The Wound Culture
What's Important… and What to Do

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Disclosures

- Opinions are expressed herein do not represent those of the Catholic Health System
- Non-FDA approved use of antibiotics will be discussed
- No Relevant Financial Relationships with Commercial Interests

Outline

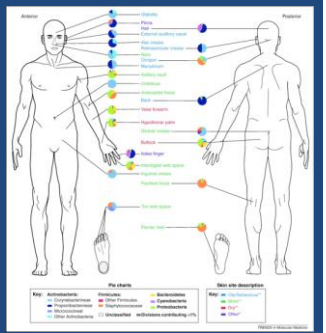
- Colonization vs. Infection
- Wound Culture Collection
- Important Pathogens & Syndromes
- Empiric Antibiotic Choices
- A Cautionary Word on Antimicrobials

Colonization or Infection?

- With few exceptions, organisms cultured from wounds do not define infection
- Infection is a Clinical Diagnosis

The Human Microbiome

- Ten Microbes for every one human cell
- Multiple "Habitats" on & in each Person
- Understanding of host-microbe interaction in health and disease is still limited



Journal of Investigative Dermatology. 2012; **132**:933–939

The Wound Habitat

- Chronic Wounds are colonized by multiple microbial species
  - Commensals and traditional "pathogens"
- Flora influenced by
  - Wound location
  - Wound age
  - Pathogenesis of wound
  - Host Factors
  - Antimicrobial Exposures

Acta Dermato-Venereologica 1995;75: 24–30.
International Journal of Dermatology. 1999;38:573–8.
International Journal of Dermatology 1998;37: 426–8.

Microbial Diversity in Venous Ulcers

Number of taxa identified by each analytic method

Taxon	No. identified by:								
	Pyrosequencing			Ibis T5000			Culture		
	Total	Range	Mean (SE)	Total	Range	Mean (SE)	Total	Range	Mean (SE)
Phylum	6	2–5	3.43 (0.25)	4	1–3	1.78 (0.19)	2	1–2	1.07 (0.18)
Class	11	3–7	4.64 (0.37)	8	1–5	2.29 (0.30)	3	1–2	1.07 (0.18)
Order	15	3–8	5.71 (0.51)	13	1–5	2.86 (0.36)	5	1–2	1.07 (0.18)
Family	27	3–12	7.86 (0.78)	15	1–5	2.93 (0.37)	7	1–2	1 (0.20)
Genus	43	3–17	9.64 (1.04)	20	1–8	3.50 (0.52)	7	1–2	1 (0.20)
Species	55	4–15	8.78 (0.87)	29	1–7	3.29 (0.50)	8	1–2	1 (0.20)

J. Clin. Microbiol. November 2011 vol. 49 no. 11 3812-3819

Microbial Diversity in Venous Ulcers

- Streptoccoci
- S. aureus
- Coagulase Negative Staph Spp.
- Pseudomonas spp.
- Anaerobes
- Enteric GNR's (e.g. Proteus)
- Diptheroids
- Non-fermenting GNR's (eg. Stenotrophomonas)

J. Clin. Microbiol. November 2011 vol. 49 no. 11 3812-3819

Distinguishing Colonization from Infection

Colonization

Microbial Co-habitation on or in host tissue *without* significant disruption to host tissue function

Infection

Microbial *invasion* of viable host tissue with consequent *injury as a result* of the microbe and microbe-specific host response

Healthy Skin

Sam Javanrouh; http://wvs.topleftpixel.com/11/10/10/

Chronic Wounds

www.wnyc.org

Infected Wounds

http://www.nydailynews.com/news/san-francisco-giants-fans-riot-world-series-win-gallery-1.1992930?pmSlide=1.1992912

When to Suspect Infection

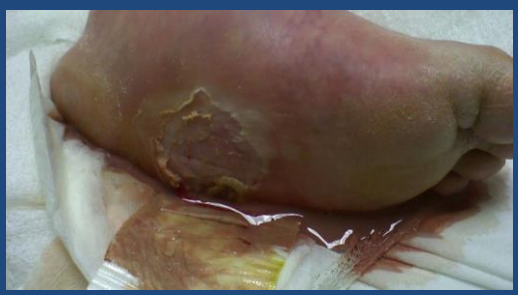
- Cardinal Signs of Inflammation
  - Pain
  - Erythema
  - Warmth
  - Swelling
- New Purulence
- Marked increase in non-purulent drainage
- Progression of Injury from prior Margins
  - Including tunneling, undermining
- New odor

