to 3 (severe).

One component may be dominant but the specific combination of scores is used to estimate the risk of limb amputation at 1 year and the need for or benefit of revascularization.[a]

Wound (W)

Grade	Ulcer	Gangrene
0	None	None
1	Small, shallow	None
2	Deep with exposed bone, joint, or tendon	Limited to digits
3	Extensive, deep, and involving forefoot and/or midfoot with or without calcaneal involvement	Extensive and involving forefoot and/or midfoot Full thickness heel necrosis with or without calcaneal involvement

Ischemia (I)

Grade	Ankle-brachial index Ankle systolic pressure	Toe pressure or transcutaneous oximetry
0	≥0.80 >100 mm Hg	≥60 mm Hg
1	0.60-0.79 70-100 mm Hg	40-59 mm Hg
2	0.40-0.59 50-69 mm Hg	30-39 mm Hg
3	≤0.39 <50 mm Hg	<30 mm Hg

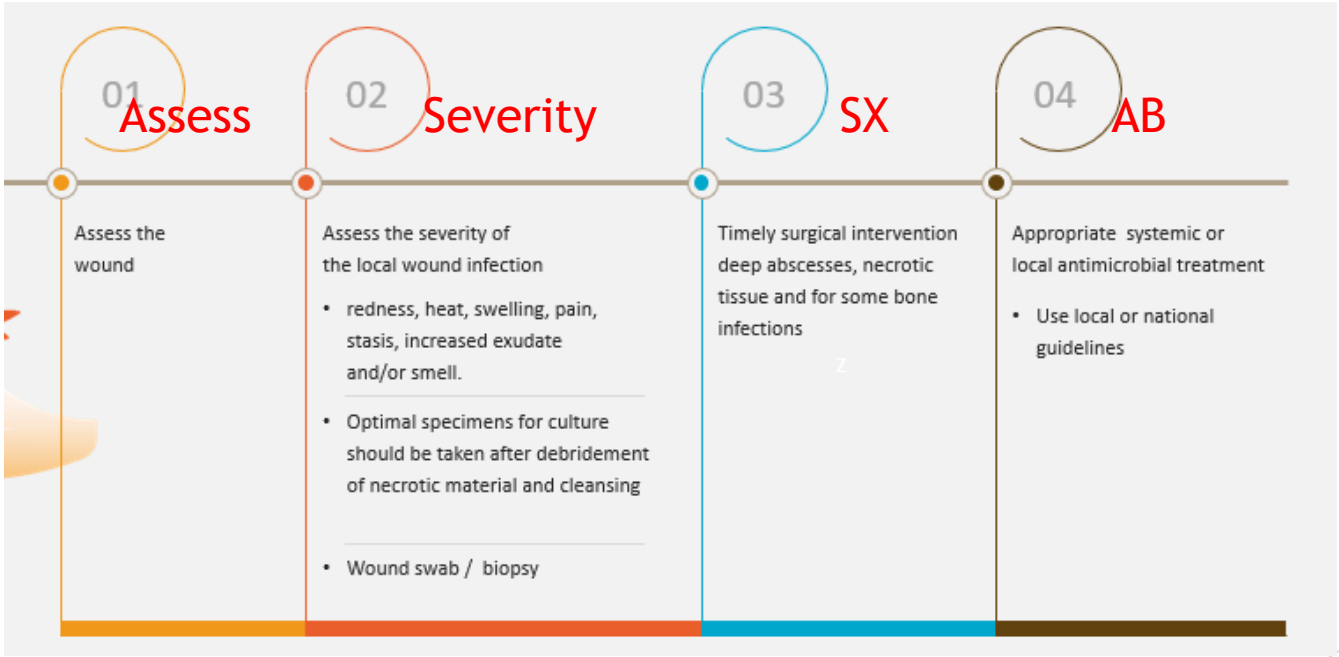
Foot infection (fI)

Grade	Clinical manifestation
0	No symptoms or signs of infection
1	Infection indicated by ≥2 of the following: • Local swelling or induration • Erythema 0.5-2.0 cm around ulcer • Local tenderness or pain • Local warmth • Purulent discharge (thick, opaque to white, or sanguineous)
2	Infection as described above with: • Erythema >2 cm around ulcer • Involving structures deeper than skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, fasciitis) • No signs of systemic inflammatory response (see below)
3	Infection as described above with ≥2 signs of systemic inflammatory response syndrome: • Temperature >38 °C or <36 °C • Heart rate >90/min • Respiratory rate >20/min or $Paco_2$ <32 mm Hg • White blood cell count >12 000/μL or <4000/μL or 10% immature forms

Table

A
B
C
D

General Principles of Infected Wound Management



When to consider hospitalization

- *Severe infection*
- *Metabolic or hemodynamic instability*
- *IV Tx needed (not available/not appropriate as outpt)*
- *Dx tests needed(not available as outpt)*
- *Severe foot ischemia*
- *Sx procedures required(more than minor)*
- *Failure of outpt management*
- *Need for more complex dressing changes than pt /caregiver can provide*

Recommendation of antibiotics

a) Use any of the systemic antibiotic regimens shown to be effective in published RCT at standard dosing to TX a Pt with DM & soft tissue infection of the foot. (Strong; High)

