Dr Aileen Boyd

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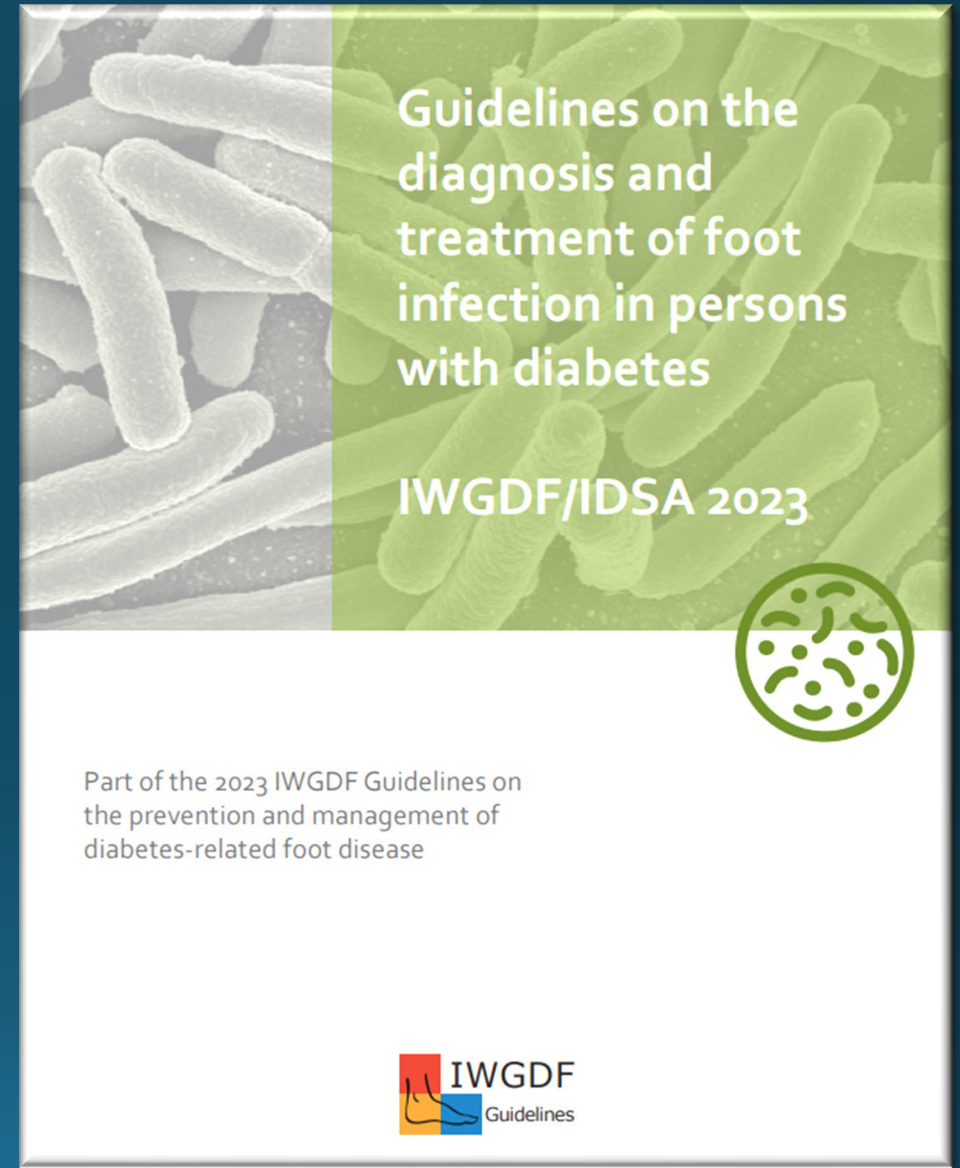
King's College Hospital NHS Trust, London

Bugs and drugs

Key microbiology takeaways for a podiatrist

No conflicts of interest



Bugs and drugs

which bug
which drug
which sample

which sample
which bug
which drug

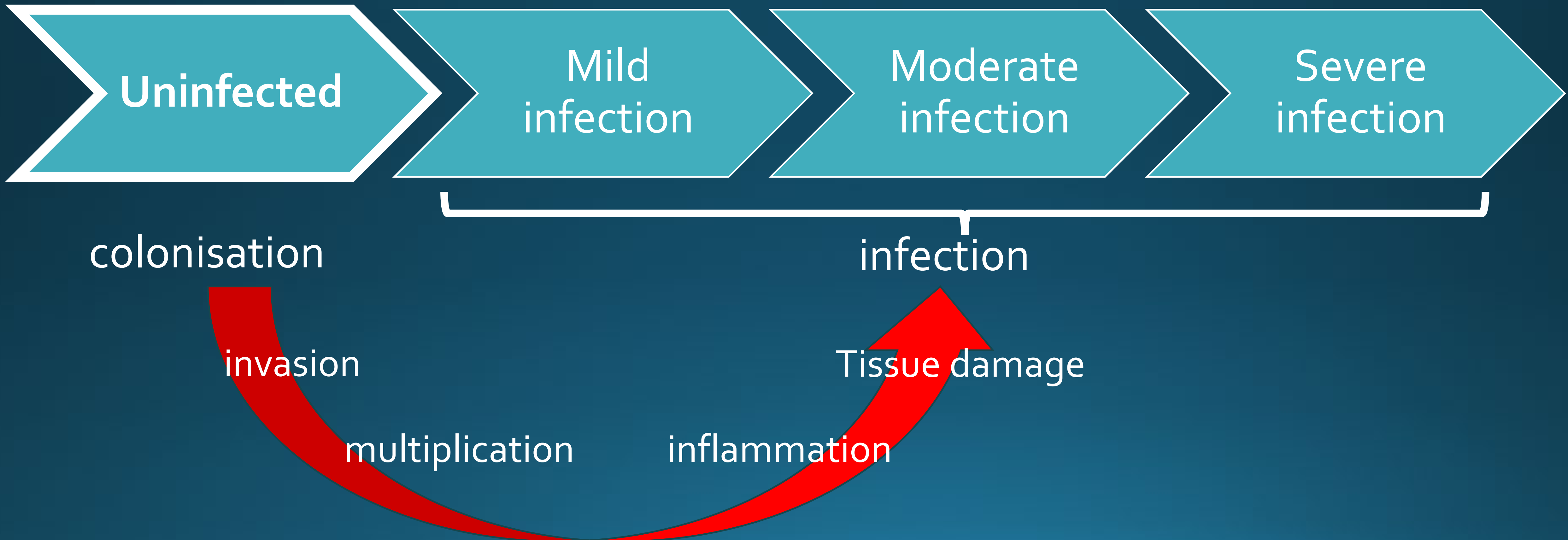
Which sample?

Which wounds NOT to sample?

colonisation

Which wounds NOT to sample?

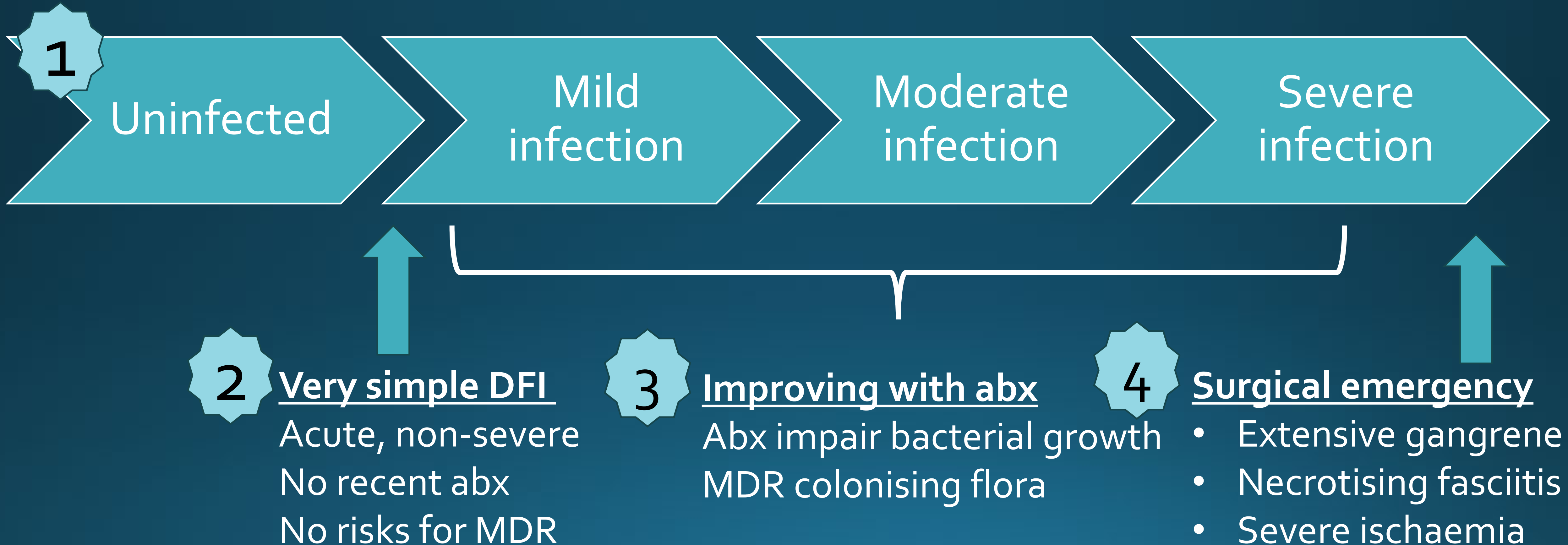
Which wounds NOT to sample?



IWGDF Infection Guideline

Clinical classification of infection, definitions	IWGDF/IDSA classification
No systemic or local symptoms or signs of infection	1 / Uninfected
Infected: At least two of these items are present: • Local swelling or induration • Erythema > 0.5 but < 2 cm around the wound • Local tenderness or pain • Local increased warmth • Purulent discharge And, no other cause of an inflammatory response of the skin (e.g., trauma, gout, acute Charcot neuro-arthropathy, fracture, thrombosis, or venous stasis)	2 / Mild

Which wounds NOT to sample?



