

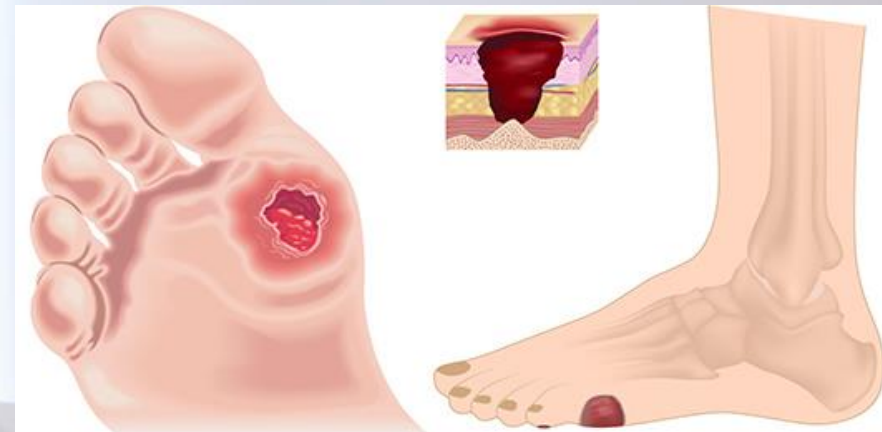
The diabetic foot

diagnostics and treatment

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Dutch Diabetes Academy 28th june 2022
1930-2000h



Disclosure belangen spreker: Max Nieuwdorp

Dutch Diabetes Academy – 28 juni 2022

(potentiële) Belangenverstrengeling

Voor bijeenkomst mogelijk relevante relaties met bedrijven

nvt

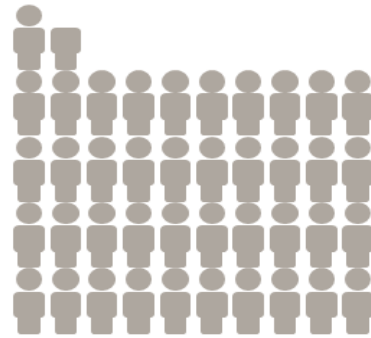
- Sponsoring of onderzoeksgeld
- Honorarium of andere (financiële) vergoeding
- Aandeelhouder
- Andere relatie, namelijk:

Caelus health

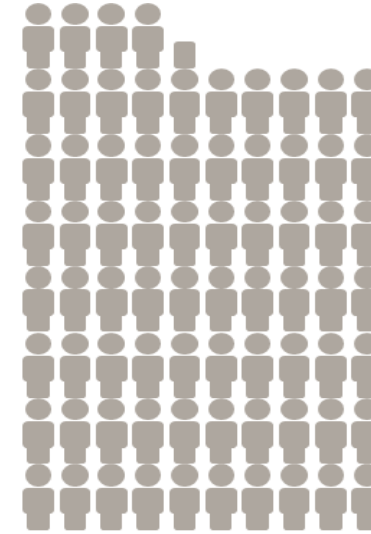
Conclusions The diabetic foot

- High morbidity and costs of diabetic foot treatment in health care!
- Diagnostic tools to classify diabetic foot ulcer: always check neuropathy and arterial pulses (for differentiation neuropathic vs vascular ulcer)
- Most infection of diabetic foot are due to multiple bacteria (grampositive > gram negative)
- Bone biopsy culture (eg via intervention radiology) better yield than superficial woundswab culture
- Osteomyelitis: diagnosis (culture + radiologic diagnosis), treatment with (oral) antibiotics followed by surgical (PTA/bypass) intervention or amputation
- Charcot foot is rare diagnosis (red foot after trauma, no wound present) diagnosis via radiological imaging, treatment is total contact cast.

Increased incidence of diabetes



415 million
2015



642 million
2040

Despite increased incidence, less mortality in DM; Thus a different complication spectrum

Diabetes-related complication in USA, 1990-2010

Less MI, more CKD peripheral artery disease: Due to use of statins and antihypertensives?

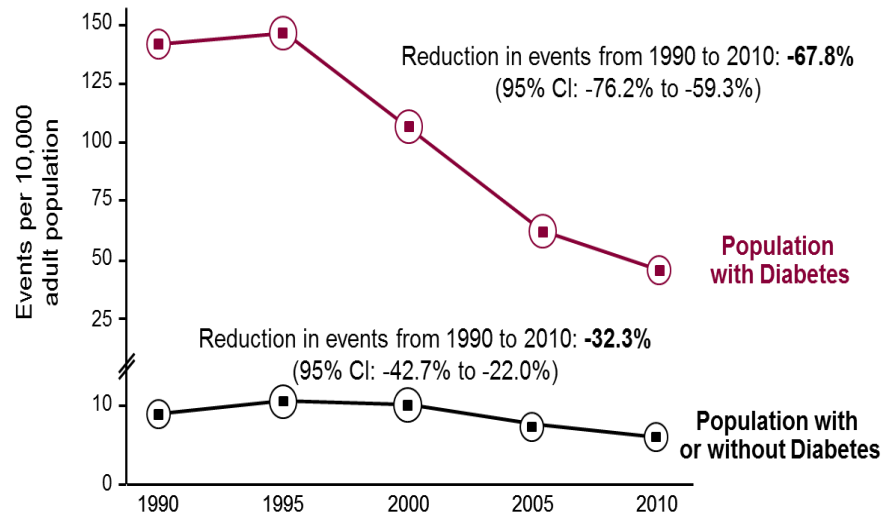


Table 2. Age-Standardized Rate of Diabetes Complications per 10,000 U.S. Adults, with or without Diagnosed Diabetes.*