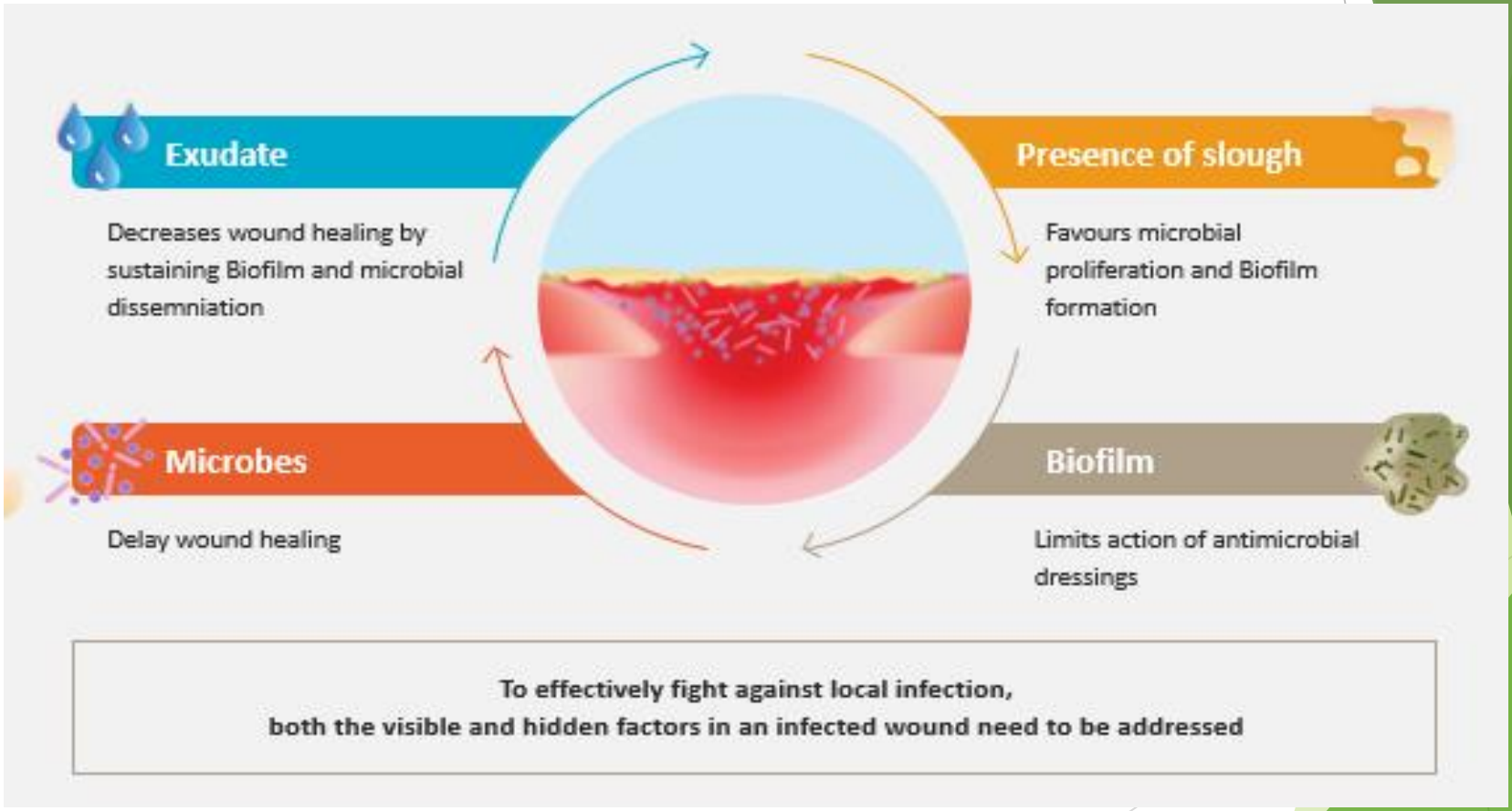
a) Administer antibiotic to a pt with **skin or soft tissue DF infection** for 1–2 wks. (Strong; High)

a) Consider continuing Tx, up to 3–4 wks, if the **infection is improving but is extensive** & is resolving slower than expected or if the pt has severe PAD. (Conditional, Low)

a) If **infection has not resolved** after 4 wks of appropriate Tx, **re-evaluate** the pt & reconsider the need for further dx studies or alternative TX. (Strong; Low).

