Diabetes is the most prevalent endocrinopathy worldwide, and in the U.S. affects 16 million Americans representing nearly 6% of the population and to >18% over age 65. Diabetes reduces life-expectancy by up to 10 years and the morbidity associated with it is staggering: Leading cause of blindness, > 50% end-stage renal disease, 1º cause for non-traumatic amputation up to 40 X risk, and 3 X risk for stroke even absent other risk factors. Incidence of peripheral neuropathy (PN) to >50%, and sometimes pre-dates its diagnosis. Likelihood of PN for every year of disease which can rapidly develop or worsen during poor glycemic control. Given prevalence of diabetes, skill is necessary in its evaluation and treatment, to include for its neurological and rheumatic manifestations.

NEUROLOGICAL MANIFESTATION OF DIABETES

Electrodiagnosis for the pattern, severity and acuity of demyelination and axonal injury:

- **Diabetic Polyneuropathy:** Motor and Sensory Peripheral Neuropathy. Thorough EMG/NCV assessment is critical –
  1. **Predominately sensory**- Mixed fiber type (small and large) , painful selective small fiber type, ataxic large fiber type. Pathology is one of segmental demyelination with distal predilection secondary to the cumulative # of internodal distances removed from the nerve cell body and impaired axonal transport. Metabolic accumulation of Polyol (Sorbitol) and other complex sugars eventually results in permanent structural injury. PN classically presents as “stock and glove” distribution.
  2. **Predominately motor**- Etiology is thought ischemic nerve infarction. If significant weakness, address functional consequences such as “foot drop” in peroneal neuropathy, or knee instability in femoral neuropathy with quadriceps loss.
  3. **Predominately autonomic neuropathy (AN)**- Autonomic dysfunction due to loss of poorly myelinated or unmyelinated pre and post ganglionic nerve fibers results in distressing manifestations including gastric and bowel dysmotility, urinary problems including urinary retention or incontinence, impotence, and postural hypotension. AN effects up to 10% of patients.

- **Proximal Motor Neuropathy (Diabetic Amyotrophy or Diabetic Lumbosacral Radiculitis)** –
  - **Symptoms:** Sudden onset, asymmetric weakness, and associated with intense proximal leg, thigh, gluteal and back pain, and prominent paresthesias/dysthesias often following poor glycemic control, and frequently associated with anorexia and weight loss. Occasionally there is a more distal lumbosacral distribution, but rarely can present as a thoracic or cervical radiculitis.
  - **Etiology:** Uncertain, but postulated to involve ischemia of vasanervorum and other inflammatory mechanisms.
  - **EMG/NCV:** May reflect vulnerability to neuropathy given presence of an underlying generalized PN, but characteristically asymmetric, active and unusually widespread denervation beyond the confines of a single nerve or root level. Correlation with anatomic scanning is often necessary to R/O a space occupying lesion such as compression by a large disc herniation, spinal stenosis or tumor. Slow, substantial but incomplete recovery should be anticipated over 12-18 months.
  - **Treatment:** Weakness can be significant and require rehabilitation measures for strengthening, bracing and walking aids to reestablish safe ambulation. Pain control can be difficult and should include all remedies directed at controlling neuropathic pain including tricyclic antidepressants (TCA), anti-epileptic drugs (AED), occasionally central alpha-blockade such as Tizanidine (Zanaflex), topical agents, and sufficiently potent analgesics to include strong opioids if necessary.

- **Subacute to Chronic Mononeuropathies** –
  - **Diabetics** are more vulnerable to common peripheral entrapment and compressive neuropathies to include but not limited to: Carpal Tunnel Syndrome (CTS), ulnar neuropathy across the elbow/Cubital Tunnel Syndrome, and Tarsal Tunnel Syndrome (TTS) with or without the presence of underlying PN.

- **Acute Mononeuropathy** –
  - Cranial: Ocular palsy (III or VI), Facial (VII), Truncal: Intercostal and abdominal, Limb: Femoral, Peroneal and others. Rarely one can see multiple acute neuropathies, known as mononeuritis multiplex (MNM).
Neurological and Musculoskeletal Manifestations of Diabetes
by Edgar S. Steinitz, M. D.