| Variable | 1990 | 1995 | 2000 | 2005 | 2010 | Change, 1990–2010 | | P Value† | |
|--|------------------|--------------------|-------------------|------------------|------------------|--------------------------|-------------------------|-------------------|--------------|
| | | | | | | Absolute Change (95% CI) | Percent Change (95% CI) | Change, 1990–2010 | Linear Trend |
| No. of adults in overall population | 177,705,141 | 189,632,670 | 201,595,867 | 213,680,406 | 226,144,631 | | | | |
| Acute myocardial infarction | | | | | | | | | |
| No. of cases | 140,122 | 183,605 | 191,011 | 158,616 | 135,743 | -4,379 | | | |
| No./10,000 persons (95% CI) | 8.5 (7.9 to 9.0) | 10.1 (9.5 to 10.6) | 9.6 (9.0 to 10.2) | 7.3 (6.8 to 7.8) | 5.7 (4.9 to 6.5) | -2.7 (-3.7 to -1.8) | -32.3 (-42.7 to -22.0) | <0.001 | 0.23 |
| Stroke | | | | | | | | | |
| No. of cases | 127,016 | 162,895 | 178,755 | 171,429 | 186,719 | 59,703 | | | |
| No./10,000 persons (95% CI) | 7.6 (7.1 to 8.2) | 8.9 (8.3 to 9.4) | 9.0 (8.4 to 9.6) | 8.0 (7.5 to 8.5) | 7.9 (6.7 to 9.1) | 0.3 (-1.0 to 1.5) | 3.4 (-13.5 to 20.3) | 0.35 | 0.86 |
| Amputation | | | | | | | | | |
| No. of cases | 50,364 | 76,531 | 80,658 | 69,074 | 73,067 | 22,703 | | | |
| No./10,000 persons (95% CI) | 3.0 (2.7 to 3.3) | 4.2 (3.8 to 4.6) | 4.0 (3.6 to 4.5) | 3.2 (2.9 to 3.5) | 3.0 (2.5 to 3.6) | -0.01 (-0.6 to 0.6) | -0.5 (-21.3 to 20.4) | 0.97 | 0.90 |
| End-stage renal disease | | | | | | | | | |
| No. of cases | 17,763 | 29,259 | 41,477 | 46,917 | 50,197 | 32,434 | | | |
| No./10,000 persons (95% CI) | 1.1 | 1.6 | 2.1 | 2.2 | 2.1 | 1.0 | 90.9 | — | — |
| Death from hyperglycemic crisis | | | | | | | | | |
| No. of cases | 2890 | 2666 | 2422 | 2254 | 2361 | -529 | | | |
| No./10,000 persons (95% CI) | 0.17 | 0.15 | 0.12 | 0.10 | 0.10 | -0.07 | -42.0 | — | — |