Infection severity	Additional factors	Usual pathogen(s)[b]	Potential empirical regimens[c]
Mild	No complicating features	GPC	Semisynthetic penicillinase-resistant penicillin (cloxacillin)
			1st generation cephalosporin (cephalexin)
	ß-lactam allergy or intolerance	GPC	Clindamycin; fluoroquinolone (levo/moxi-floxacin); trimethoprim-sulfamethoxazole; doxycycline
	Recent antibiotic exposure	GPC + GNR	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam)
			Fluoroquinolone (levo/moxi-floxacin); trimethoprim-sulfamethoxazole
	High risk for MRSA	MRSA	Linezolid; trimethoprim-sulfamethoxazole; clindamycin; doxycycline, fluoroquinolone (levofloxacin, moxifloxacin)
Moderate or severe[d]	No complicating features	GPC ± GNR	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam)
			2nd, 3rd generation cephalosporine (cefuroxime, cefotaxime, ceftriaxone)
	Recent antibiotics	GPC ± GNR	ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam)
			2nd, 3rd generation cephalosporine (cefuroxime, cefotaxime, ceftriaxone) group 1 carbapenem (ertapenem); (depends on prior therapy; seek advice)
	Macerated ulcer or warm climate	GNR, including *Pseudomonas* sp.	ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam) semisynthetic penicillinase-resistant penicillin (cloxacillin) + ceftazidime or ciprofloxacin group 2 carbapenem (mero/imi-penem)
	Ischaemic limb/necrosis/gas forming	GPC ± GNR ± strict anaerobes	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam) or ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam)
			Group 1 (ertapenem) or 2 (mero/imi-penem) carbapenem
			2nd (cefuroxime)/3rd (cefotaxime, ceftriaxone) generation cephalosporin + clindamycin or metronidazole
	MRSA risk factors	MRSA	Consider adding, or substituting with, glycopeptides (vancomycin, teicoplanin); llLinezolid; daptomycin; fusidic acid, trimethoprim-sulfamethoxazole; doxycycline
	Risk factors for resistant GNR	ESBL	Carbapenem (erta/mero/imi-penem); fluoroquinolone (ciprofloxacin); Aminoglycoside (amikacin); colistin

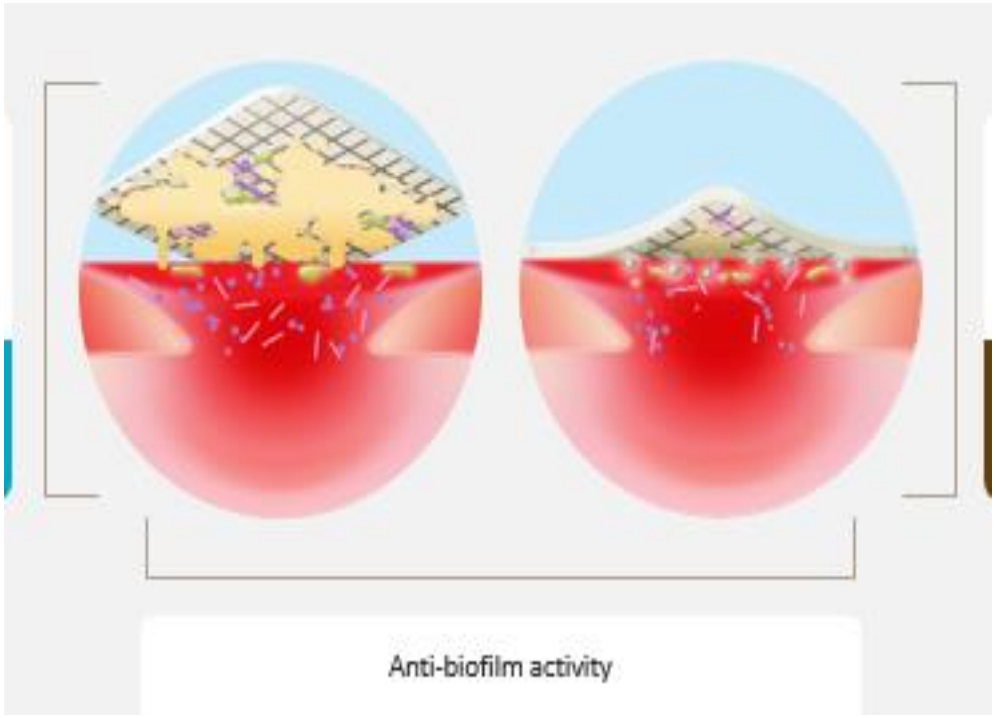
Wound infection creates a vicious cycle that causes tissue damage and delayed healing



To effectively fight against local infection,
both the visible and hidden factors in an infected wound need to be addressed

Stop the vicious cycle of wound infection

Complete & continuous cleaning action



Antimicrobial activity

Combined cleaning and antimicrobial action defeats biofilms and prevent their reattachment

AMPUTATION:

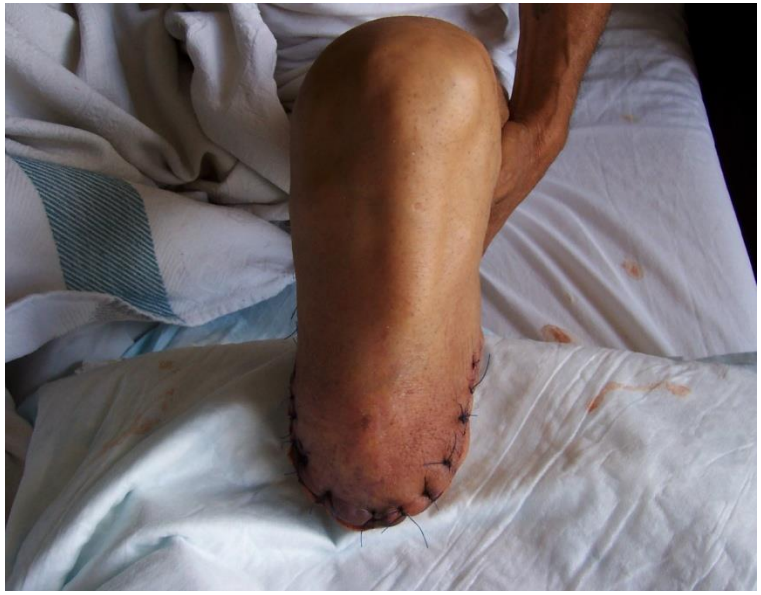
- ***INDICATIONS:***

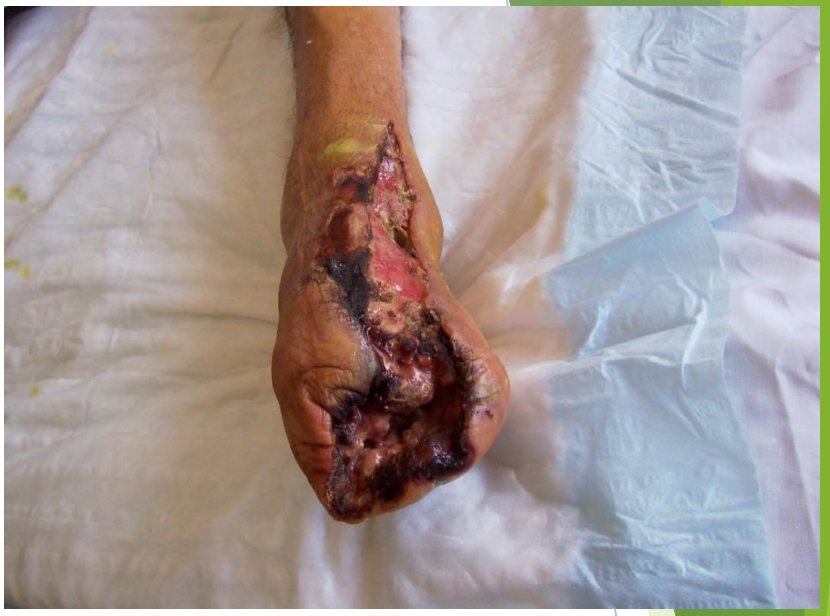
1. Advanced ischemia with little viable tissue left on wt-bearing area .
2. Lack of target vessel.
3. Patients with advanced sepsis & unfitness for multiple operations .

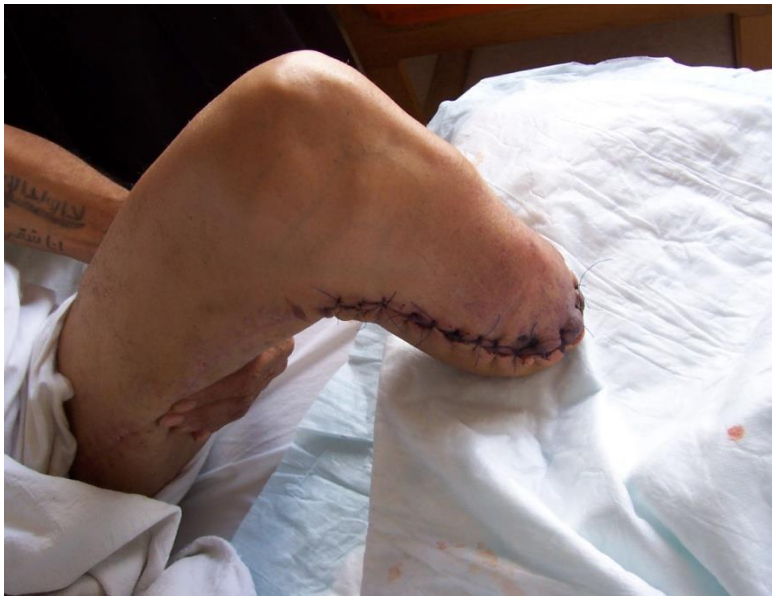
Level of amputation is determined by extent of tissue involvement & expected healing site

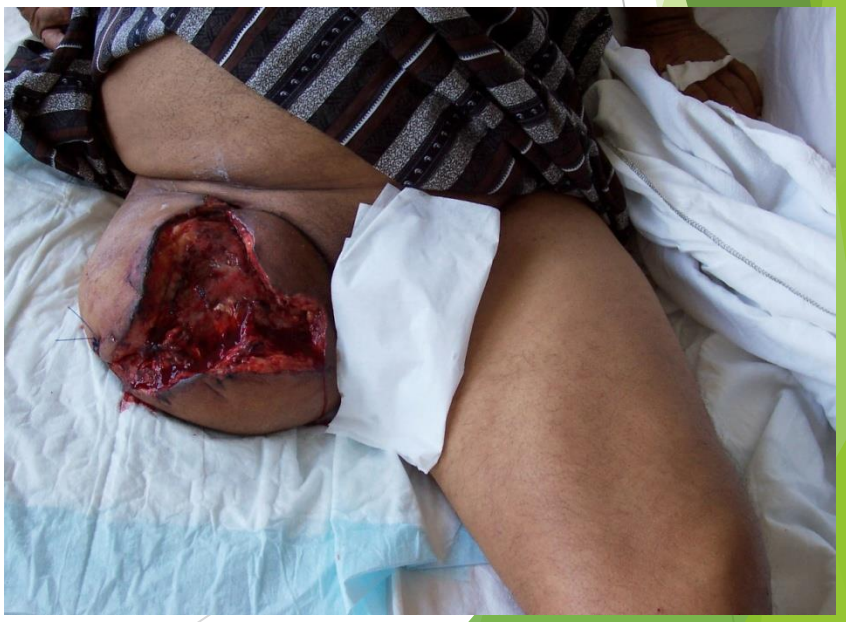
TcO_2 >40 mmHg

- Levels :
  - Simple digit amputation
  - Ray amputation
  - Transmetatarsal
  - lisFranc
  - Chopart amputation
  - Syme
  - B.K.A.
  - Through knee
  - A.K.A.
  - Disarticulation.









