Diabetic Foot Osteomyelitis:
What is New in Diagnosis &Treatment

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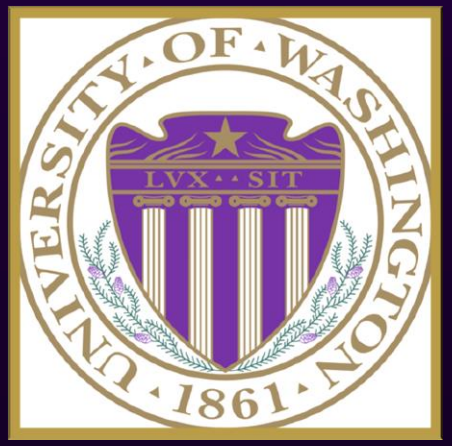

Lipsky BA, "Bone of Contention: Diagnosing DFO". *Clin Infect Dis* 2008;47:528

Overview of Diabetic Foot Osteomyelitis

- Epidemiology: common problem with high morbidity
- Pathophysiology: spread from soft tissue infection
- Microbiology: mostly *S. aureus*; often polymicrobial
- Diagnosis: tests insensitive early; non-specific late
  - Clinical (especially probe-to-bone); biomarkers
  - Imaging: X-ray; MRI; SPECT/CT; PET/CT
  - Bone culture/histopathology
- Treatment: clinician/center dependent
  - Surgical: standard; combined with antibiotics
  - Antibiotic: can be used alone; long duration
- Follow-up: difficult; at least 1 year

DIABETES/METABOLISM RESEARCH AND REVIEWS
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REVIEW ARTICLE

Diabetic foot osteomyelitis: a progress report on diagnosis and a systematic review of treatment†

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Summary

The International Working Group on the Diabetic Foot appointed an expert panel to provide evidence-based guidance on the management of osteomyelitis in the diabetic foot. Initially, the panel formulated a consensus scheme for the diagnosis of diabetic foot osteomyelitis (DFO) for research purposes, and undertook a systematic review of the evidence relating to treatment. The consensus diagnostic scheme was based on expert opinion; the systematic review was based on a search for reports of the effectiveness of treatment for DFO published prior to December 2006.

The panel reached consensus on a proposed scheme that assesses the probability of DFO, based on clinical findings and the results of imaging and laboratory investigations.

The literature review identified 1168 papers, 19 of which fulfilled criteria for detailed data extraction. No significant differences in outcome were associated with any particular treatment strategy. There was no evidence that surgical debridement of the infected bone is routinely necessary. Culture and sensitivity of isolates from bone biopsy may assist in selecting properly targeted antibiotic regimens, but empirical regimens should include agents active against staphylococci, administered either intravenously or orally (with a highly bioavailable agent). There are no data to support the superiority of any particular route of delivery of systemic antibiotics or to inform the optimal duration of antibiotic therapy. No available evidence supports the use of any adjunctive therapies, such as hyperbaric oxygen, granulocyte-colony stimulating factor or larvae.

We have proposed a scheme for diagnosing DFO for research purposes. Data to inform treatment choices in DFO are limited, and further research is urgently needed.

IDSA GUIDELINES

Clinical Infectious Diseases 2012;54(12):132–173
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2012. DOI: 10.1093/cid/cis346

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

Prepared by the IWGDF Working Group on Foot Infections

Authors

B. A. Lipsky[1], J. Aragón-Sánchez[2], M. Diggle[3], J. Embil[4], S. Kono[5], L. Lavery[6], É. Senneville[7], V. Urbancic-Rovan[8], S. Van Asten[6,9], E. J. G. Peters[9]; on behalf of the International Working Group on the Diabetic Foot (IWGDF)

Institutions

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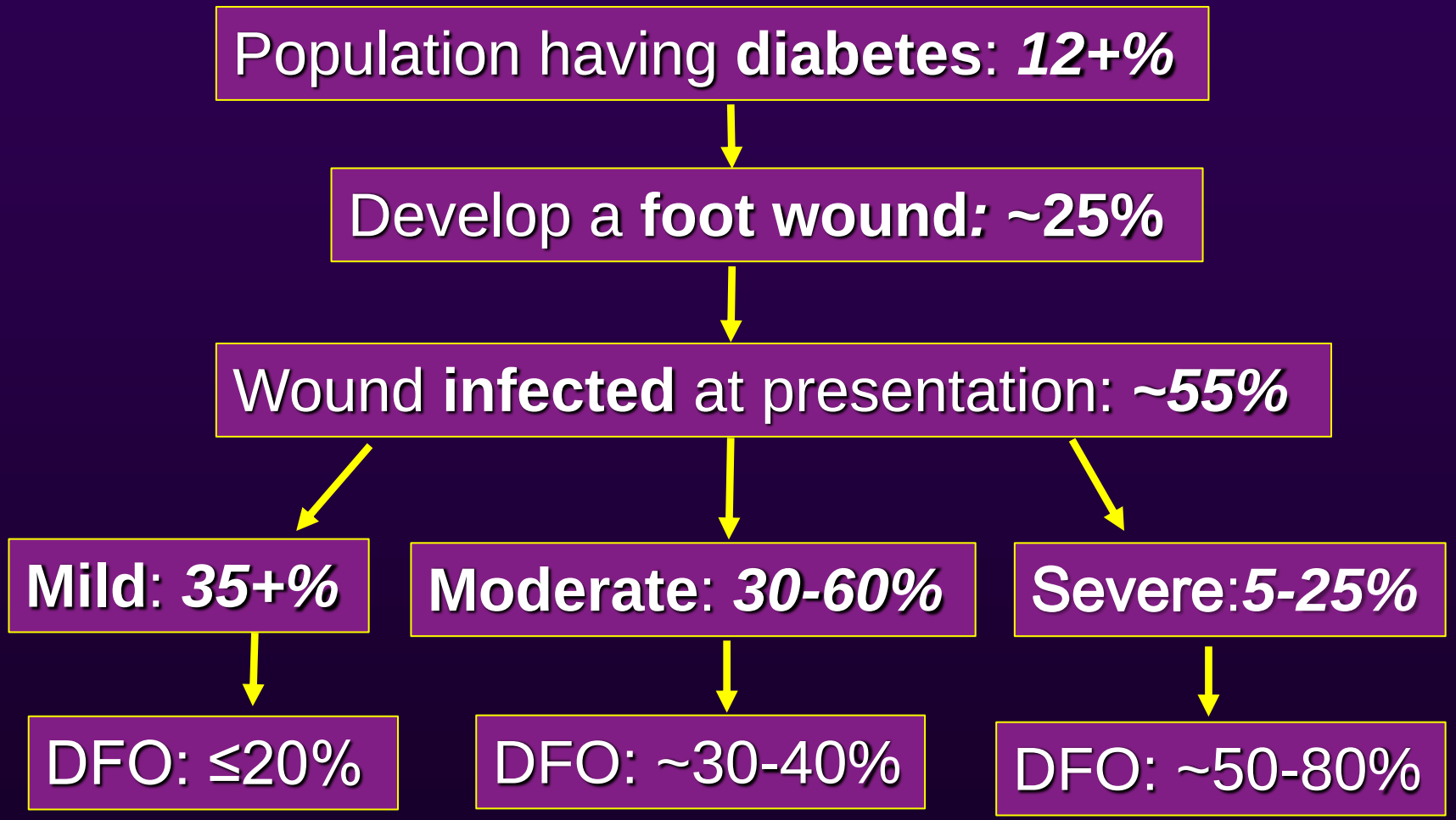
iwgdf.org/guidelines/guidance

Diab Metab Res Rev 2016;32 Suppl 1:45

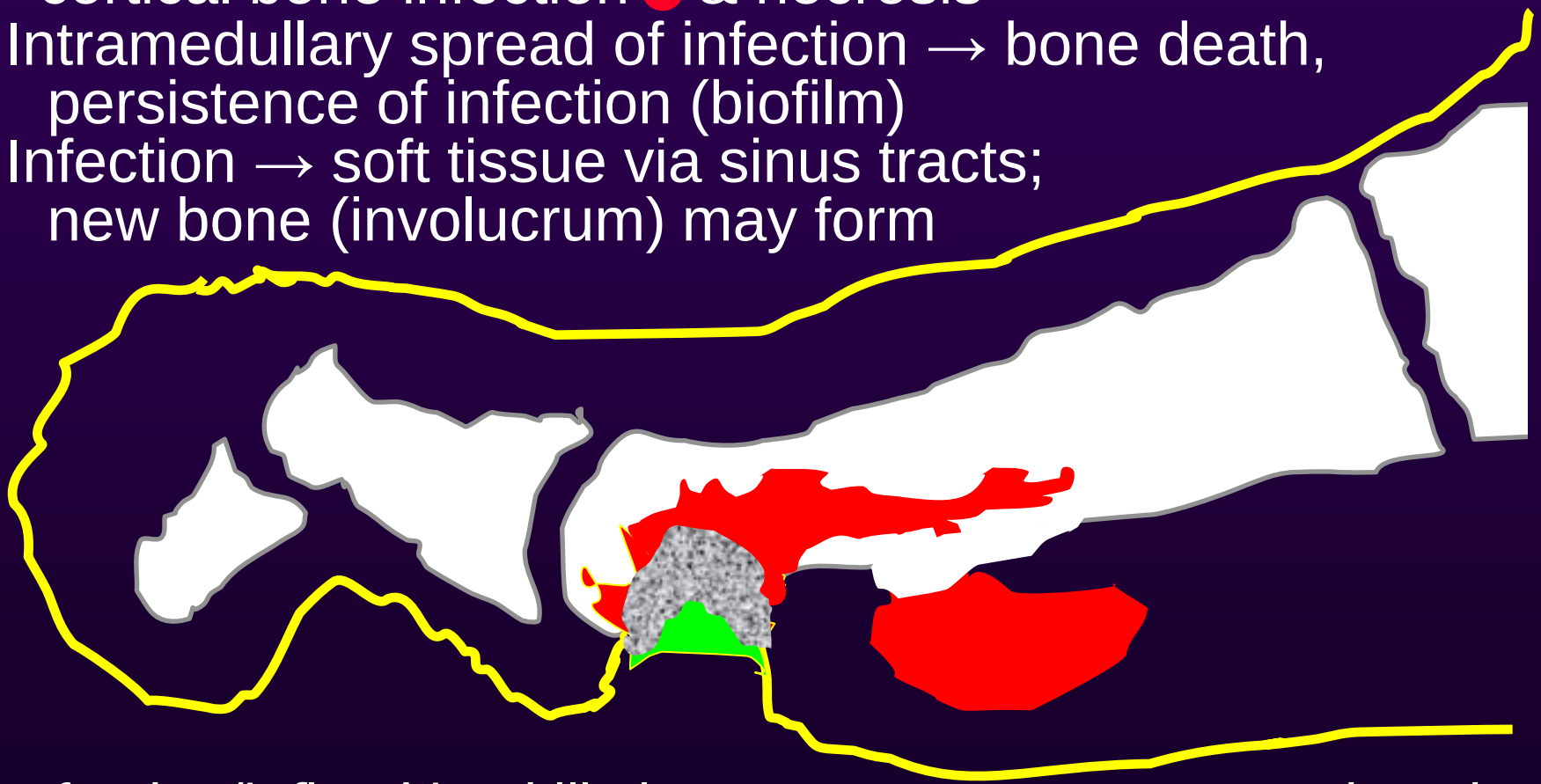
Epidemiology of Diabetic Foot Infections



Lipsky et al, *Clin Infect Dis* 2012;54:132

Pathogenesis Diabetic Foot Osteomyelitis

- Soft tissue loss & infection leads to contiguous cortical bone infection & necrosis
- Intramedullary spread of infection → bone death, persistence of infection (biofilm)
- Infection → soft tissue via sinus tracts; new bone (involucrum) may form



- Infection/inflam'tion kills bone → sequestrum; may detach

Lipsky, Berendt. *American College Physicians Medicine* 2011

Implications of Presence of Osteomyelitis in DFI

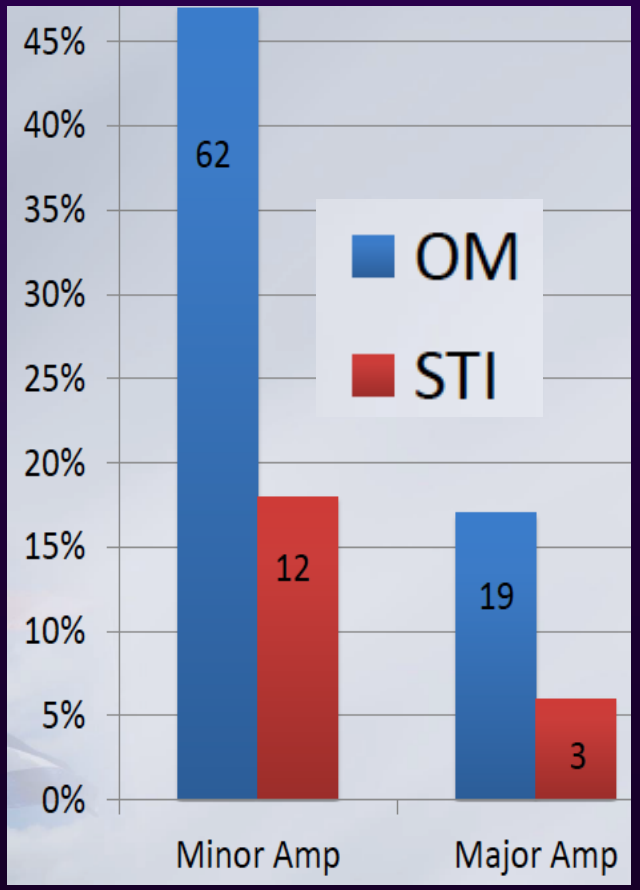
Pts hospitalized for DFI; 1 center (Istanbul) in 2 years

	Osteomyelitis (n=37)	***No Osteo*** (n=36)	p-Value
Length hospitlzn (d)	42 (29-51)	20 (13-30)	<0.001
Durtn antibiotic (d)	47 ± 20	22 ± 15	<0.001
Durtn IV antibiotic(d)	44 (31-65)	33 (23-46)	0.030
Time wound heal (d)	183 ±95	141 ± 65	0.030
Surgical procedures	24 (65%)	11 (31%)	<0.003
Minor amputation	22 (59%)	5 (14%)	<0.001

Multluoglu, Lipsky et al, *Scand J Infect Dis* 2013;45:497

DFI: Worse Outcomes with *Bone* vs *Soft Tissue* Infxn

- Retrospective review 200 pts hospitalized with DFI
- DFO dx: + bone culture or histology
- 133 pts (67%) had DFO, 80% forefoot
- Compared to STI, DFO significantly⇧
  - **Overall amptns**: 61% v 22%, OR 5.4
  - **Minor amptns**: 47% v 18%, OR 4.0
  - **Major amptns**: 17% v 5%, OR 3.6
  - Mean **length of stay**: 9.8 v 7.7 d, p=0.06



Hobizal et al, ISDF, The Hague 20 May 2015

Microbiology: Pathogens on Bone Biopsy DFO

Variables	*Lesens*	*Senneville*	*Aragon-Sanchez*
# Samples	80	76	176
Mean isol/sample	1.6 ± 1	1.54	–
%, by pathogen			
Staph aureus	33%	26%	47%
[MRSA	19%	10%	17%]
Coag-neg staph	14%	26%	11%
Streptococci	9%	12%	3%
Enterococci	12%	8%	1%
Gram − rods	20%	18%	29%
Pseud aerug	8%	2%	9%
Anaerobes	4%	5%	–

