

Peripheral Neuropathy: Diagnosing and Evaluation

Eddie Patton Jr., M.D.

Neurologist, Neuromuscular Disease Specialist
Methodist Sugar Land Neurology Associates

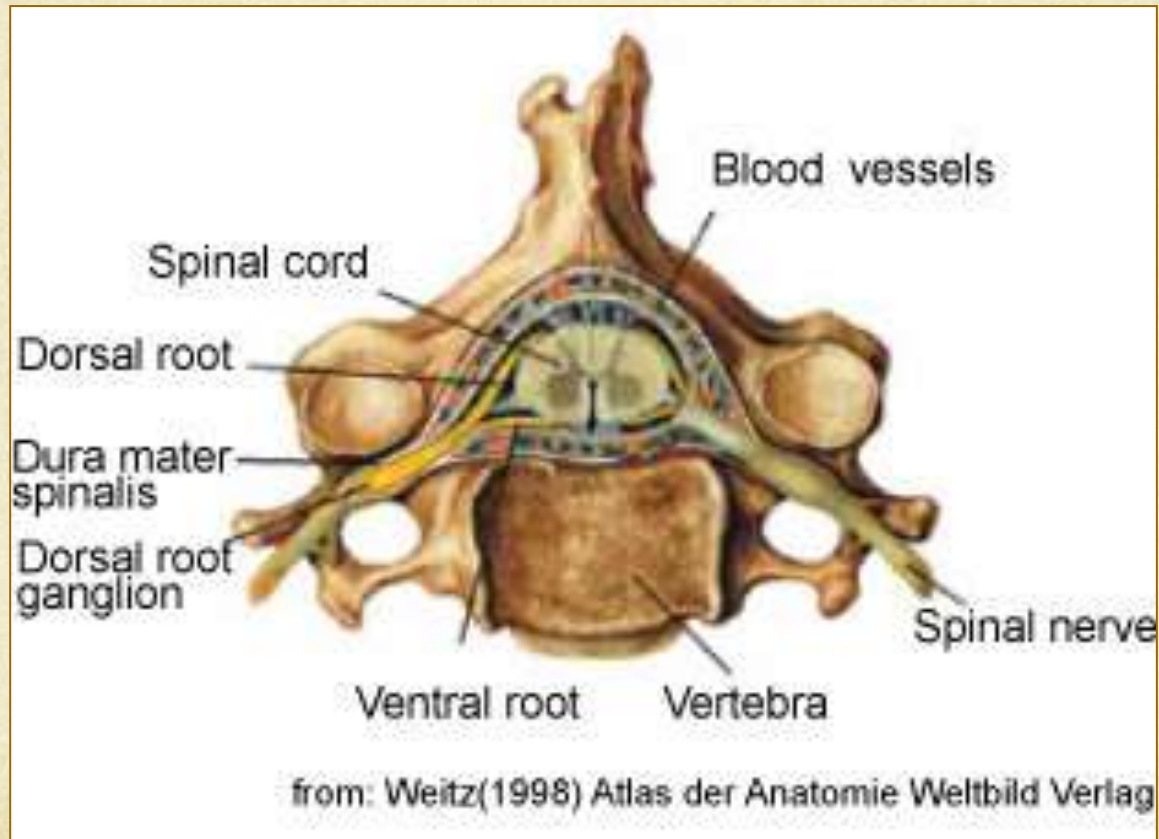
Overview

- Define peripheral neuropathy
- Highlight different causes of neuropathy with a focus on the most common causes
- Discuss pertinent history and examination findings
- Discuss the work-up including lab tests and ancillary studies
- Questions