Avoiding Amputation

Solutions

- Improve awareness .
- Prevention better than cure .
- Improve referral system .
- Increase facilities .

MEDICAL TREATMENT:

- **ALPROSTADIL** (Prostavasin) ~ PGE1

1. Effects on **plt activity**: impaired aggregation & adhesion ,counteract TXA2
2. **Haemostatic** effect: ^ local fibrinolysis,impair plts hyperactivity
3. **Hemorheological** effect: decrease viscosity , ^ RBC ‘s flexibility.
4. **Antiatherosclerotic** effect : decrease proliferation & mitosis of S.M. decreased intracellular matrix synthesis

- **In Diabetics** :

1. Improves claudications
2. Relief rest pain
3. Healing of trophic tissues & reduction of amputation.

- **Indications:**

1. primary conservative Tx where revascularization is not possible.
2. Post angioplasty.

HBO:

- Improves oxygenation of tissues : may increase TcO2
- Enhances the killing capacity of neutrophils
- Inhibits growth of anaerobic organisms

TREATMENT:

- **MULTIDISCIPLINARY APPROACH.**

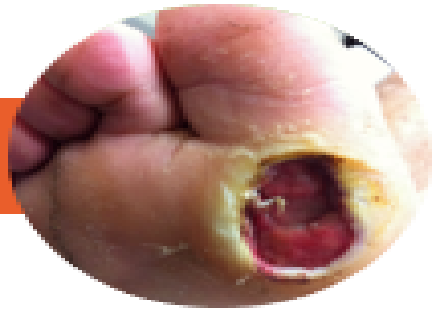
- FUNDIMENTAL AIMS of foot salvage in D.M patients are : eradication of all sepsis, removal of all irreversibly damaged tissue ,adequate vascularity & creation of a functional foot.

- Diabetic foot clinic should include :Diabetic physician, Diabetic education nurse ,orthopedic nurse ,vascular nurse ,podiatrist, vascular & orthopedic surgeons available at call.

THANK YOU

Why Diabetic Foot Ulcers are at Risk of Infection?

Complex open wounds



Environmental conditions are conducive to bacterial multiplication.

Skin integrity compromised, moisture, plentiful supply of nutrients, poor blood supply etc.

Wounds become contaminated by environmental organisms from surroundings and /or patients' flora,

They increase in numbers forming biofilms, which inhibit healing and can lead to local infections.

Biofilm Based Wound Care

Debridement, cleaning, topical treatment with systemic treatment if indicated.

Category 1
No infection

Standard treatment / dressing

Category 2 Mild infection

No systemic manifestations and only skin and subcutaneous tissue involved. Erythema does not extend >2cm around the wound–
Treatment: debridement/ cleansing / antimicrobial dressing

Category 3
Moderate infection

No systemic manifestations, tendons, muscle, joint and bone may be involved. Erythema extends >2cm around the wound
Treatment: – debridement / cleansing/ antimicrobial dressing - consider antibiotics

Category 4
Severe infection

Associated manifestations of systemic inflammatory response syndrome (SIRS)temp > 38'C, increased heart rate, raised WBC, bone involvement
Treatment: - debridement / cleansing / antimicrobial dressing – systemic antibiotics – consider sepsis

Foot infection (fI)

Grade	Clinical manifestation
0	No symptoms or signs of infection
1	Infection indicated by ≥2 of the following: • Local swelling or induration • Erythema 0.5-2.0 cm around ulcer • Local tenderness or pain • Local warmth • Purulent discharge (thick, opaque to white, or sanguineous)
2	Infection as described above with: • Erythema >2 cm around ulcer • Involving structures deeper than skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, fasciitis) • No signs of systemic inflammatory response (see below)
3	Infection as described above with ≥2 signs of systemic inflammatory response syndrome: • Temperature >38 °C or <36 °C • Heart rate >90/min • Respiratory rate >20/min or $Paco_2$ <32 mm Hg • White blood cell count >12 000/μL or <4000/μL or 10% immature forms

Received: 22 June 2023 | Accepted: 23 June 2023

DOI: 10.1002/dmrr.3687

RESEARCH ARTICLE

WILEY

IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023)