Lesens et al, *Clin Microbiol Infect* 2011;17:285

Microbiome in DFO: PCR vs Culture of Bone

Conventional Culture (n=26)		**16s rRNA Sequencing** (n=23)	
Gram + cocci	20 (77%)	Gram+ cocci	23 (100%)
S. aureus, total	13 (50)	*Staphylococcus* spp.	20 (87)
Coag – staphylococci	11 (42)	Coag – staphylococci	Not tested
Streptococcus spp.	6 (23)	*Streptococcus* spp.	13 (57)
Enterococcus spp.	2 (8)	*Enterococcus* spp.	0
Gram + bacilli	1 (4)	Gram + bacilli*	18 (78)
Corynebacterium spp.	1 (4)	*Corynebacterium* spp.	18 (78)
Gram – bacilli	13 (50)	Gram – bacilli	10 (44)
P. aeruginosa	4 (15)	*Pseudomonas* spp.	5 (22)
Anaerobes	6 (23)	Anaerobes*	20 (87)
- Facultative	3 (12)	- Facultative	17 (74)
- Obligate	3 (12)	- Obligate	20 (87)
Polymicrobial infxn	16 (64)	Polymicrobial infxn	21 (91)

* $p<0.001$ for conventional vs molecular 16s

van Asten et al, *Eur J Clin Micro Inf Dis* 2016;35:293

Diagnosing DFO: Current Methods

- Clinical
  - *History*: long wound duration; recurrent infections
  - *Exam*: deep (>3mm)/large (>2 cm^2) ulcer; bony prominence; visible bone/joint; "sausage" toe
  - *Probe-to-bone*: useful if done/interpreted correctly

Dinh et al *Clin Inf Dis* 2008;47:519; Butalia et al *JAMA* 2008;299:806
Berendt et al. *Diabetes Metab Res Rev* 2008;24 Suppl 1:S145

The Probe-to-Bone Test in DF Osteomyelitis

Method (Grayson, *JAMA* 1995):

- 14 F blunt metal probe
- Bone: gritty, hard feel

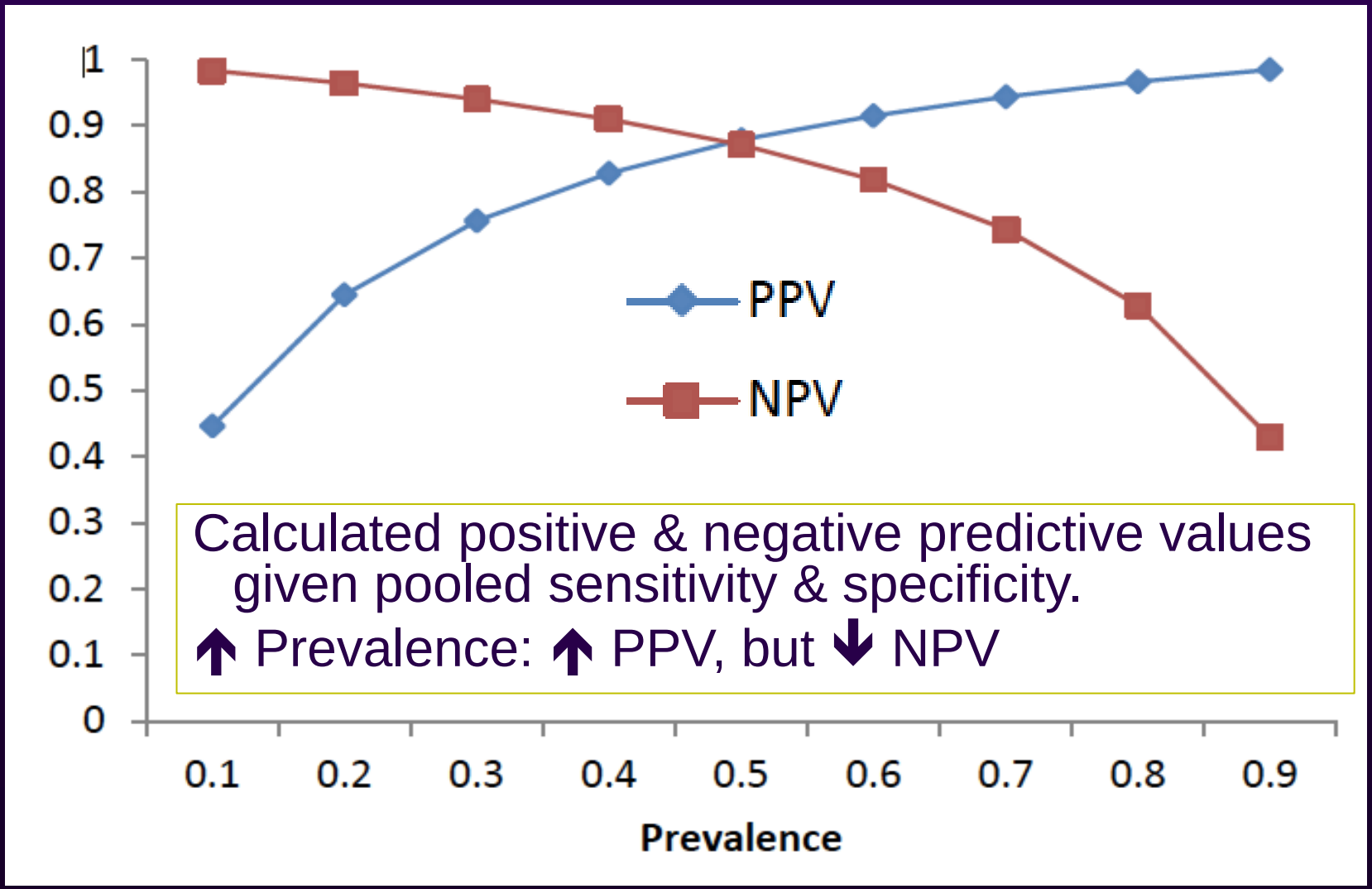
Ertugrul BM, Lipsky BA. *Diab Foot Ankle* 2013;4:10

Performance Characteristics PTB Test

Reference,yr	Pts	Sensi	Specif	PPV	NPV	DxOR
Grayson, 1995	75	.66	.85	.89	.56	11
Lavery, 2007	247	.87	.91	.57	.98	64
Aragon, 2011	338	.94	.98	.99	.83	630
Lozano, 2010	132	.98	.78	.94	.91	180
Mutluoglu, 2012	65	.67	.85	.87	.63	11
Zaiton, 2014	102	.83	.77	.92	.59	16
Pooled	**959**	**.87**	**.88**	**.92**	**.84**	**49**

Lam et al, *Clin Infect Dis* 2016 (in press)

The Importance of Prevalence in PTB Test



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Berendt et al. *Diabetes Metab Res Rev* 2008;24 Suppl 1:S145

Meta-analysis*: Biomarkers for Diagnosing DFO

Test	Sensitivity	Specificity
Single test (pooled studies)		
- ESR (n=6)	.81 (.71-.88)	.90 (.75-.96)
- WBC (n=3)	.56 (.36-.74)	.84 (.76-.90)
Combinations (1 study each)		
- CRP (>3.2)	.85	
+ depth (>3mm)	1.00	.55
- CRP (>1.4)	.85	.83
+ PCT (>0.3)	.81	.71

*8/195 studies met inclusion criteria

van Asten et al, *Curr Diabetes Rev* 2015 (epub Jul 12)

Value of Inflammatory Markers in DFO: Pilot Study

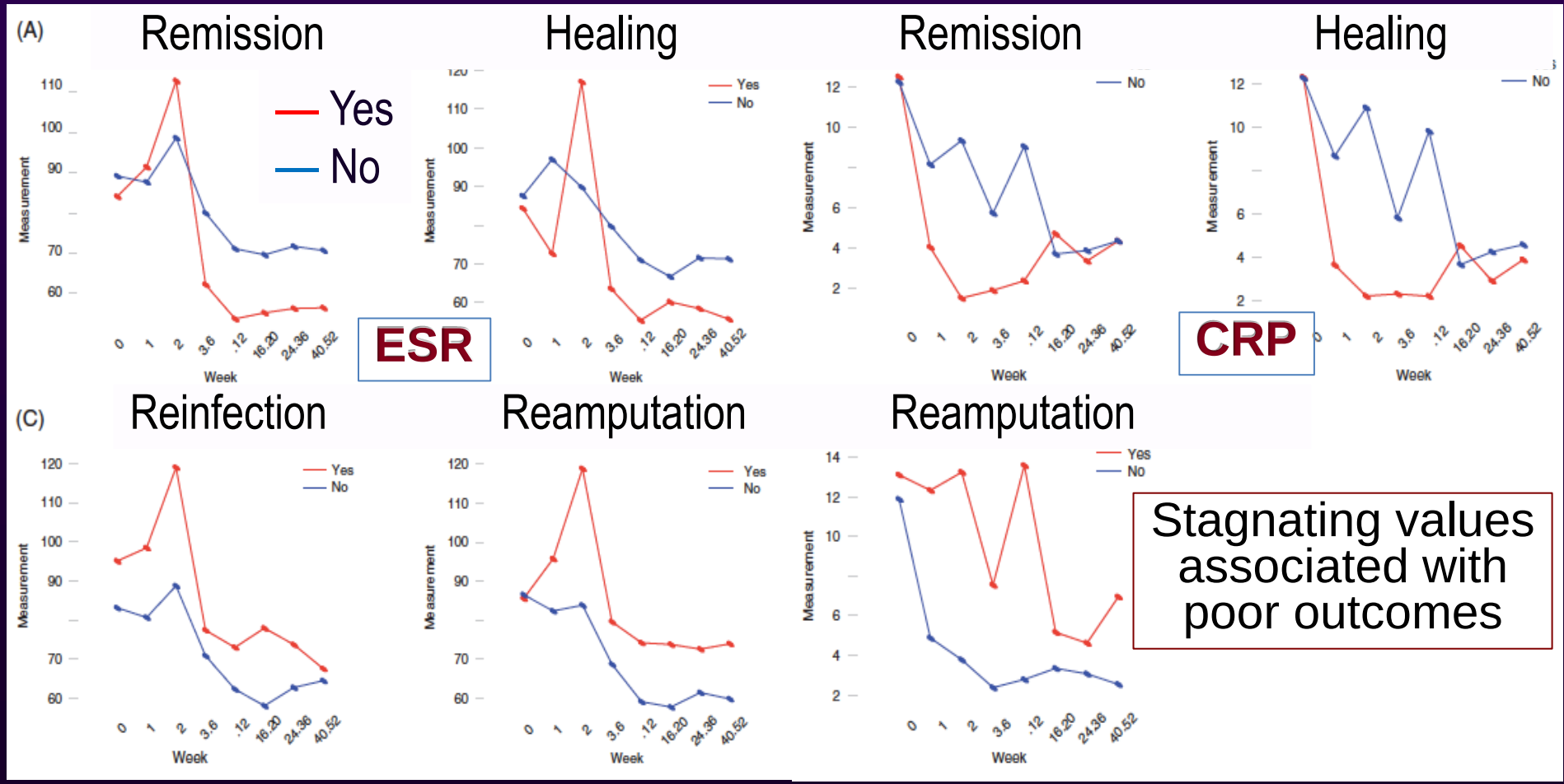
- 35 pts hospitalized with infected DFU; 24 with DFO
- Inflammatory markers measured @ baseline, 3, 6 wks

  ESR, CRP, PCT, IL-6, IL-8, tumor necrosis factor alpha (TNFα), monocyte chemotactic protein-1 (MCP-1), macrophage inflammatory protein-1 alpha (MIP1α)
- Results: no significant differences between grps except:
  - **PCT ↑** in non-osteo group at *baseline* (p=0.05)
  - **CRP, ESR, PCT, IL-6 ↓** w/ therapy in DFO (but not non-osteo) group (p=0.05)
  - **MCP-1 ↑** increased with therapy (p=0.002)
- Conclusion: inflammatory markers have limited use for differentiating bone vs soft tissue DFI

van Asten et al, *Int Wound J* 2015 (epub 3 Dec)

Inflammatory Markers Over 1 Year F/U of DFO

122 pts with bone bx proven DFO; overall ulcer healing rate 38%



van Asten et al, *Int Wound J* 2016 (epub March)

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- Imaging
  - *Plain x-ray*: limited sensi (early) & specif (late)
  - *Radionuclide scans*: WBC>bone; non-specific
  - *MRI*: best current test; marrow edema, soft tissue
  - SPECT/CT, PET/CT, PET/MRI promising; F/U

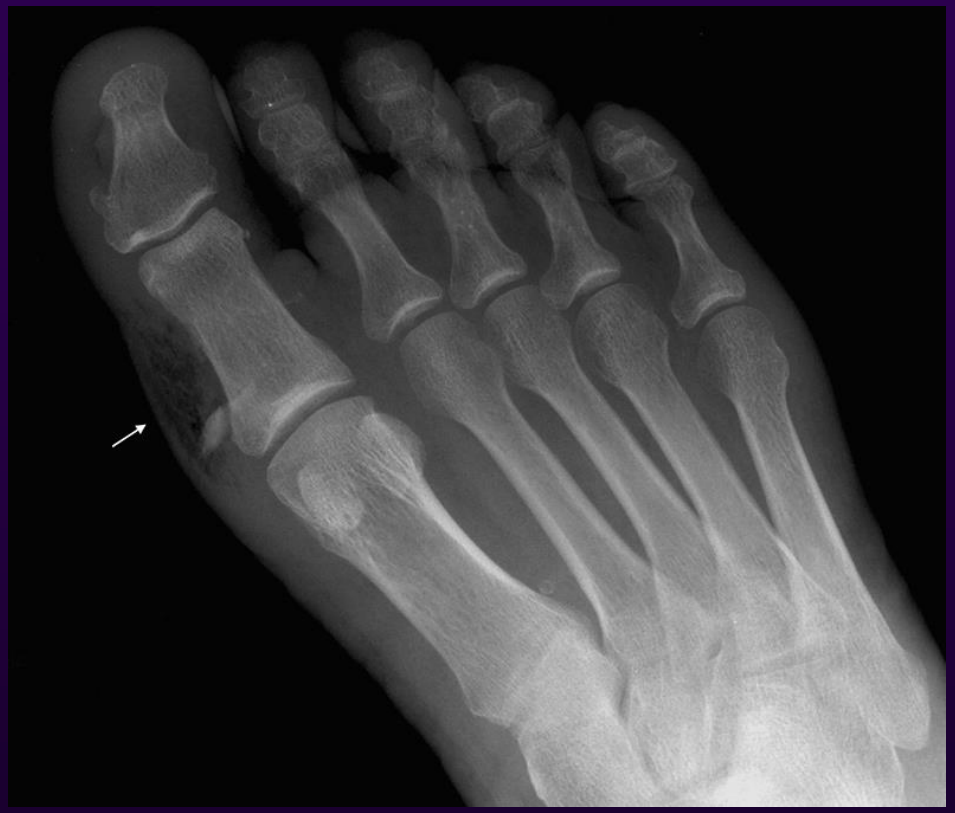
Dinh et al *Clin Inf Dis* 2008;47:519; Butalia et al *JAMA* 2008;299:806
Berendt et al. *Diabetes Metab Res Rev* 2008;24 Suppl 1:S145