**Every 20 seconds somewhere in the world
a leg is lost as a consequence of diabetes**



Epidemiology of diabetic foot

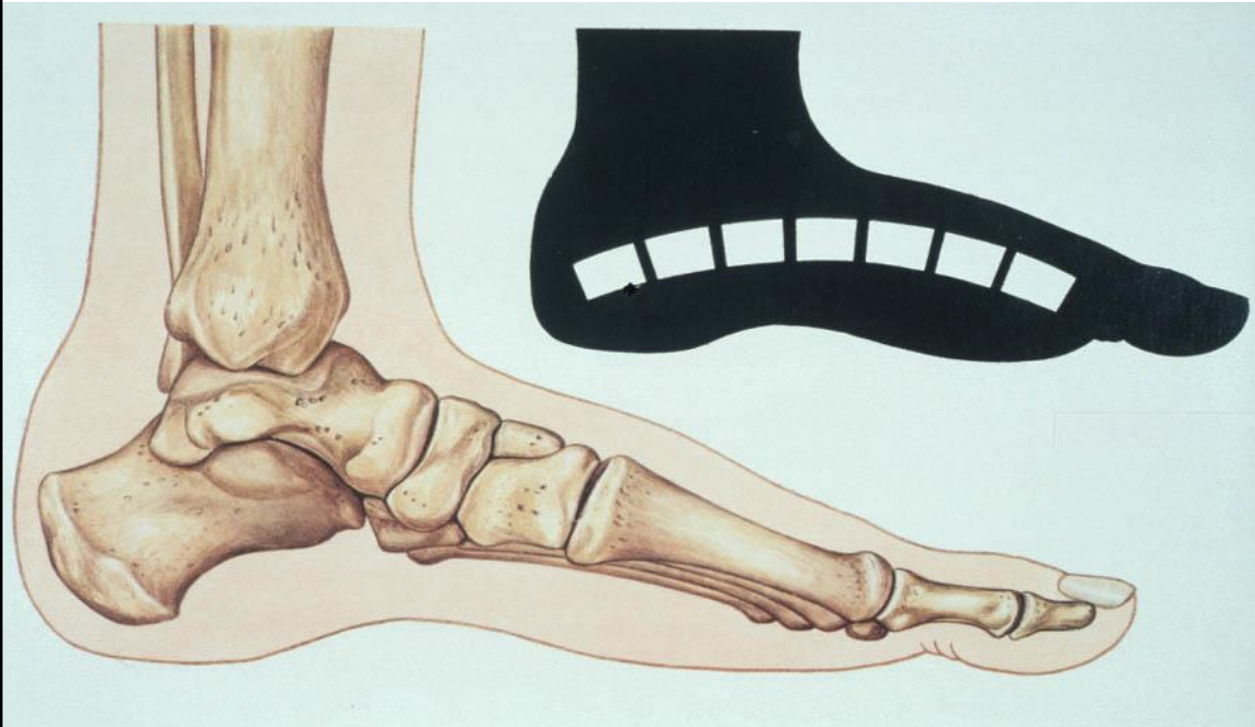
- Amount of patients with diabetes in Netherlands: 1.100.000(2019 and expected to be 1,3 miljoen in 2040 (data RIVM)
- Incidence of diabetic foot ulcer in NL: 2,2% (~ 22.000 per year)
- Takes up 30 - 40% of healthcare costs spent on diabetes in Netherlands
- Yearly in Netherlands about 3500 amputations due to diabetes
- High disease burden for both patient voor patiënt (**QoL = smallcell lung cancer**) and for health care

- At Amsterdam UMC data (100 new patients per year at our footclinic, 1150 patients analysed of the last 10 years):
 - - about 70-80% of patients is cured
 - - only 15% ends up with amputation of toe / (part of) leg
 - -average time of woundhealing : 2-3 months
 - -recurrence: 40% in 1 year



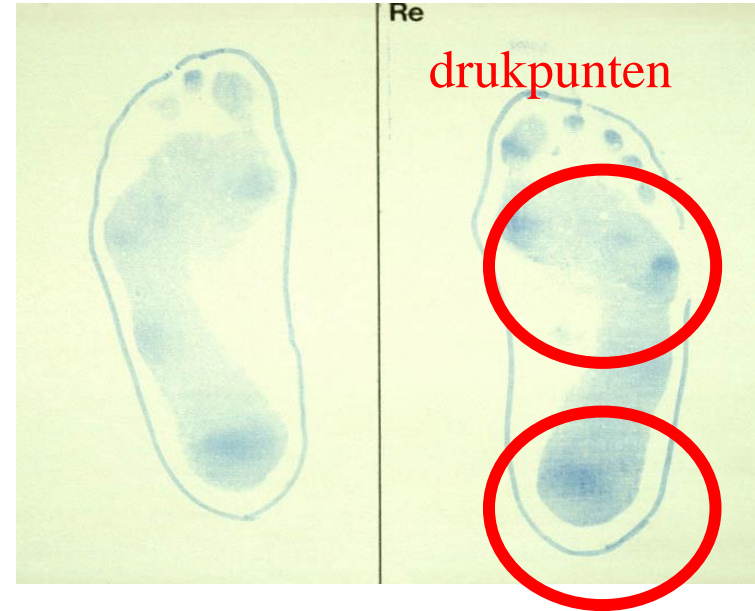
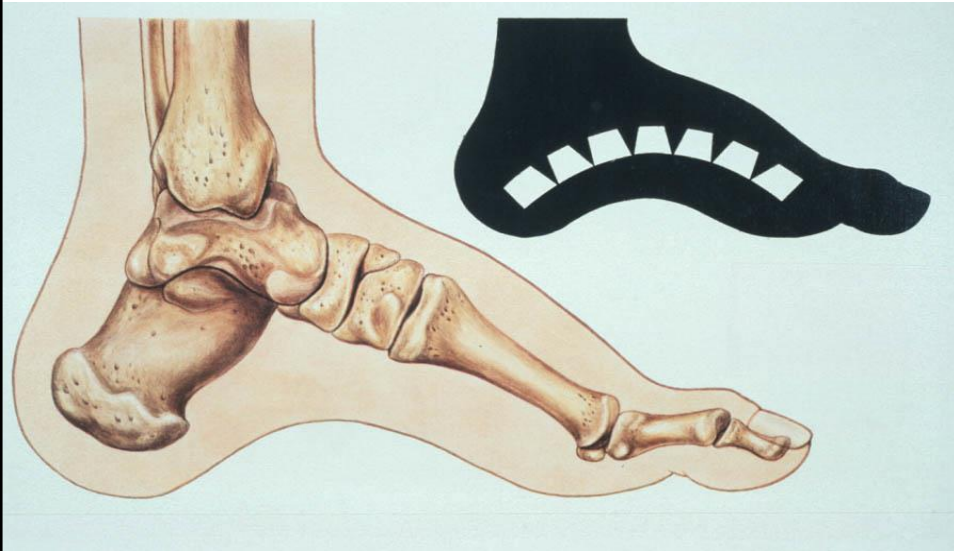
Aetiology Diabetic foot: role of neuropathy and muscle atrophy