Pain, Erythema, Swelling, Warmth

Purulence, Pain, Progression

Progression, Pain, Purulence, Odor

Warmth, Swelling, Purulence



The Wound Culture

Benefits

- Allows identification of potentially resistant pathogens
- Can help narrow antimicrobial selection
- Allows for evaluation of rare pathogens

Harms

- Rarely diagnostic on its own
  - Do not Culture wounds without signs of infection
- Colonizers and Contaminants can confound results
- Deep tissue infections may not be detected from superficial specimens

Basic Wound Culture Principles

- Wound Cultures can cause Harm if performed without cause
- Do not culture necrotic debris
- Superficial Swabs are of limited utility
- Deep tissue specimens are more useful
- Ideally, deep cultures should be collected prior to antimicrobials (especially for bone specimens)
- If suspect unusual organisms alert the lab

Tissue Biopsy for Culture

- Debride and cleanse Superficial areas
- Using Aseptic Technique resect viable tissue with punch biopsy or scalpel
- Routine and Anaerobic specimens

Needle Aspiration

- Disinfect Overlying tissue
- Insert 18-22 gauge needle and aspirate contents
- Routine and Anaerobic specimens

Unroofing

- Disinfect Overlying tissue
- Unroof tissue overlying region of interest
- Insert swab into cavity below
- Routine and Anaerobic specimens

Superficial Swabs

- Swab surface of wound
- Throw swab in garbage can

Diabetic Foot Infection Guidelines

"We recommend sending a specimen for culture that is from deep tissue, obtained by biopsy or curettage after the wound has been cleansed and debrided. We suggest avoiding swab specimens, especially of inadequately debrided wounds, as they provide less accurate results."

Clinical Infectious Diseases 2012;54(12):132–173

Superficial Cultures: Multiple Organisms -Significance Not Clear

Deep Culture Specimen: S. aureus; MRSA

I've got My culture. Which Organisms Should I be Concerned About?

Culprit Organisms by Syndrome

Narrow Spectrum → Broad Spectrum

Non-Purulent Cellulitis | Purulent Cellulitis & Abscess | Diabetic Foot Infection | Sacral, Perianal & Genital Deep Tissue infections | Necrotizing Fasciitis, Sepsis & Extensive Antibiotic Exposures

Streptococci >>>

Staph aureus >>

Enteric GNR' >>>>>>>>>>>>>>>>>>>>>>>>>>>

Pseudomonas>>>>>>>>>>>>>>>>>

Resistant GNR's>>

Wounds with Surrounding Cellulitis

"The vast majority of SSTIs are caused by S. aureus and β-haemolytic streptococci, usually Lancefield groups A, C and G, with group B occurring in diabetics and the elderly"

-2014 IDSA Practice Guidelines for Skin and Soft Tissue Infections

Clinical Infectious Diseases 2014;59(2):e10–52
Clin Infect Dis 2001;32:S114-32

Wounds complicated by Extensive Necrosis, Deep Penetration or multiple Antibiotic Exposures

- S. aureus
- Group A, B, C, G Streptococci
- Enteric Gram Negatives (E. coli, Klebsiella, Serratia, Proteus etc).
- Anaerobes
- Pseudomonas, Acinetobacter

Organisms That Rarely Cause Invasive Disease

- Most Coagulase Negative Staph*
  - S. lugdinensis is major exception
  - Underlying foreign materials (e.g. vascular grafts, prosthetic joints) may be infected by Coag Neg Staph
- "Diptheroids"
- Bacillus species
  - Anthrax rare exception
- Corynebacteria
  - C. diptheriae is a rare exception

Bocher et al. JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2009, p. 946–950

