5th Annual
Multidisciplinary Management
of the High Risk Diabetic
Foot Conference

Birmingham, Alabama
November 20, 2008

Diabetic Foot Infections: *Presentation, Diagnosis and Treatment*

Gary M. Rothenberg, DPM, CDE, CWS
Director of Resident Training
Attending Podiatrist
Miami VA Healthcare System

Miami VA Healthcare System

The Burden of the Problem: *Infection*

- 20% of diabetes related hospital admissions
- 15% of people with diabetes will ulcerate over their lifetime
- Ulcerations and infections are the leading risk factors for amputation

Prevention, prompt diagnosis and appropriate treatment are necessary to prevent morbidity

The Acutely Infected Diabetic Foot is Not Adequately Evaluated in an Inpatient Setting

Edelson, et al *Arch Intern Med*, Vol 156, Nov 1996

A retrospective review to evaluate the standard of treatment of the diabetic foot infection at a university teaching institution

- 255 consecutive admissions between Jan 1991 – Dec 1994
- Dx of "Infected diabetic foot ulceration"
- 144 male/111 female
- Mean age 59.9

The Acutely Infected Diabetic Foot is Not Adequately Evaluated in an Inpatient Setting

Edelson, et al *Arch Intern Med*, Vol 156, Nov 1996

Minimum Evaluation Competency

- Wound Characteristics
  - Depth
  - Size
- General Wound Description
  - Drainage
  - Margins
  - Viability of base
- Radiographs
- Pulse Examination
- Sensory Examination

- 10.2% documented wound depth or involvement of underlying structures
- 37.5% had the size of their wound recorded
- 40.4% Sensory exam performed
- 63.2% described wound exudate
- 68.6% pulse examination

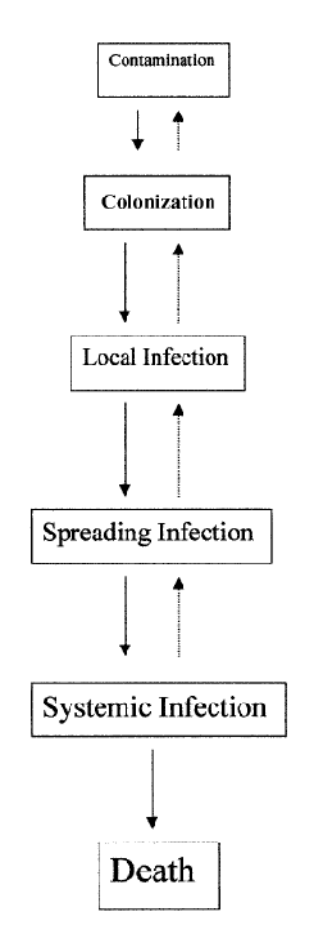
The Acutely Infected Diabetic Foot is Not Adequately Evaluated in an Inpatient Setting

Edelson, et al *Arch Intern Med*, Vol 156, Nov 1996

Less than 14% of patients met all criteria for minimum evaluation competency

Results highlight the need for a systematic, detailed lower extremity examination for every diabetic person admitted to the hospital

Useful Definitions



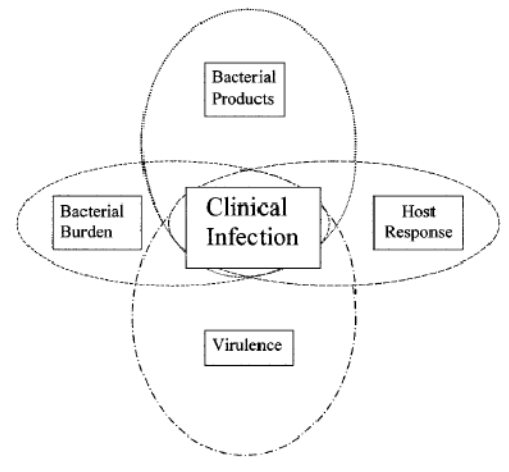
- **Contamination**- presence of bacteria on the wound surface
- **Colonization** – presence of and multiplication of surface microbes / bacterial contaminants without infection
- **Critical Colonization** – multiplication of bacteria within the wound to the stage where the host defenses are unable to maintain balance
- **Infection** – Invasion and multiplication of microorganisms in body tissues resulting in local cellular injury

Factors that Influence Infection Rates

Risk of wound infection varies according to the following equation:

Dose of bacterial contamination x Virulence

Resistance of the Host



- **Wound characteristics**
- **Nonviable contamination**
- **Vascular insufficiency**
- **Host immunocompetence**

Clinical Presentation: *Local vs. Systemic Signs*

- Rubor
- Calor
- Dolor
- Tumor
- Loss of function
- Purulent drainage

- Leukocytosis
- Fever
- Chills
- Malaise
- Pain
- Hyperglycemia

Risk Factors for Foot Infections in Individuals with Diabetes

Lavery, et al *Diabetes Care*, Vol 29, Number 6, June 2006

Prospective study of the epidemiology of foot infections in 1,666 patients enrolled in a disease management program

- Average follow-up 27 months
- 151 patients (9.1%) developed 199 foot infections
  - 97/151 (64.2%) outpatient
  - 54/151 (35.8%) hospitalized
- 30 patients (19.9%) developed bone culture proven osteomyelitis

Risk Factors for Foot Infections in Individuals with Diabetes

Lavery, et al *Diabetes Care*, Vol 29, Number 6, June 2006

Statistically significant risk factors for foot infection

- Wound depth to bone
- Wound duration >30 days
- Recurrent foot wound
- Traumatic wound etiology
- Peripheral vascular disease

The risk of developing an infection was 2,193 times greater in subjects who develop a foot wound than in those without a wound

Classification of Foot Infections

- Severity
- Extent or depth of involvement
- Clinical characteristics
- Anatomic location
- Etiology
- Purulent secretion
- Local signs of inflammation or infection
- Systemic / metabolic instability

Classification of Foot Infections

Clinical Description	IDSA	IWGDF
▪Wound without purulence or any manifestation of inflammation	Uninfected	1
▪>2 manifestations of inflammation: purulence, erythema, pain, tenderness, warmth or induration ▪Erythema <2cm periulcer, infection of skin/subq ▪No systemic illness	Mild	2
▪Pt. Systemically well, metabolically stable but cellulitis>2cm, lymphangitis, deep abscess, gangrene, muscle, joint or bone involvement	Moderate	3
▪Systemic toxicity/metabolic instability (fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, hyperglycemia, azotemia)	Severe	4

Validation of the Infectious Diseases Society of America's Diabetic Foot Infection Classification System

Lavery et al, *Clin Inf Dis* 2007;44:562-565

- 1,666 patients prospectively enrolled in prevention program
- Mean f/u 27.2 months
- 247 (14.8%) wound
- 151 (9.1%) infection
  - 71 (47%) mild
  - 52 (34%) moderate
  - 27 (17.9%) severe

- Increased risk for amputation
- Increased anatomic level of amputation
- Increased need for hospitalization

- Neuropathy
- Peripheral vascular disease
- History of amputation

- Deeper wounds
- Osteomyelitis
- Multiple infections

Presentation of the Infected Diabetic Foot

Summary

Presentation of infection is not always straightforward

Inflammatory response to injury or infection may be reduced because of impaired cellular function, vascular disease and neuropathy

History and Physical
Risk Factors
Classify Infections

Classic signs may be absent and so we rely on laboratory tests…

To Culture or Not to Culture.....

If performed properly, cultures are vital to guiding effective antibiotic therapy

- **Intra-op / wound base currettage**
- **Pre-therapy cultures**
- **Gram stain / C&S**
- **Blood cultures**
- **Repeat cultures**

Mild Infections

Monomicrobial

Staph / Strep

Severe Infections

Polymicrobial

Gram pos cocci and Gram neg rods, anaerobes

Emerging role of MRSA

Miniaturized Oligonucleotide Arrays

A new tool for discriminating colonization from infection due to *Staphylococcus aureus* in diabetic foot ulcers

Sotto, et al *Diabetes Care*, Vol 30, Number 8, August 2007

The future of clinical microbiology?