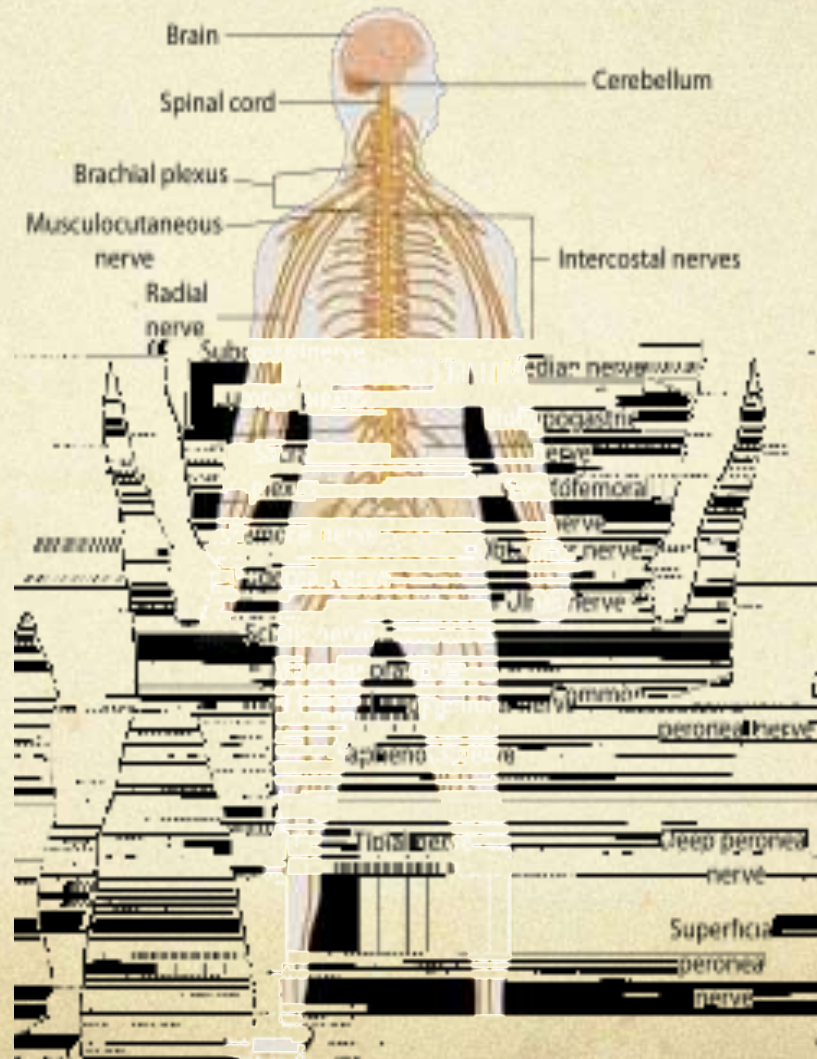
What is a peripheral neuropathy?

- PN is estimated to affect more than 20 million Americans
- Prevalence higher in older people > 55 yo (8%) than general population (2.4%)
- Annual cost to Medicare exceeds \$3.5 billion
- Neuropathy can severely decrease a persons quality of life and productivity
- Secondary complications includes falls, fractures, foot ulcers, amputations, cardiac arrhythmias
- Any disorder of the peripheral nervous system

