Evaluation of Neuropathy in the Diabetic Foot

Javier La Fontaine, DPM, MS
Associate Professor
Department of Plastic Surgery
University of Texas Southwestern Medical Center
Dallas, Texas
• Success is the ability to go from one failure to another with no loss of enthusiasm.
  – Sir Winston Churchill
  *British politician (1874 - 1965)*

• ‘PAIN – God’s greatest gift to mankind’
  - Paul Brand
Impact of Diabetic Neuropathy

- 15% of Diabetics will develop an ulcer
- 85,000 amputations per year
- 1 every 2 minutes
- $13.7 billion industry
- 27% direct medical cost of Diabetes

(Diabetes Care 26:1790-1795, 2003)
Diabetic Neuropathy

• Affects up to 50% of DM patients
• Epidemiology and natural history still poorly understood
• Definition: “The presence of S/S of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes” (International consensus, 1998)
• Rochester Neuropathy Study- 10% from other causes (Neurology 43, 1993)
## Stages of Diabetic Peripheral Neuropathy

<table>
<thead>
<tr>
<th>No neuropathy</th>
<th>No symptoms or signs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical neuropathy</strong></td>
<td></td>
</tr>
<tr>
<td>Chronic painful</td>
<td>Burning, shooting, reduced DTRs, stabbing, pins and needles</td>
</tr>
<tr>
<td>Acute painful</td>
<td>As above but severe hyperesthesiaes, “insulin neuritis”</td>
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<tr>
<td>Painless with complete sensory loss</td>
<td>Numbness, painless injury absent DTR’s, reduced normal sensitivity</td>
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<tr>
<td>Late complications</td>
<td>Ulcers, Amputations, Charcot</td>
</tr>
</tbody>
</table>

Etiology of Diabetic Neuropathy

- Hyperglycemia
- Other
  - Oxidative stress
  - Polyol Pathways
  - AGE’s
  - PKC inhibition
  - Growth factors
  - Insulin like growth factors
  - C-peptide
  - VEGF
  - Immune mechanisms
Classification of Diabetic Neuropathy
(Thomas: Diabetes 46, 1997)

• Focal and Multifocal neuropathies
  – Focal Limb
  – Proximal Motor (Amyotrophy)
  – Thoracolumbar radiculoneuropathy
  – Cranial

• Rapidly reversible
  – Hyperglycemic neuropathy

• Generalized Symmetrical polyneuropathy
  – Sensorimotor
  – Acute sensory
  – Autonomic
Focal Limb

• Mononeuritis
  – sudden onset
  – usually single nerve
  – Infarction of nerve
  – Common nerve: median, ulnar, peroneal (drop foot)
  – resolves spontaneously
  – not progressive
  – Tx: symptomatic

• Entrapment
  – gradual onset
  – single n. exposed to trauma
  – Common nerve: same but tarsal tunnel
  – Progressive
  – 1 in 3 DM patients
  – Tx: splints, rest, injection, surgery
Generalized Symmetrical Polyneuropathy

• Acute sensory
  – Rapid onset
  – Severe burning, wt. loss, depression
  – Signs: mild sensory, motor unusual
  – NCV normal, minor abnormalities
  – Complete recovery within 12 months

• Chronic sensorimotor
  – Gradual onset
  – Burning pain, paresthesiae, numbness
  – Signs: mild-moderate
  – NCV unusually abnormal
  – May persist for years

(Thomas: Diabetes 46, 1997)
Chronic Sensorimotor Neuropathy

(Anatomy)

Sensory
- Myelinated
  - Touch
  - Vibration
  - Position
- Thinly myelinated
- Unmyelinated

Small Fibers

Autonomic
- Thinly myelinated
  - HR
  - BP
  - Sweating
  - Gut function
- Unmyelinated

Motor
- Myelinated
  - Motion control
Electrophysiology

- Provides a sensitive but nonspecific onset of neuropathy
- Trace the progression of neuropathy and provide information of the severity of it
- Insensitive to many pathological changes in DPN
- *To rule out other causes of neuropathy
Initial Management

• Exclude nondiabetic causes
  – Malignancy, metabolic, toxic, infective, medication related, DICP

• Education and practical measures

• Assess level of blood glucose control

• Aim for optimal stable control

• Consider pharmacological therapy

(Boulton AJ et.al.: Diabetic Somatic Neuropathies, Diabetes Care 27(6), 2004)
Starling’s Curve of Pain