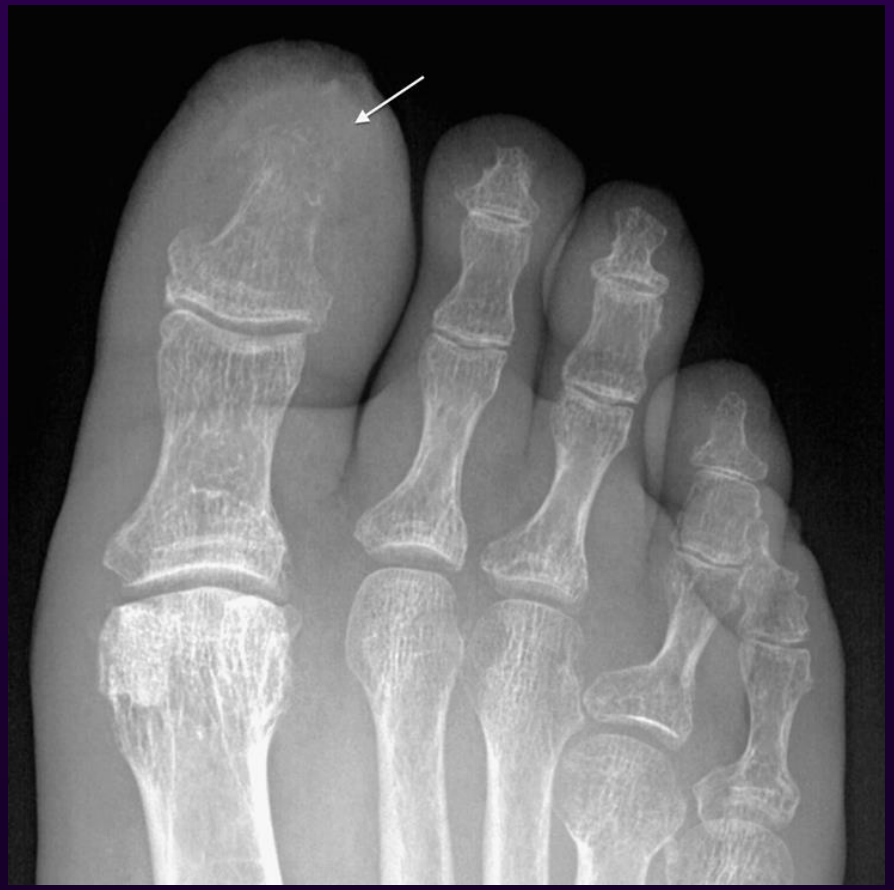
Typical Features DFO on Plain X-rays

- *Periosteal* reaction or elevation
- Loss of bone *cortex* with bony *erosion*
- Focal loss cortical *trabecular* pattern
- *Lucency* in bone marrow
- Bone *sclerosis*, with or without erosion
- Presence of *sequestrum*: dead bone; radiodense
- Presence of *involucrum*: layer of new bone growth
- Presence of *cloacae*: opening in involucrum or cortex
- Evidence of *sinus tract* from bone to soft tissue

Lipsky et al, *Diab Metab Res Rev* 2016 Jan;32 Suppl 1:45

Radiographic Features of Osteomyelitis



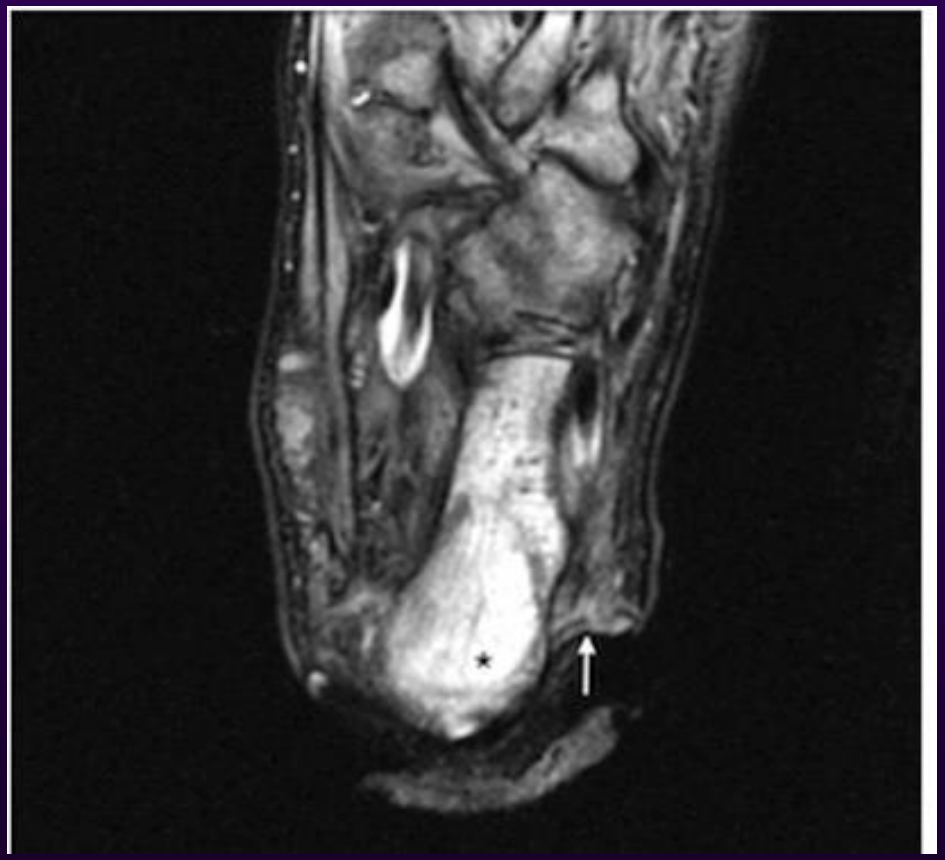


Relative Utility MRI Findings for Dx DFO

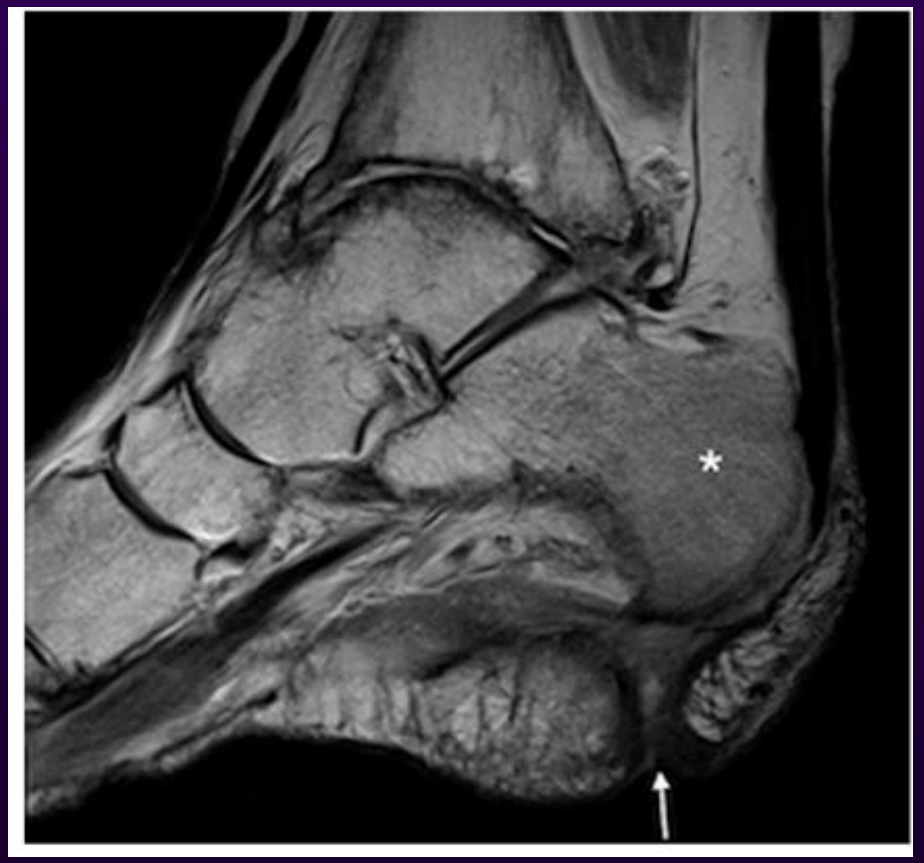
Finding	Relative Utility
⑩ ↓marrow intensity T1-w; ↑ on fluid-sensitive sequences; post-contrast enhancement	Equivocal
• Joint effusion & enhancement, subluxation & dislocation, bone frag^{mentation} & proliferation, erosion &destruction, intraarticular bodies	Equivocal
• Periosteal reaction	*
• Subtending skin ulcer	*
• Ulcer: area >2 mm or depth >3 mm	**
• Tenosynovitis	*
• Focal involvement	*
• Septic arthritis	***
• The “ghost sign” (contrast)	***
• Sinus tract, or abscess	***

Leone et al, *Skel Radiol* 2016; epub 17 Feb

MRI in Diabetic Foot Osteomyelitis



Axial T2 fat-suppressed



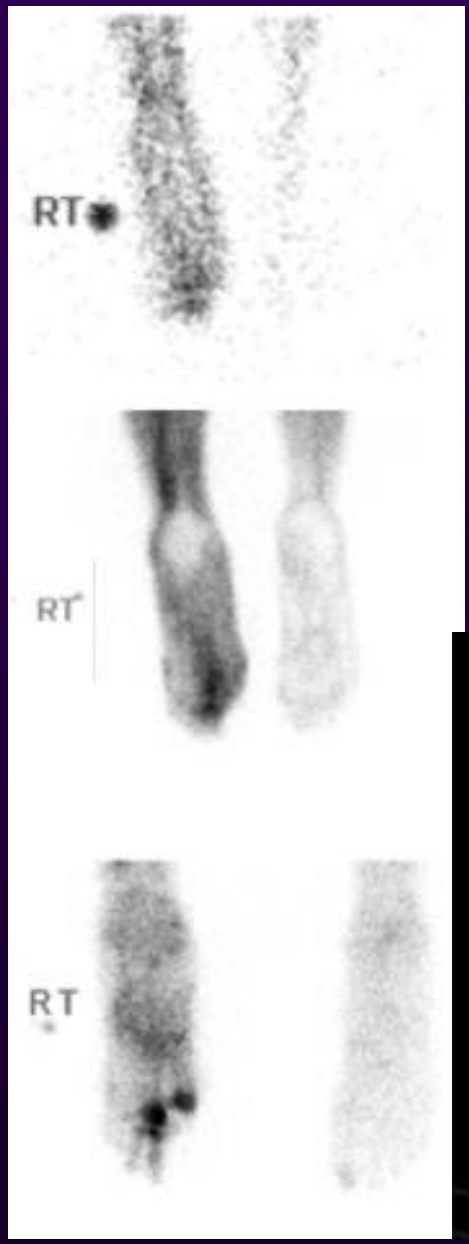
Sagittal T1

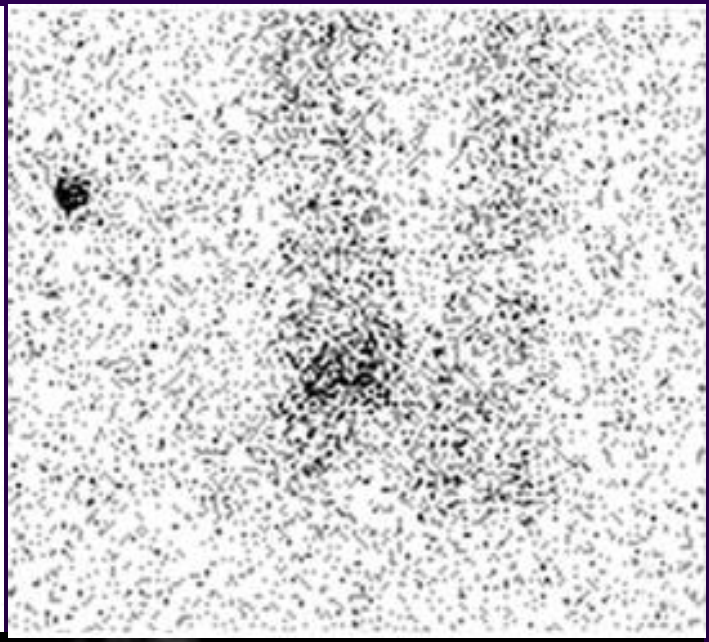
SPECT/CT

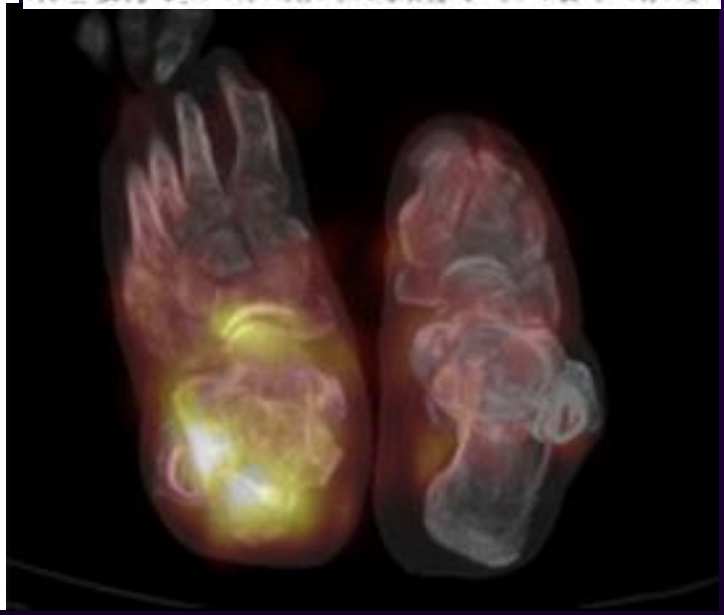
3 phase bone scan: can't differentiate recent post-op change in 1st & 2nd toes from midfoot osteomyelitis

In^{111} WBC differentiates infection from post-op changes but poor anatomical correlation

Fusion WBC SPECT/CT ⇧ specificity & good anatomical detail



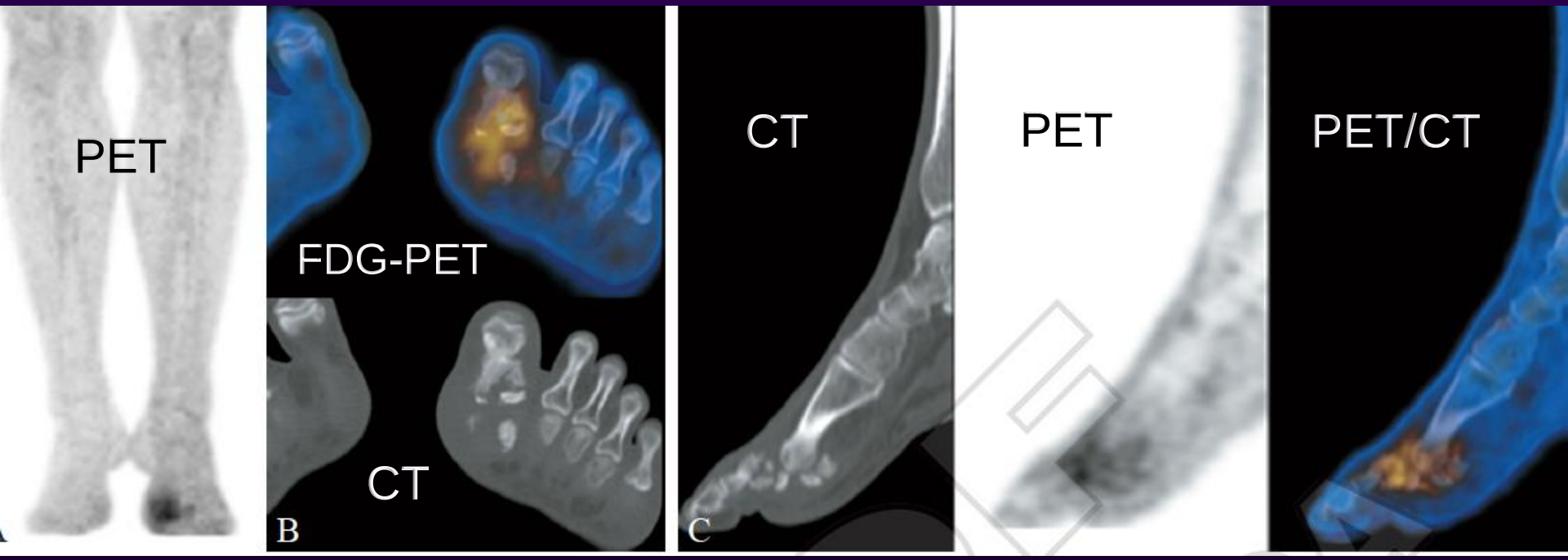




Fridman et al, *Clin Pod Med Surg* 2014;31:43

FDG-PET/CT for Diabetic Foot Osteomyelitis

L foot plantar ulcer (A) FDG-PET maximal intensity projection with focus of ⇧FDG uptake 1st toe; (B) coronal, (C) sagittal CT PET/CT: focus of uptake in fragmented 1st MT (+ bone culture)