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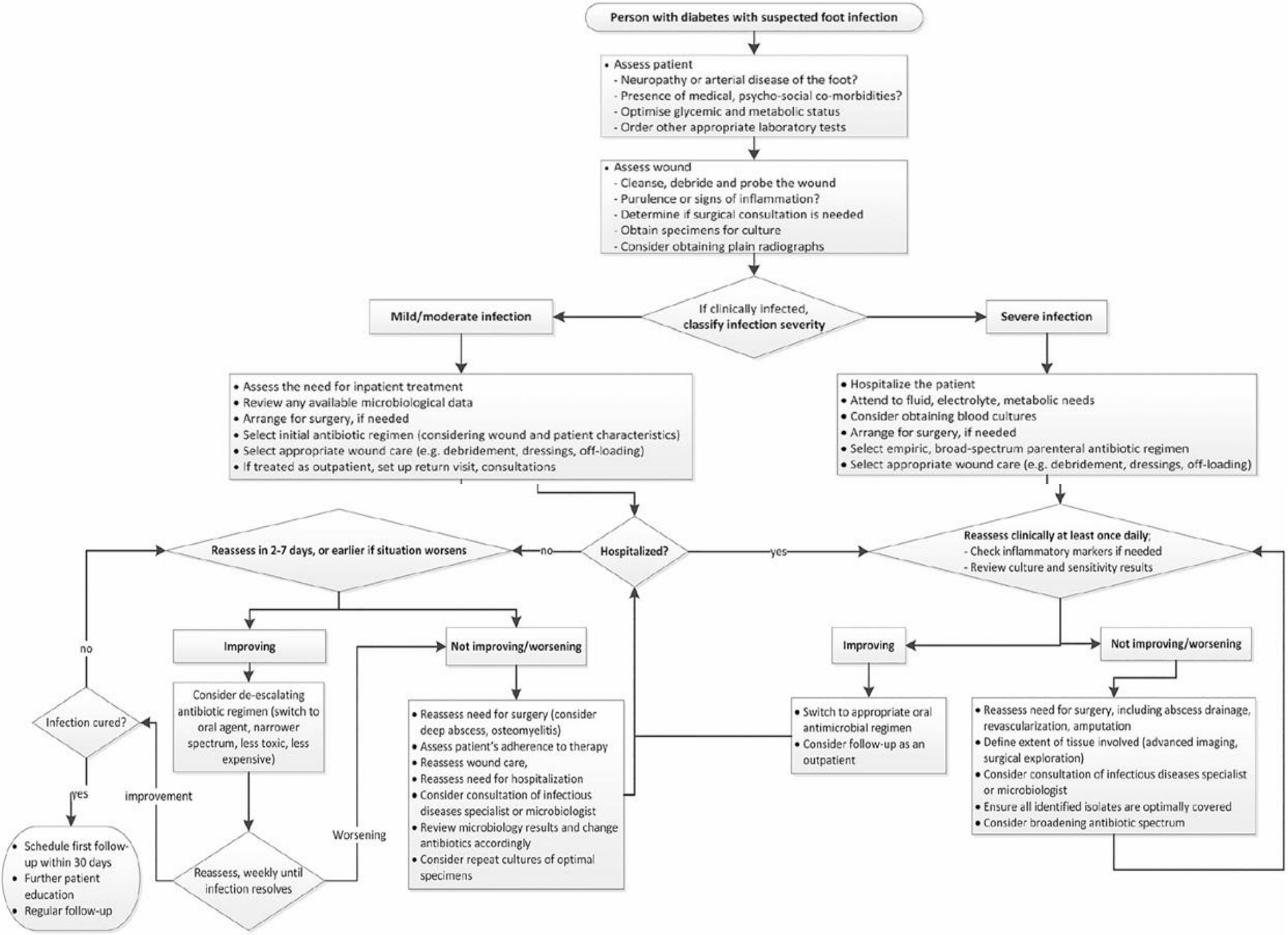
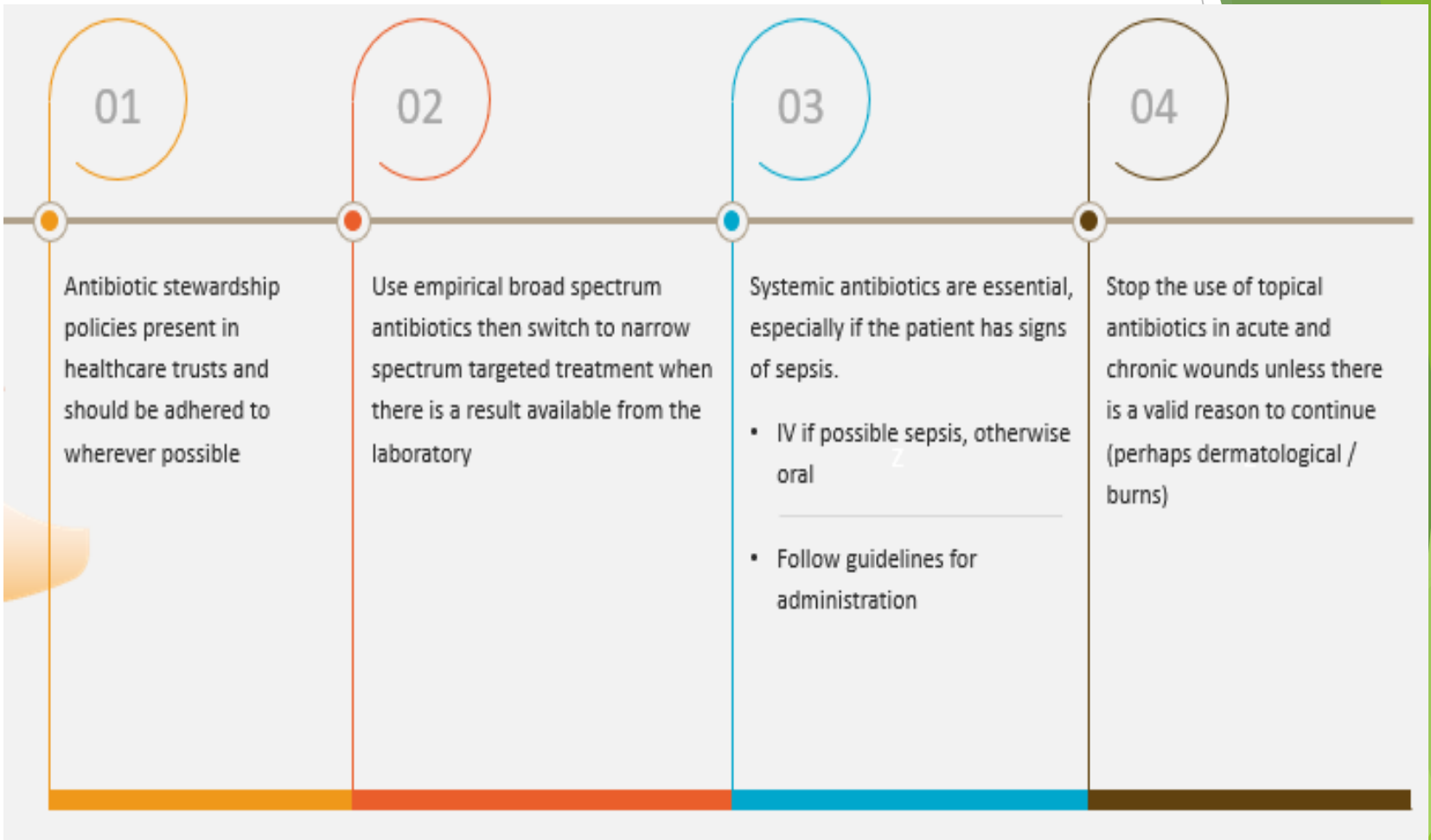
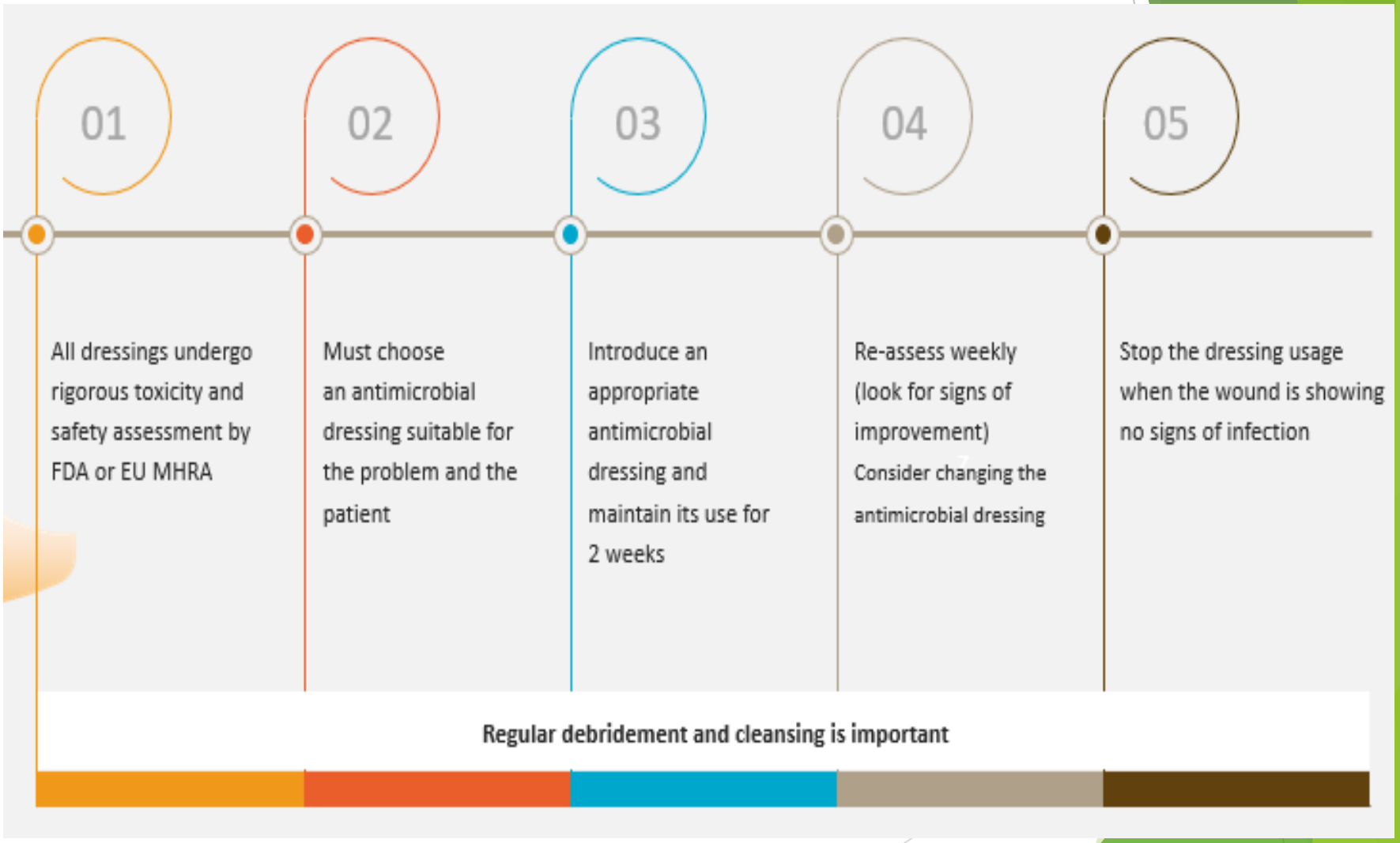