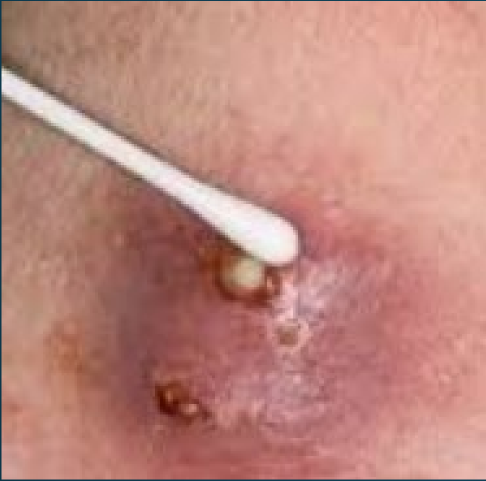
Severe infection

Surgical emergency

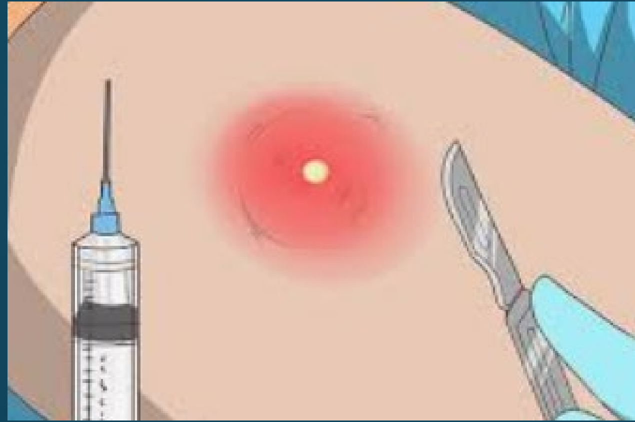
- Extensive gangrene
- Necrotising fasciitis
- Severe ischaemia

Urgent referral

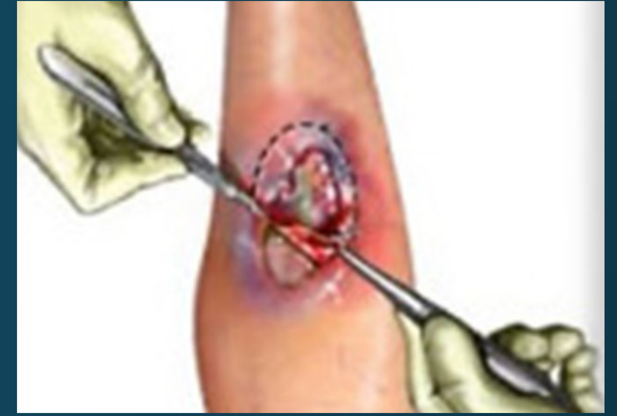
Orthopaedic surgeon
Vascular surgeon
Plastic surgeon



Pus swab

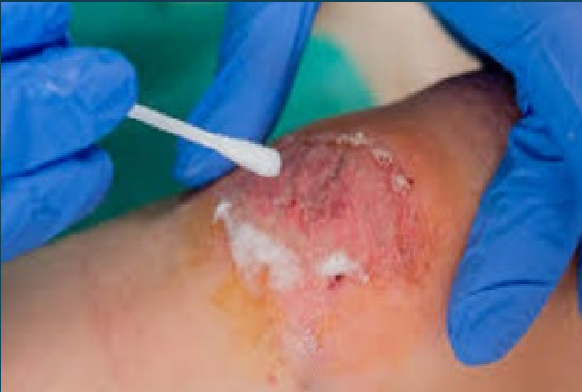


Pus aspirate



Tissue/bone biopsy

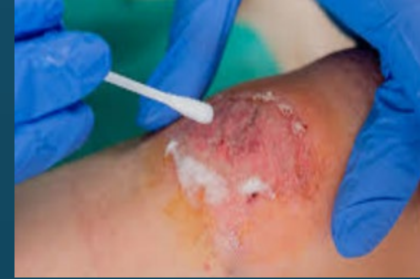
Swab

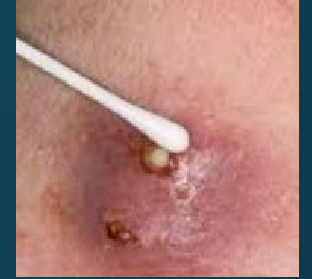


Which sample type and when?

Percutaneous bone biopsy

Swab and pus swab





PROS

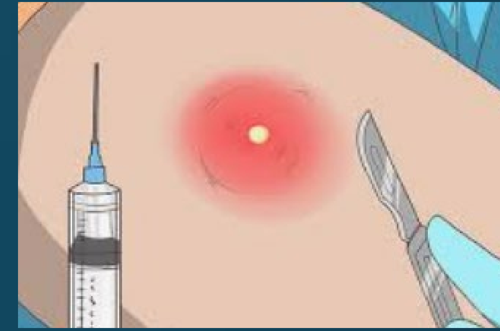
- Easy
- Some bugs always pathogens

  e.g. Group A strep

CONS

- Small volume (0.1ml)
- Surface flora
- No Gram stain
- Basic culture only – no specific tests for mycobacteria / fungi

Pus aspirate



PROS

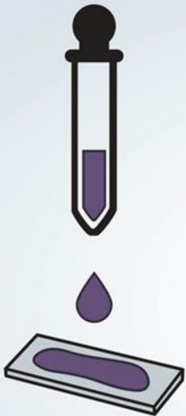
- Easy
- Greater volume
- Longer viability of organisms
- Gram stain