normal foot

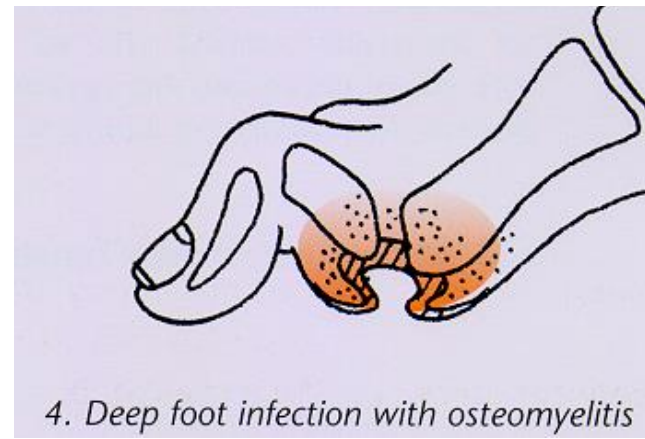
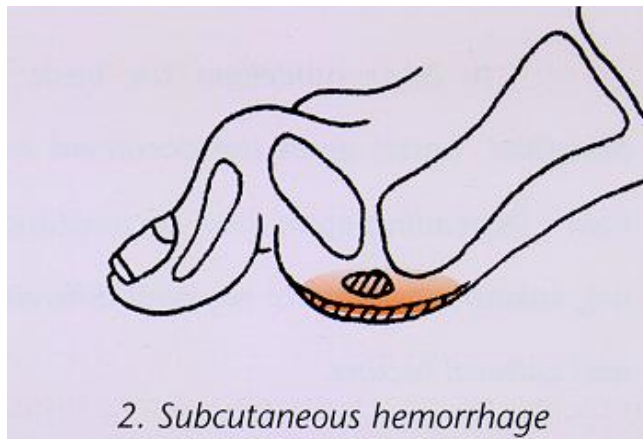
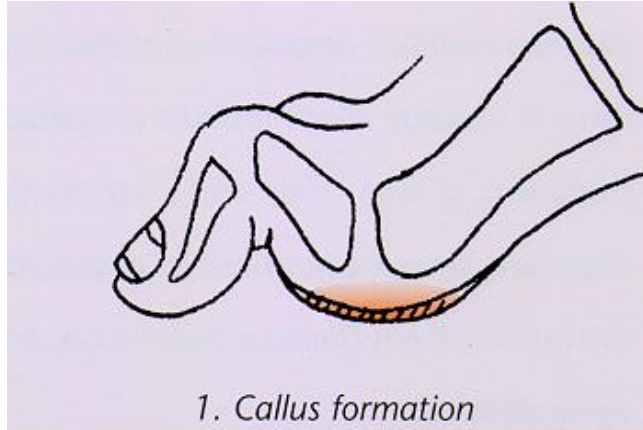


Aetiology Diabetic foot: role of neuropathy and muscle atrophy

diabetic foot



From high footpressure to wound/infection



Diabetic foot, not always infection

Dhr K. 56 years

DM type 1 since 1997, poorly regulated

3 weeks ago swollen and red left foot to GP

GP: starts Augmentin on the diagnosis of cellulitis

However, no wound /infection parameters in blood, no effect on antibiotics

LO: neuropathy from knee down, good arterial pulsations. At conventional xray; midfoot white;



Differential diagnosis

DD:

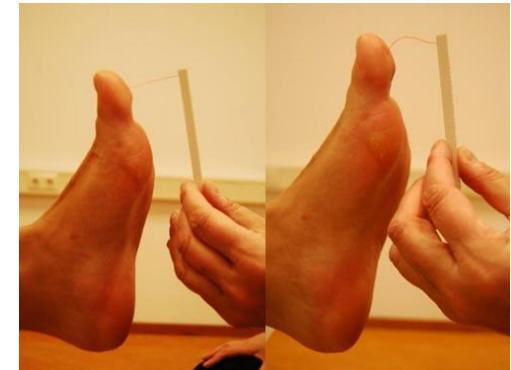
- Cellulitis
- Osteomyelitis
- Gout
- Charcot foot
- Deep venous thrombosis
- Rheumatoid arthritis



Diabetic neuropathy

Diagnostics: testing sensoric and gnostic function

Sensoric function: Semmes-Weinstein monofilament



Gnostic function: tuning fork or vibratip



Peripheral artery disease: feel a dorsalis pedis en tibialis posterior pulsations



Dutch guideline for diabetic foot 2017 (1)

- 1. How to investigate diabetic foot ulcer?**
- 2. Interventions to reduce risk of (recurrent) ulcer**
- 3. Classification ulcer**
- 4. Diagnosis and severity of diabetic foot infection**
- 5. Diagnosis & treatment of osteomyelitis**
- 6. Diagnosis PAOD and effect vascular intervention on healing**
- 7. Foot Pressure lowering interventions on healing**