- *Describe a genotyping method that detects the presence of genes that encode for various virulence factors and antibiotic resistance in less than 1 day*

- Diabetic, hospitalized patients with wounds
- No recent antibiotics
- Wound cultures that grew **ONLY** *S. aureus*

Miniaturized Oligonucleotide Arrays

A new tool for discriminating colonization from infection due to *Staphylococcus aureus* in diabetic foot ulcers

Sotto, et al *Diabetes Care*, Vol 30, Number 8, August 2007

- Virulence factors were present in infected wounds (9% Grade 1 / 98% Grade 2)
- *S. aureus* is a remarkably persistent colonizer, recovered 60% on follow-up culture
- Only a few S. aureus isolates from first episode wounds were MRSA compared to all those from recurrent wounds
- MRSA wounds had overall worse outcomes
- More resistance was seen with more severe infections

Value of White Blood Cell Count With Differential in the Acute Diabetic Foot Infection

Armstrong, et al *JAPMA* Vol 86, Number 5, May 1996

Preliminary retrospective review to determine the average admission white blood cell count and the prevalence of leukocytosis and elevated polymorphonuclear leukocytes in patients admitted for treatment of pedal infections at multiple sites

- 338 consecutive admissions (203 male / 135 female)
- Average age 60.2
- Three centers

- Mean admission WBC 11.9 +/- 5.4/mm3
  - 56% WBC WNL
- Average PMN leukocyte 71.4 +/- 11.1%
  - 83.7% PMN leukocyte % WNL

Value of White Blood Cell Count With Differential in the Acute Diabetic Foot Infection

Armstrong, et al *JAPMA* Vol 86, Number 5, May 1996

- Leichter et al, 1988 reviewed “serious pedal infections”
  - Average WBC 9.7
- Armstrong, et al, 1995 reviewed diabetic foot infections
  - Mean admission WBC 9.8

*In the diagnosis of infectious disease, laboratory values are **adjunctive**. A normal WBC and differential should not deter from appropriate, early and aggressive treatment of potentially limb threatening infections.*

The Diagnosis of Osteomyelitis in Diabetes Using Erythrocyte Sedimentation Rate: A Pilot Study

Kaleta, et al *JAPMA* Vol 91, Number 9, October 2001

- Retrospective review 29 patients (17 male / 12 female) admitted during a one year period with cellulitis / suspected osteomyelitis
- Osteomyelitis confirmed via pathology of those treated surgically or 2/3 positive bone scan, MRI, and radiograph or ability to probe to bone

- 19 patients with osteomyelitis
- Mean ESR Osteo = 104 mm/h
- Mean ESR Cellulitis = 44 mm/h

ESR > 70 mm/h in diabetic foot infections is highly suspicious of osteomyelitis

- *89.5% Sensitivity*
- *100% Specificity*
- *100% PPV*
- *83% NPV*

Puncture Wounds: Normal Laboratory Values in the Face of Severe Infections in Diabetics and Non-Diabetics

Lavery, et al *Am Jour Med*, Vol 101, 1996

*Using infected puncture wounds, this study asks the question whether WBC and ESR is **lower** in diabetics as compared to non-diabetics*

- Hospitalized patients with clinically infected plantar puncture wounds between 1985 and 1992
- Retrospective chart review
- 77 Diabetic (51 male/26 female) average age **52.5**
- 69 Non-diabetic (55 male/14 female) average age **34.1**

Puncture Wounds: Normal Laboratory Values in the Face of Severe Infections in Diabetics and Non-Diabetics

Lavery, et al *Am Jour Med*, Vol 101, 1996

	Diabetes	No Diabetes
WBC (4-11)	**12.3** +/- 4.4	**10.2** +/- 2.9
ESR (0-20)	**62.1** +/- 38.7	**20.2** +/- 17.3
Oral Temp (C)	37.7 +/- 0.6	37.3 +/- 0.5

- ***Pain*** is the most frequent complaint in non-diabetic population
- ***Erythema and drainage*** were the complaints of the diabetics

Puncture Wounds: Normal Laboratory Values in the Face of Severe Infections in Diabetics and Non-Diabetics

Lavery, et al *Am Jour Med*, Vol 101, 1996

	Diabetes			No Diabetes	
	Osteo	**ST**		**Osteo**	**ST**
WBC	**13.4**	11.8		9.5	10.3
ESR	**71**	**58**		33.6	17.5
Temp	38	37.5		37.8	37.2

- Delay before seeking medical attention was significantly greater in Diabetics vs. Non-Diabetics (8.7 +/- 18.9 vs. 5.3 +/- 8.4 days)

Laboratory values are adjunctive, utility is variable and unreliable

Procalcitonin as a Diagnostic Aid in Diabetic Foot Infections

Uzun et al *Tohoku J Exp Med* Vol 213 (4), 2007

To determine the serum PCT levels in diabetic patients with foot ulcers and assess usefulness as an infection marker in comparison with ESR, WBC, and C-reactive protein