Rarely Cause Significant Invasive Infection Alone

- Enterococcus (including VRE)
- Candida Species
- Stenotrophomonas

Organisms That (Almost) Always Require Treatment

- Mycobacterium tuberculosis
- Dimorphic Fungi (Coccidiodes, Histoplasma, Blastomycosis)
- Cryptococcus
- Mucormycetes
- Sporothrix
- B. anthracis
- Nocardia
- Leishmania
- C. perfringens
- Group A Strep ? (S. pyogenes)

http://www.regionalderm.com/Regional_Derm/Afiles/afb.html

Caveats

- Extreme Immune Suppression
  - Commensals and Rare Organisms become Pathogens
- Foreign Material Associated Infections
  - Coag negative Staph spp. cause real disease
- Consider impact of antimicrobials given at the time of Culture collection
  - May not grow the invading organism
  - May only grow non-invading but resistant co-habitants (e.g. VRE, Pseudomonas, Stenotrophomonas)

Empiric Antimicrobials

- Empiric Treatment not always necessary → Sometimes it may be better to wait for more data:
  - C. difficile history
  - Multiple allergies
  - Concern for unusual organism or resistant organism
  - Concern for osteomyelitis (get bone cultures off Antimicrobials)
- Severity of Infection, Host Susceptibility & Systemic Symptoms should influence decision for empiric coverage
  - Typically Want Staph aureus and Streptococcus coverage
  - Coverage for other organisms should take into account wound location, wound appearance, systemic symptoms, host risk factors

Cellulitis (non-purulent).

Non-purulent cellulitis is characterized by diffuse erythema, pain and warmth at the infected site. Streptococcal bacteria cause most cases.

Treatment Duration: 5-7 days

Preferred Oral Agents:
Dicloxacillin 500 mg PO q6h X 5-7 days
Non-severe penicillin allergy: Cephalexin 500 mg PO q6h X 5-7 days
Severe penicillin allergy: Clindamycin 300 mg PO q8h 5-7 days

Preferred Intravenous Agents*:
Cefazolin 1 to 2 gm IV q8h
Non-severe penicillin allergy: Cefazolin 1 to 2 gm IV q8h
Severe penicillin allergy: Vancomycin IV (per pharmacy dosing) or Clindamycin 600 mg IV q8h.

*Conversion to oral agent can be made when improvement is demonstrated by fever resolution, cessation of spread and improvement in inflammatory markers.

Skin Abscess/Purulent Cellulitis

Purulent skin infections are typically caused by Staphylococcus aureus (MSSA and MRSA).

Incision and drainage is the cornerstone to therapy for skin abscesses.

Preferred Empiric Agents:
Trimethoprim-Sulfamethoxazole 1 DS tab PO q12h 5-7 days
Doxycycline 100 mg PO q12h 5-7 days
Vancomycin IV (per pharmacy dosing)

Preferred MSSA Agents:
Dicloxacillin 500 mg PO q6h X 5-7 days
Non-severe penicillin allergy: Cephalexin 500 mg PO q6h X 5-7 days
Severe penicillin allergy: *see MRSA below*

Preferred MRSA Agents (refer to resistance report to confirm sensitivities)
Trimethoprim-Sulfamethoxazole 1 DS tab PO q12h 5-7 days
Doxycycline 100 mg PO q12h 5-7 days
Clindamycin* 300 mg PO q8h 5-7 days
Vancomycin IV (per pharmacy dosing)

*Clindamycin resistance occurs in 25-30% of *S. aureus* isolates in Western New York. Sensitivity to Clindamycin should be confirmed before using as definitive therapy.

DM FOOT INFECTIONS -MILD-	Preferred Empiric Therapy	PCN Allergy
• Cellulitis ≤ 2 cm • Infection limited to skin/superficial subcutaneous tissues • No local complications or systemic illness	Dicloxacillin 500 mg PO q6h OR Cephalexin 500 mg PO Q6H OR Cefadroxil 1 gram PO Q12H OR Amoxicillin/clavulanate 875 mg PO Q12H	Levofloxacin 500 mg PO daily

Clinical Infectious Diseases 2012;54(12):132–173

DM FOOT INFECTION -MODERATE-	Preferred Empiric Therapy	PCN Allergy
Patients must be systemically well and must have any 1 of the following: • Cellulitis ≥ 2 cm • Lymphangitis • Spread beneath fascia • Deep tissue involvement or abscess Gangrene	Amoxicillin/clavulanate 875 mg PO Q12H OR Ampicillin/sulbactam 3.0 grams IV Q6H OR Ceftriaxone 1gm IV q24h AND Metronidazole 500 mg PO Q12H **Concern for MRSA:** Consider adding: Vancomycin IV OR TMP/SMX 1 DS q12h PO OR Doxycycline 100 mg PO Q12H	Levofloxacin 500 mg PO daily AND Metronidazole 500 mg PO Q12H Concern for MRSA: Consider adding: Vancomycin IV OR TMP/SMX 1 DS q12h PO OR Doxycycline 100 mg PO Q12H

