# DIABETIC NEUROPATHY

Dr. Waddah Kazkaz

# Definition

The presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes.

# Epidemiology

- Involvement of peripheral and autonomic nervous system is probably the most common complication of diabetes.
- Diabetic neuropathy is the most common neuropathy in western world.
- Clinical and subclinical neuropathy has been estimated 10-100 % of diabetic patient depending upon the diagnostic criteria and patient populations examined.

# Risk factor

# A- Modifiable risk factors

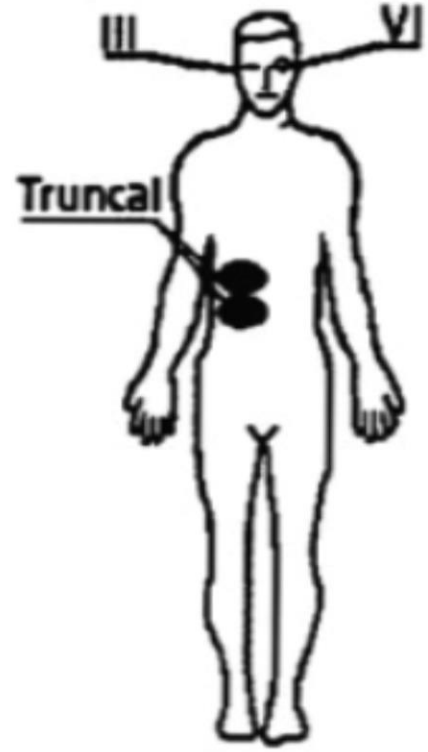
1. poor glycemic control
2. alcohol
3. hypertension
4. cigarette smoking
5. hypertriglyceridemiae genotype

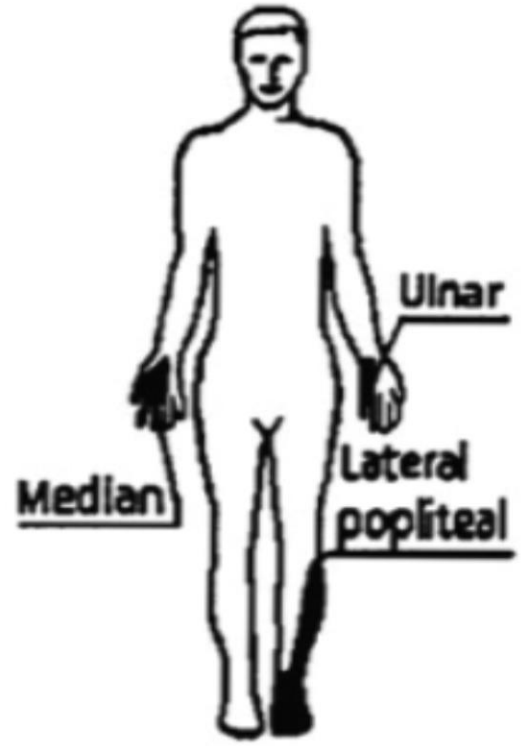
# B- Non-modifiable risk factor

1. obesity.
2. older age.
3. male set.
4. family history of neuropathic disease.
5. longer duration of diatestes.
6. APOE genotype.
7. aldose reductase gene hyperactivity.
8. angiotensin_converting enzyme.