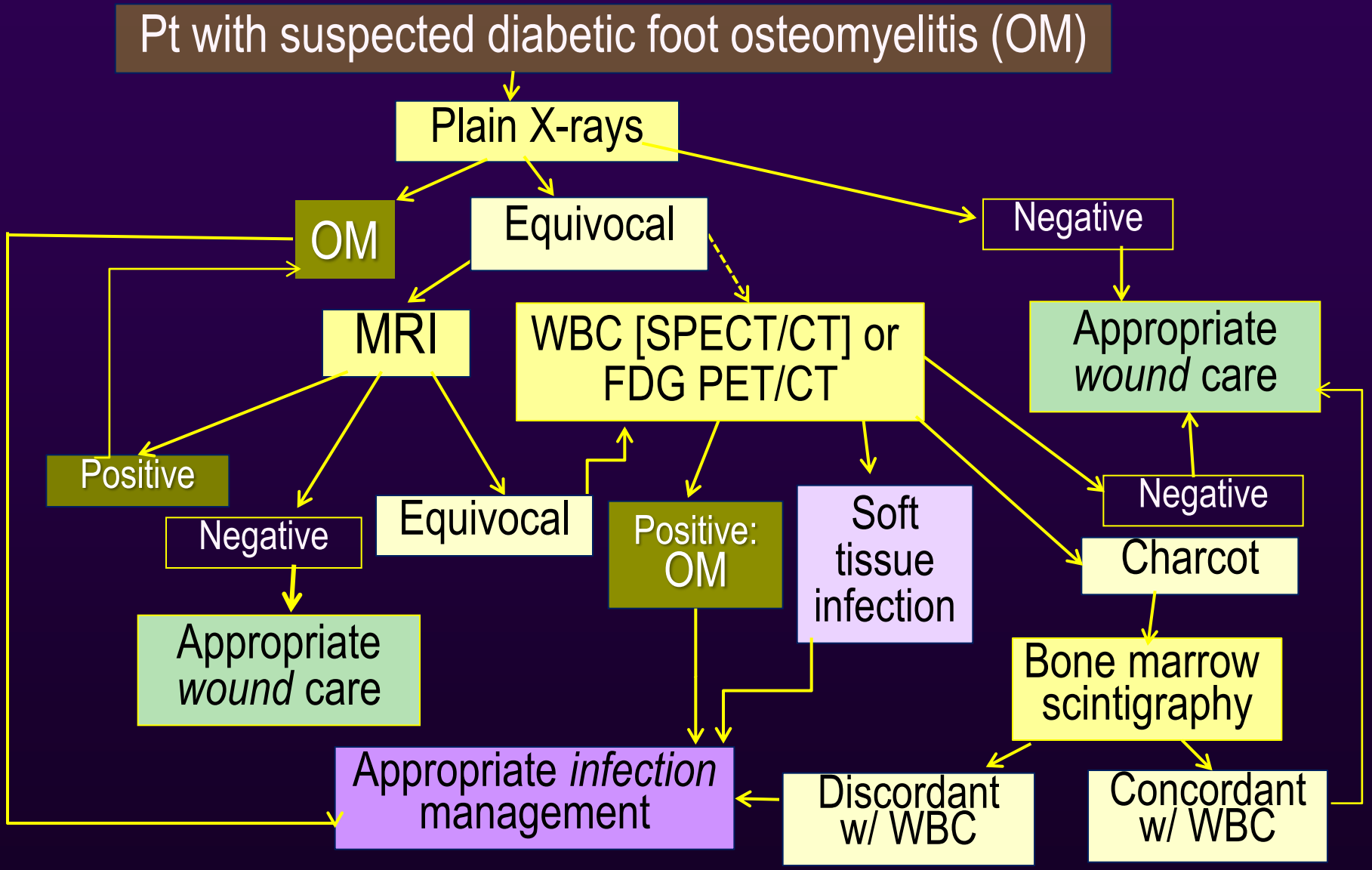
Israel, Sconfienza, Lipsky. *QJ Nucl Med Mol Imag* 2013;58:33

Advanced Imaging for Diabetic Foot Osteomyelitis

Imaging technique	+ LR	– LR	Advantages	Limitations
MRI	3.8	0.14	Good spatial resolution, high accuracy, can assess both soft tissues and bone	Reduced performance with severe ischemia
18F-FDG PET	5.6	0.4	Good spatial resolution	Limited availability; high cost
^{99m}Tc / ^{111}In labelled-leukocytes scans	4.73 / 2.31	0.12 / 0.38	High sensitivity; moderate specificity	Requires blood handling; time consuming
^{99m}Tc or ^{67m}Ga SPECT/CT	3.0	0.18	Good spatial resolution	Limited availability
^{99m}Tc-UBI 29-41 scan	Max* [*Specificity=100%]	Min*	Very high predictive values	Limited clinical data
^{99m}T bone scan	1.11	0.71	Widely available	Low specificity

Lipsky et al, *Diab Metab Res Rev* 2016 Jan;32 Suppl 1:45

Approach to Diagnosing Diabetic Foot Osteomyelitis



Israel, Sconfienza, Lipsky. *Quart J Nucl Med Molec Imag* 2013;58:33

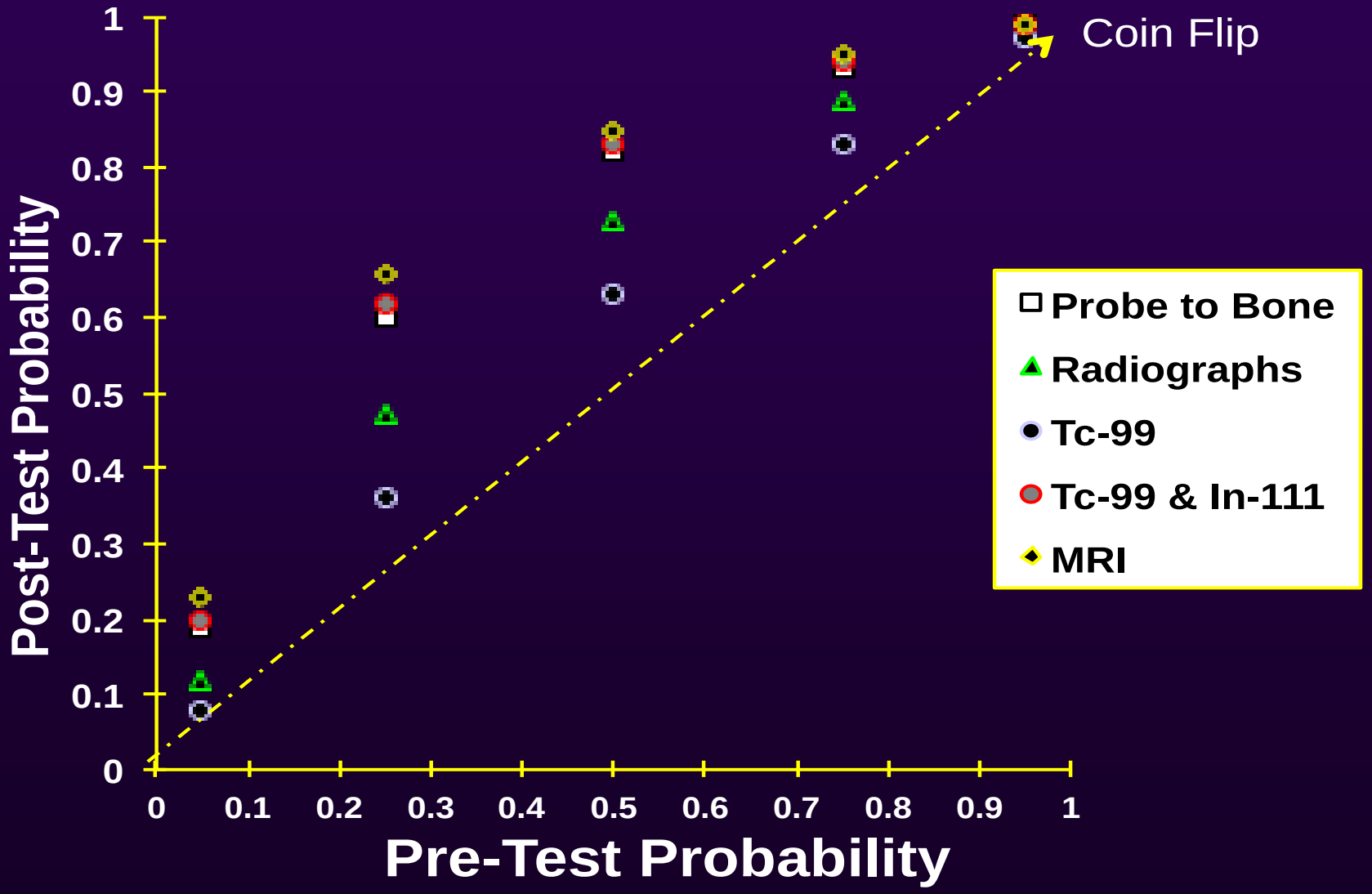
Likelihood Ratios of Diagnostic Tests for DFO*

	Diagnostic Test	+ LR	− LR
Clinical	Clinical gestalt	5.5	0.54
Clinical	***Ulcer area >2cm²***	***7.2***	0.48
Clinical	Ulcer inflammation	1.5	0.84
Biomarker	***Probe-to-bone test***	***6.4***	***0.39***
Biomarker	***ESR >70 mm/hr***	***11.0***	***0.34***
Imaging	Plain X-rays	2.3	0.63
Imaging	^{99}Tc 3 phase bone scan	1.4	0.40
Imaging	***Tc/In labeled WBC scan***	4.7/2.3	***0.12/.038***
Imaging	MRI	3.8	**0.14**
Imaging	SPECT/CT	3.0	**0.18**
Imaging	FDG-PET	5.6	0.40

*Approximations based on variable number of heterogeneous studies

Lipsky et al, IWGDF DFI guidance 2015; Markanday *OFID* 2014; 1(2):ofu060

Importance of Pre-test Probability in Dx DFO



Wrobel *JAPMA* 1998;88:337

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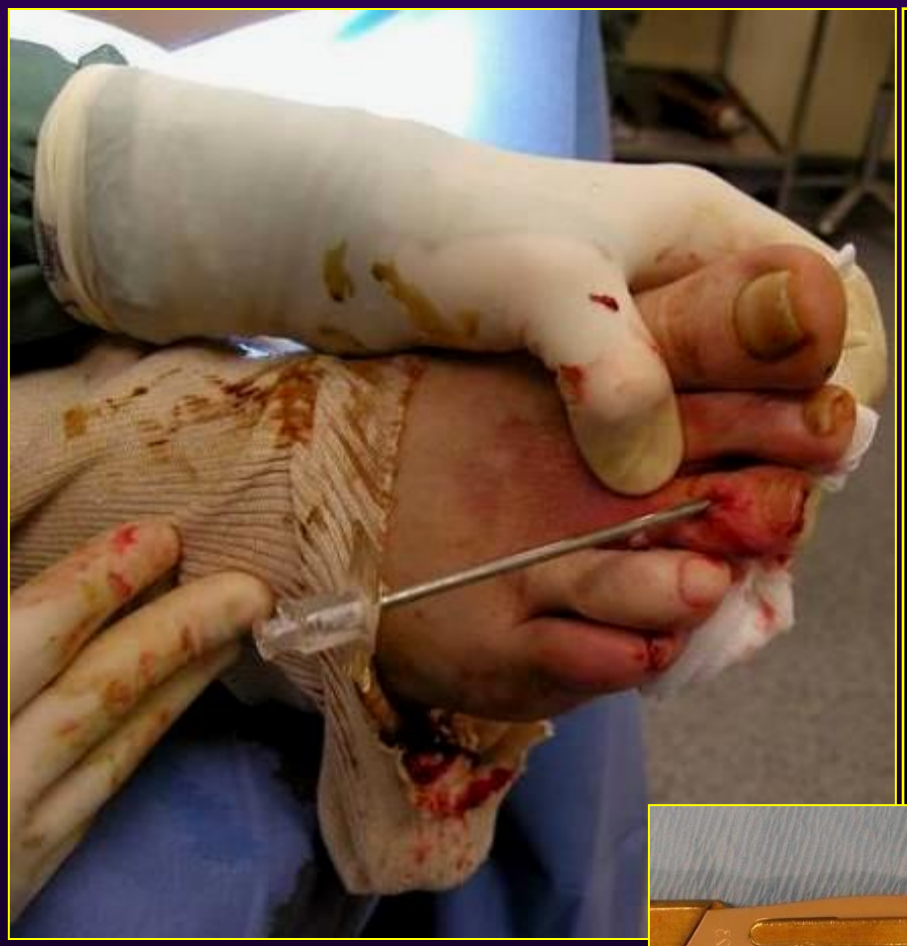
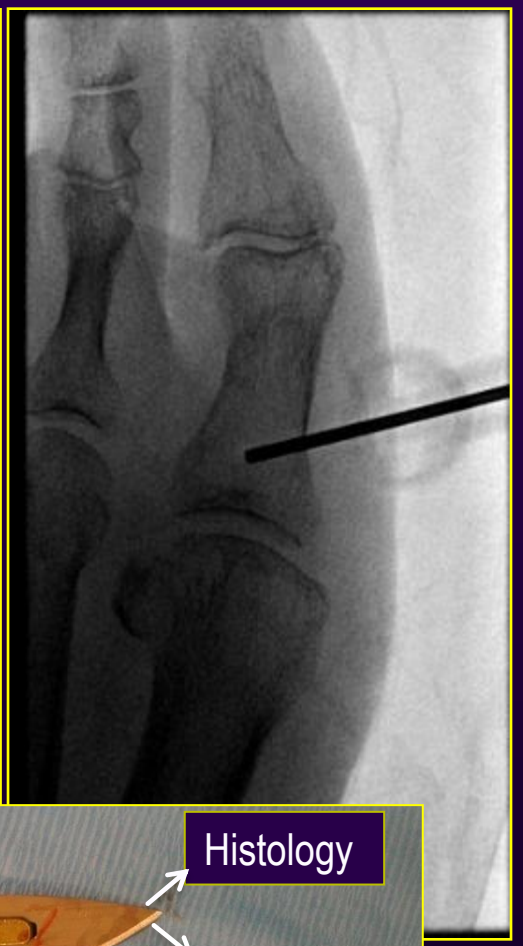
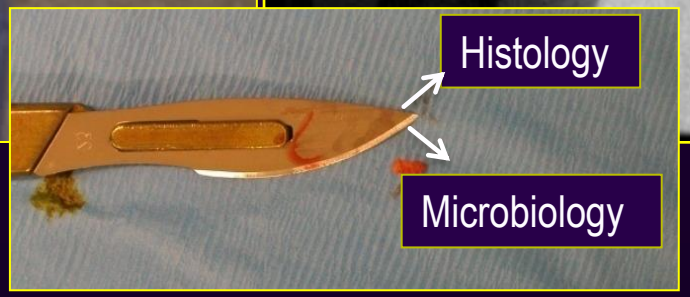
  - *MRI*: best current test; marrow edema, soft tissue
  - SPECT/CT, PET/CT, PET/MRI quite promising
- Bone Biopsy: *culture & histology*- criterion standard