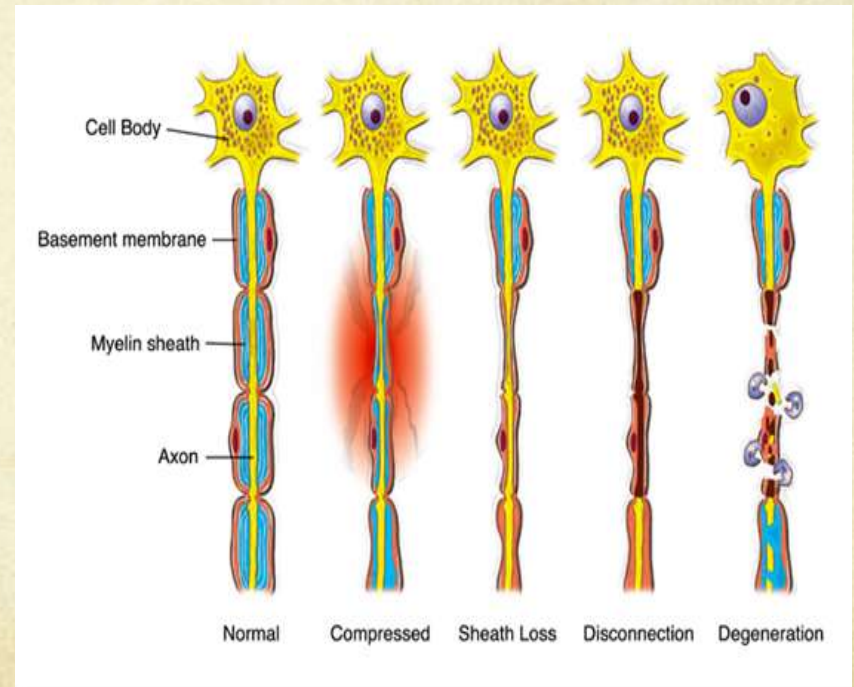
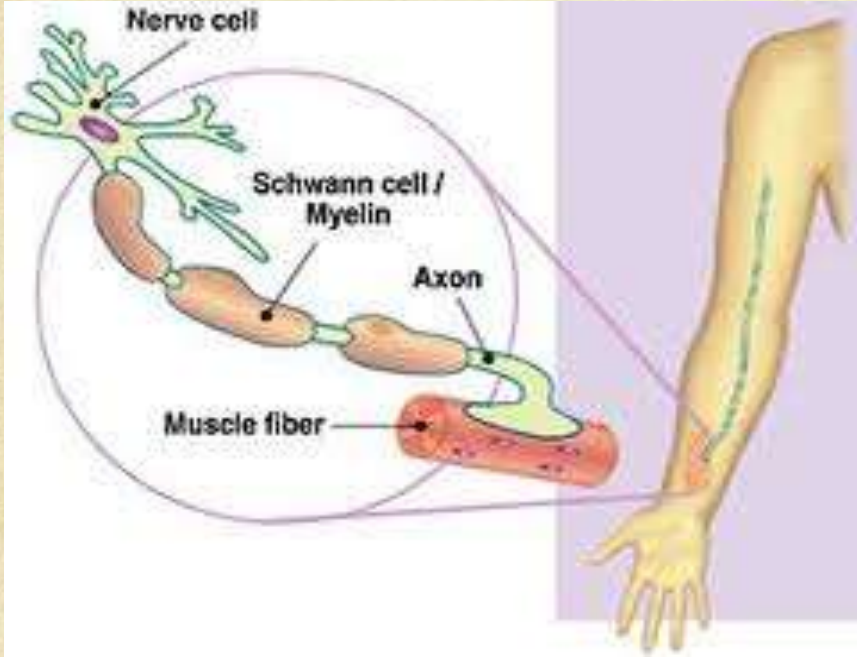
Peripheral Neuropathy



Peripheral neuropathy



Axonal vs Demyelinating



Causes of distal symmetric polyneuropathies

- Endocrine diseases
 - Diabetes mellitus
 - Hypothyroidism
 - Acromegaly
- Nutritional diseases
 - Alcoholism
 - Vitamin B12 deficiency
 - Folate deficiency
 - Whipple's disease
 - Postgastrectomy syndrome
 - Gastric restriction surgery for obesity
 - Thiamine deficiency
- Hypophosphatemia
- Critical illness polyneuropathy
- Connective tissue diseases
 - Rheumatoid arthritis
 - Polyarteritis nodosa
 - Systemic lupus erythematosus
 - Churg-Strauss vasculitis
 - Cryoglobulinemia
- Amyloidosis
- Gouty neuropathy
- Carcinomatous axonal sensorimotor polyneuropathy
- Lymphomatous axonal sensorimotor polyneuropathy
- Infectious diseases
 - Acquired immunodeficiency syndrome
 - Lyme disease
- Sarcoidosis
- Toxic neuropathy
 - Acrylamide
 - Carbon disulfide
 - Dichlorophenoxyacetic acid
 - Ethylene oxide
 - Hexacarbons
 - Carbon monoxide
 - Organophosphorus esters
 - Glue sniffing
- Metal neuropathy
 - Chronic arsenic intoxication
 - Mercury
 - Gold
 - Thallium
- Medications

Causes of peripheral neuropathy

- 30 % of neuropathies are caused by diabetes
- 30 % are idiopathic (or unknown)
- The rest are due to other disorders but one of the most common in this category is nutritional and alcohol consumption