Clinical Infectious Diseases 2012;54(12):132–173

DM FOOT INFECTION -Severe-	Preferred Empiric Therapy	PCN Allergy
Hemodynamic Instability or Systemic Toxicity PLUS any 1 of the following: • Cellulitis ≥ 2 cm • Lymphangitis • Spread beneath fascia • Deep tissue involvement or abscess Gangrene	Vancomycin IV AND Piperacillin/tazobactam 3.375 GM grams IV Q8H (extended infusion) OR Cefepime 2 g IV Q8H AND Metronidazole 500 mg Q12H	Levofloxacin 750 mg IV daily AND Metronidazole 500 mg IV Q12H AND Vancomycin IV

Clinical Infectious Diseases 2012;54(12):132–173

When to Consider Empiric MRSA Coverage for Skin and Soft Tissue

- Mild Infections when local prevalence ≥50% S. aureus are MRSA
- History of MRSA past year
- Moderate and Severe Infections
- Failure to Improve on MSSA therapy
- Dialysis Patients

Oral MRSA Options

Drug	Dose	Strep Coverage	Cost	Select Adverse Effects
Doxycycline	100mg q12h	+/-	$	GI upset, Photosensitivity
Minocycline	100mg q12h	++	$$	GI upset, Photosensitivity
TMP/SMX	1 DS q12h	+/-	$	Interactions, Renal Adjustments
Linezolid	600 mg q12h	+++++	$$$	Interactions, Thrombocytopenia
Clindamycin	300-450mg q8h	+++	$	C diff, Variable Covg. S. aureus & Group B Strep
Levofloxacin	500 mg q24	+++	$	High rate resistance S. aureus, C. diff

When to Consider Pseudomonas

- Severe Systemic Illness
- Heavy Antimicrobial Exposure History
- Wounds with significant water exposure
- Humid Environments
- Heavily Immunocompromised

Pseudomonas

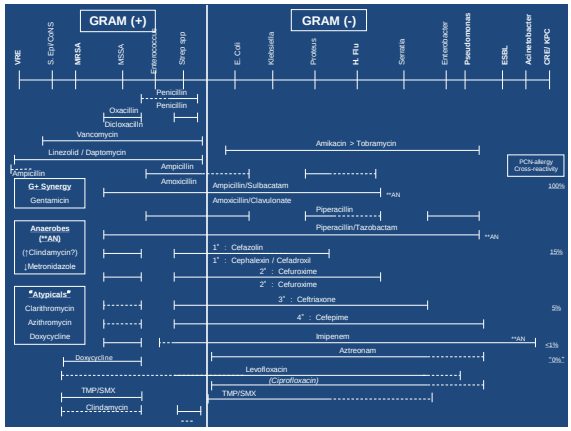
Treating Foot Infections in Diabetic Patients: A Randomized, Multicenter, Open-Label Trial of Linezolid versus Ampicillin-Sulbactam/ Amoxicillin-Clavulanate

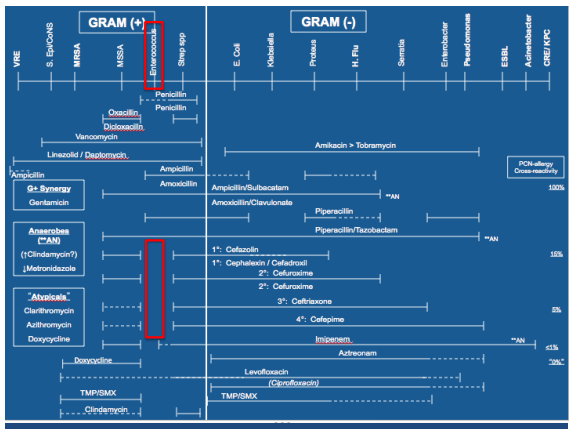
Benjamin A. Lipsky,[1] Kamal Itani,[2] Carl Norden,[3] and the Linezolid Diabetic Foot Infections Study Group*