Dutch guideline for diabetic foot 2017 (2)

- 8. (Evidence based) wound treatment products**
- 9. Systemic hyperbaric oxygen therapy**
- 10. Amputation: when, how and which specialists to be involved?**
- 11. Optimal timing of these treatment modalities**
- 12. patient information about selfcare/management and
alarmsymptoms**
- 13. Diagnosis and treatment of acute Charcot foot**
- 14. Multidisciplinary team for treatment of diabetic foot**

Most important updates in this new guideline: ***prevention, risk classification and bonebiopsy***

- 1. kidneydialysis patients = high risk category for amputation upon diabetic foot**
- 2. When In doubt about vascular status : have toe (Doppler) blood and oxygenpressure analysed**
- 3. Orthopedic Shoes made based on plantar foot pressure measurements**
- 4. For identification of bacteria driving osteomyelitis: use botbiopsy/deep wound culture instead of superficial woundswab**
- 5. Motivate patient to do daily foot temperature measurements to prevent ulcer recurrence and drive early treatment**

Diabetes ulcer treatment-1



- **Wagner Classification (also measure size/depth wound and make picture for objective followup)**
- **Feel pulations (+ pressure measurement))**
- **Early use of endovascular intervention (PTA)**
- **Hyperbaric oxygen treatment is investigated**
- **Culture (deep woundculture) or osteomyelitis (ultrasound guided) botbiopsy for anaerobic culture**

| Grade | Description of ulcer |
|-------|--|
| 0 | intact skin in patients who are at risk |
| I | superficial ulcers with exposed subcutaneous tissue |
| II | exposed tendon and deep structures |
| III | ulcers extend to the deep tissue and have either associated soft tissue abscess or osteomyelitis |
| IV | ulcers include feet with partial gangrene |
| V | feet ulcers with more extensive gangrenous tissue |

Wagner classification for diabetic foot ulcers

Diabetes ulcer treatment-2

- **Time = tissue !**
- **Window for vascular diagnostics < 1 -2 weeks**
- **Total contact cast (TCC)/Gips = best choice if a foot plantar pressure ulcer keeps recurring**
- **Wondressing products: no evidence of faster healing**
- **Criteria for multidisciplinary diabetic foot ulcera team**
- **Certified diabetic foot ulcer centers in netherlands**

Multidisciplinary Diabetic foot ulcer team

Amsterdam UMC, location AMC

100 new patients

300 controls per
jaar



Internist

Vascular Surgeon

podiatrist

rehabilitation

physician

Every 2 weeks
multidisciplinary
radiology meeting



Diagnostic algorithm for footulcer



- Establish with temperature or your hand if there is **> 2 C temperature difference** between both feet
- Test for signs of neuropathy
- Ask for signs of vascular disease (claudicatio intermittens and resting pain)
- **Feel foot pulsations, if absent determin** ankle-arm index and toe oxygen/bloodpressure
- Check systemic signs of infection (fever and endocarditis stigmata)
- establish **size and depth** of ulcer after removing callus (bonecontact?)
- Make picture of wound for objective followup.
- Ask for cause of ulcer.
- Check and (also feel) and feel in shoes of patients