Alcohol Misuse

- New AAN Distal Symmetric Polyneuropathy discusses the fact that patients initially evaluated for peripheral neuropathy should also be screened for alcohol misuse
- Alcohol is neurotoxic and will make any peripheral neuropathy worse
- Same is true for tobacco

Diabetes and Pre-diabetes

- According to the American Diabetes Association
 - Total: 25.8 million children and adults in US with DM
 - 8.3% of the population
 - Prediabetes: 79 million
 - New Cases: 1.9 million in people aged 20 or older in 2010
- Neuropathy affects 50% of patients with diabetes
- Diabetes accounted for over \$62.3 billion in healthcare cost in 1996

Causes of peripheral neuropathy

- Recent evidence has shown that there is a strong connection with metabolic syndrome
 - Poor glycemic control
 - Visceral obesity and height
 - Hypertension
 - Age
 - Smoking
 - Hypoinsulinemia
 - Dyslipidemia

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Clinical evaluation

- Length-dependent process:
 - Symptoms usually occur distally at first (toes, soles) and symmetrical
 - Sensory sx early – numbness, burning, paresthesias, dysesthesias. Positive sensory symptoms highly suggestive.
 - Motor sx – weakness of **toe extensors** and **ankle dorsiflexors**
 - Ankle jerks are lost/reduced first
 - Symptoms progress in an ascending manner

Clinical Evaluation

- When sensory symptoms reach upper **calves/knees**, fingers & hands become affected
 - Numbness, dysesthesias in finger tips
 - Difficulty opening jars; turning keys; buttoning
 - By now patients c/o gait unsteadiness because of proprioception loss and weakness of extensor muscles
 - Distal muscle wasting and weakness prominent

Clinical Evaluation

- Autonomic symptoms are frequent in small fiber neuropathies:
 - Bladder dysfunction
 - Constipation/Diarrhea
 - Impotence
 - Gastroparesis
 - Orthostatic hypotension, arrhythmias
 - Sweating disturbances (anhidrosis, hyperhidrosis)
 - Dry eyes/mouth, blurred vision
 - Tonic pupils

Clinical evaluation

- Other important information:
 - Other medical conditions/systemic diseases
 - Recent viral/infectious illness/vaccination
 - Medications (including “herbs”, OTC)
 - Toxins – alcohol, smoking, heavy metals, organic solvents
 - Family history

Features on exam

- **Atrophy** → axonal loss
- **Weakness and early loss of DTR's without atrophy** → myelin loss (or acute axonal loss)
- **Fasciculations** → proximal lesion (root or motor neuron)
- **Pes cavus, high arched feet, cocked toes** → chronic, and likely inherited
- Most common finding is distal sensory loss in a “stocking or glove” distribution
 - Vibration one of the first sensory components affected

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Routine Lab Tests (almost all patients)

- CBC
- ESR, ANA, RF, dsDNA
- BUN, creatinine, Ca, Phos, albumin, LFTs, electrolytes
- Fasting blood sugar and HbA1C if diabetes or glucose intolerance suspected
 - **Most specific test is a 2-5 hour oral glucose tolerance test**
- TSH, B12, Folate, SPEP, Serum IFE, Immunoglobulin levels

Selective Patients (if routine labs inconclusive)

- 24 hr urine for heavy metals
- Porphyrin levels
- Urine protein electrophoresis and IFE for free light chains
- Special immunologic and genetic tests
- VDRL, Lyme, WNV, HIV
- Skin/fat pad/rectal biopsy for amyloid
- 2 hour GTT
- CSF examination
- Clinical exam, NCS of relatives if gene tests negative
- X-ray skeletal survey

Investigations

- EMG/NCS
 - Usually can establish that a neuropathy is the cause of a patient's symptoms
 - Exceptions: small fiber neuropathy +/- autonomic neuropathies
 - Helps separate neuropathy from e.g. myelopathy, hysteria, orthopedic causes etc.
 - Can broadly categorize neuropathies as **primarily axonal** or **demyelinating**