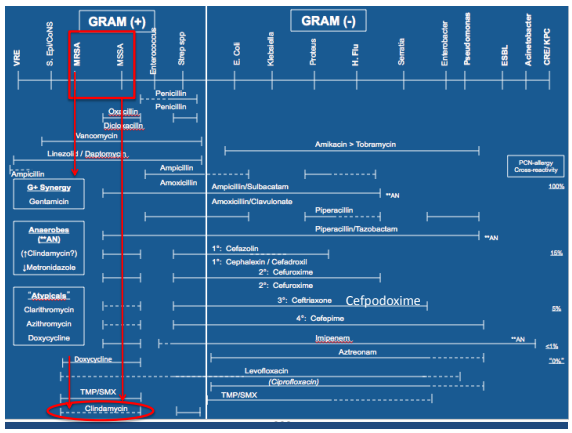
[1]Antibiotic Research Clinic, Veterans' Affairs Puget Sound Health Care System, and Department of Medicine, University of Washington, Seattle, Washington; [2]Department of General Surgery, Veterans' Affairs Medical Center, Houston, Texas, and [3]Pfizer, Peapack, New Jersey

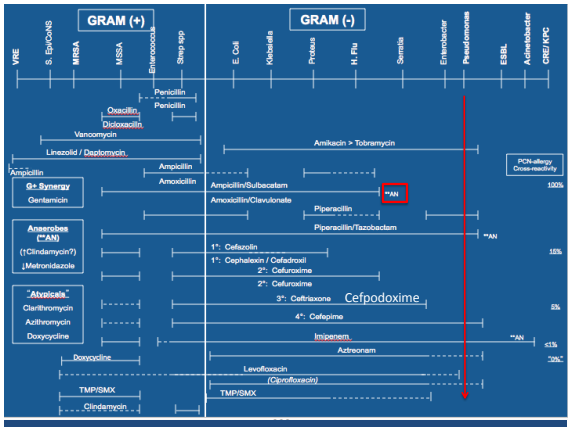
"Among linezolid-treated patients infected with both gram-positive and gram-negative pathogens, clinical success rates were similar regardless of whether aztreonam was added to the treatment regimen, supporting the concept that addressing the primary gram-positive pathogens is most important."

Benjamin A. Lipsky et al. Clin Infect Dis. 2004;38:17-24









Sometimes the Best Antibiotic is Cold Hard Steel

Consequences…..

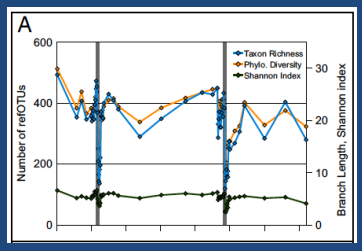
- Antimicrobials Can Have Lasting (Negative) Effects
- Wound cultures can be very helpful….but also very harmful

Antibiotic Exposure and C. difficile Risk

Drug	Odds of CDI
Carbapenem	1.86-2.5
Flouroquinolones	**2.8-5.2**
Clindamycin	**2.86-20.3**
3rd Gen Cephalosporins	**3.2-4.6**
Penicillins	1.75
Macrolides	1.4
TMP-SMX	1.78
Proton Inhibitors	**1.69-2.16**
Doxycycline	0.91

1. *J. Antimicrob. Chemother. (2014) 69 (4): 881-891.2.*
2. Janarthanan et al. Am J Gastroenterol. 2012 Jul;107(7):1001-10.
3. Loo et al. N Engl J Med 2011;365:1693-703.

Antibiotics and The Human Microbiome



4554–4561 |Les Dethlefsena and David A. Relman PNAS | March 15, 2011 | vol. 108 | suppl. 1

Human Microbiome in Health And Disease

- Clostridium difficile
- Obesity
- Autoimmune Disorders
- Inflammatory Bowel Disease
- Neurological Disorders

Summary

- Most Wounds will Culture Microorganisms
- The diagnosis of infection is made on clinical grounds, not by culture
- Superficial Swabs have limited utility in differentiating invasive disease from colonization
- Treating major gram positive pathogens (Step and Staph aureus) will cure many wound related infections
- Treatment of other pathogens should be influenced by culture data, severity of illness and wound characteristics
- The use of antimicrobials and wound cultures carries risk to the patient which should be considered in clinical decision making