Texas classification of ulcer

- Neuropathic 50%
- Ischemic (PAOD) 10%
- Neuro-ischemic 40%

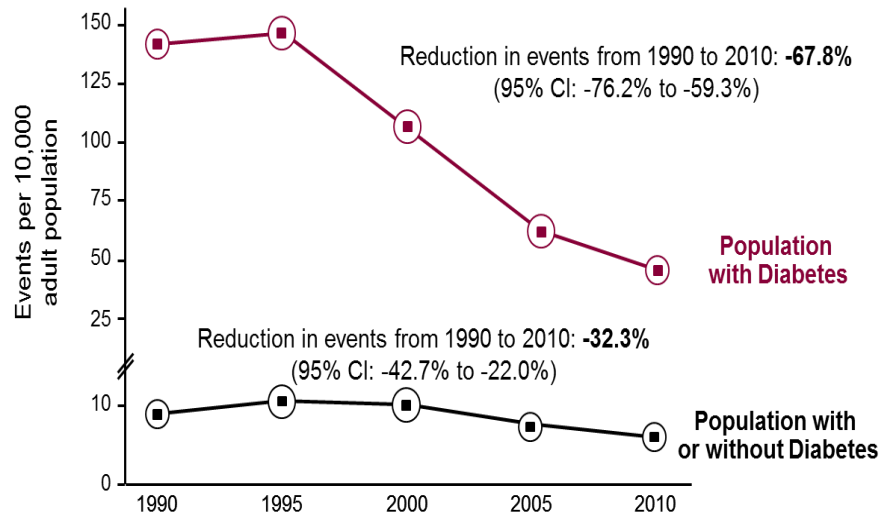


Neuropathisch ulcus



Neurovasculair ulcus

Texas classification



UT Diabetic Foot Wound Classification System

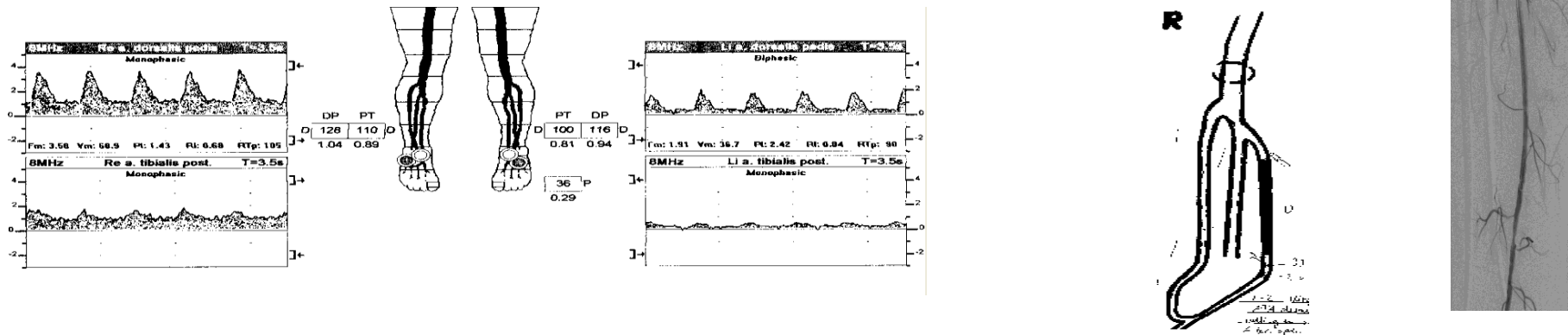
| Grade | 0 | 1 | 2 | 3 |
|-------|--|---|--|------------------------------------|
| A | Pre or postulcerative lesion completely epithelialized | Superficial wound, not involving tendon, capsule, or bone | Wound penetrating to tendon or capsule | Wound penetrating to bone or joint |
| B | with infection | with infection | with infection | with infection |
| C | with ischemia | with ischemia | with ischemia | with ischemia |
| D | with infection and ischemia | with infection and ischemia | with infection and ischemia | with infection and ischemia |

University of Texas Diabetic Foot Wound Classification System. 27

Changes in ulcer pathophysiology over 10-20 years due to CVD medication and better glycemic control

Diagnostics of (neuro)vascular ulcer

- Check claudicatio intermittens, (resting) ischemic pain and check foot pulsations as well as perform ankle/arm index of both legs



- If ankle-arm index < 0.9 or > 1.3 (**vals verhoogd**) \rightarrow have additional radiological evaluation (CT angio) or echo duplex **affected limb** done

Interventions to improve PAOD: dotter procedure or vascular Bypass

- When toe pressure is <50 mmHg;
- Ankle arm index is $<0,5$, with toepressure <30 mmHg and/or;
- Oxygen toepressure is (tcpO <25 mmHg).

- Also, consider vascular intervention if there is;-
 - large (infected) wound (>5 cm)
 - deep wound (texas > 3);
 - Wound of calcaneus
 - When a patient is on hemodialysis or has chronic kidney failture (creatin clearance < 20 ml/min)

When you think of a osteomyelitis, that is best prognostic value!

Table 2. Diagnostic Accuracy of Physical Examination and Laboratory Investigations for Lower Extremity Osteomyelitis in Patients With Diabetes Mellitus

| Source | Examination Maneuver/Finding | Positive LR (95% CI) | Negative LR (95% CI) |
|-----------------------------------|---|----------------------|----------------------|
| Newman et al, 1991 ⁹ | Bone exposure ^a | 9.2 (0.57-146) | 0.70 (0.53-0.92) |
| Newman et al, 1991 ⁹ | Ulcer area >2 cm ^{2a} | 7.2 (1.1-49) | 0.48 (0.31-0.76) |
| Newman et al, 1991 ⁹ | Ulcer inflammation (erythema, swelling, purulence) ^a | 1.5 (0.51-4.7) | 0.84 (0.56-1.3) |
| Clinical Gestalt | | | |
| Newman et al, 1991 ⁹ | Clinical judgment ^a | 9.2 (0.57-147) | 0.70 (0.53-0.92) |
| Vesco et al, 1999 ⁴⁰ | Wagner grade >2 ^a | 13 (0.82-203) | 0.48 (0.27-0.86) |
| Enderle et al, 1999 ²⁴ | Wagner grade >2 ^a | 3.9 (0.96-16) | 0.04 (0-0.70) |
| Summary LR ^b | | 5.5 (1.8-17) | 0.54 (0.30-0.97) |

What to do when you think of an osteomyelitis under the ulcer

- A probe-to-bone test (PTB) by probing the wound to check if you feel bone (=clinical diagnosis)
- Perform lab (CRP/sedimentation/hb/leukocytes + diff) to check for increased systemic inflammation
- Perform a conventional x ray of the foot (preferably when patient is standing) .
- Remember that sensitivity and specificity of all of these tests are not 100% , clinical judgment and low threshold to start antibiotics (after taking wound swab for culture) is key!
- Time = tissue

Usual suspect bacterial strains in diabetic wound ulcer infections (find the bug!)