Dinh et al *Clin Inf Dis* 2008;47:519; Butalia et al *JAMA* 2008;299:806
Berendt et al. *Diabetes Metab Res Rev* 2008;24 Suppl 1:S145

Bone Biopsy for Diabetic Foot Osteomyelitis







Courtesy: Drs. E. Senneville & E. Beltrand

Value of Bone Culture in DFO

59 consecutive diabetic patients with foot osteomyelitis
Initially treated *without bone surgery*

3 died, 6 lost to F/U

50 evaluable patients

22: ***Bone***-culture based Rx*		28: ***Swab***-culture based Rx*
18 (82%) in remission†	p=.02	14 (50%) in remission†
18 (69%%) got rifampin	p=.0006	5 (21%) got rifampin

*Median duration 12 wks

† ≥1 year after end of Rx

Senneville et al, *Diabetes Care* 2008;31:637

Value of a Negative Bone Culture

341 pts with suspected DFO: percutaneous bone bx; ≥2 yr F/U

275 culture **+**

66 culture **–**

[25 lost to F/U or excluded]

41 enrolled

16 (39%) healed

25 unhealed

10 clinically/imaging stable

15 repeat bone bx

6 likely *not* osteo

4 suspected osteo

9 culture **–**

6 cult **+**

True negative : 31 (75%)
False negative: 10 (25%)

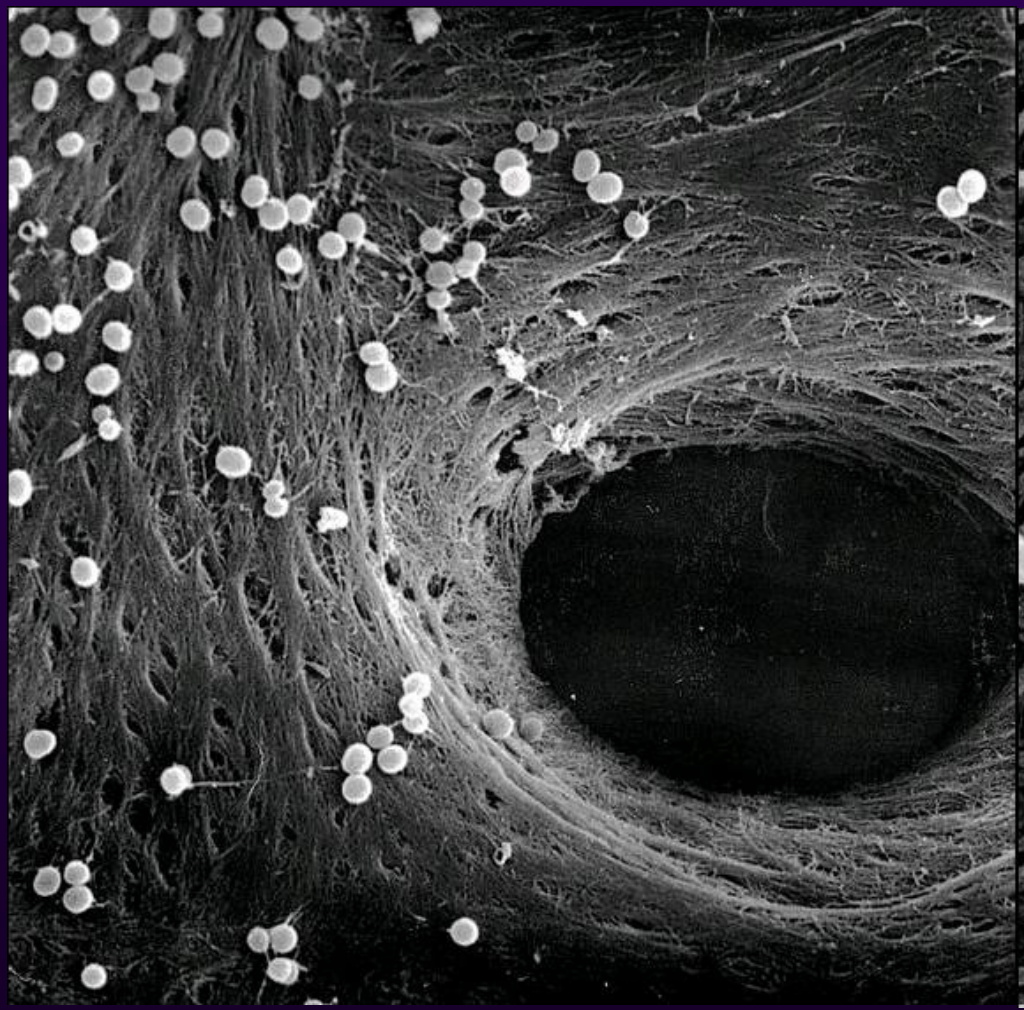
Senneville et al, *Diabet Med* 2012;29:56

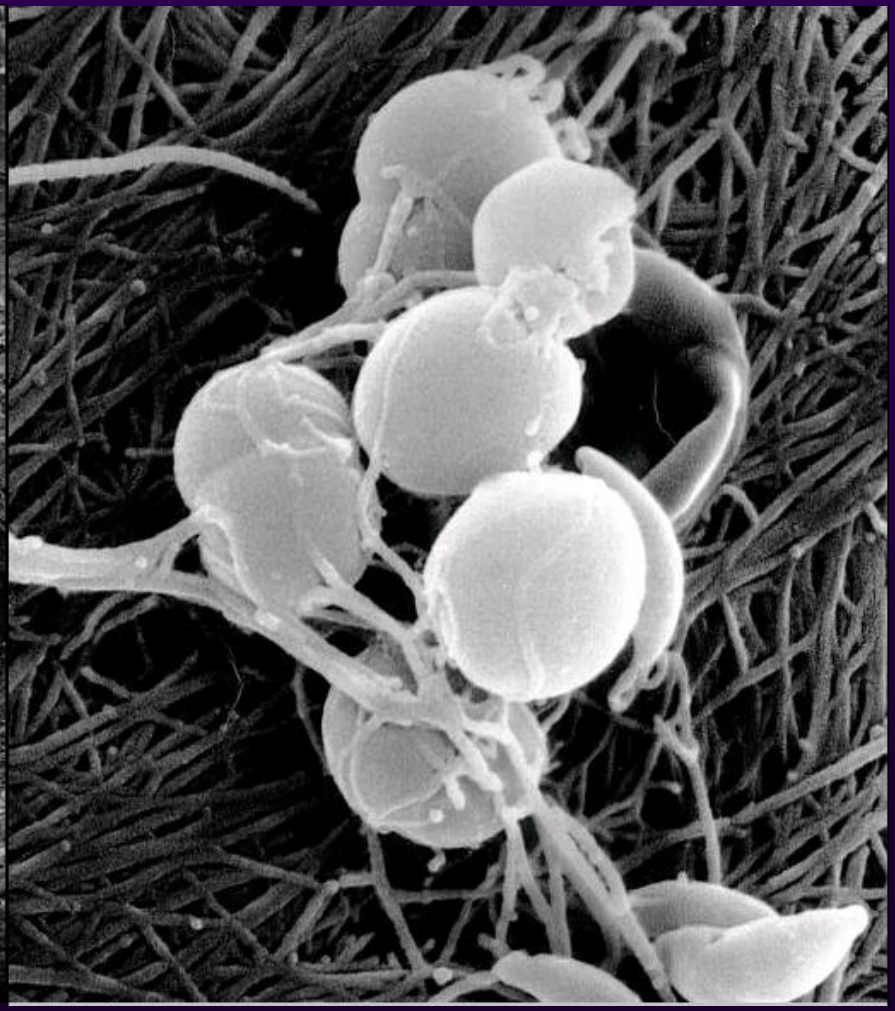
In Which Situations Is Diagnostic Bone Biopsy Most Recommended?

- Uncertainty regarding the *diagnosis* of osteomyelitis despite clinical and imaging evaluations
- Culture data from *soft tissue* specimens unclear
- Failure to *respond* to empiric antibiotic therapy
- Plan to insert *metalware* in bone at affected site
- Desire to use antibiotic *agents* that may be especially effective for osteomyelitis but have a high potential for selecting resistant bacteria (eg, rifampin, FQs)

Lipsky et al, [IDSA DFI guidelines] *Clin Infect Dis* 2012;54:1679
Lipsky et al, [IWGDF DFI guidance] *Diab/Metab Res Rev* 2015 (in press)

Treating Diabetic Foot Osteomyelitis



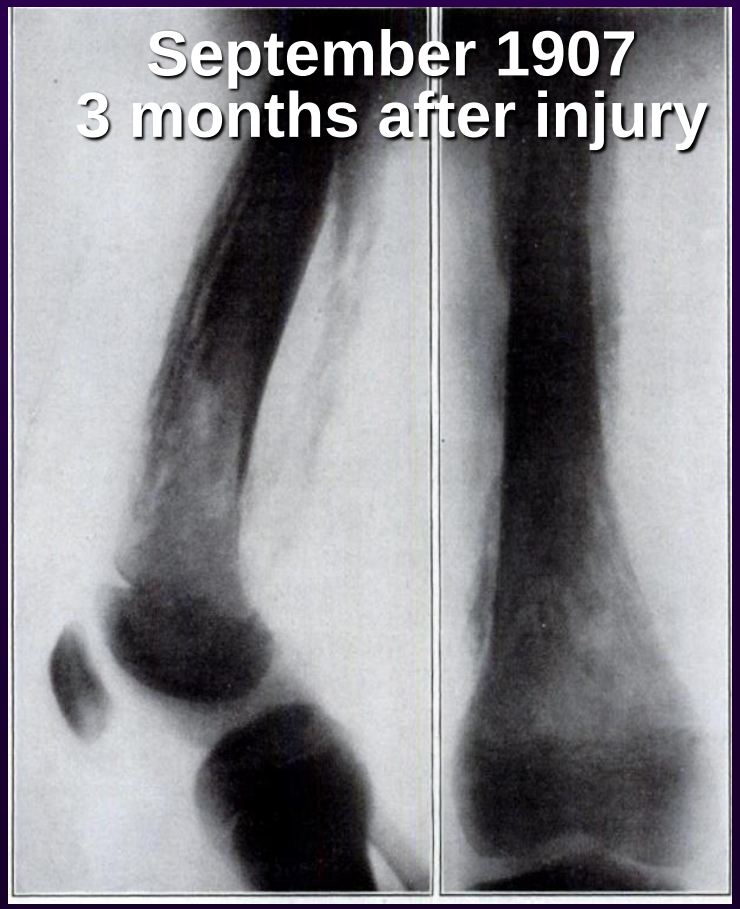


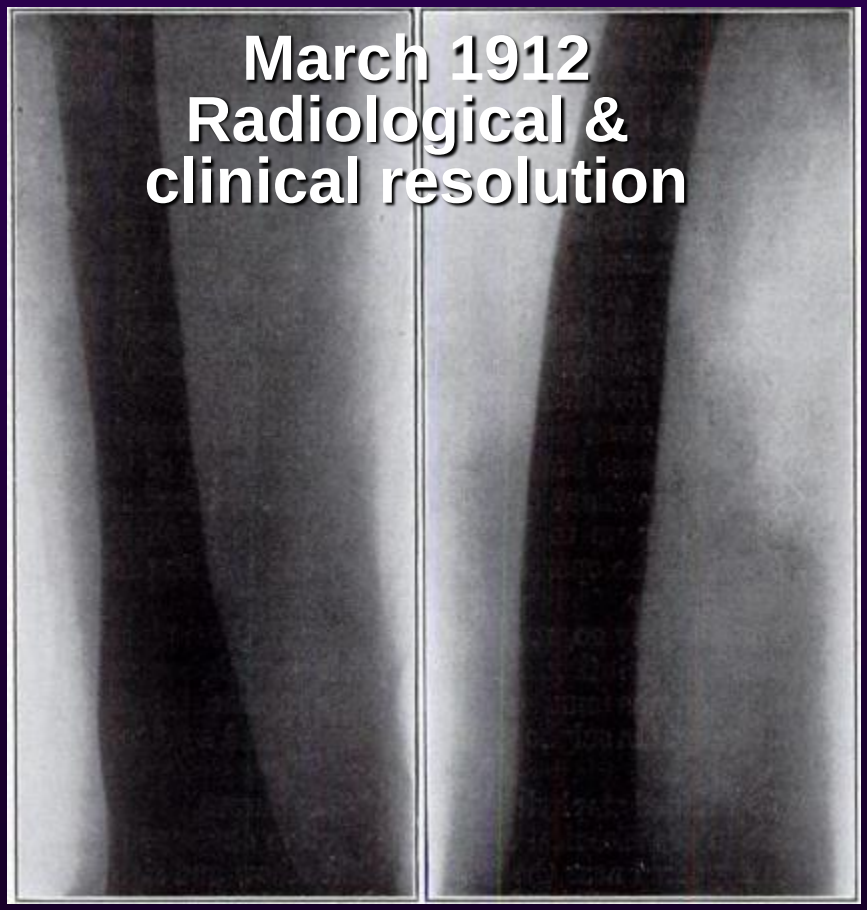
Key Questions About Treatment of Diabetic Foot Osteomyelitis

- What are the most appropriate **antibiotic** regimens
  - Specific single, or combinations of, *agent(s)*
  - *Route* of therapy (IV vs oral vs local)
  - *Duration* of therapy
- When is **surgical** resection of bone required
- How do we know when we have achieved **remission** or cure?