MUSCULOSKELETAL MANIFESTATIONS OF DIABETES

1. **Cheiroarthropathy**– A syndrome of limited joint mobility, also known as ‘diabetic stiff hand syndrome’ which occurs in up to 75% of long-standing diabetics. It is characterized by thickening and induration of the skin which can take on a waxy appearance, which results in soft tissue and flexion contractures of the fingers diminishing hand function. Histopathology reveals excessive and abnormal collagen deposition. Medications and therapy may help, but good glycemic control is thought important to slow progression.

2. **Adhesive Capsulitis with ‘Frozen Shoulder’**
3. **Flexor Tenosynovitis**
4. **Dupuytrens Contracture**
5. **Charcot Arthropathy**
6. ‘RSD’/CRPS I & II (Reflex Sympathetic Dystrophy/Complex Regional Pain Syndrome)
7. ‘DISH’ Syndrome (Diffuse Idiopathic Skeletal Hyperostosis)
8. **Osteopenia**

**Clinical Pearls in the Assessment of PN**

- **Peripheral Neuropathy** explains > 60% of all falls and ↑ falls risk 13-15 X normal
- **Proprioceptive Sense** is necessary for balance and its normal function is critical to prevent falls and injury, and a far more important factor than visual or vestibular function relative to falls risk.
- **Unipedal Stance Time**
  - Inability to succeed with unipedal stance is very predictive of falls, and this in distinction from results of the Romberg sign
  - Problems with unipedal stance time predicts nearly 50% of all falls
  - Unipedal stance is often < 3 seconds if PN with H/O falls, < 9 seconds in the presence of PN, yet >30 seconds is normal
  - Test unipedal stance over 3 trials:
    - ≥ 30 seconds unipedal stance predicts no PN over 90% of the time with very low risk for falls (≤ 5%)
    - < 10 seconds unipedal stance predicts PN virtually all of the time with a high risk for fall and injury
- **Nociceptive Perception.** Risk for diabetic foot ulceration and Charcot joint escalates with degree of sensory loss. It is important to test ability to detect pinprick, and to discriminate sharp versus dull
- **Joint Position Sense.** Assess by 1 cm displacements of the great toe over 10 trials. Normal is 100%, abnormal if ≤ 80%
- **Vibratory Sense.** Place a maximally struck tuning fork at IP joint of the great toe, and then at the medial malleolus
  - Quantitate # seconds of vibratory perception over several trials:
    - ≥ 10 seconds at IP joint great toe is normal
    - < 10 seconds vibratory sense at the malleolus correlates with PN over 90% of the time

**Treating Neuropathic Pain**

When TCA are ineffective, or only partially control pain, consider:

“Gabapentin for Symptomatic Treatment of Painful Neuropathy in Diabetes”– JAMA, 12/2/98-Vol 280, #21

- Gabapentin monotherapy is efficacious for: Decreasing pain, improving sleep, positive effect on mood and quality of life (p < .001)
- 83% completed study with a decreased pain score from 6.4 to 3.9 out of 10 on the Likert scale
- > 60% of patients described a moderate improvement in pain

Gradually increase the dose towards 900 mg daily as 300 mg t.i.d., but some benefit from dosages as high as 3600 mg per day

Clinically, several medications in conjunction usually best– If non-opioid analgesics, including NSAIDs, and topicals insufficient, then combinations of TCAs (less often SSRIs), AEDs (Gabapentin & others), Mexilitine, opioids, and rarely Baclofen or Tizanidine.

**Rehabilitation**

1. A thorough musculoskeletal, neurological, vascular and functional examination is mandatory.
2. Assessment should include cognitive abilities; visual, vestibular and proprioceptive function; strength, coordination and balance.
3. Examination findings are placed in the context of environmental and architectural barriers, and the psychosocial support system.
4. Importance of education to prevent complications with emphasis on diabetic foot care can not be overemphasized.
5. Should BKA amputation be necessary, consider immediate post-op prostheses (IPOP) whenever possible in order to control edema, minimize intensity and duration of phantom pain, and to more quickly reestablish ambulation and functional ability.

Electrodiagnosis & Rehabilitation: Experience and Expertise brings Excellence