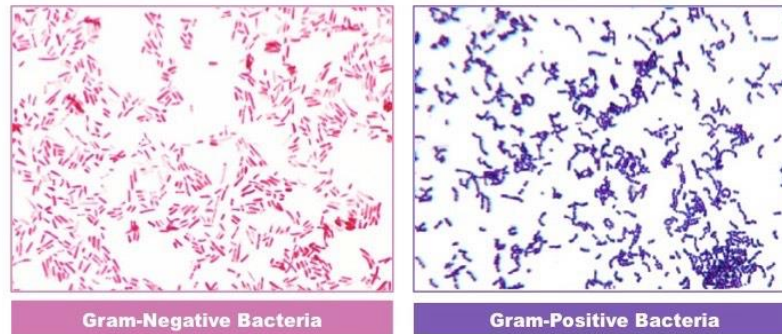
Deep wound swab (or if possible take a part of the ulcer tissue) for for gram staining (within hours) and regular microbiology cultures (2-3 days)

Ask about previous antibiotic courses!!

Gram stain:

redictive value of Gram stain is 93%, but less good for gram positive strains (75% predictive voor groei grampositieve bacterie), than gram negative ((82% voorspellende waarde voor groei gram negatieve bacterie kweek)

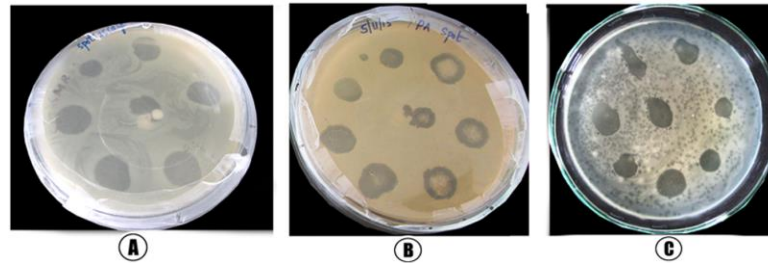
Gram-Negative Versus Gram-Positive Bacteria



Usual suspect bacterial strains in diabetic wound ulcer infections (find the bug!)

Microbiological culture:

- Bacterial flora in swab culture
- 92% bacterial strains could be types (also usually mycosis)
- -2/3 more **Gram+ bacterial strains** than gram negative



Start broad spectrum antibiotics and taper based on culture and clinical effect

Treat (toe) mycosis if present

When after first round of antibiotics, no signs of osteomyelitis curation are seen, consider bonebiopsy (with equipment for crista biopsy for hematological diagnosis)

Antibiotics treatment

Antibiotics (think of kidney function and adapt dosage) in case of woundinfection for 2 wks

- - ulcer < 1 cm; augmentin 3dd 625 mg
- ulcer > 1 cm: flucloxacilline 4dd 500mg en ciproxin 2dd 500mg

Antibiotics (think of kidney function and adapt dosage) in case of osteomyelitis suspicion for 6 wks

- flucloxacilline 4dd 1000mg / clindamycine 3dd 600mg
- ciproxin 2dd 750mg



Acute and chronic pressure offloading

- **Acute offloading**
- Felt (vilt) treatment
- TCC casts



- **Chronic offloading (shoes and surgery)**
- Achillestendon elongation
- Flexor tenotomy of toes (to resolve clawing of toes)
- Inlays and Orthopedic shoes



Complications (longterm) of diabetic ulcus/osteomyelitis

- Sepsis due to osteomyelitis with soft tissue infection
- More rare: -Spondylodiscitis
- Endocarditis
- Amputation (usually start of more amputations)

What can the patient do him/herself?

Only walk inside and outside on sandals or shoes (not on bare foot)

- Daily inspection of feet by patient self (or by partner)
- Also, do temperature measurement of both feet (either with thermometer or by back of the hand)

* 1x 4 to 6 weeks to pedicure/podotherapeut

- If there is a temperature difference ($> 2\text{ C}$) with an ulcer, than high likelihood of infection

* In that case, directly contact huisarts



Diabetic foot, not always infection

Dhr K. 56 years

DM type 1 since 1997, poorly regulated

3 weeks ago swollen and red left foot to GP

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LO: neuropathy from knee down, good arterial pulsations. At conventional xray; midfoot white;



Differential diagnosis

DD:

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- Osteomyelitis
- Gout
- Charcot foot
- Deep venous thrombosis
- Rheumatoid arthritis



Acute Charcotfoot

Acute / chronic phase:

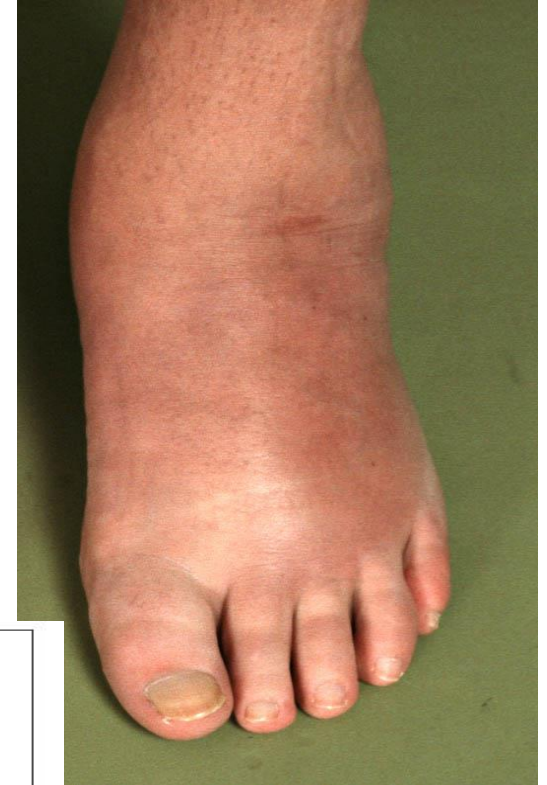
Spontaneous fractures of bone in foot

Pathophysiology not well known (but often seen after infection or small trauma)

Only in diabetes patients with neuropathy!

Presentation:

Redness, increased temperature of the foot ($>2^{\circ}\text{C}$), swelling-edema, usually no pain



"Stage 0" - hot foot, normal Xrays. MR shows bone oedema and fractures



Stage 1 - fragmentation, bone resorption, dislocations, fractures



Stage 2 - coalescence, sclerosis, fracture healing, debris resorption



Stage 3 - remodelling

Therapy of charcot foot

- Strict immobilization (3-6 months)
- With Gips (total contact cast of TCC)
- Surgery only when there is an instable foot (fixation) despite TCC cast
- Currently no medication advised in guidelines



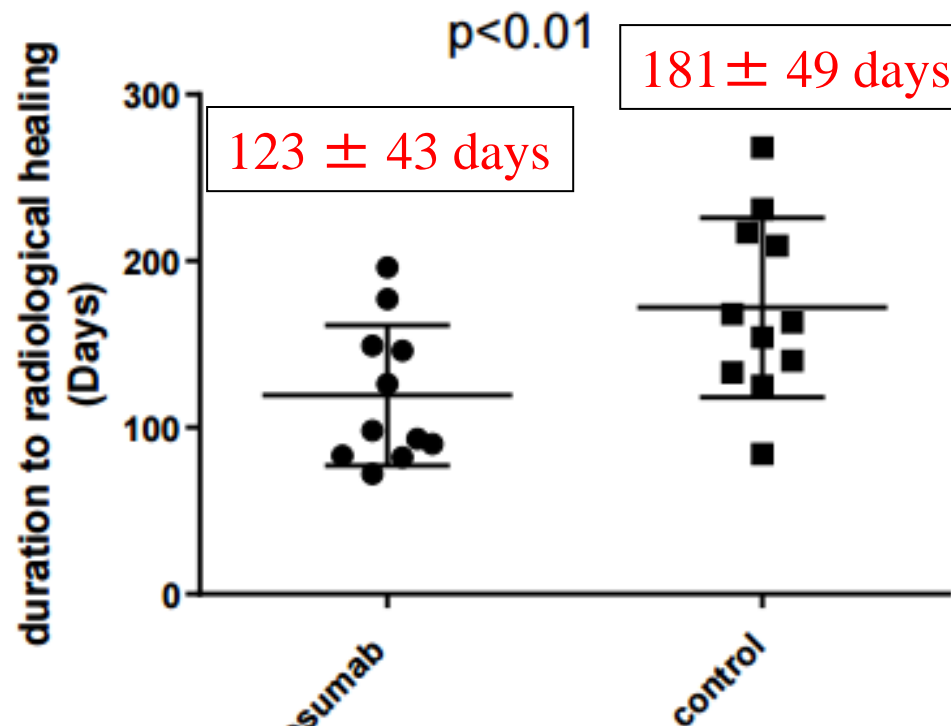
Denosumab might help to shorten TCC cast duration and prevent foot deformation upon Charcot



Effect of Single Dose of RANKL Antibody Treatment on Acute Charcot Neuro-osteopathy of the Foot

<https://doi.org/10.2337/dc17-1517>

Tessa E. Busch-Westbroek,^{1,2}
Kamiel Delpeut,^{1,2} Ron Balm,^{1,3}
Sicco A. Bus,^{1,2} Tim Schepers,^{1,3}
Edgar J. Peters,^{1,4} Frank F. Smithuis,^{1,5}
Mario Maas,^{1,5} and
Max Nieuwdorp^{1,4,6}



Thus, 2 months shorter in TCC cast after single denosumab (injection costs 60 dollar)

The phase after acute Charcot foot

Recovery

- No redness and no volume difference between both feet
- no temperature difference ($< 2^{\circ}\text{C}$)
- On conventional x ray: consolidation of fractures

Then what:

- Have people walk on orthopaedic shoes
- Explain that there is a high risk of ulcers and reinfection



Conclusions The diabetic foot

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- Osteomyelitis: diagnosis (culture + radiologic diagnosis), treatment with (oral) antibiotics followed by surgical (PTA/bypass) intervention or amputation
- Charcot foot is rare diagnosis (red foot after trauma, no wound present) diagnosis via radiological imaging, treatment is total contact cast.