- 49 admitted patients with diabetic foot wounds Jan 2005 – June 2005
  - 22 non-infected
  - 27 infected
  - 22 healthy control

Procalcitonin as a Diagnostic Aid in Diabetic Foot Infections

Uzun et al *Tohoku J Exp Med* Vol 213 (4), 2007

Group	PCT (ng/ml)	CRP (mg/dl)	WBC (10/L)	ESR (mm/h)
Control N=22	<0.06	4.4	6.4	14.7
NDFI N=22	0.06	11.0	8.0	31.4
DFI N=27	**0.18**	49.4	**11.4**	**62.7**

- *CRP has the lowest diagnostic accuracy*
- *PCT has superior specificity but comparable sensitivity to WBC and ESR*
- *PCT may not rise sufficiently in localized infections*

Diagnosis of Foot Infections

Summary

Early diagnosis is important before involvement of deep structures

Laboratory and microbiological analysis may be misleading

Do not rely on any single value

Subtle findings such as lack of wound healing may indicate infection

Cultures

Labs

WBC / ESR / CRP

PCT

Osteomyelitis:
The Diagnostic Dilemma

- Occurs in 20% of patients with a foot wound
- Markedly increases the risk of amputation
- Distinguishing from soft tissue infection and Charcot arthropathy is difficult
- Early diagnosis may have a significant effect on amputation outcomes

- Bone biopsy
- Probe to bone
- MRI
- Bone Scans
- CT
- PET

Diabetic Foot Osteomyelitis: a progress report on diagnosis and a systematic review of treatment

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

Diagnosis

- History
- Physical Exam
- Plain Radiographs
- Bone Scans
- PET
- MRI
- Bone Biopsy

Treatment

- Indications for surgery
- Choice of surgical intervention
- Effectiveness of non-surgical management
- Emperical choice of antibiotics
- Duration of antibiotics
- Route of administration
- Effectiveness of adjunct therapies
- Prognosis
- Aftercare

Diabetic Foot Osteomyelitis: a progress report on diagnosis and a systematic review of treatment

Berendt et al, *Diab Metab Res Rev* 2008;24 (Suppl 1)

Category	Post-test prob of OM	Mgmt advice	Criteria
Definite	>90%	Treat	▪Bone bx +culture/+ histo OR ▪Purulence in bone OR ▪Ulcer with bone detatched OR ▪Intramedullary abscess on MRI
Probable	51-90%	Consider treating	▪Visible bone in ulcer OR ▪+MRI (bone edema and other signs) OR ▪+Culture / - histo or visa versa
Possible	10-50%	Treatment may be justifiable	▪Cortical destruction on x-ray OR ▪MRI with bone edema OR ▪+Probe to bone OR ▪ESR >70 OR ▪wounds >6 weeks non healing / >2 weeks infx
Unlikely	<10%	No need for treatment	▪No S/S inflammation, nl x-ray and superficial ulcer <2 weeks ▪Normal MRI ▪Normal Bone scan

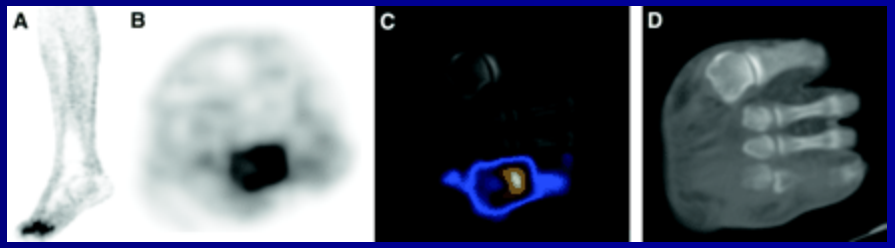
The Diabetic Foot: Initial Experience with 18F-FDG PET/CT

Keidar, et al *J Nuclear Med* Vol 46, Number 3, March 2005

To assess the role of PET/CT using 18F-FDG for the diagnosis of diabetic foot osteomyelitis

- Positron Emission Testing
- Computerized Tomography
- 18F-fluorodeoxyglucose

- 14 consecutive diabetic patients with clinically suspected osteomyelitis
- 10 male / 4 female
- Mean age 54 years
- All patients underwent bone scan and PET/CT