CONS

- Need 0.5ml pus

Gram stain

Crystal Violet

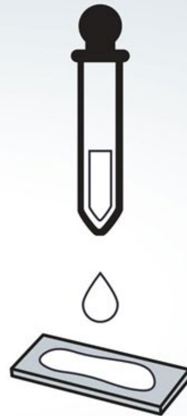


All Purple

Iodine

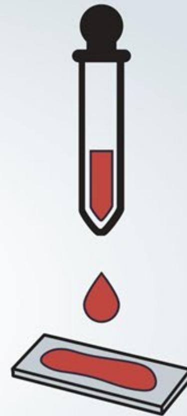
All Purple

Alcohol

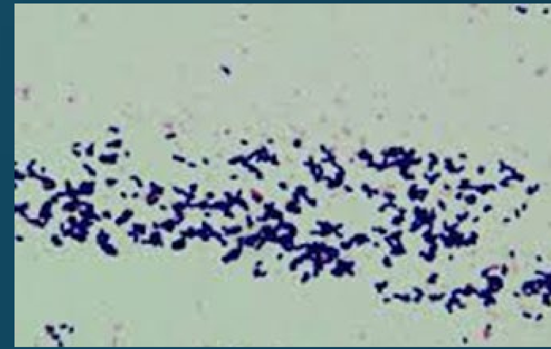


G+ = Purple
G- = Colorless

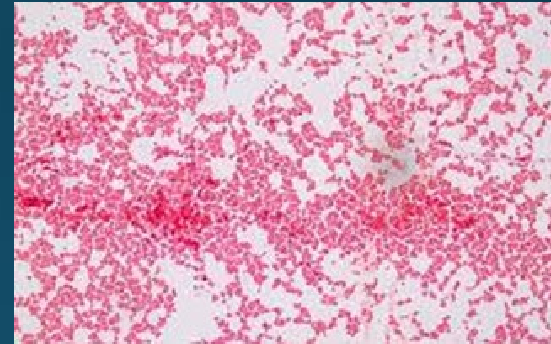
Safranin



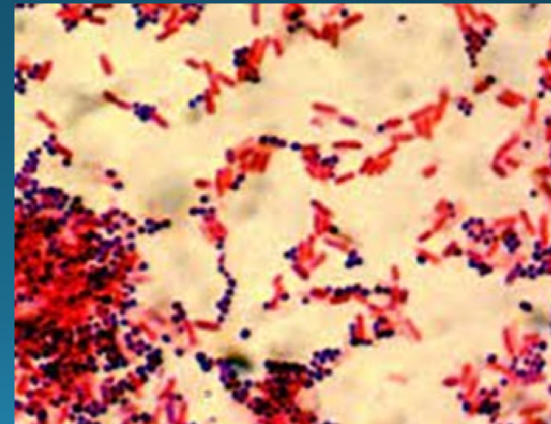
G+ = Purple
G- = Red



Gram positive

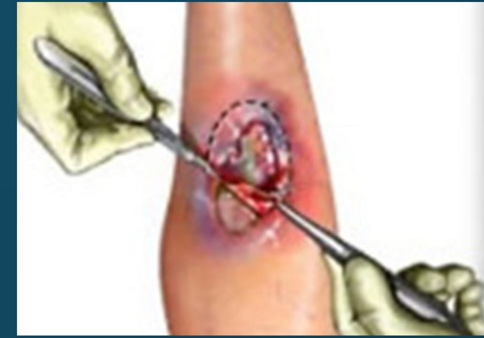


Gram negative



Mixed Gram positive and Gram negative

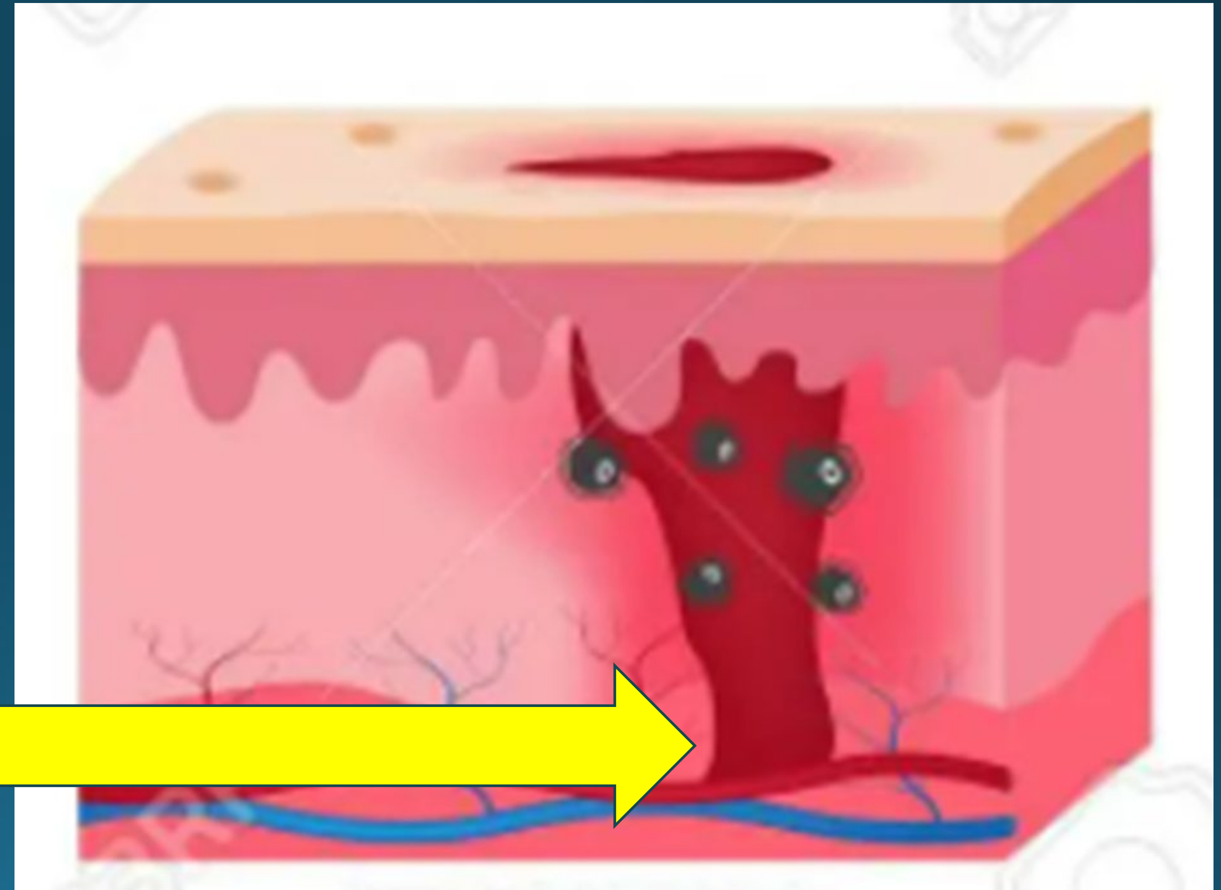
Tissue biopsy



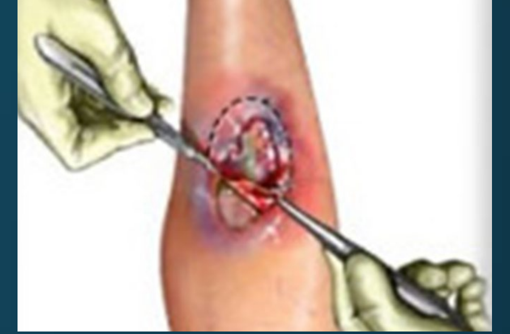
PROS

- Higher sensitivity
- Higher specificity
- Gram stain
- Extended tests

predominance of pathogenic bacteria



Tissue biopsy via wound



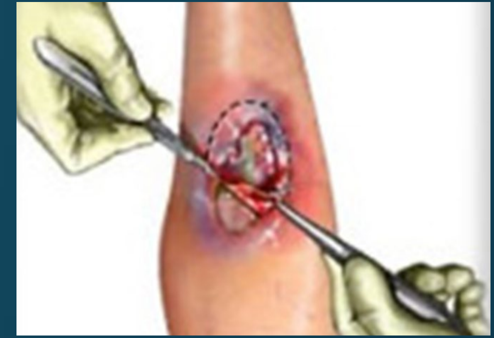
PROS

- Higher sensitivity
- Higher specificity
- Gram stain
- Extended microbiology tests

CONS

- Technical skill?
- Patient discomfort?
- Risk of introducing infection into deeper tissue?

Bone biopsy via wound



PROS

- Relatively easy
- Usually confirms OM

CONS

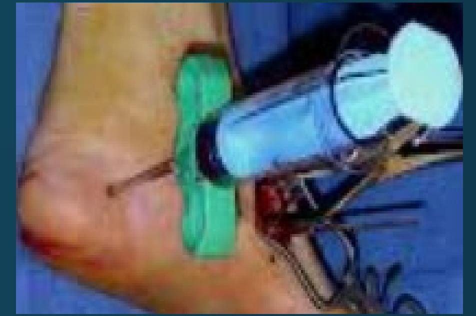
- Contaminated with colonisers from wound

Resection margin biopsy

Separate instruments!

Poor histological correlation with culture?

Percutaneous bone biopsy



PROS

- Highly specific
- Few adverse events
- Can be done in clinic
- Gold standard?

CONS

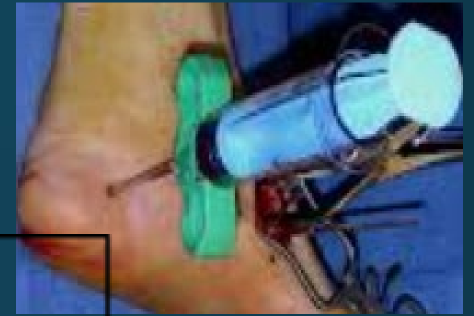
- Needs trainings

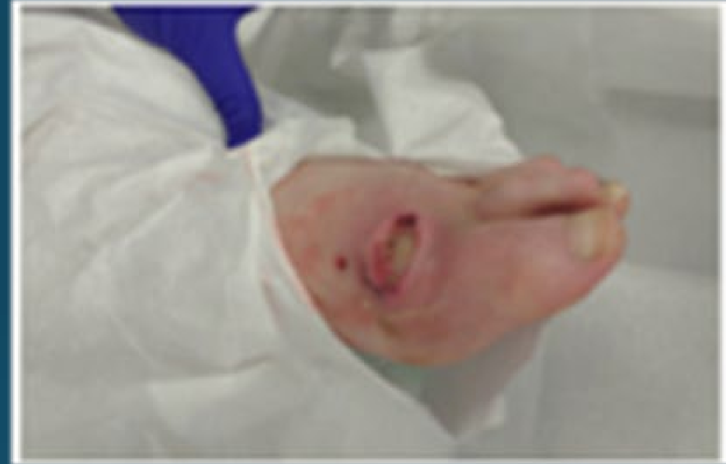
> Trials. 2021 Aug 3;22(1):517. doi: 10.1186/s13063-021-05472-6.

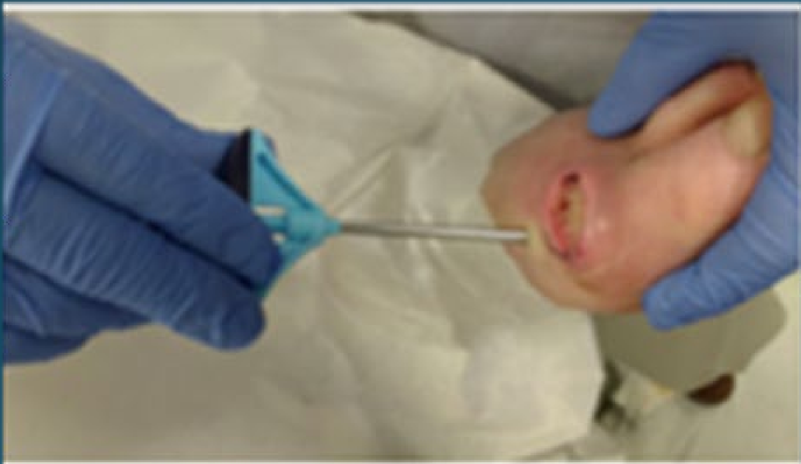
Using a BonE BiOPsy (BeBoP) to determine the causative agent in persons with diabetes and foot osteomyelitis: study protocol for a multicentre, randomised controlled trial

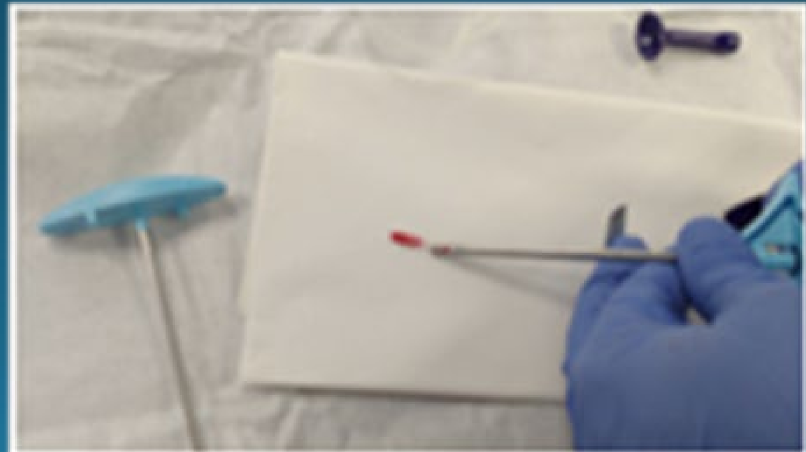
Meryl Cinzía Tila Tamara Gramberg [1], Rimke Sabine Lagrand [2], Louise Willy Elizabeth Sabelis [2], Martin den Heijer [3], Vincent de Groot [2], Max Nieuwdorp [4], Willemijn Kortmann [5], Elske Sieswerda [6], Edgar Josephus Gerardus Peters [3]

Percutaneous bone biopsy









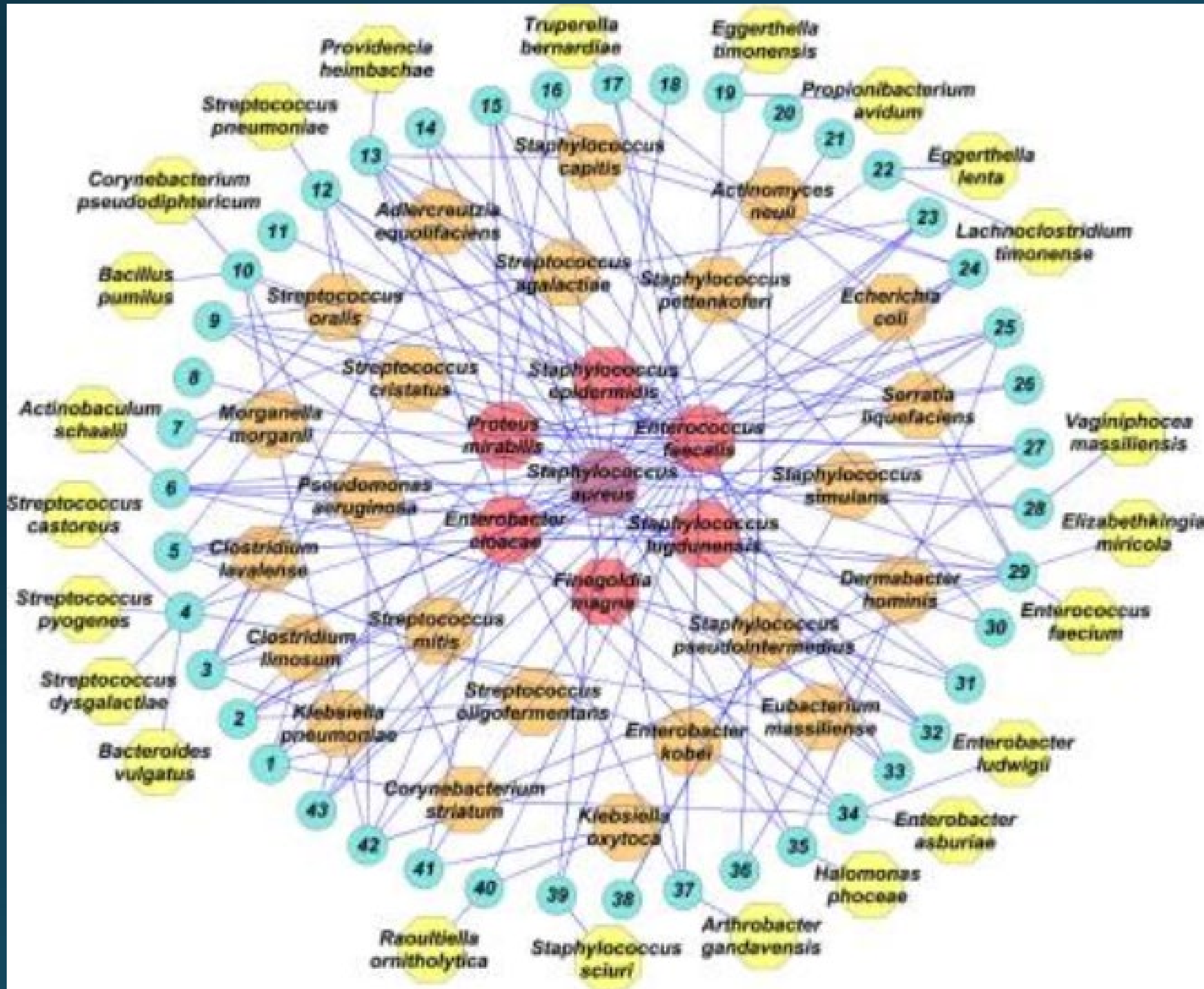
Slide courtesy of Maureen Bates, KCH podiatrist

Sampling tips…

- antibiotic-free period
- drop of saline to prevent desiccation
- get to lab promptly

1. Infected wounds
2. Tissue /bone
3. Prior to abx

Which bug?