Onset of Diabetes

Pain Threshold

No Pain

Time

Good

Bad

Neural Functions
New DPN Pain Guidelines
First-tier drugs

- Duloxetine
- Pregabalin
Honorable Mentions

- Topical Capsaicin
- Lidocaine
- Bupropion
- Citalopram
- Paroxetine
- Phenytoin
- Topiramate
- Opioid Methadone
Identifying patients with neuropathy
Light pressure

- 10g monofilament
- Short life expectancy
- Fatigued
- Test on at least 3 sites: Plantar toe, Metatarsal heads
- Avoid areas of callus
- One negative response indicates at-risk foot
Monofilaments in screening of ‘at risk’ feet

- Comparative of supposed 10g monofilaments
- Not all ‘10g’ monofilaments actually buckle at 10g
- Reliable filaments produced by:
  - Bailey instruments
  - Owen Mumford

Booth & Young, Diabetes Care 2000;23:984
Armstrong, Diabetes Care; 23:887
Is Semmes-Weinstein Monofilament Testing Accurate & Reliable?

- Wide variability in the load characteristics at baseline and with continued loading
- Reproducibility decreases with repetitive loading
- Recovery after 24 hours improves accuracy of the test

Booth: Diabetes Care, 2000
Yong R: J Foot Ankle Surg. 1999
What is the Service Life of a Semmes-Weinstein Monofilament?

• New Touch-Test Sensory Monofilament
• Initial average force generated $9.8 \pm 0.3 \text{ g (9.2-10.2g)}$
• After 500 loading cycles $\sim 1.3\text{g decrease}$
  $8.6 \pm 0.3\text{g (8.1-9.0g)}$
• 24 hour recover improved accuracy
  $9.6\text{ g (9.1-10.0g)}$

North Coast Medical

Yong R: J Foot Ankle Surg. 1999
Is Semmes-Weinstein Monofilament Testing Accurate & Reliable?

• Compared 4 commercially available 10g SWM
• Identified large variation in loading forces
• 20-100% demonstrated buckling ± 1.0g (9.0-10.0 grams)

Booth: Diabetes Care, 2000
What is the Service Life?

- After 100 loading cycles “most” monofilaments were within 10% of 10g
- After 200 cycles only 50% were ± 1.0g

Booth: Diabetes Care, 2000
Brand Averages

![Graph showing force (grams) against loading cycle for different brands.](image-url)
Monofilament Failure – what is the service life?

• Require frequent replacement ???
• Calibrated instruments should be used
• “throw away” or “give away” devices are of uncertain quality-durability
Vibration perception

• 128 Hz tuning fork
• Cheap and widely available
• Can be negative in hypothyroidism and alcoholism
Vibration perception

• Test over another part of the body e.g. elbow
• Patient must close eyes
• Vibrate fork by springing two limbs of TF with thumb and forefinger
• Apply flat surface of TF to tip of toe
• If no response test on medial malleolus
Vibration Sensation: Tuning Fork

• 3 groups
• 24 patients with neuropathic DFU
• 24 patients without DPN
• 21 without diabetes

Meijer et al., Diabetes Care 2005
Tuning fork

• Positive and negative predictive values:

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<tbody>
<tr>
<td>ICDF 1:</td>
<td>64</td>
<td>100</td>
<td>TF, PP, MF, AJ</td>
<td>5m</td>
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<tr>
<td>ICDF2:</td>
<td>63</td>
<td>100</td>
<td>As above + CW</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NDF1:</td>
<td>64</td>
<td>100</td>
<td>TF, CW, MF, AJ</td>
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<tr>
<td>NDF2:</td>
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<td>97</td>
<td>TF</td>
<td>30s</td>
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<tr>
<td>NDF3:</td>
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<td>TF, MF</td>
<td>60s</td>
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<tr>
<td>NDF4:</td>
<td>82</td>
<td>84</td>
<td>MF</td>
<td>30s</td>
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Meijer et al., Diabetes Care 2005
Conclusion

• Neuropathy is common
• Painful vs. Identifying patients “at risk”
• Control glucose before treating painful symptoms
• Leads to expensive complications
• Easy to screen
• Tuning fork is the best screening tool