Exclusively Surgical Treatment of Osteomyelitis

10 yo with post-traumatic osteomyelitis of L femur;
pus drained, sequestrum removed; later sinus curetted

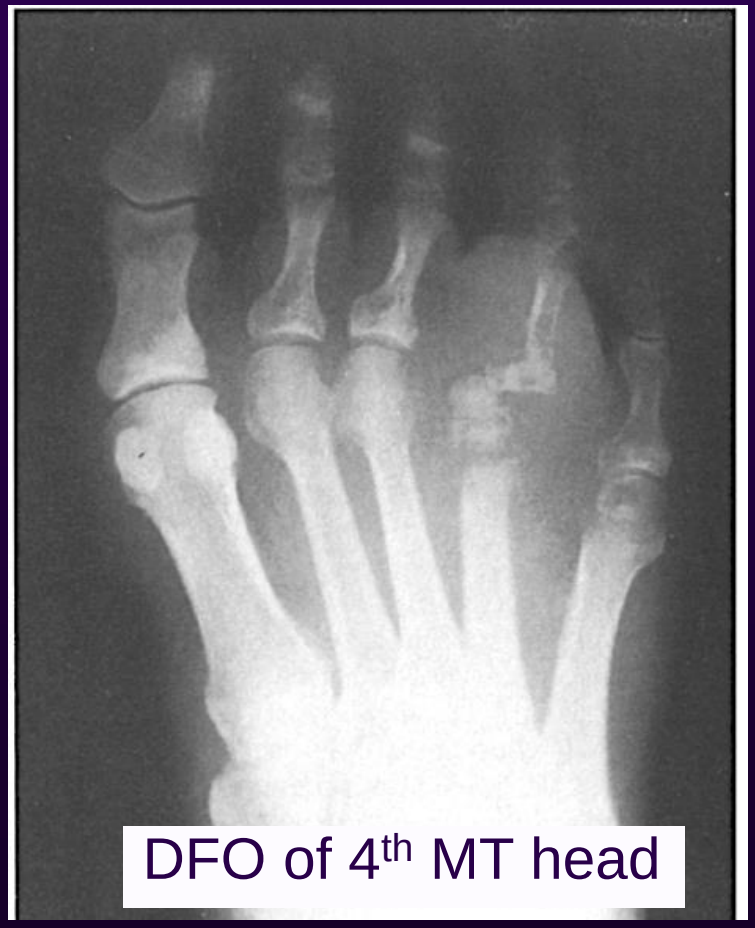


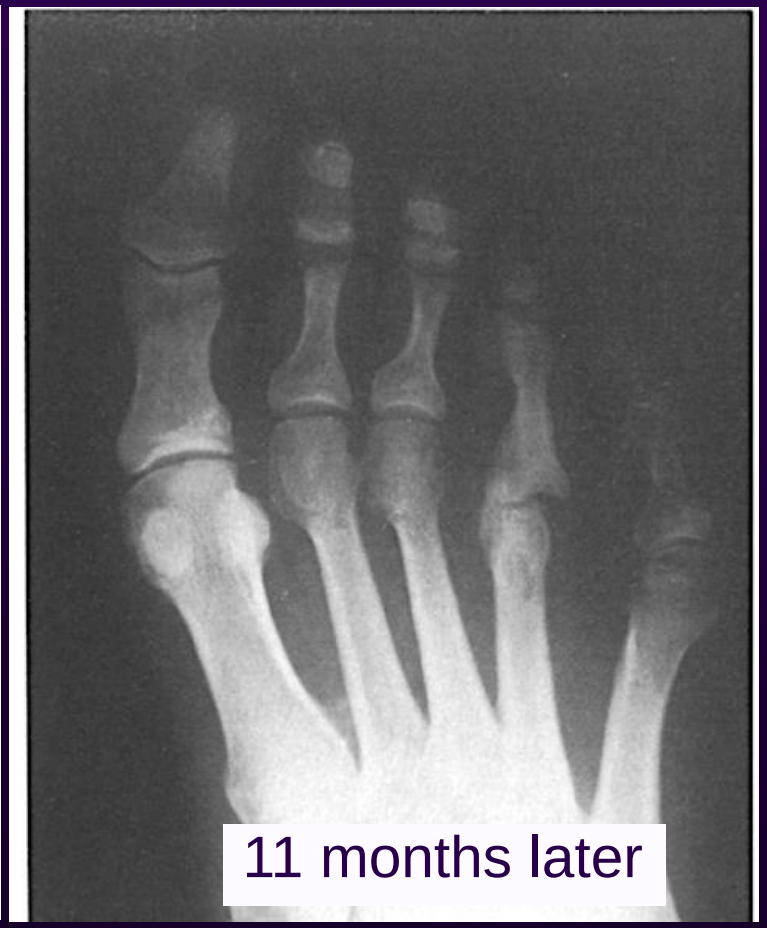


R. Hammond, *J Bone Joint Surg Am* 1913;s 2-10:569

Exclusively Antibiotic Therapy of DFO

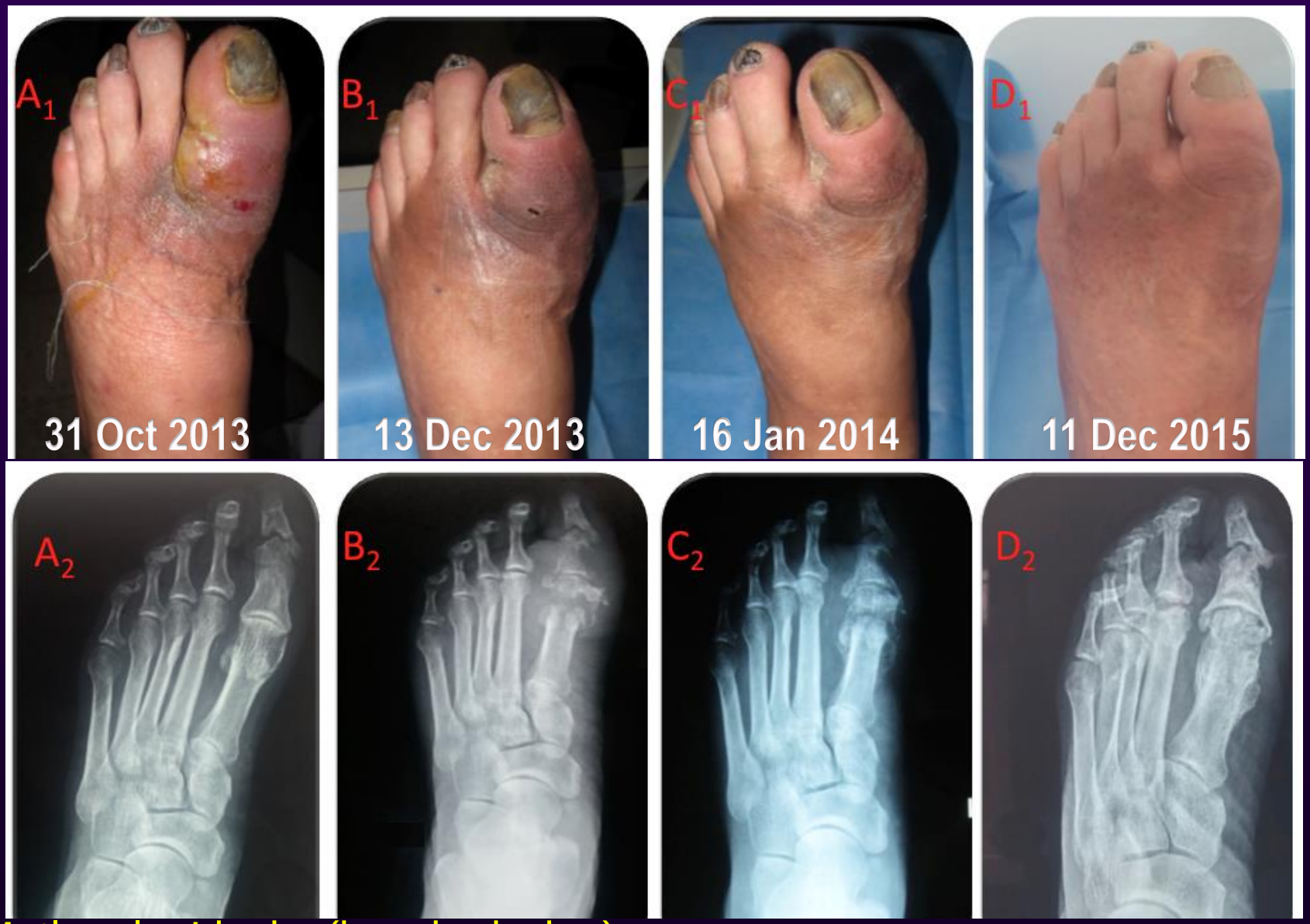
Of 51 cases, 53% resolved with antibiotic w/o bone surgery





Bamberger et al *Am J Med* 1987;83:653

Resolution of DFO With Antibiotic Therapy Alone



Mutluoglu, Lipsky (in submission)

Can Osteomyelitis Be Cured ***Without*** Surgical Resection of Bone?

- Review of reported patients managed with antibiotics & little or no surgical debridement[1]
  - 546 total patients in 11 studies from 1987-2002
  - Mostly given oral fluoroquinolones, for ≥3 mos
  - Satisfactory response seen in ~65% (25-88%)
- In 4 more recent observational studies[2-5] (total of 443 patents): 63-79% remission rates
- All *retrospective* studies, mostly forefoot cases

[1]Jeffcoate, Lipsky. *Clin Infect Dis* 2004;39 Suppl 2:S115;
[2]Acharya et al, *Diab Res Clin Pract* 2013 Sep;101(3):e18
[3]Ulcay et al, *Pak J Med Sci* 2014;30:28; [4]Zeun et al, *IJLEW* 2015 (1 Sept)
[5]Jordano-Montanez et al, *Enferm Infecc Microbiol Clin* 2014;32:555

Outcome of *S. aureus* DFO by Treatment Type

Retrospective cohort study 74 pts; + bone culture (35% MRSA)
Bone surgery in 47% (mostly forefoot); rest antibiotic alone

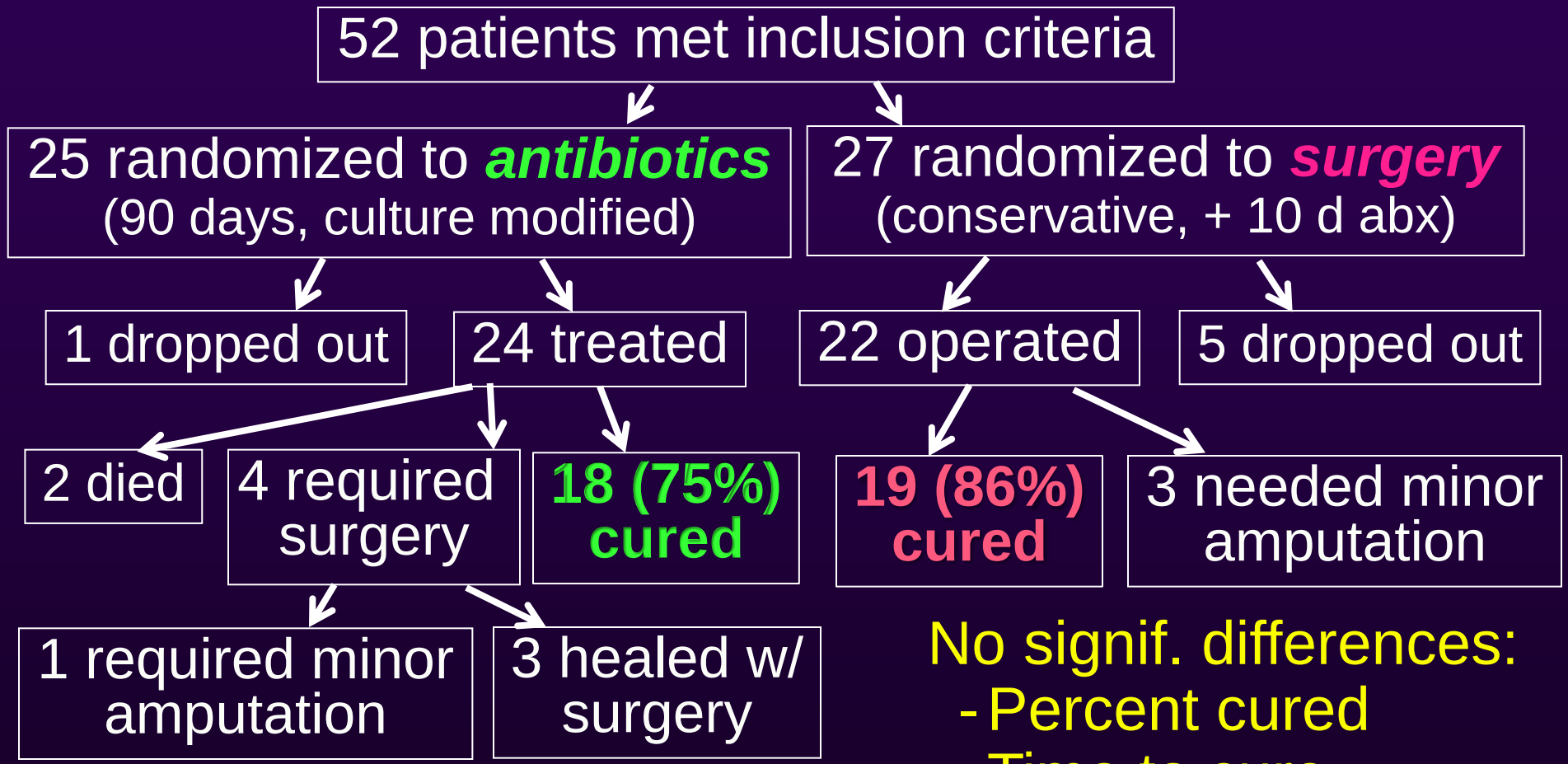
	Medical	**Surgical**	P
-Favorable outcome	87%	80%	NS
-Hospitalized >24 hours	49%	94%	<.001
-Mean hospital LOS (days)	17 ± 3	50 ± 12	.004
-*Median* duration abx (wks)	8 (6-52)	5 (2-44)	.001
-Antibiotic d/c 2° side effects	33%	9%	.01

- Mortality on F/U (mean 21 months): 20%
- New episode (noncontiguous) DFO: 32%

} No significant diff medical v surgical

Lesens et al, *Int J Lower Extrem Wounds* 2014; Dec 16 pii

RCT of Primarily Antibiotic vs Surgery for DFO



Reulceration: 9.5% abx; 21% surgery

No signif. differences:
- Percent cured
- Time to cure
- Complications

Lazaro-Martinez et al, *Diabetes Care* 2014; 37:789

Primarily Surgical vs Medical Treatment for DFO: Individualizing the Choice

Surgical

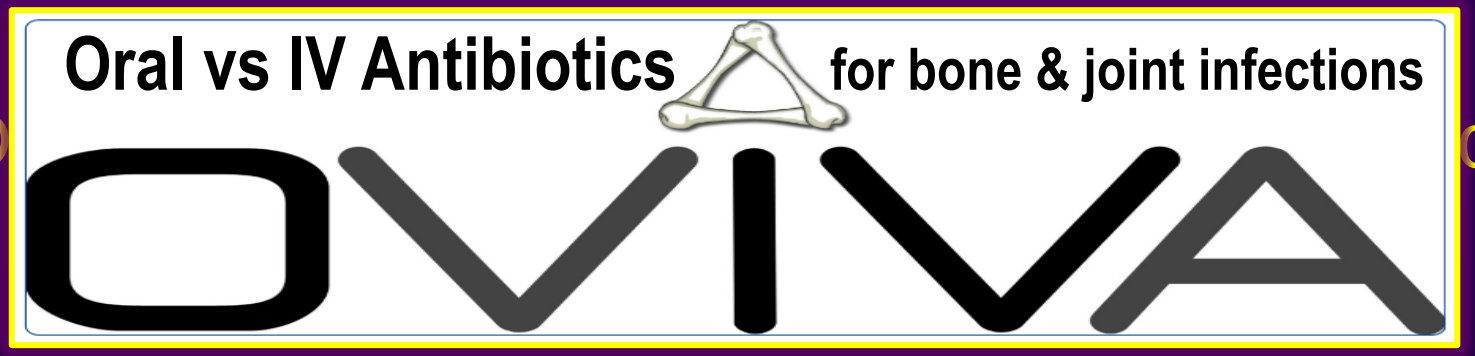
- Substantial bone necrosis
- Fxnly non-salvageable foot
- Pt is non-ambulatory
- ⇧ risks antibiotic problems
- No available active antibiotic
- Uncorrectable foot ischemia
- Patient preference

Medical

- Pt too unstable for surgery
- Bad post-op mechanics likely
- No other need for surgery
- Small, forefoot lesion
- No skilled surgeon available
- Surgery costs prohibitive
- Patient preference

Lipsky BA. *Diabetes Care* 2014;37:593

D o?