Person with diabetes with suspected foot infection
• Assess patient
- Neuropathy or arterial disease of the foot?
- Presence of medical, psycho-social co-morbidities?
- Optimise glycemic and metabolic status
- Order other appropriate laboratory tests
• Assess wound
- Cleanse, debride and probe the wound
- Purulence or signs of inflammation?
- Determine if surgical consultation is needed
- Obtain specimens for culture
- Consider obtaining plain radiographs
If clinically infected, classify infection severity
Mild/moderate infection
Severe infection
• Assess the need for inpatient treatment
• Review any available microbiological data
• Arrange for surgery, if needed
• Select initial antibiotic regimen (considering wound and patient characteristics)
• Select appropriate wound care (e.g. debridement, dressings, off-loading)
• If treated as outpatient, set up return visit, consultations
• Hospitalize the patient
• Attend to fluid, electrolyte, metabolic needs
• Consider obtaining blood cultures
• Arrange for surgery, if needed
• Select empiric, broad-spectrum parenteral antibiotic regimen
• Select appropriate wound care (e.g. debridement, dressings, off-loading)
Hospitalized?
no
yes
Reassess in 2-7 days, or earlier if situation worsens
Reassess clinically at least once daily;
- Check inflammatory markers if needed
- Review culture and sensitivity results
Improving
Not improving/worsening
Improving
Not improving/worsening
Consider de-escalating antibiotic regimen (switch to oral agent, narrower spectrum, less toxic, less expensive)
• Reassess need for surgery (consider deep abscess, osteomyelitis)
• Assess patient's adherence to therapy
• Reassess wound care,
• Reassess need for hospitalization
• Consider consultation of infectious diseases specialist or microbiologist
• Review microbiology results and change antibiotics accordingly
• Consider repeat cultures of optimal specimens
• Switch to appropriate oral antimicrobial regimen
• Consider follow-up as an outpatient
• Reassess need for surgery, including abscess drainage, revascularization, amputation
• Define extent of tissue involved (advanced imaging, surgical exploration)
• Consider consultation of infectious diseases specialist or microbiologist
• Ensure all identified isolates are optimally covered
• Consider broadening antibiotic spectrum
no
Infection cured?
yes
improvement
Worsening
Reassess, weekly until infection resolves
• Schedule first follow-up within 30 days
• Further patient education
• Regular follow-up