Patient	Bone Scan	PET	CT	PET/CT	Final dx
1	+	+	-	4th met	Osteo
2	+	+	+	1st met	Osteo
	+	+	+	2nd met	Osteo
	+	+	Equiv	1st met	Osteo
3	+	+	+	1st met	Osteo
	+	+	+	Cuneif	Osteo
4	+	+	+	Lat mall	Osteo
	+	+	Equiv	Calc	Osteo
5	+	+	+	ST	ST
6	+	+	+	ST	ST
7	+	+	Equiv	ST	ST
8	+	+	-	ST	ST
9	+	+	Equiv	ST	ST
10	+	+	Equiv	3rd met	Charcot
11	-	-	-		No infx
12	-	-	-		No infx
13	+	-	-		No infx
14	-	-	Equiv		No infx

Osteomyelitis

PET/CT 8/8

CT alone 5/8

No Osteo

PET/CT 5/5

CT alone 2/5

Infection

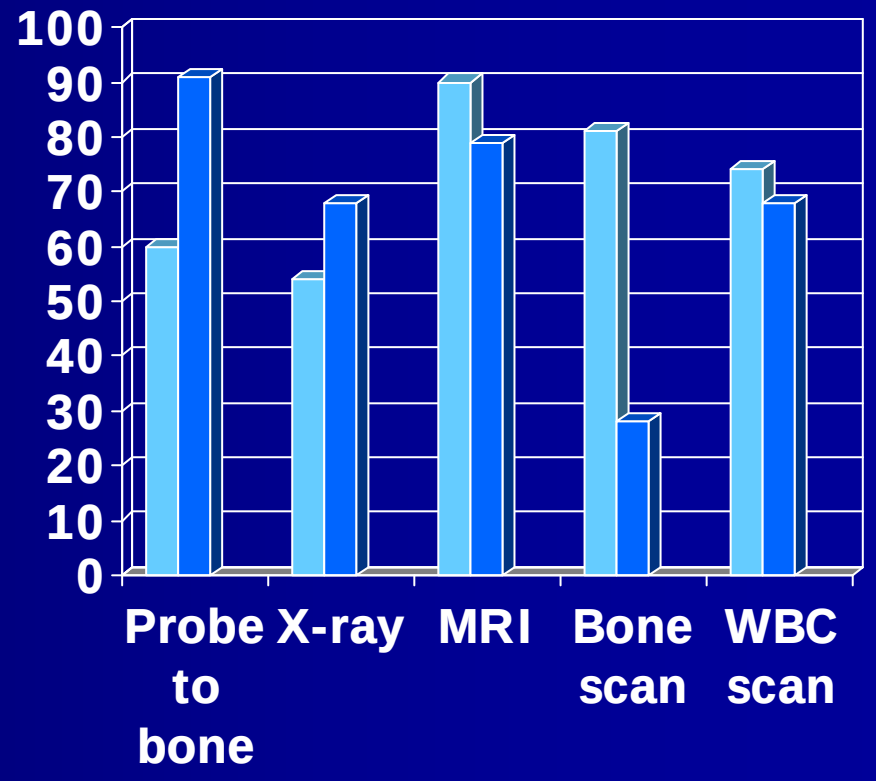
PET/CT 13/14

93% accuracy

Diagnostic Accuracy of the Physical Examination and Imaging Tests for Osteomyelitis Underlying Diabetic Foot Ulcers: Meta Analysis

Dinh et al, *Clin Inf Dis*, 2008:47:519-27

- Meta-analysis of the accuracy of diagnostic tests for osteomyelitis in diabetic patients 1966 – 2007
- 9 studies - histopath
- Exposed bone and + Probe to bone suggest osteomyelitis
- Limited studies
- MRI is the most accurate imaging modailty



Treatment of Diabetic Foot Infection

Summary

- Non infected ulcers do not require antibiotics
- Mild soft tissue infections can be treated with oral antibiotics
- Severe soft tissue infections should be treated with IV antibiotics
- Osteomyelitis treatment is controversial but generally requires surgery and IV antibiotics in the acute phase and transition to orals
- Soft tissue infections treatment duration 1-4 weeks
- Osteomyelitis treatment 6-12 weeks
- All definitive antibiotic therapy should be culture-driven

Outcomes and Prevention

- Goals of treatment are to eliminate clinical evidence of infection and avoid soft tissue loss / amputation
- 80-90% of mild-moderate infections should respond well to treatment
- Re-infection occurs in 20-30%
- Education and the team approach are extremely important