Jneid J, Cassir N, Schuldiner S, Jourdan N, Sotto A, Lavigne JP, La Scola B.
Exploring the Microbiota of Diabetic Foot Infections With Culturomics.
Front Cell Infect Microbiol. 2018

Which bugs to worry about?

Operative sample
Percutaneous bone bx
Tissue biopsy near metalwork

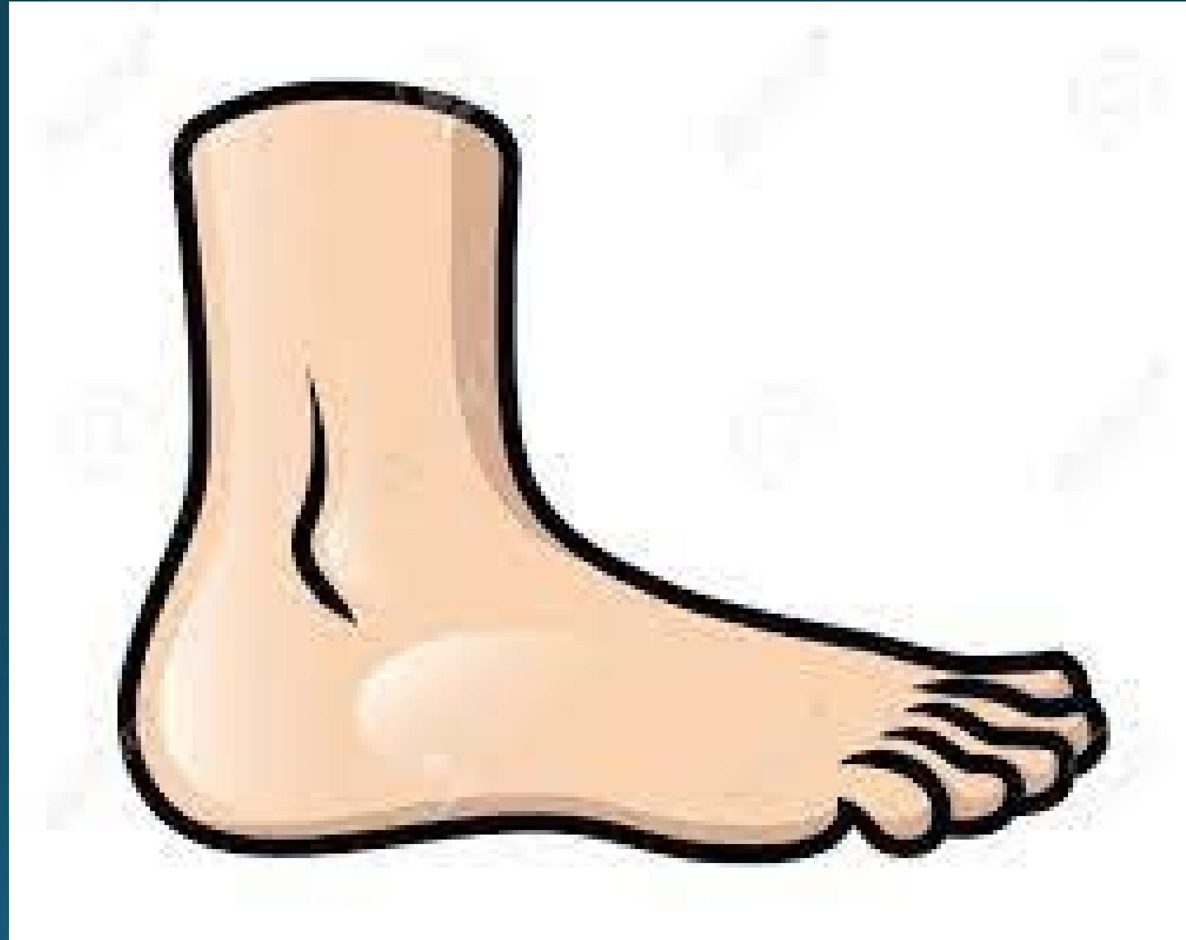
→ ANY bug!

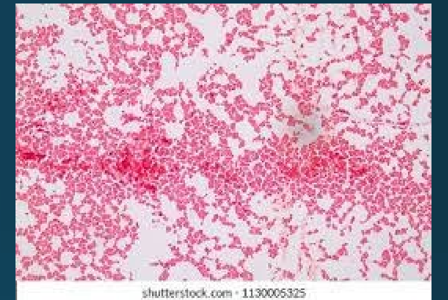
Swabs
Per-wound tissue /bone

→ skin flora
or
pathogen

Normal skin flora

Gram positive
Coagulase negative staphylococci,
micrococci,
corynebacteria,
cutibacteria

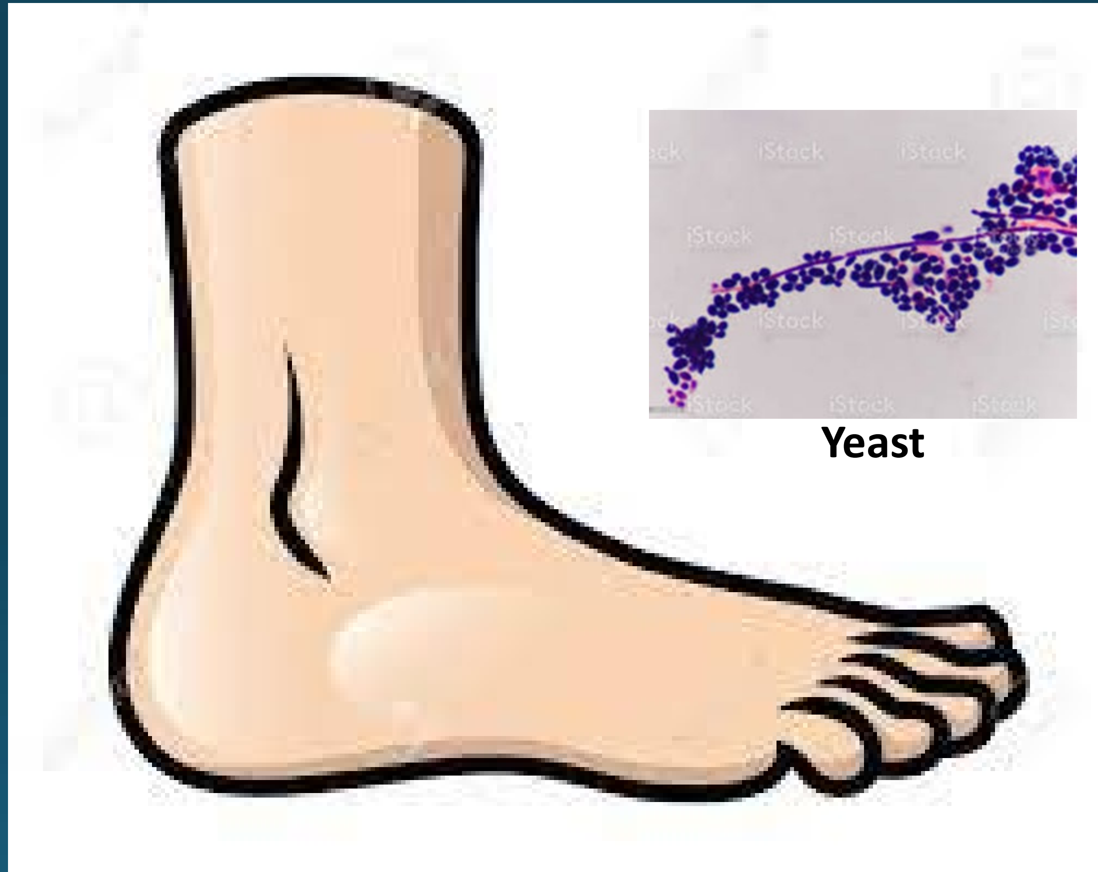


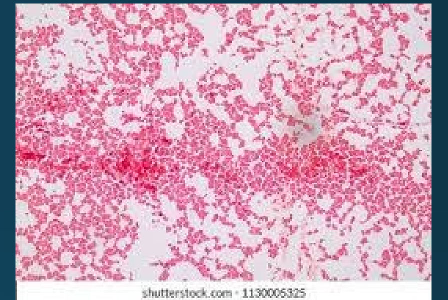


Gram negative,
E coli,
Klebsiella,

Normal skin flora in patient with DM

<u>Gram positive</u>
Staph aureus ++
Streptococci
Fewer coagulase negative staphylococci
micrococci,
corynebacteria,
cutibacteria





<u>Gram negative ++</u>
Acinetobacter,
E coli,
Klebsiella,
Enterobacter,
Proteus

And lots more!

Which Gram positive bug is a worry?