- Pilot study in Oxford; then enrolled 1060 pts in 30 UK centers
- Bacterial infection types: osteomyelitis (DFO); prosthetic joint infection; orthopedic device/bone-graft; spinal infection
- Open label: ~1 wk IV abx for all, then randomized to ≥5 wks of IV or oral antibiotic regimen (clinicians' choice of agent[s])
- Outcomes: assessed at one year follow up visit
  - 1° is definite failure (+ culture or dx histology from bone or periprosthetic tissue, draining sinus or pus from bone
  - 2° : SAE, IV line compltn, Rx failure; early Rx termination; resource allo^{cation}; QoL; hip/knee score; Rx adherence
- Endpoint review committee (blind to Rx): all potential failures

Li et al. *Trials* 2015;16:583

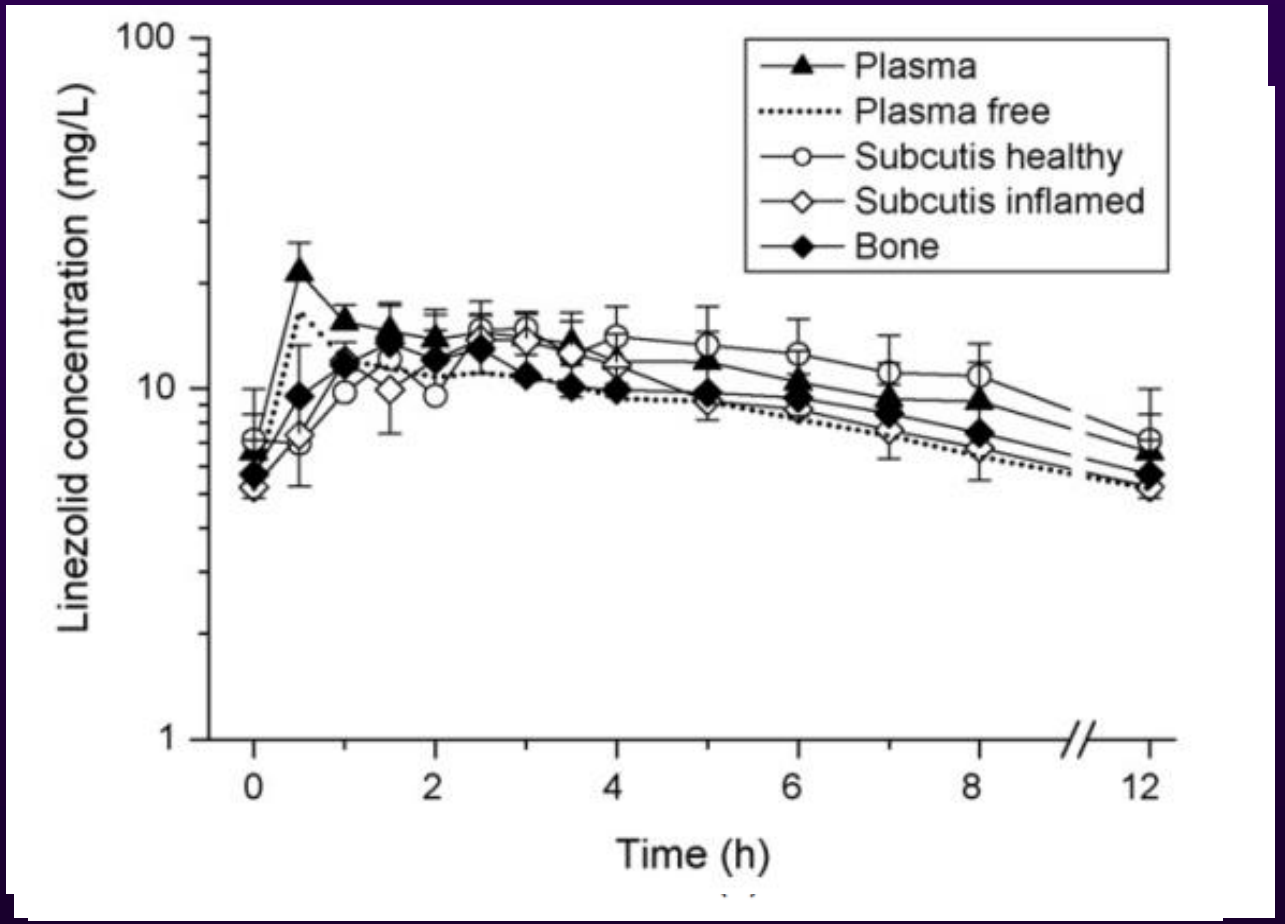
Bone Penetration of Antibiotics

Antibiotic	Mean [Bone/Serum] Ratios
Levofloxacin	0.36-1.0
Ciprofloxacin	0.27-1.2
Moxifloxacin	0.33-1.05
Vancomycin	0.05-0.67
Linezolid	0.2-0.51
Daptomycin	1.17
Clindamycin	0.21-0.45
Cefazolin	0.179
Ceftriaxone	0.07-0.17
Cefuroxime	0.04-0.55
Rifampin	0.08-0.57

Lalani T. *UpToDate* 2014

Bone Penetration of Antibiotic Agents in DFO

- Fosfomycin [1]
- Daptomycin [2]
- Linezolid [3]



Substantial variability in mean bone penetration among drugs, studies

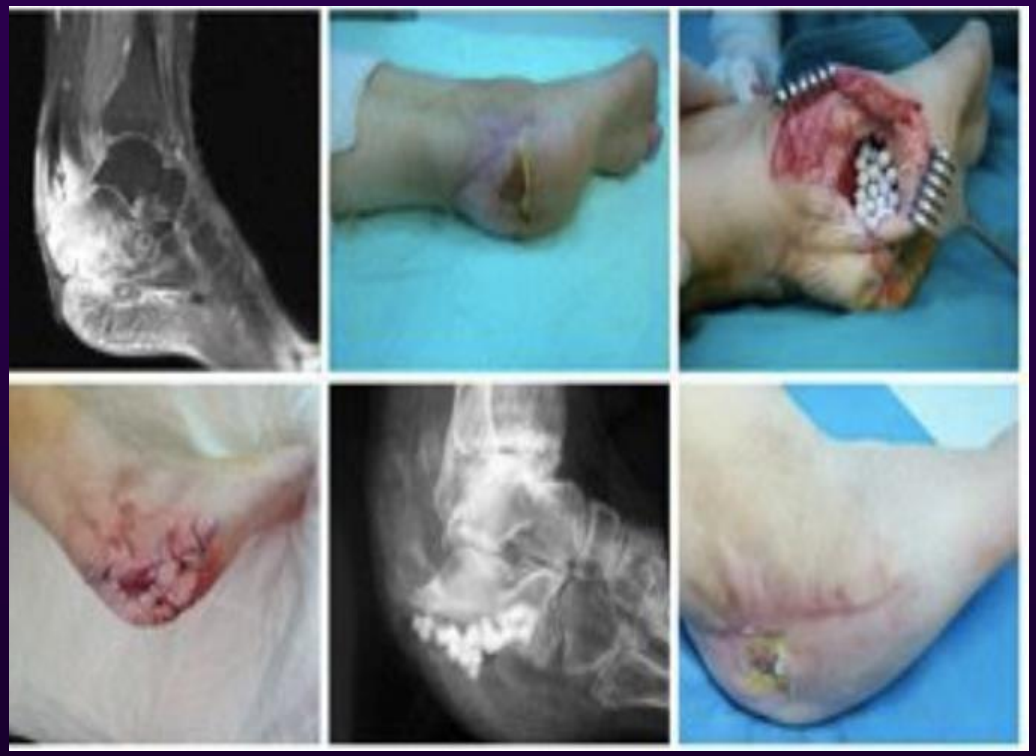
[1]Schintler V *et al. J Antimicrob Chemother* 2009; [2]Traunmüller F et al. *J Antimicrob Chemother* 2010; [3]Traunmüller F *Int J Antimicrob Agents* 2010

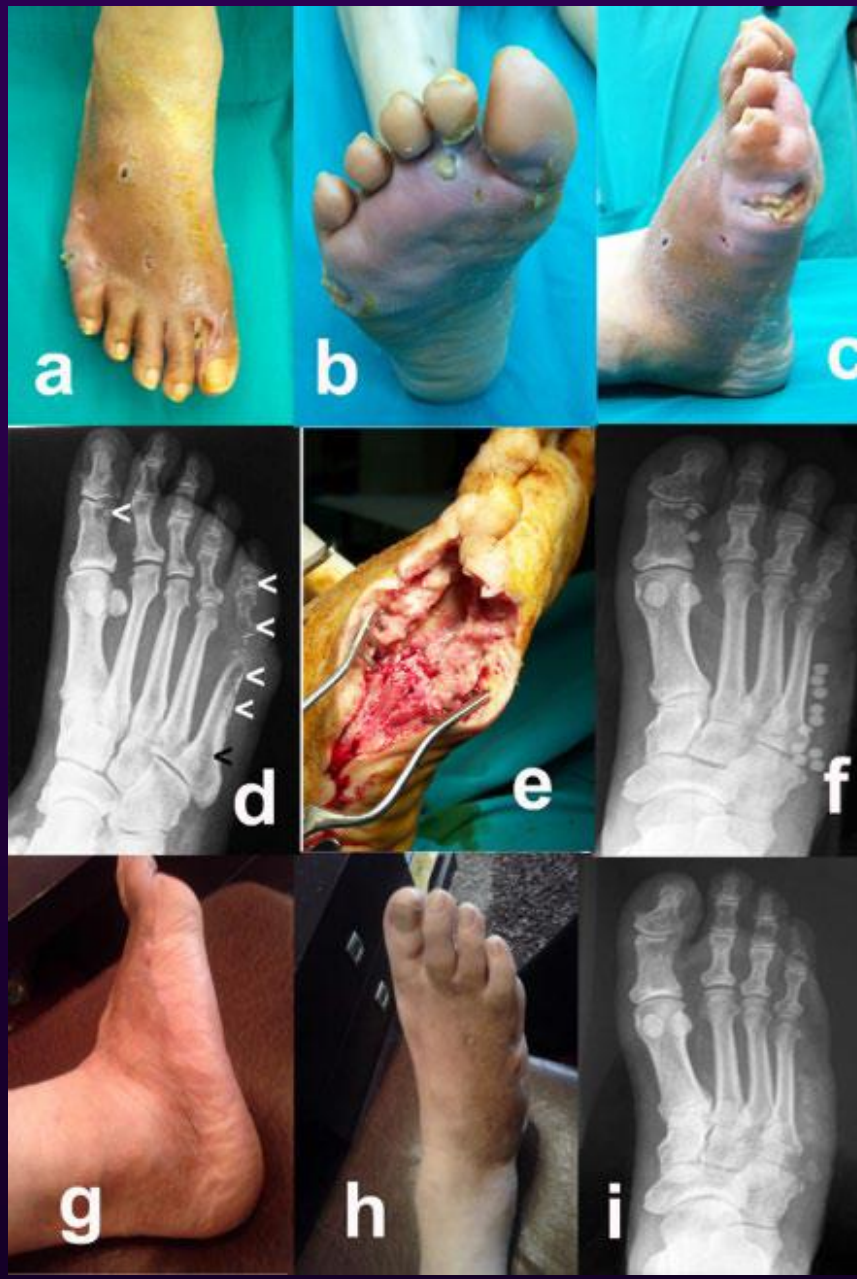
Duration of Antibiotic Treatment for DFO

- Multicenter RCT: 6 vs 12 weeks of antibiotic therapy
  - Pts w/ + bone culture; w/o ischemia; no surgical Rx
  - Remission: no evidence infection, stable/improved x-rays, overlying wound healed X ≥12 months f/u
- Results: 40 pts enrolled 2007-2009
  - Characteristics of 2 treatment groups similar
  - Remission rates:
    6 weeks: 12/20 (60%)
    12 weeks: 14/20 (70%) [p=NS]
  - Signif. ↓ GI adverse events with 6 wks (15 v 45%)
  - No differences: relapse; need for resection; spread

Tone et al, *Diabetes Care* 2015;38:302

Antibiotic Beads or Bone Grafts for Treating DFO





Panagopoulos *Int J Low Extrem Wounds* 2015;14:87

Xanthopoulou et al, ECCMID 2016

Local Antibiotics for Treating Osteomyelitis

PMMA (beads, cement), $CaSO_4$ (pellets, beads), Polylactic acid

Advantages

- Hi local antibiotic level
- Fills dead space
- Low systemic concentrations
- PLA & $CaSO_4$ don't require bead removal

Disadvantages

- Variable formulations, sizes
- Requires pharmaceutical grade antibiotic powders
- Subinhib conc → resistance
- ? Inhibition of bone healing
- Operation to remove PMMA

*Literature search (July 2014) 3770 papers: ? best system, antibiotic, duration, need for surgery or systemic antibiotics

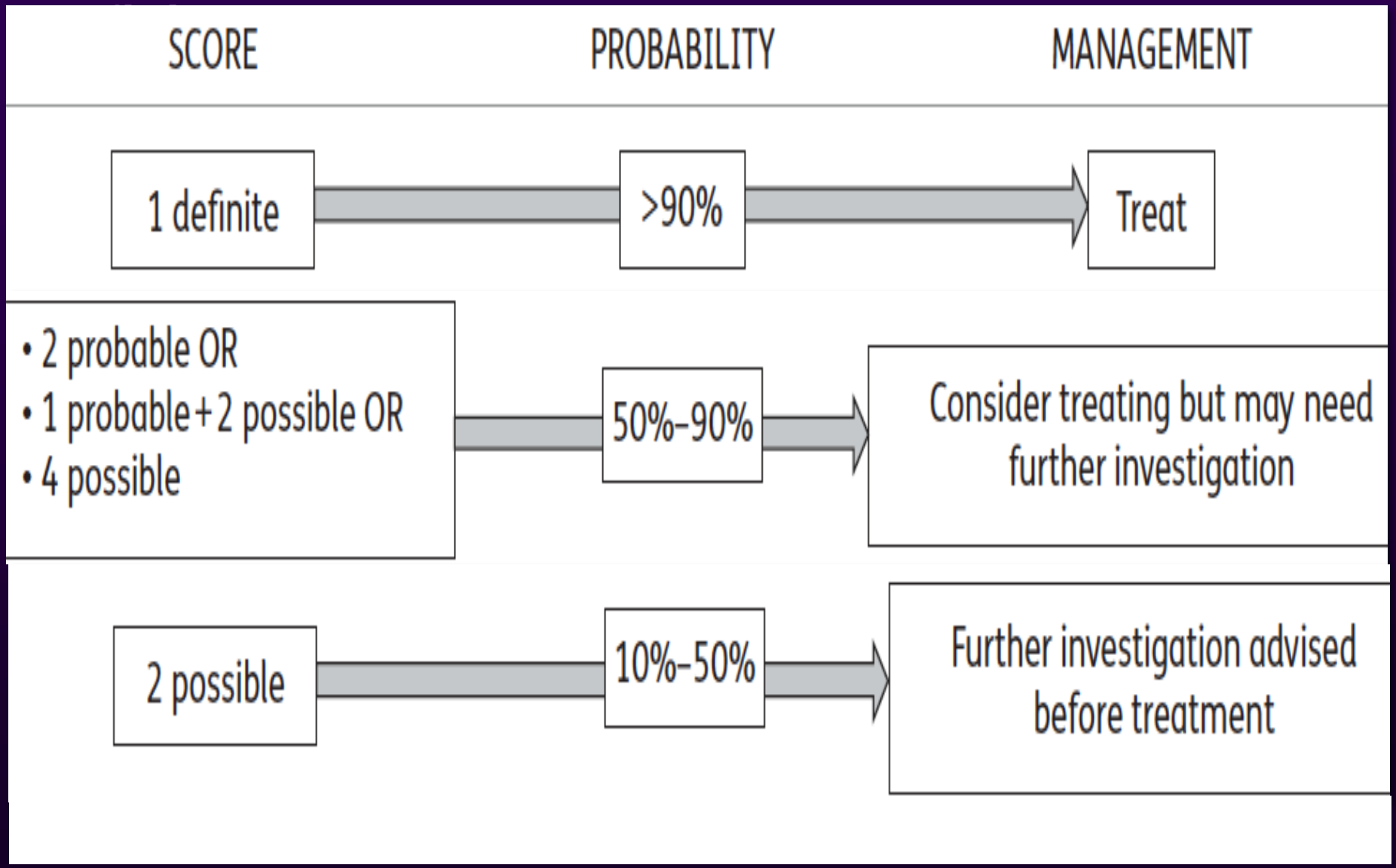
Barth et al, *Int J Antimicrob Ag* 2011;38:371
*Panagopoulos, et al *Int J LE Wound* 2015;14:87