# Classification

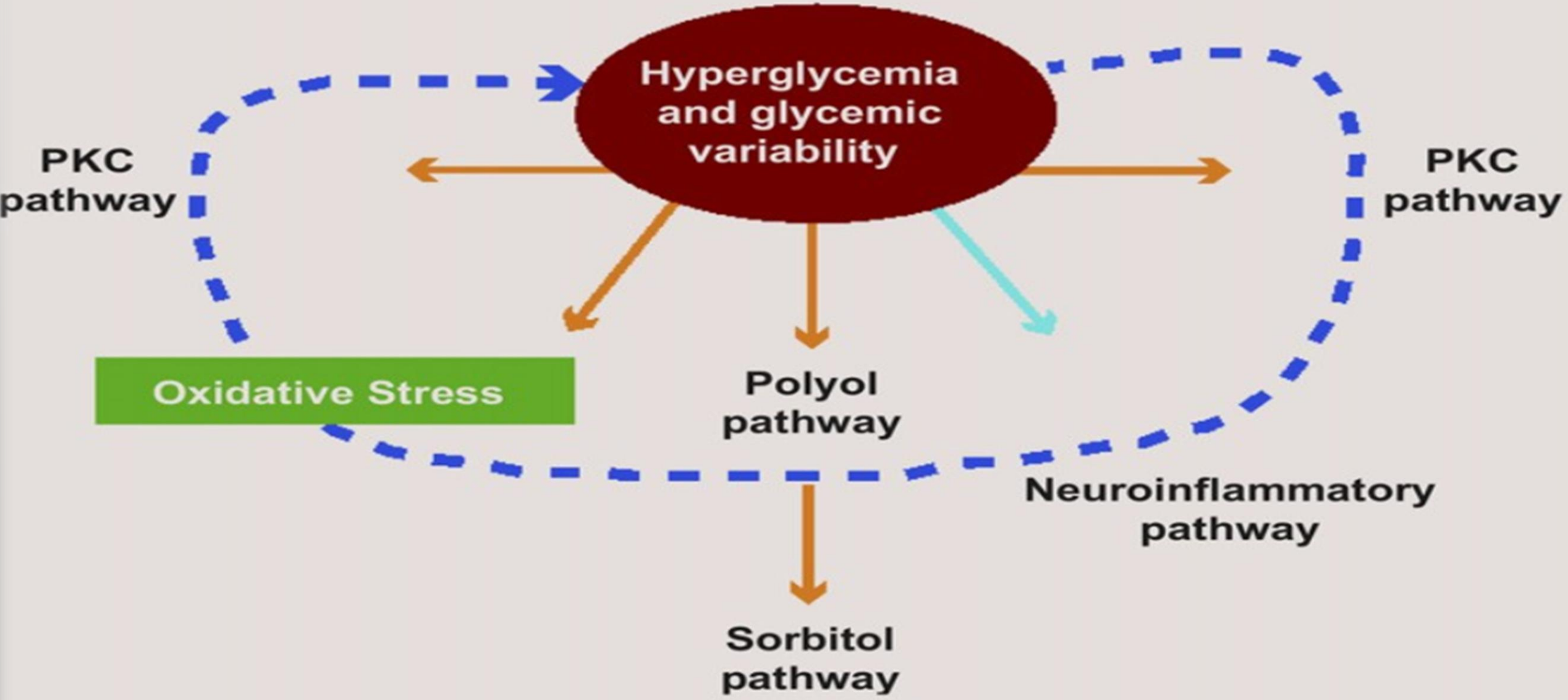
1. Distal symmetric polyneuropathy.
2. Autonomic neuropathy.
3. Thoracic and lumbar nerve root disease causing polyradiculopathies.
4. Individual cranial and peripheral nerve involvement causing focal mononeuropathy, especially affecting oculomotor nerve and the median nerve.
5. Asymmetric involvement of multiple peripheral nerves resulting in mononeuropathy multiplex.
6. Acute painful diabetic neuropathies:
   - treatment induced diabetic neuropathy
   - diabetic neuropathic cachexia
   - diabetic amorexia




| Large fiber Neuropathy | Small fiber Neuropathy | Proximal motor Neuropathy | Acute mono Neuropathies | Pressure Palsies |
|---|---|---|---|---|
| Sensory loss: 0→ +++ (Touch, vibration)<br>Pain: + → +++<br>Tendon reflex: N → ↓↓↓<br>Motor deficit 0 → +++ | Sensory loss: 0 → +<br>(thermal , allodynia)<br>Pain: + → +++<br>Tendon reflex: N → ↓<br>Motor deficit: 0 | Sensory loss: 0 → +<br>Pain: + → +++<br>Tendon reflex: ↓↓<br>Proximal Motor deficit:<br>+ → +++. | Sensory loss: 0 → +<br>Pain: + → +++<br>Tendon reflex: N<br>Motor deficit:<br>+ → +++ | Sensory loss in Nerve distribution: + → +++<br>Pain: + → ++<br>Tendon reflex: N<br>Motor deficit: + → +++ |

# Pathogenesis of Diabetic Neuropathy



# Symptoms and Diagnosis

- The earliest sign of diabetic polyneuropathy probably reflect the gradual loss of integrity of both large myelinated and small myelinated and unmyelinated nerve fiber.
- Loss of vibratory sensation and altered proprioceptiom.
- Impairement of pain light touch and temperature.
- Decreased or absent ankle reflexes occur early in the disease while more widespread loss of reflexes and motor weakness are late finding.