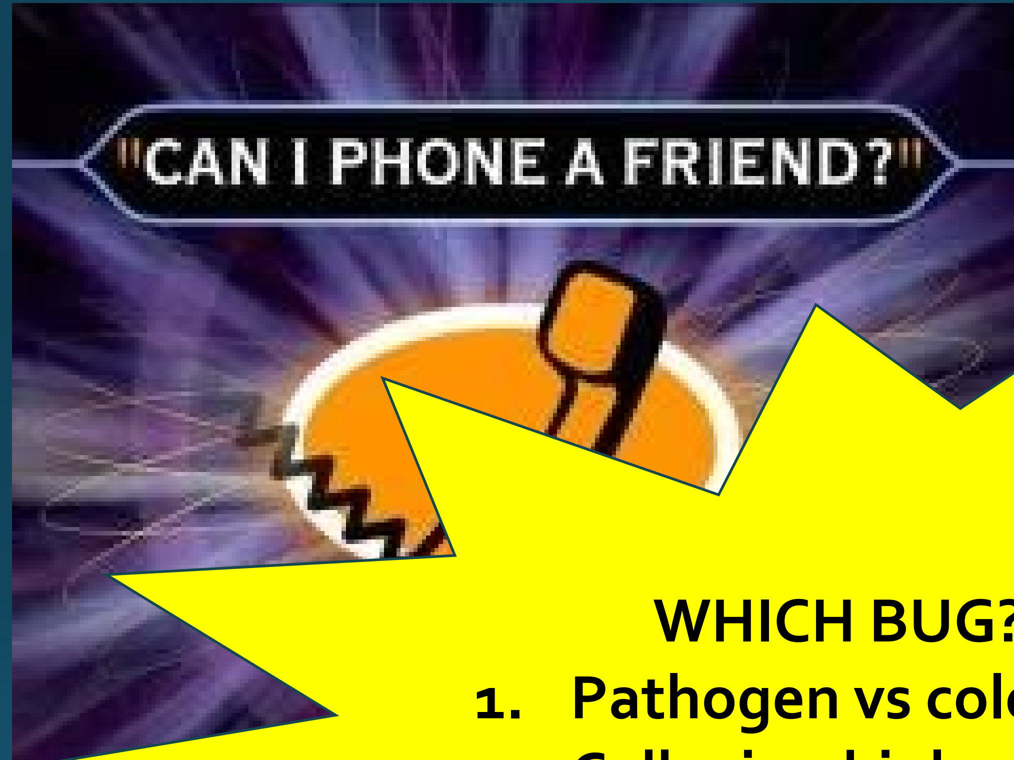
- Staph aureus
  - MSSA
  - MRSA
- Staph lugdunensis
- Beta-haemolytic streptococci
  - Strep pyogenes (Group A strep)
  - Strep agalactiae (Group B)
  - Strep dysgalactiae (Group C/G)
- Strep anginosus group

Enterococci

Which Gram negative bug?

- Proteus
- E coli
- Klebsiella
- Serratia
- Morganella
- Enterobacter
- Pseudomonas
- Bacteroides
- etc

- Stenotrophomonas
- Acinetobacter



WHICH BUG?

1. Pathogen vs coloniser?
2. Call microbiology!

Which drug?

Which drug?

- Right antibiotic
- Right dose
- Right time
- Right duration
- Right route

WAAW

18 - 24 November 2025

Which drug?

- Right antibiotic
- Right dose
- Right time
- Right duration
- Right route

Which drug?

- Right time
- Right antibiotic
- Right dose
- Right duration
- Right route

Right time

When NOT to treat!

1. Prior to biopsy
2. Prior to blood cultures
3. Uninfected ulcers

Primum non nocerum

C difficile diarrhoea

photosensitivity

diarrhoea

AKI

Bone marrow suppression

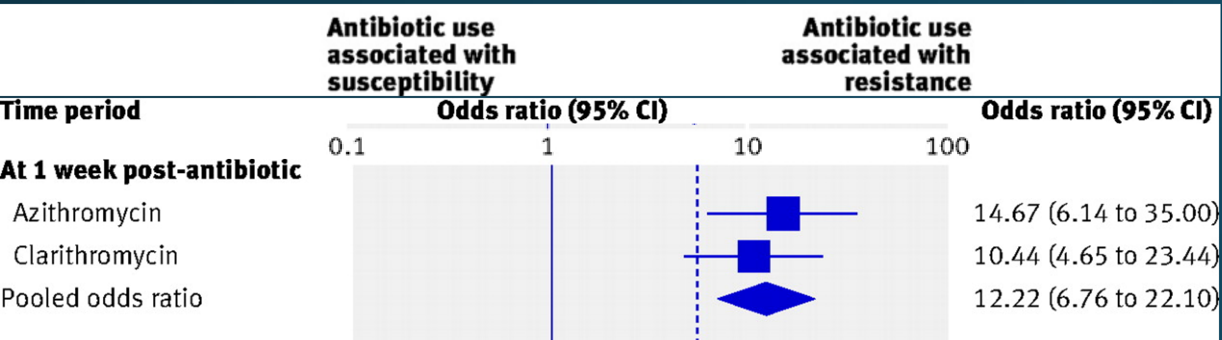
AMR

Acute hepatitis

IV line thrombus

Drug interactions

IV line infection



AMR after one course of abx

Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis

Céire Costelloe et al. BMJ 2010;340:bmj

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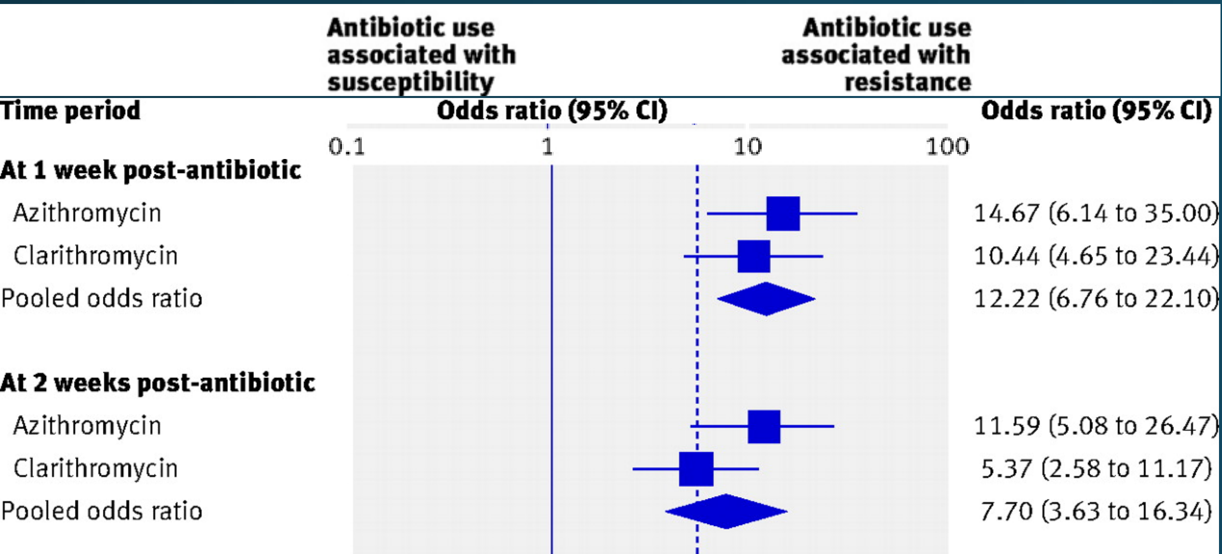

thebmj

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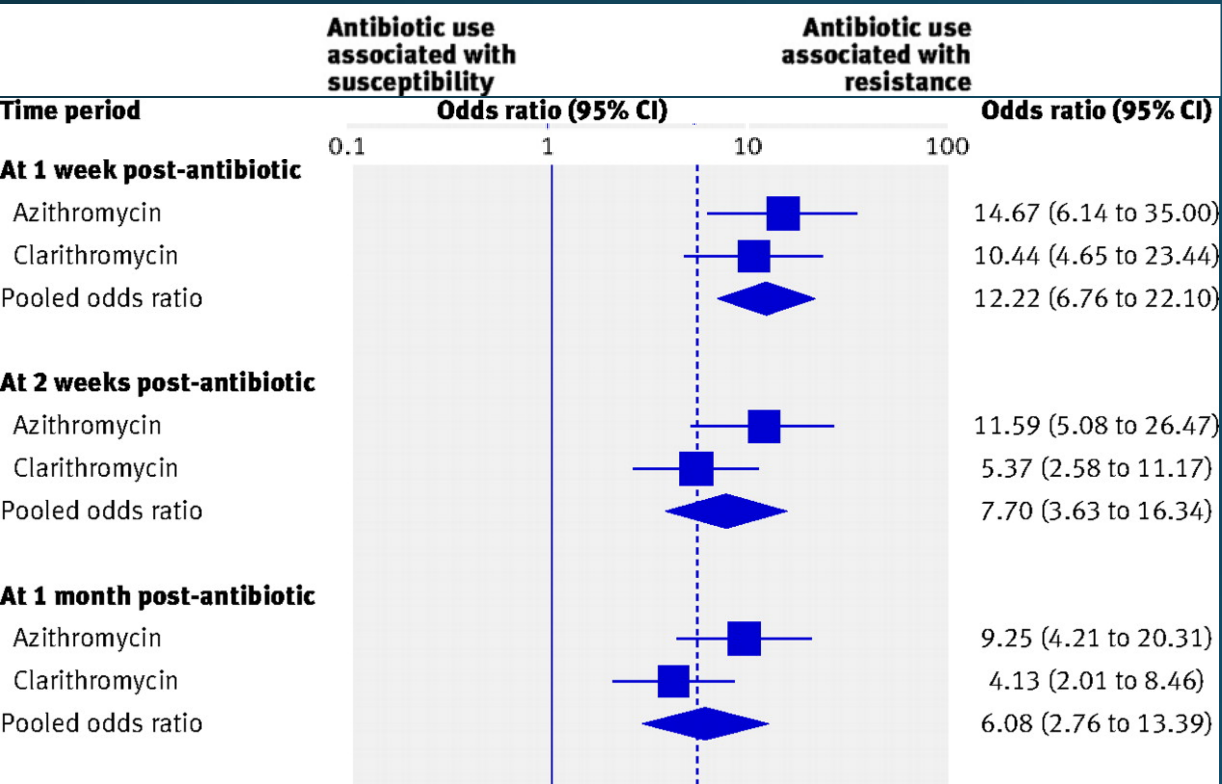

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Antibiotic use associated with susceptibility

Antibiotic use associated with resistance

Time period	Odds ratio (95% CI)
At 1 week post-antibiotic	
Azithromycin	14.67 (6.14 to 35.00)
Clarithromycin	10.44 (4.65 to 23.44)
Pooled odds ratio	12.22 (6.76 to 22.10)
At 2 weeks post-antibiotic	
Azithromycin	11.59 (5.08 to 26.47)
Clarithromycin	5.37 (2.58 to 11.17)
Pooled odds ratio	7.70 (3.63 to 16.34)
At 1 month post-antibiotic	
Azithromycin	9.25 (4.21 to 20.31)
Clarithromycin	4.13 (2.01 to 8.46)
Pooled odds ratio	6.08 (2.76 to 13.39)
At 2 months post-antibiotic	
Azithromycin	4.37 (2.13 to 8.98)
Clarithromycin	3.00 (1.48 to 6.08)
Pooled odds ratio	3.61 (2.18 to 5.97)
At 6 months post-antibiotic	
Azithromycin	1.89 (0.88 to 3.77)
Clarithromycin	2.47 (1.20 to 5.07)
Pooled odds ratio	2.16 (1.30 to 3.61)

Odds ratio (95% CI): 0.1 1 10 100

Antibiotic use associated with susceptibility

Antibiotic use associated with resistance

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Resistance in urinary tract bacteria (E coli)