IDSA DFI Guidelines on Treating Bone Infection

Extent of Surgery	Route of Rx	Duration of Rx
No residual infected tissue (eg, post-amputation)	Parenteral or oral	2 - 5 days
Residual infected soft tissue only	Parenteral or oral	2 – 4 weeks
Residual infected (but viable) bone	Initial parenteral then oral switch	4 – 6 weeks
Dead bone present no bone resection	Initial parenteral then oral switch	? ≥ 3 months

Lipsky et al,[IDSA DFI guidelines] *Clin Infect Dis* 2012;54:132

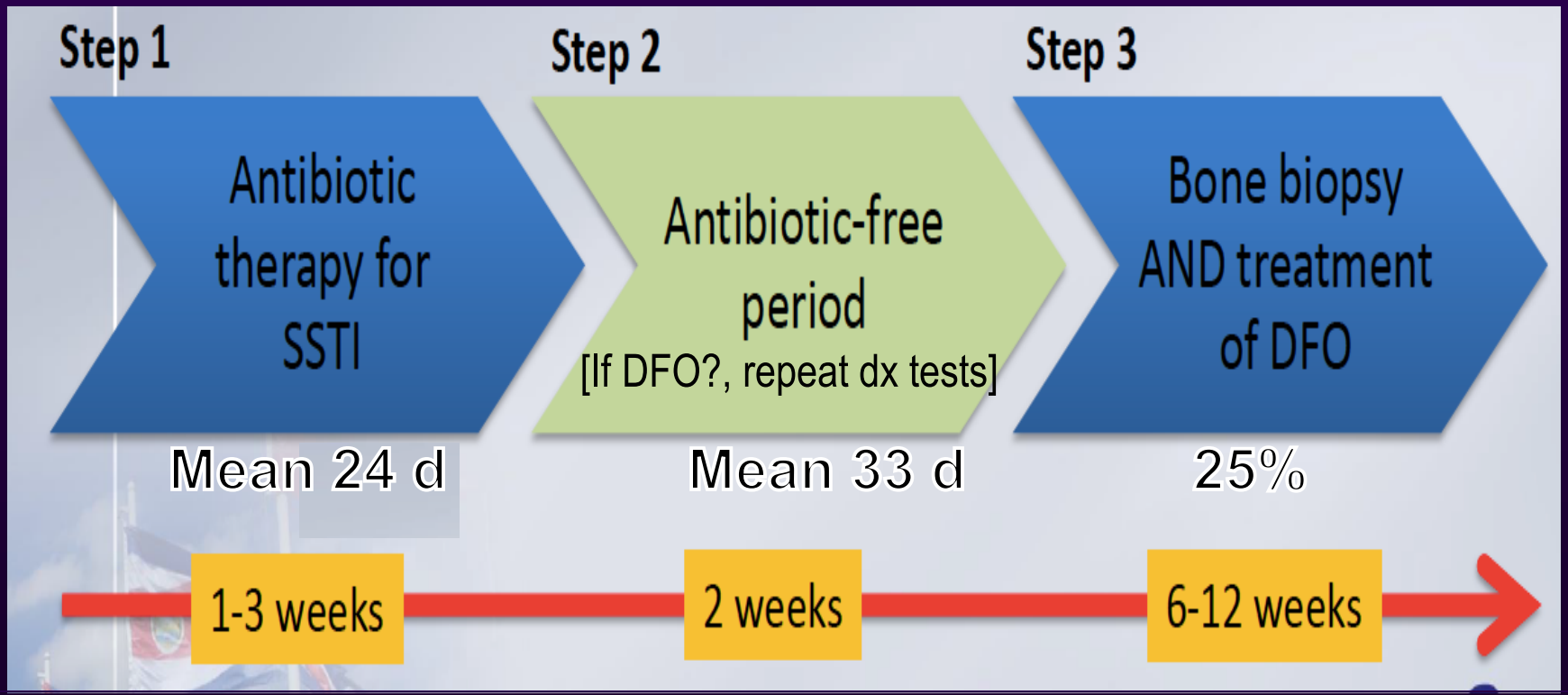
Proposed Management Scheme DFO: IWGDF



Berendt et al, *Diab Metab Res Rev* 2008;24 Suppl 1:S145

Proposed Sequential Approach for Concomitant Soft Tissue Infection & Suspected Osteomyelitis

Retrospective study, 32 pts, Tourcoing 2006-13

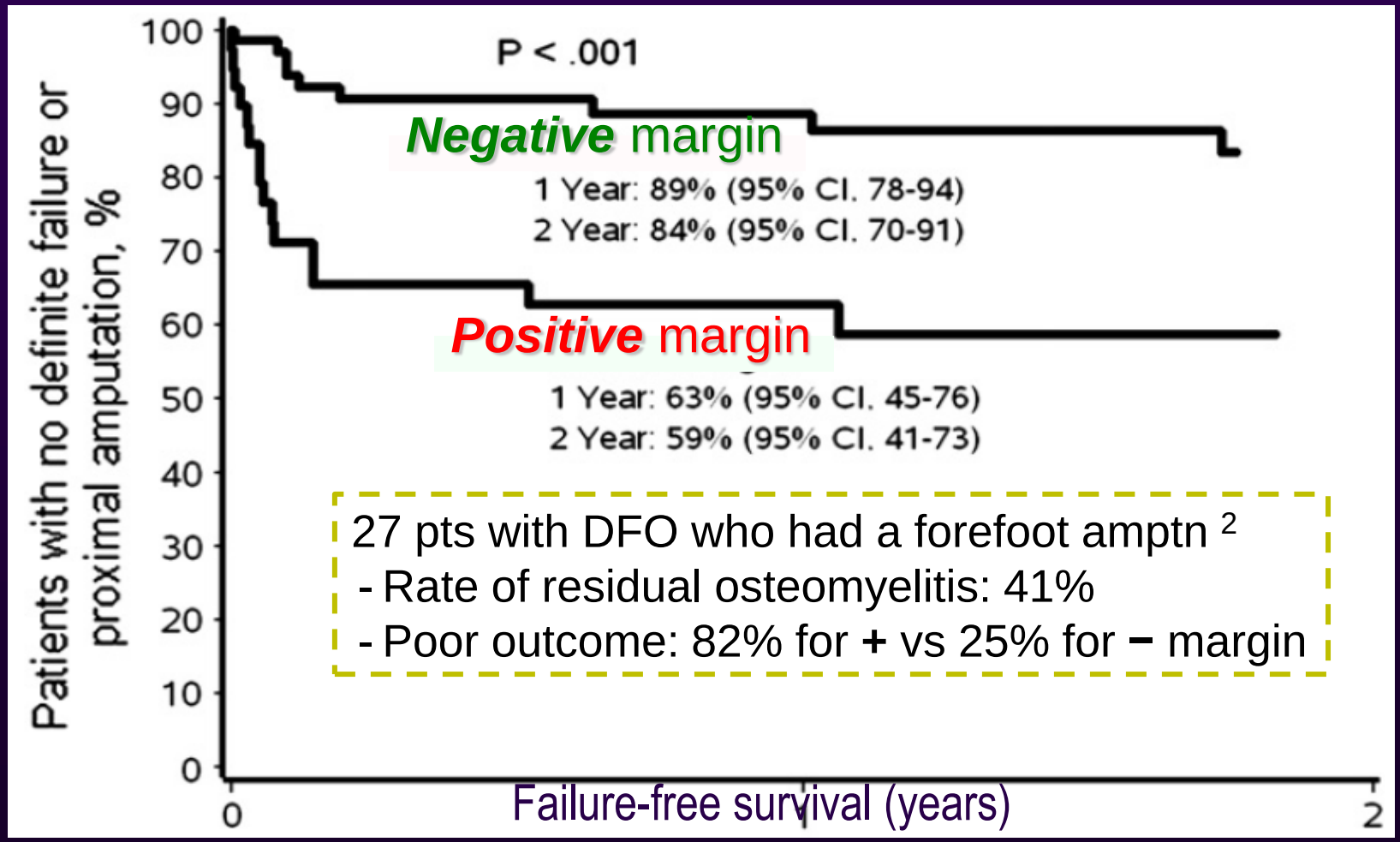


41% had DFO; 59% in remission @ final f/u (mean 3.9 y)

Berthol, Int Symp Diab Foot, Hague 2015; Markanday *OFID* 2014; 1(2):ofu060

Effect of Residual Osteomyelitis After Resection

111 DFO pts: 39 (35%) histology + margins for osteomyelitis[1]



27 pts with DFO who had a forefoot amptn [2]
- Rate of residual osteomyelitis: 41%
- Poor outcome: 82% for **+** vs 25% for **−** margin

[1]Kowalski et al, *J Foot Ankle Surg* 2011;50:171

[2]Atway et al, *J Foot Ankle Surg* 2012;51:749

How Do We Know if a Patient is Responding To Antibiotic Treatment?

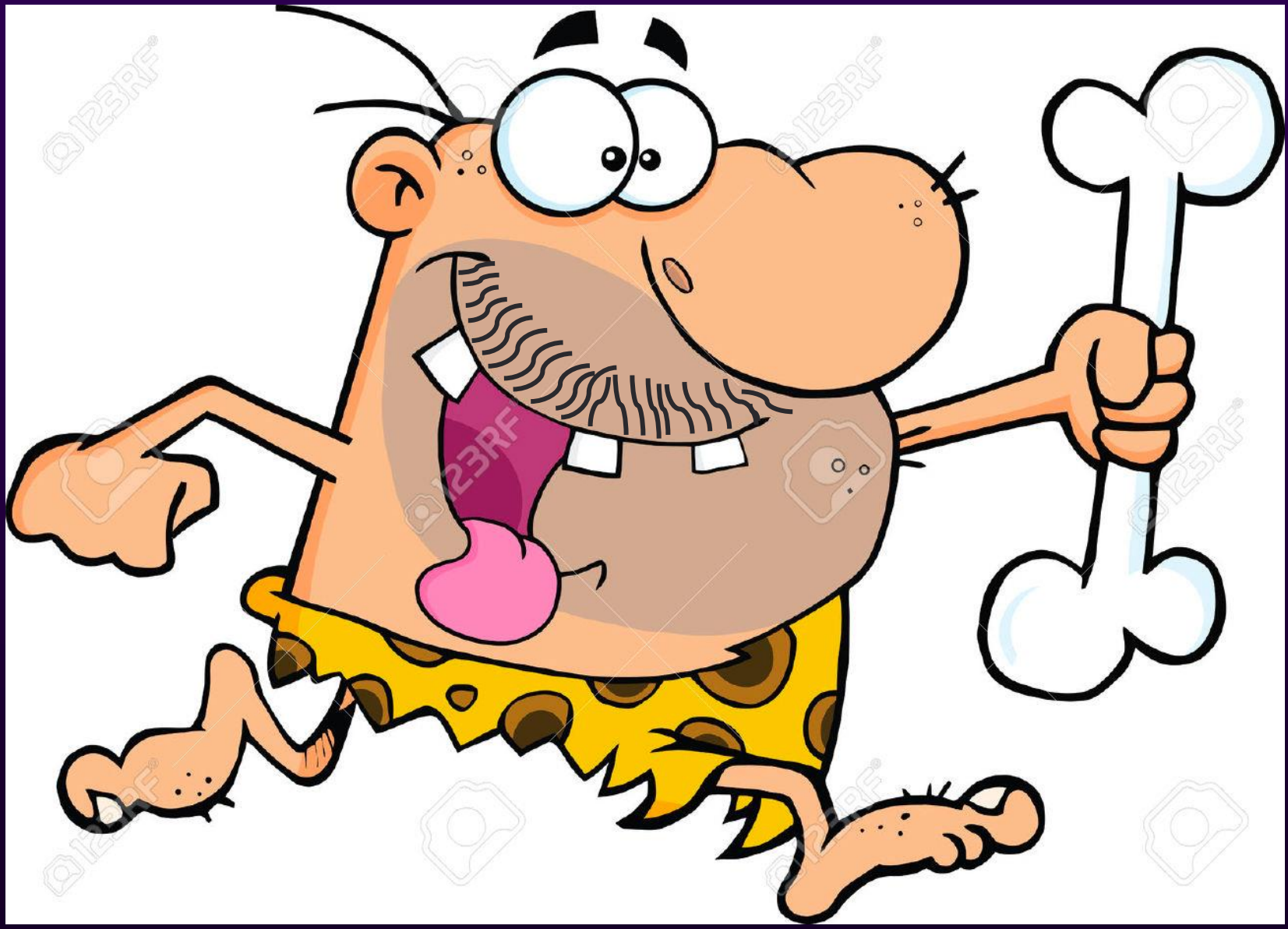
- Decreasing inflammatory markers
- Resolution of local soft tissue infection
- Healing of adjacent/overlying wound
- Evolving radiographic findings c/w healing
- Lack of uptake on radionuclide studies

Consider “in remission” until F/U @ least 1 year

Lipsky BA, et al. IDSA: *Clin Infect Dis* 2012;54:132
Lipsky BA, IWGDF: *Diab/Metab Res Rev* 2016;32 Suppl 1:45

Conclusions: Strategies for Managing DFO

- Diagnosis
  - *PTB* test is useful if done & interpreted correctly
  - *ESR* is probably still best serological test
  - If advanced imaging needed, *MRI* usually preferred, but *SPECT/PET/CT/MRI* promising
  - *Bone biopsy* (culture/histology) criterion standard
- Treatment
  - *Bone culture* & sensitivity helps guide therapy
  - *Oral antibiotic* therapy usually adequate
  - Therapy for *6 weeks* usually adequate
  - Many patients can be treated *without surgery*
  - Defining "*remission*" is still difficult



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