# Criteria for dignosis

| Michigan Neuropathy Screening Instrument (MNSI) | | |
|---|---|---|
| Appearance of feet | Right | Normal = 0<br>Abnormal = 1 |
| | Left | Normal = 0<br>Abnormal = 1 |
| Ulceration | Right | Absent = 0<br>Present = 1 |
| | Left | Absent = 0<br>Present = 1 |
| Ankle reflexes | Right | Present = 0<br>Reinforcement = 0.5<br>Absent = 1 |
| | Left | Present = 0<br>Reinforcement = 0.5<br>Absent = 1 |
| Vibration perception at great toe | Right | Present = 0<br>Reduced = 0.5<br>Absent =0 |
| | Left | Present = 0<br>Reduced = 0.5<br>Absent = 1 |
| Total | | 8 points |

✓ A score greater than 2 indicate neuropathy with both a high specificity 95% and sensitivity 80%.

# Electrodiagnosis tests

- Asymmetry of symptoms or signs.
- Intial pressention with weakness more than sensory loss.
- Proximal greater than distal signs and symptoms.
- Rapidly progressive disease course.

# Monitoring

- Type I diabetis of more than five years duration.
- Type II diabetes in all patients.
- In any patient presenting with idiopathic painful neuropathy.

# Diabetic neuropathy, or neuropathy in diabetic patient !??

1) CIDP.

2) B12 deficiency.

3) Uremia.

4) Hypothyroidism.

5) Monoclonal gammopathies.

# Treatment

# Anticonvulsants

- If clinically appropriate, pregabalin should be offered for the treatment of PDN (Level A).
- Gabapentin and sodium valproate should be considered for the treatment of PDN (Level B).
- There is insufficient evidence to support or refute the use of topiramate for the treatment of PDN (Level U).
- Oxcarbazepine, lamotrigine, and lacosamide should probably not be considered for the treatment of PDN (Level B).

**Valproate may is potentially teratogenic, be avoided in women of childbearing age. Due to weight gain and potential worsening of glycemic control, this drug is unlikely to be the first treatment choice for PDN .**

# Antidepressants

- Amitriptyline, venlafaxine, and duloxetine should be considered for the treatment of PDN (Level B). Data are insufficient to recommend one of these agents over the others.
- Venlafaxine may be added to gabapentin for a better response (Level C).
- There is insufficient evidence to support or refute the use of desipramine, imipramine, fluoxetine, or the combination of nortriptyline and fluphenazine in the treatment of PDN (Level U).

# Opioids

- Dextromethorphan, morphine sulfate, tramadol, an oxycodone should be considered for the treatment of PDN (Level B). Data are insufficient to recommend one agent over the other.

- **The use of opioids for chronic nonmalignant pain has gained credence over the last. Both tramadol and dextromethorphan were associated with substantial adverse events (e.g., sedation, nausea, and constipation).**
- **The use of opioids can be associated with the development of novel pain syndromes such as rebound headache.**
- **Chronic use of opioids leads to tolerance and frequent escalation of dose.**

# Other pharmacologic agents

- Capsaicin and isosorbide dinitrate spray should be considered for the treatment of PDN (Level B).
- Clonidine, pentoxifylline, and mexiletine should probably not be considered for the treatment of PDN (Level B).
- The Lidoderm patch may be considered for the treatment of PDN (Level C).
- There is insufficient evidence to support or refute the usefulness of vitamins and -lipoic acid in the treatment of PDN (Level U).

❖ **Although capsaicin has been effective in reducing pain in PDN clinical trials, many patients are intolerant of the side effects, mainly burning pain on contact with warm/hot water or in hot weather.**

# NONPHARMACOLOGIC MODALITIES ?

- Percutaneous electrical nerve stimulation should be considered for the treatment of PDN (Level B).
- Electromagnetic field treatment, low-intensity laser treatment, and Reiki therapy should probably not be considered for the treatment of PDN (Level B).
- Evidence is insufficient to support or refute the use of amitriptyline plus electrotherapy for treatment of PDN (Level U).

| | Recommended drug and dose | Not recommended |
|---|---|---|
| **Level A** | Pregabalin, 300–600 mg/d | |
| **Level B** | Gabapentin, 900–3,600 mg/d | Oxcarbazepine |
| | Sodium valproate, 500–1,200 mg/d | Lamotrigine |
| | Venlafaxine, 75–225 mg/d | Lacosamide |
| | Duloxetine, 60–120 mg/d | Clonidine |
| | Amitriptyline, 25–100 mg/d | Pentoxifylline |
| | Dextromethorphan, 400 mg/d | Mexiletine |
| | Morphine sulphate, titrated to 120 mg/d | Magnetic field treatment |
| | Tramadol, 210 mg/d | Low-intensity laser therapy |
| | Oxycodone, mean 37 mg/d, max 120 mg/d | Reiki therapy |
| | Capsaicin, 0.075% QID | |
| | Isosorbide dinitrate spray | |
| | Electrical stimulation, percutaneous nerve stimulation ×3–4 weeks | |

THANKS ☺