Time period, study	Antibiotic exposure	Resistance in unexposed (control) group (%)	Odds ratio (95% CI)
0-1 month			
Donnan[17]	Trimethoprim	NR	4.45 (3.78 to 5.21)
Hillier[19]	Trimethoprim	20	4.85 (2.63 to 8.94)
Hillier[19]	Amoxicillin	20	3.11 (1.57 to 6.17)
Pooled odds ratio			4.40 (3.78 to 5.12)
Test for heterogeneity: I^2=0.0%, P=0.576			
0-3 months			
Donnan[17]	Trimethoprim	NR	2.60 (2.04 to 3.33)
Hillier[19]	Trimethoprim	39	2.62 (1.69 to 4.07)
Hillier[19]	Amoxicillin	39	2.26 (1.41 to 3.62)
Hay[18]	Any antibiotic	20	1.93 (1.06 to 3.51)
Pooled odds ratio			2.48 (2.06 to 2.98)
Test for heterogeneity: I^2=0.0%, P=0.796			
0-6 months			
Steinke[23]	Any antibiotic*	19	1.36 (1.14 to 1.61)
Donnan[17]	Trimethoprim	NR	1.67 (1.32 to 2.10)
Steinke[23]	Trimethoprim	19	3.95 (3.04 to 5.12)
Hillier[19]	Amoxicillin	28	1.83 (1.39 to 2.42)
Donnan[17]	Any antibiotic*	NR	1.65 (1.10 to 2.46)
Hillier[19]	Trimethoprim	28	2.57 (1.83 to 3.61)
Metlay[24]	ST	28	4.10 (2.20 to 7.50)
Pooled odds ratio			2.18 (1.57 to 3.03)
Test for heterogeneity: I^2=89.2%, P=0.000			
)-12 months			
Donnan[17]	Trimethoprim	NR	1.22 (1.16 to 1.28)
Donnan[17]	Any antibiotic*	NR	1.18 (1.06 to 1.32)
Hillier[19]	Amoxicillin	19	1.62 (1.18 to 2.23)
Hay[18]	Any antibiotic*	38	1.13 (0.79 to 1.63)
Hillier[19]	Trimethoprim	19	2.36 (1.59 to 3.50)
Pooled odds ratio			1.33 (1.15 to 1.53)
Test for heterogeneity: I^2=71.9%, P=0.007			

0.1 | 1 | 10

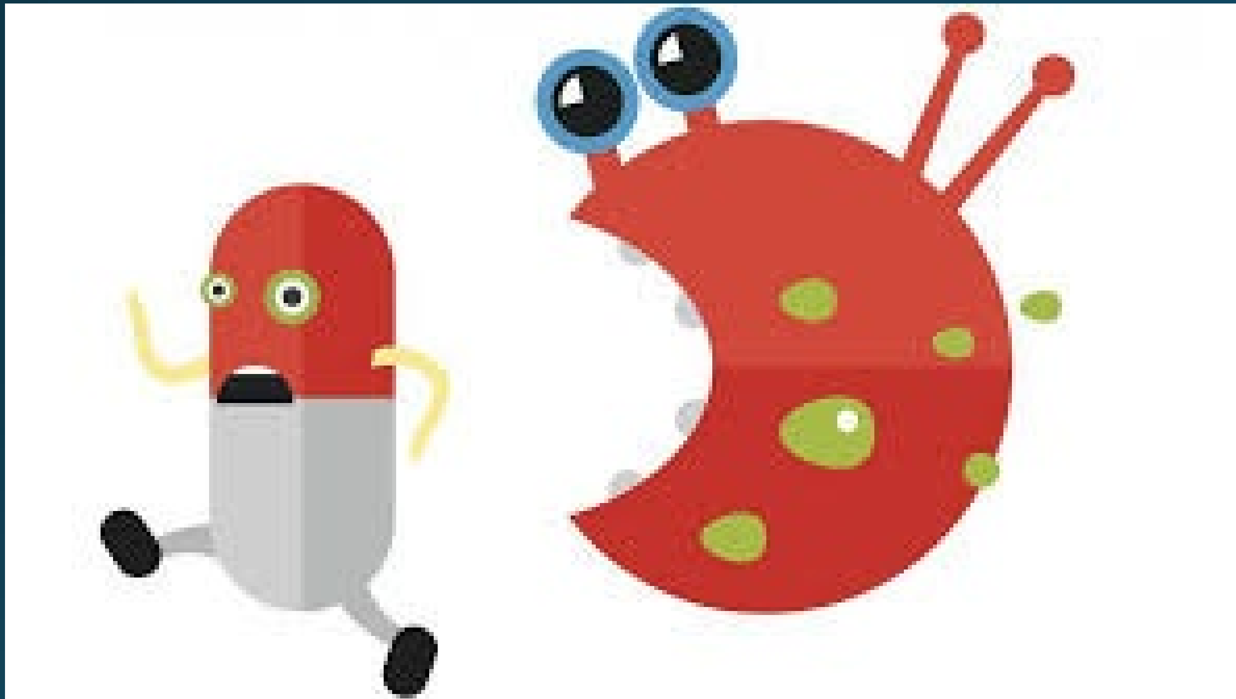
Antibiotic use associated with susceptibility | **Antibiotic use associated with resistance**

* Any antibiotic other than trimethoprim. ST=sulfamethoxazole-trimethoprim. NR=not reported

One short course of abx

Risk of AMR
one year later!

Antimicrobial resistance (AMR)



- Higher morbidity
- Longer length of stay
- Increased healthcare costs
- Higher mortality
- Risk of transmission

Empirical Rx

Targeted Rx

Right drug & dose

King's College Hospital NHS
NHS Foundation Trust

GUIDELINES FOR THE MICROBIOLOGICAL MANAGEMENT OF DIABETIC FOOT INFECTIONS PRESENTING ACUTELY TO HOSPITAL

Document Information		
Version Number	*5*	***Please complete all fields***
Is this a new guideline? *(Yes / No)*		*No*
Is this an update of an existing guideline? *If yes, please state the title of the guideline being replaced. Also state the key changes from previous guideline.*		*Yes (Guidelines for the Microbiological Management of Diabetic Foot Infections)*

Severity of infection	Category of infection			
	'Empiric'	Recent antibiotic treatment for DFIRe	Penicillin allergy	High risk for MRSA
MILD INFECTION (If patient discharged ensure follow up in diabetic foot outpatient clinic)	**Flucloxacillin** PO 500mg QDS	**Co-amoxiclav** PO 625mg TDS	**Non-severe allergy:** **CefALEXin** PO 500mg TDS **Severe allergy:** **Doxycycline** PO 200mg OD Or **Co-trimoxazole** PO 960mg BD	**Doxycycline** PO 200mg OD Or **Co-trimoxazole** PO 960mg BD
Moderate infection (If patient discharged ensure follow up in diabetic foot outpatient clinic)	**Co-amoxiclav** PO 625mg TDS PLUS **Amoxicillin** PO 500mg TDS		**Non-severe allergy:** **CefALEXin** PO 1.5g TDS + if necrosis present **Metronidazole** PO 400mg TDS **Severe allergy:** **Co-trimoxazole** PO 1440mg BD + if necrosis present **Metronidazole** PO 400mg TDS	**Co-trimoxazole** PO 1440mg BD + if necrosis present **Metronidazole** PO 400mg TDS Or **Linezolid** 600mg BD PO
Severe infectionModerate or severe infectionMod **CONSIDER DEEPER INFECTION** • **Involve Diabetic Foot Team ASAP** • **Involve on-call vascular team if surgery is deemed necessary** If patient known to be colonised with multi-resistant Gram negative organisms (e.g. ESBL or CPE producing) then discuss with microbiology	**Co-amoxiclav** IV 1.2g TDS + if patient septic, stat **Amikacin** 15mg/kg	**Piperacillin-tazobactam** IV 4.5g QDS + if patient septic, stat **Amikacin** 15mg/kg	**Non-severe allergy:** **IV CefTRIAXone 2g BD** + **Metronidazole** PO 400mg TDS **Severe allergy:** **Teicoplanin** IV 10-12mg/kg BD for 3 doses then once daily + **Ciprofloxacin** PO 750mg BD + **Metronidazole** PO 400mg TDS (use **Ciprofloxacin** 400mg IV TDS + **Metronidazole** 500mg IV TDS if unable to take PO) + if patient septic, stat **Amikacin** 15mg/kg	**Add** **Teicoplanin** IV 10-12mg/kg BD for 3 doses then once daily

Severity of infection	Category of infection			
	'Empiric'	Recent antibiotic treatment for DFIRe	Penicillin allergy	High risk for MRSA
MILD INFECTION (If patient discharged ensure follow up in diabetic foot outpatient clinic)	Flucloxacillin PO 500mg QDS	Co-amoxiclav PO 625mg TDS	**Non-severe allergy:** CefALEXin PO 500mg TDS **Severe allergy:** Doxycycline PO 200mg OD Or Co-trimoxazole PO 960mg BD	Doxycycline PO 200mg OD Or Co-trimoxazole PO 960mg BD
Moderate infection (If patient discharged ensure follow up in diabetic foot outpatient clinic)	Co-amoxiclav PO 625mg TDS PLUS Amoxicillin PO 500mg TDS		**Non-severe allergy:** CefALEXin PO 1.5g TDS + if necrosis present Metronidazole PO 400mg TDS **Severe allergy:** Co-trimoxazole PO 1440mg BD + if necrosis present Metronidazole PO 400mg TDS	Co-trimoxazole PO 1440mg BD + if necrosis present Metronidazole PO 400mg TDS Or Linezolid 600mg BD PO