What About Systemic Treatments? Use of Antibiotics?



What About Topical Dressings?



Q.A.M.H / VASCULAR UNIT / DISTAL BYPASS / OUR EXPERIENCE

- 33 LIMBS 2002 -2004.
- 82 % were Males
- Age 30 – 82 yrs
- Bilateral 6.8 %
- Risk factors 55 % were D.M
- Pathology 80 % Atherosclerosis.

Presentation:

- 10 pts with rest pain.
- 13 pts with dry gangrene .
- 5 pts with wet gangrene .
- 5 lost follow up .

Procedure :

- RLSV in 23 Pts
- Composite in 4 Pts .
- Synthetic (PTFE) with vein cuff in one Pt.

Inflow source: vessel		Runoff
23	CFA	9 ATA
3	POP A	18 PTA
1	SFA	1 TPT
1	Distal Ax-Fem	

Follow up Results :

- peri op : 63% were patent.
- 3 months : 54 %
- One year : 47 %

Vascular Amputations at Q.A.M.H./Our Experience :

- Years 2003 & 2004.
- 109 in 81 patients
- 61 BKA & 48 AKA
- 23 converted from BKA to AKA
- 66 Males & 15 Females
- Age 30 - 85 years, peak 60-70 years
- R.F : 67 % diabetics, 59 % smokers, 48 % HTN

- Study on 30 pts given prostavasin , 35 – 88 yrs
- 50% D.M , 63 % smokers
- Indication :64 % forefoot gangrene,36 % rest pain or claudication.
- F.U. = 1 m – 3 yrs
- Results : **43 % had viable limb** , 50 % had major amputations.
- S.E. : mild phlebitis.
- **Conclusion :** in non operable POVD with crippling pain or early gangrene ,its use is JUSTIFIED.

Conclusion

1. Identification of local infection is difficult and usually determined on clinical assessment.

2. Guidelines are available to help with identification of local infection created by a panel of experts and all available evidence (IWGDF 2023 update)

3. Need of a combined action to fight local infection: Debridement, cleansing , topical antiseptic dressing (only use systemic antibiotic if indicated)

4. Refer your DFU patients to specialist centers when appropriate.

PRE AMPUTATION EVENTS :

- 48 Patients had open vascular procedure ,17 Pts with distal bypass.
- 6 Pts had angioplasty alone .
- 25 had no vascular procedure / 16 had presented with advanced gangrene.
- 2 had surgery outside

Amputation

Reasons

- No Medical insurance / late presentation.
- Medical ignorance .
- Diabetes & its poor control
- Multi level disease
- Buerger’s disease & patient compliance
- Increased load with limited facility