Goals

• Evaluate peripheral neuropathy symptoms

• Recognize and be able to diagnose diabetic peripheral neuropathy

• Review recommendations for treating neuropathic pain
Types of DM Neuropathy:

- Symmetric peripheral axonopathy
- Autonomic neuropathy
- Focal mononeuropathy (cranial nerve & peripheral/limb)
- Thoracic and lumbar radiculopathy (including amyotrophy)
- Mononeuropathy multiplex
Why the nerves in DM?

- Accumulation of glycosylated proteins/products
- Sorbitol accumulation
- Oxidative stress
- Ischemia? Inflammation?
- Other (hexosamine pathway & protein kinase C pathway disruption)
How Common is DM Neuropathy?

• The most common complication of DM

• The most common neuropathy in Western Society

• About 50% of DM patients develop clinically evident neuropathy (*average 7 year lag between onset and dx)

• However, many estimate 100% have neuropathy (depending on criteria)
Sensory Complaints
Feet feel odd
Red Flags

1. Proximal involvement (non-length dependent)
2. Gait ataxia
3. Finger joint position loss (severe ataxia)
4. Autonomic Nervous System Involvement
5. Multifocality
6. Acute or subacute onset (sudden or rapidly progressing)
Lumbar Radiculopathy
(Dermatome Map)
Clinical Presentation

*Sensory Loss*
Diabetes Defined

1. DM
   - Fasting blood glucose $\geq 126 \text{ mg/dl}$
   - 2 hr glucose $\geq 200 \text{ mg/dl}$ on 75-g OGTT
   - HbA1c $\geq 6.5\%$ (* ADA new recs. 2010)

2. Impaired fasting glucose
   - Fasting blood glucose 101-125 mg/dl

3. Impaired glucose tolerance
   - 2 hr glucose 140-199 mg/dl on 75-g OGTT
89 patients w/ idiopathic PN
- 28 pts (31%) DM
- 12 pts (13%) IGT
- 3 pts (3%) IFG

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- 43 pts (48%) abnormal glucose metabolism
- 2 hr OGTT is the most sensitive measure of demonstrating abnormal glucose metabolism in cases of idiopathic PN

Value of OGTT in PN Work-Up

- 100 patients with idiopathic PN (previously screened for DM)
  - 2003 Revised ADA Criteria (101-125 = impaired fasting)
    - 61% normal glucose metabolism
    - 39% abnormal glucose metabolism
      - 36% impaired fasting glucose
      - 3% diabetes mellitus
  - 2hr-OGTT (23 out of 61 patients)
    - 38% normal glucose metabolism
    - 62% abnormal glucose metabolism (37% increase in Dx)
      - 38% impaired glucose tolerance
      - 24% diabetes mellitus

AAN Guidelines 2009

• Distal symmetrical PN
  – Fasting blood glucose
  – 75 gram 2 hour OGTT if FBG negative
  – Vit B12, homocysteine, & MMA
    • (↑ 5-10% detection where B12 200-500)
  – Serum immunofixation
  – EMG
  – Autonomic test
  – Skin biopsy may be useful
Specific Medications

- Amitriptyline greater anticholinergic SE than nortriptyline, doxepin in cardiac patients

- Duloxetine (cymbalta - SNRI): nausea common, can combine with AED

- Venlafaxine (effexor): nausea/somnolence

- Pregabalin (lyrica):

- Gabapentin (neurontin):

- Lidoderm patches

- Mexilitine (mexitil): limited benefit

- Capsaicin cream:

- Alpha-lipoic acid: nausea/vertigo (600 mg/once/day)
AAN Guidelines 2011

• EFFECTIVE: pregabalin

• PROBABLY EFFECTIVE:
  – TENS (transcutaneous electrical nerve stimulation)

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AAN Guidelines 2011

• PROBABLY NOT EFFECTIVE:
  – Oxcarbazepine, lamotrigine, lacosamide, clonidine, pentoxifylline, mexiletine, magnetic field treatment, low-intensity laser therapy, Reike therapy, anodyne light therapy

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Prevent DM Neuropathy?

Over 10 years intensive insulin treatment (HbA1C 2 % lower) associated with:

• 60-70 % reduction in development of definite neuropathy
• 44 % decrease in abnormal NCS
• 53% decrease in autonomic dysfunction

•** For each 1% rise in HbA1c there is a 1.3 m/s slowing of NCS over 8 years


Oslo Study: Diabetologia 1994; 37;579
References