Empirical Rx

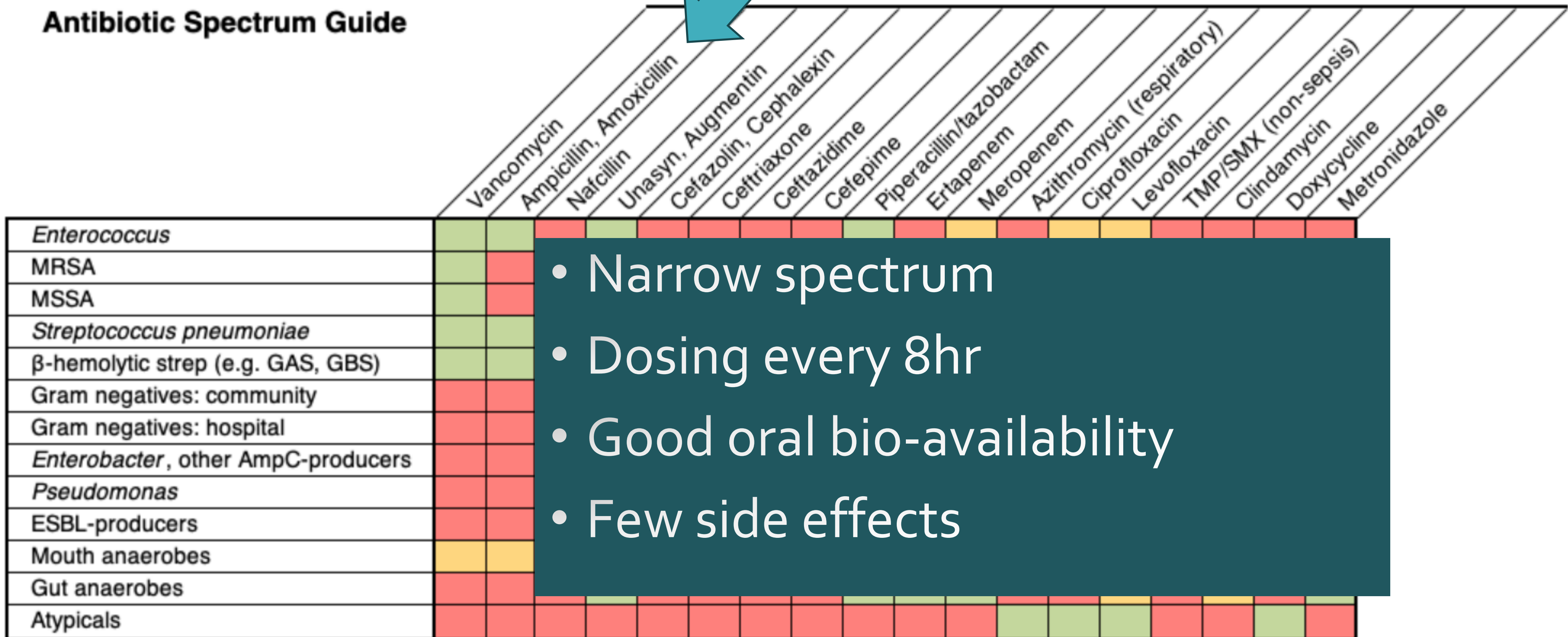
Targeted Rx

Right drug & dose

	Staphylococcus aureus	
	DISC DIFFUSION	
Cefoxitin	30 mm	Susceptible *
Cefuroxime		
Ciprofloxacin	29 mm	**Susceptible, maximum dose** *
Clarithromycin		
Clindamycin	30 mm	Susceptible *
Co-amoxiclav		
Co-trimoxazole	33 mm	Susceptible *
Doxycycline		
Erythromycin	29 mm	Susceptible *
Flucloxacillin		
Fusidic acid	35 mm	Susceptible *
Linezolid	30 mm	Susceptible *
Mupirocin	37 mm	Susceptible *
Neomycin	18 mm	Susceptible *
Rifampicin	33 mm	Susceptible *
Tetracycline	31 mm	Susceptible *
Trimethoprim	27 mm	Susceptible *

- Narrowest spectrum
- Fewest side effects
  - Allergy /intolerance
  - Kidney function etc
- Fewest drug interactions
- Easiest regimen

Amoxicillin



- Narrow spectrum
- Dosing every 8hr
- Good oral bio-availability
- Few side effects

Flucloxacillin

Antibiotic Spectrum Guide

Vancomycin
Ampicillin, Amoxicillin
Nafcillin
Unasyn, Augmentin
Cefazolin, Cephalexin
Ceftriaxone
Ceftazidime
Cefepime
Piperacillin/tazobactam
Ertapenem
Meropenem
Azithromycin (respiratory)
Ciprofloxacin
Levofloxacin
TMP/SMX (non-sepsis)
Clindamycin
Doxycycline
Metronidazole

Enterococcus
MRSA
MSSA
Streptococcus pneumoniae
β-hemolytic strep (e.g. GAS, GBS)
Gram negatives: community
Gram negatives: hospital
Enterobacter, other AmpC-producers
Pseudomonas
ESBL-producers
Mouth anaerobes
Gut anaerobes
Atypicals

- Narrow spectrum
- Dosing every 6hr
- 50% oral bio-availability
- Side effects not common

Shading Key: good to excellent activity some activity little to no activity

Erythromycin / clarithromycin

Antibiotic Spectrum Guide

ancomycin
mpicillin, Amoxicillin
afcillin
nasyn, Augmentin
efazolin, Cephalexin
eftriaxone
eftazidime
efepime
iperacillin/tazobactam
rtapenem
eropenem
Azithromycin
Ciprofloxacin
Levofloxacin
TMP/SMX (non-sepsis)
Clindamycin
Doxycycline
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Gut anaerobes
Atypicals

- Narrow spectrum
- Dosing every 12hr
- Good oral bio-availability
- GI side effects ++

Shading Key: good to excellent activity; some activity; little to no activity

Co-trimoxazole (TMP-SMX)

Antibiotic Spectrum Guide

ancomycin
mpicillin, Amoxicillin
afcillin
nasyn, Augmentin
efazolin, Cephalexin
eftriaxone
eftazidime
efepime
iperacillin/tazobactam
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eropenem
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Pseudomonas
ESBL-producers
Mouth anaerobes
Gut anaerobes
Atypicals

- Broader spectrum
- Dosing every 12hr
- Good oral bio-availability
- Side effects - AKI, sudden death,

Shading Key: good to excellent activity; some activity; little to no activity

Doxycycline

Antibiotic Spectrum Guide

Doxycycline
Metronidazole

Enterococcus
MRSA
MSSA
Streptococcus pneumoniae
β-hemolytic strep (e.g. GAS, GBS)
Gram negatives: community
Gram negatives: hospital
Enterobacter, other AmpC-producers
Pseudomonas
ESBL-producers
Mouth anaerobes
Gut anaerobes
Atypicals

- Narrow spectrum
- Dosing every 12hr
- Good oral bio-availability
- Side effects - photosensitivity

Shading Key: good to excellent activity; some activity; little to no activity

Ciprofloxacin

Antibiotic Spectrum Guide

ancomycin
mpicillin, Amoxicillin
lafcillin
Inasyn, Augmentin
efazolin, Cephalexin
eftriaxone
eftazidime
efepime
iperacillin/tazobactam
rtapenem
eropenem
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Gram negatives: hospital
Enterobacter, other AmpC-producers
Pseudomonas
ESBL-producers
Mouth anaerobes
Gut anaerobes
Atypicals

- Broad spectrum
- Dosing every 12hr
- Good oral bio-availability
- Side effects ++

Shading Key: good to excellent activity | some activity | little to no activity

Ciprofloxacin

Medicines & Healthcare products Regulatory Agency

Published
22 January 2024

Fluoroquinolone antibiotics: must now only be prescribed when other commonly recommended antibiotics are inappropriate

disabling and potentially long-lasting or irreversible side effects.

- Tendon injury
- Aortic aneurysm & dissection
- Sleep disorders, anxiety, panic attacks, confusion or depression etc

Right duration

Table 5: Duration of antibiotic therapy according to the clinical situation

Infection severity (skin and soft tissues)	Route	Duration
Class 2: mild	oral	1-2 weeks*
Class 3 / 4: moderate / severe	[illegible] iv	2-4 weeks
Bone/joint	[illegible]	Duration
Resected	oral/initially iv	2-5 days
Debrided (soft tissue infection)	oral/initially iv	1-2 weeks
Positive culture or histology of bone margins after bone	oral/initially iv	3 weeks
resection	oral/initially iv	6 weeks
No surgery or dead bone		

*: 10 days following surgical debridement

needs MDT

Rx until the infection has resolved
NOT until the wound has healed!

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Positive culture or histology of bone margins after bone resection	oral/initially iv	3 weeks
No surgery or dead bone	oral/initially iv	6 weeks

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*: 10 days following surgical debridement

Right route

- PO
- IV
- local

IV antibiotics

"Serious" infections

But…

- Venous catheter complications
- Prolonged hospital stays
- Increased drug costs
- Increased nursing costs
- High carbon footprint

OVIVA

Oral Versus Intravenous Antibiotics for Bone and Joint Infection trial

2019

NEJM

N = 1054

(527 each group)

6 weeks IV or PO

(enrolled within 7days)

20% DM

Oral abx non-inferior

Treatment failure

- IV 14.6%
- PO 13.2%

IWGDFI guidelines for DFO

Bugs don’t care how the drugs get there!

Highly oral bioavailable

Local antibiotics

Sprinkling abx powder onto surgical site?

- *Persist for max few days*
- *No standardised dose*
- *No RCT showing efficacy*
- *NOT recommended in any guidelines*

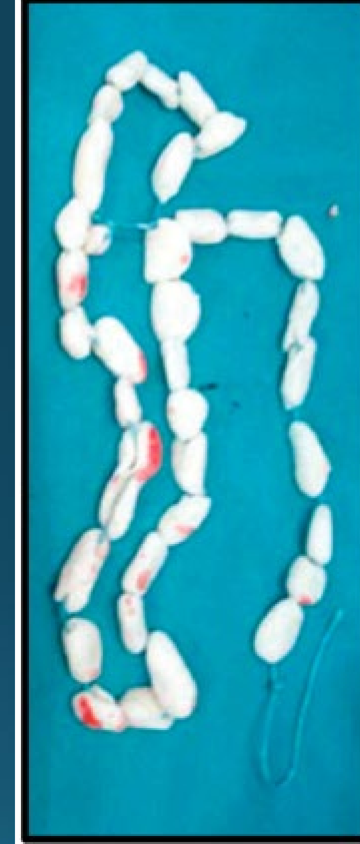
Abx with a carrier?

