Is Neuropathy the root of all evil in the diabetic foot?

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The Global Burden of Diabetes

For the first time in the history of mankind non-communicable diseases have become the leading cause of global mortality and morbidity (60%)

Diabetes is now responsible for 3.2 million deaths each year and it has overtaken HIV/AIDS which is responsible for 3 million deaths per year (WHO 11 May 2004)
Society in Transition
Amputation – most feared complication of diabetes
ROOT: Definitions

- Anchor of a plant
- Underground or hidden part
- A fundamental or essential part
- The source or origin of a thing
- An offshoot
Diabetic Peripheral Neuropathy

Definition:

‘The presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes: the diagnosis cannot be made without a clinical examination’

Diabetic Neuropathies – Clinical Classification

Polyneuropathies
- Sensory
  - Chronic sensorimotor
  - Acute sensory
- Autonomic
- Proximal motor
- Trunchal

Mononeuropathies
- Isolated peripheral
- Cranial
- Mononeuritis multiplex
- Trunchal

Boulton AM, Ward JD. Clin Endocrinol Metab. 1986;15:917-931.
Chronic Sensorimotor Neuropathy

The most common form

• Of insidious onset
• Positive symptoms
  – Burning, stabbing, shooting, hyperaesthesiae, paraesthesiae
• Negative symptoms
  – Numbness
• Nocturnal exacerbation

Boulton AM, Ward JD. Clin Endocrinol Metab. 1986;15:917-931.
Human Diabetic Neuropathy
Impact of Diabetic Peripheral Neuropathy (DPN)

- Most common peripheral neuropathy in developed nations
- Accounts for more hospitalizations than all other diabetic complications combined
- Contributes to 50%-70% of all nontraumatic amputations in the US
- There are 85,000 amputations in the US each year, 1 every 10 minutes, 87% due to neuropathy, cost $37B

Boulton et al. Diabetes Care 2004;27:1458-1486
Clinical Impact of Diabetic Distal Symmetric Polyneuropathy (DSP)

Agent X

Painful neuropathic symptoms

Impairment Disability Handicap

DSP

Neuropathic deficits

Foot ulcers

Infection (skin, bone)

Charcot foot

Surgery, Amputation

Quality of life ↓

Mortality ↑

Cost ↑
Clinical Consequences of Diabetic Peripheral Neuropathy

NEUROPATHY

PAIN

Burning
Paraesthesia
Hyperaesthesia
Allodynia
Nocturnal-exacerbation

INSENSITIVITY

Foot ulceration;
at least 50%
preventable

Paul Brand CBE, MD, FRCS
1914-2003

• The Gift of Pain
• Pain: the Gift nobody wants

• Surgeon and missionary: worked in leprosy and diabetes
• He took the foot from art to science
Diabetic Neuropathy

‘PAIN – God’s greatest gift to mankind’

Paul Brand
‘I shall never be free until I can feel pain’

Leprosy patient in Madras: cited by Dr Paul Brand
‘If I were to choose between pain and nothing ..... I would choose pain’

William Faulkner
Do not walk barefoot

- Burn to sole of foot
- Need footwear for protection
Loss of proprioception
Who is at risk of Foot Ulceration?

- Neuropathy
- Peripheral Vascular Disease
- Past history of foot ulceration
- Microvascular Complications (especially nephropathy)
- Elderly, living alone
- Foot deformity
- Amputation
Does Neuropathy Lead to Ulceration? A Prospective Study

- 469 diabetic patients screened in 1988
- Vibration perception assessed by biothesiometry
- All foot ulcers recorded

Young et al, Diabetes Care 1994;17:557
Prospective Foot Ulcer Study

Results — Foot Ulcers

<table>
<thead>
<tr>
<th></th>
<th>VPT&lt;15</th>
<th>VPT 16-24</th>
<th>VPT&gt;25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ulcers 1988-92</td>
<td>6</td>
<td>2</td>
<td>41</td>
</tr>
<tr>
<td>Risk per patient</td>
<td>2.9%</td>
<td>3.4%</td>
<td>19.6%</td>
</tr>
<tr>
<td>Risk/patient/year</td>
<td>0.7%</td>
<td>0.9%</td>
<td>4.9%</td>
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</table>
Predicting Diabetic Foot Ulcer Risk

- North West Diabetes Foot Care Study (NWDFCS)
- Population-based prospective study in NW UK – 6 health-care districts
- 16,000 patients included in total
- First study on 9,710 diabetic patients

NWDFCS: THE NDS

- 3 sensory modalities
  - Vibration (128 Hz tuning fork – hallux)
  - Pin-prick (Neurotip): dorsal distal hallux
  - Hot/cold rods: dorsal distal hallux

ALL: normal = 0, abnormal = 1
Ankle reflex: normal = 0, absent = 2, reinforcement = 1
MAX TOTAL 5 each leg: =10

Abbott et al, 2002
NWDFCS: Results

- 9710 diabetic patients followed for 2 years
- 291 ulcers developed:
  male to female: 1.6:1.0
- NDS best baseline predictor
  NDS < 6: 1.1% annual ulcer incidence
  NDS > 6: 6.3% annual ulcer incidence

Abbott et al, 2002
A Case of PUO?