Local antibiotic carriers

Carrier	Materials	Antibiotics	Benefits	Disadvantages
PMMA	Polymethylmethacrylate	Heat stable only (Aminoglycosides, Glycopeptides, Tetracyclines, and Quinolones)	Availability, Occupies dead space	Not absorbable, long elution profile
Ceramics	Calcium sulfate, calcium phosphate, or a combination	Aminoglycosides Glycopeptides Lipopeptides	Absorbable, faster resorption and elution profiles	Possible toxicity or hypercalcemia (rare), wound drainage, cost
Hydrogels	PCLA-PEG-PCLA tri-block, poly(ether ester) SynBiosys, etc.	Variable	Absorbable, fast resorption, variety	Shorter release period, lack structural integrity, cost

PMMA

- Oldest carrier - used since 1970s
- Rigid polymer – formed into beads
- Requires removal
- ?useful in trauma setting



Ceramics – Cerement® & Stimulan®

- Absorbable
- Calcium sulphate or phosphate
- ~6 weeks abx delivery

Cerement®

- 60% calcium sulphate
- 40% hydroxyapatite – stimulates bone growth

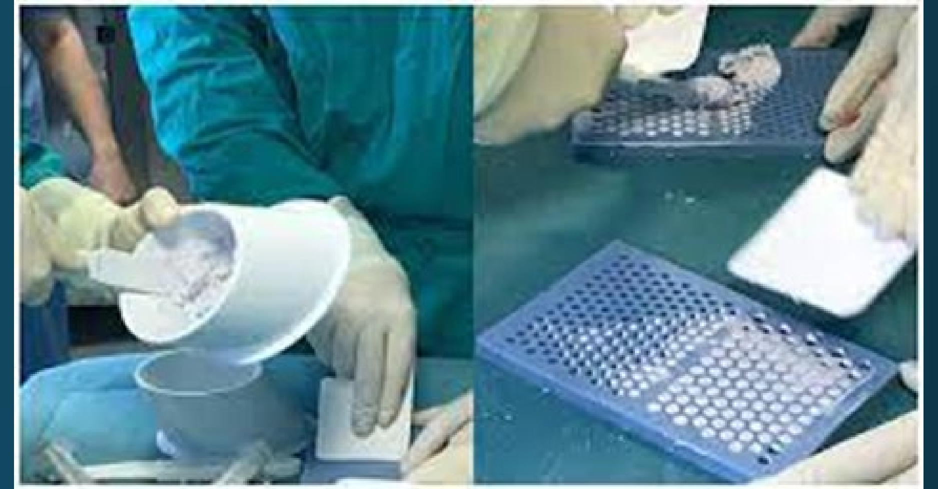
Cerement - bone void filler

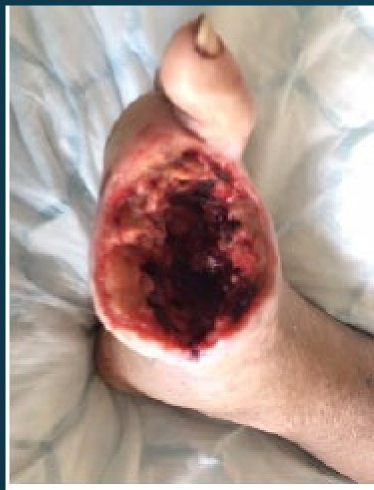
CementG - Gentamicin *"64-150x higher than MIC"*

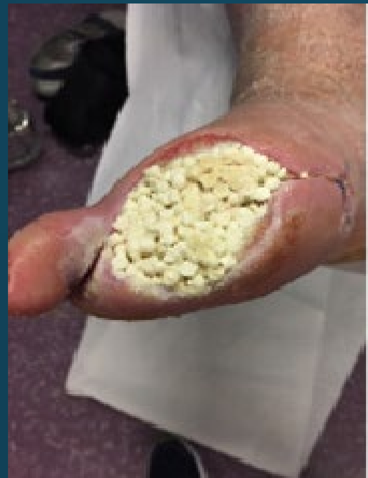
Cerement V - Vancomycin *"3000 x the MIC of MRSA"*

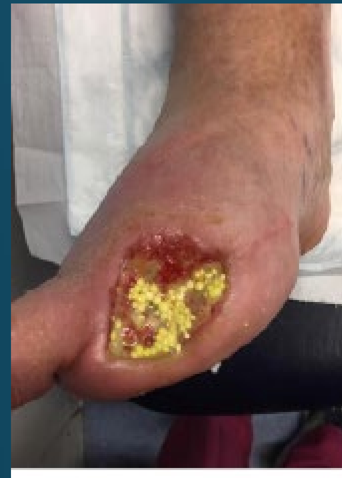
Stimulan®

- Calcium sulphate carrier
- Licence for soft tissue infection & OM
- Exudate ++
- For vancomycin or gentamicin
- Needs non-adherent dressing
- Can be reapplied

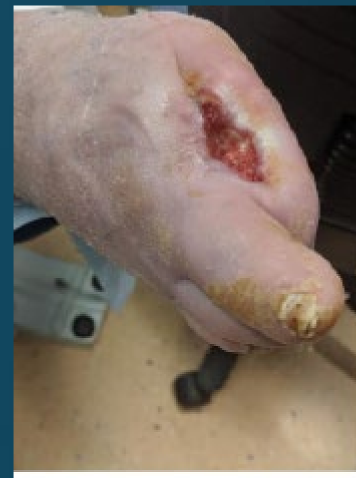




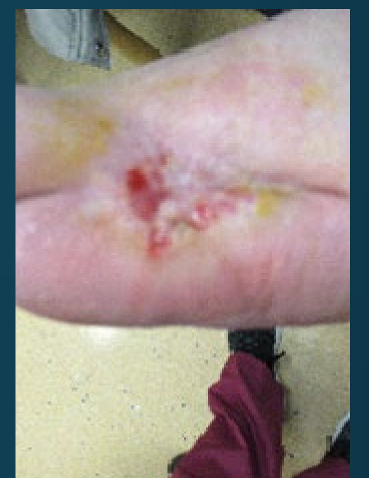




8 weeks



14 weeks



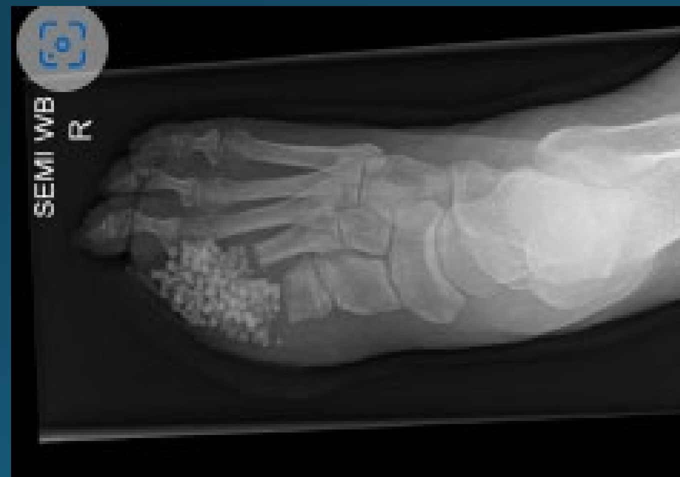
25 weeks

70yoM T2DM. DFI

Bone – Proteus mirabilis and Pseudomonas ciproR
Pt self-d/c
Attended clinic – not septic. Debridement ++

Stimulan G
No PO or IV abx

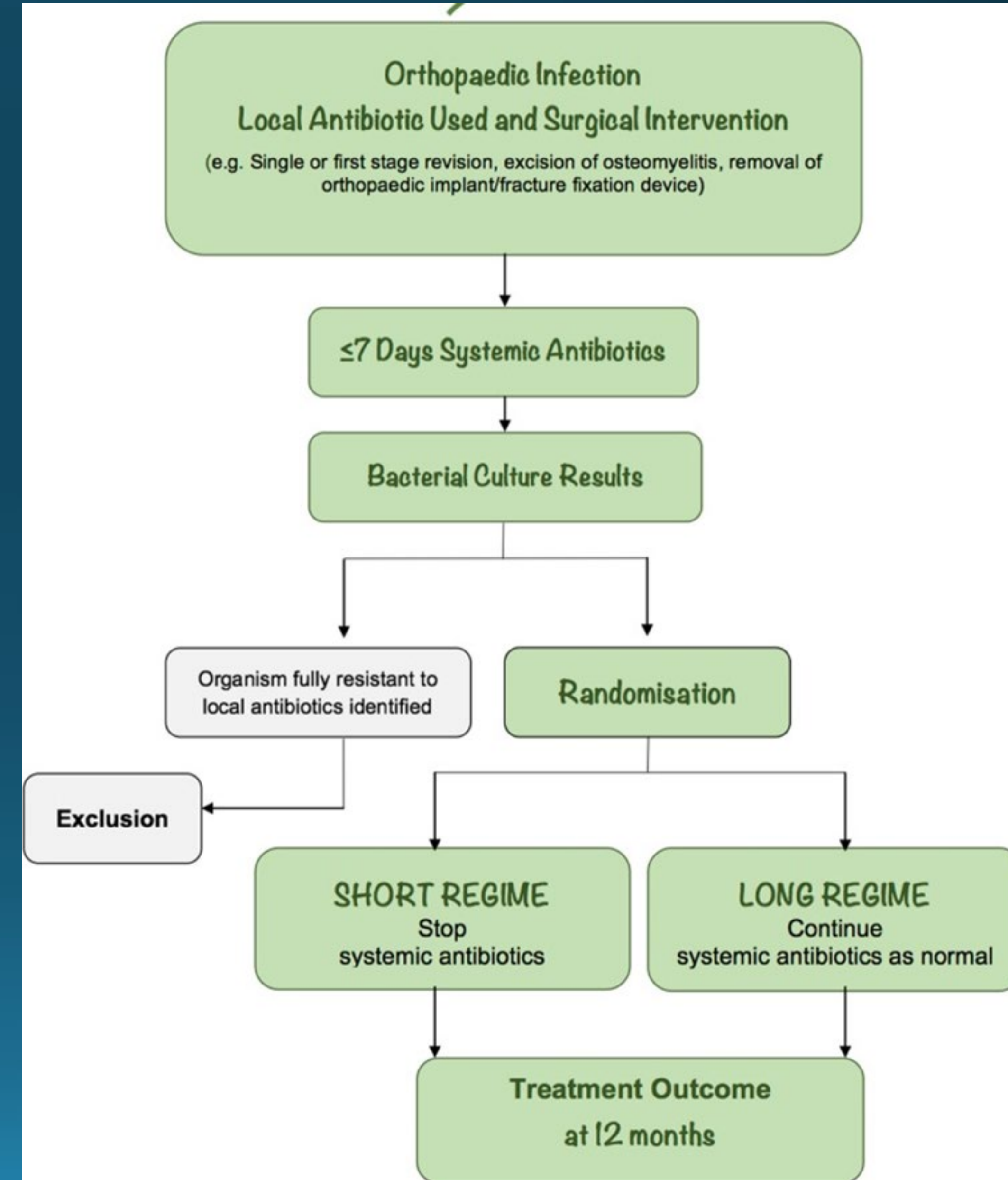
7 days of PO abx



Short or Long Antibiotic regimes in orthopaedics

SoLARIO

- Multi centre, RCT
- Surgically treated BJI
- Oxford, UK
- Local abx plus either
  - 7 days abx
  - 4-6 weeks abx
- Presented at EBJIS 2025
- Publication pending



BLADE -VG2 study

STIMULAN® VG v Standard of Care (SoC) for DFO

- Multi-centre RCT
- Debridement and either

  Stimulan®VG with <5 days systemic abx

  OR

  4-6 weeks systemic abx
- Review cure rates at one year
- Started 2023
- Completed June 2025
- Results ?Jan 2026

Which drug?

- Right antibiotic
- Right dose
- Right time
- Right duration
- Right route

- **Follow guidelines**
- **Or ask microbiology**
- **Local abx - watch this space!**

Key takeaways!

which bug
which drug
which sample

- *Pathogen vs coloniser*
- *Deep samples*
- *Infected wounds*
- *Follow Rx guidelines*
- *Micro are here to help!*

Thank you for listening