• Temp 38.3C. Tachycardia, normotensive
• CVS/RS nad
• Abdomen – no tenderness – exit site slight discharge.
• Legs – moderate oedema – bandage over R hallux
• CNS ‘grossly inact’
A Case of PUO?

- Hb 10.9g%, wbc 15.5 platelets normal
- Urea 34, Creat 766, K 5.0
- Blood cultures negative
- CXR, ECG - unremarkable
- PD fluid culture negative
- Exit site culture 'skin commensals'
- U/S and CT abdomen - unremarkable
A Case of PUO?

- Started on broad spectrum antibiotics
- No improvement after holiday weekend
- Diabetes team referral Tuesday
- Feet examined, dressing removed
- ..........
A Case of PUO: Motto of story

In diabetes, ALWAYS examine the feet: lack of symptoms ≠ lack of Neuropathy
Other Associations with Foot Ulceration End-stage Renal Disease

- Association between start of dialysis and incidence of foot ulceration
- Up to 40% of dialysis patients have past or current ulceration
- Related to lack of diabetes follow-up
- Ethnic protection lost

Game et al 2005, 2010; Ndip et al 2010
Dialysis and Foot Ulceration

• Dialysis is an independent risk factor for foot ulceration
• When compared to ESRD patients not on dialysis, 4.2x increased risk of foot ulceration
• Mortality after amputation - 290% increase in hazard for those on dialysis
• Need for foot care on dialysis units

Ndip A et al, Diabetes Care 2010;33: 878-880 and 33;1811-1816
CDFE
Report of a Task force of the ADA

Meeting, Chicago, January 2008

Co-Chairs: AJM Boulton and DG Armstrong

Members: S Albert, R Frykberg, R Hellman, Sue Kirkman, L Lavery, J LeMaster, J Mills, M Mueller, P Sheehan, D Wukich.
Comprehensive Diabetic Foot Exam (CDFE)

AIMS

To review the recent literature and recommend key constituents of the CDFE for adult persons with diabetes
Recommendations
1. History and general exam
   • Peripheral Vascular Disease
   • Past foot ulceration or amputation
   • Renal status
   • Footwear assessment
   • Dermatological
   • Foot deformity
Recommendations

2. Neuropathy Assessment

- 10 g monofilaments tested at 4 sites (MTH 1, 3 & 5 and hallux plantar) AND ONE OTHER OF
- 128 Hz tuning fork vibration - hallux
- Pinprick sensation – dorsal hallux
- Ankle reflexes
- VPT – biothesiometer/VPT meter
EURODIALE STUDY: DIFFERENCES ACROSS EUROPE

- Study in 14 European hospitals in 10 countries
- 1229 new diabetic foot ulcer patients included
- More non-plantar ulcers seen (52%): PVD in 49%, Infection in 58%: 31% both infection and PVD.
- Severity of diabetic foot ulcers greater than previously reported
- Those with PVD + infection more likely to have other serious co-morbidities.

Nerve Damage + Mechanical Stress

Inflammation

Ulceration + Faulty Healing

Infection

Vascular Disease

Amputation

Stop
Advanced Monitoring using Temperature Assessment ...
<table>
<thead>
<tr>
<th>Study Population</th>
<th>Sample Size</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lavery Diabetes Care 2004 Ulcer history</td>
<td>N=85 6 mos</td>
<td>Temp 2% Standard 20% OR 10.3</td>
</tr>
<tr>
<td>Lavery Diabetes Care 2007 Ulcer history</td>
<td>N=173 15 mos</td>
<td>Temp 8.5% Standard 29.3% Structured 30.4% OR 4.5</td>
</tr>
<tr>
<td>Armstrong Am J Med 2007 Ulcer history</td>
<td>N=225 18 mos</td>
<td>Temp 4.7% Standard 12.2% OR 3.0</td>
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</table>
Conclusions: Is neuropathy the root of all evil?

- Anchor of a plant  x
- Underground or hidden part  √
- A fundamental or essential part  √
- The source or origin of a thing  ±
- An offshoot  x
For one mistake made for not knowing, ten mistakes are made for not looking.

J A Lindsay
Thank you for your kind attention