EMG/NCS

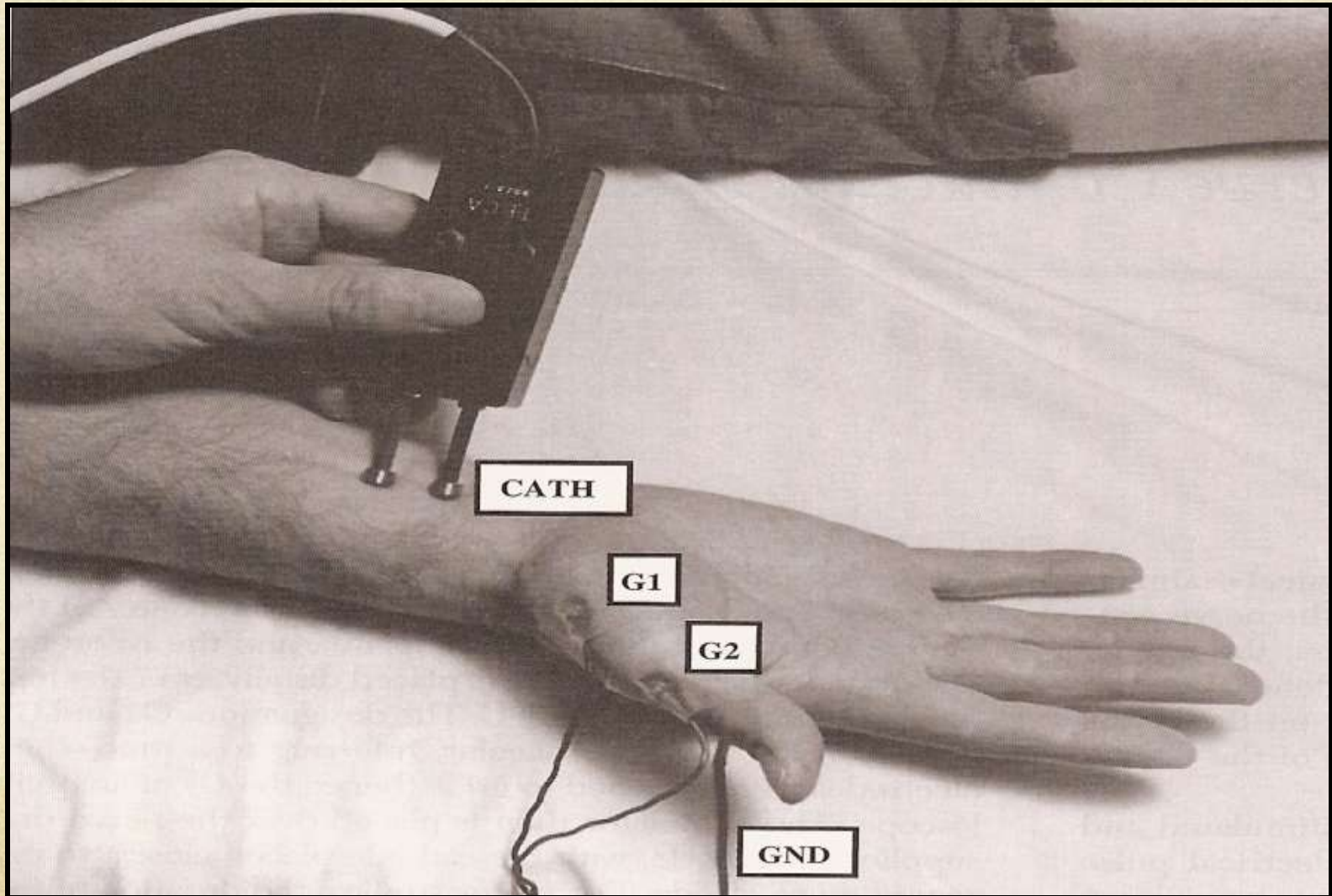
- AAN clinical guidelines
 - The combination of neuropathic symptoms, signs, and abnormal electrodiagnostic studies provides the most accurate diagnosis of distal symmetric polyneuropathy

Basic Equipment

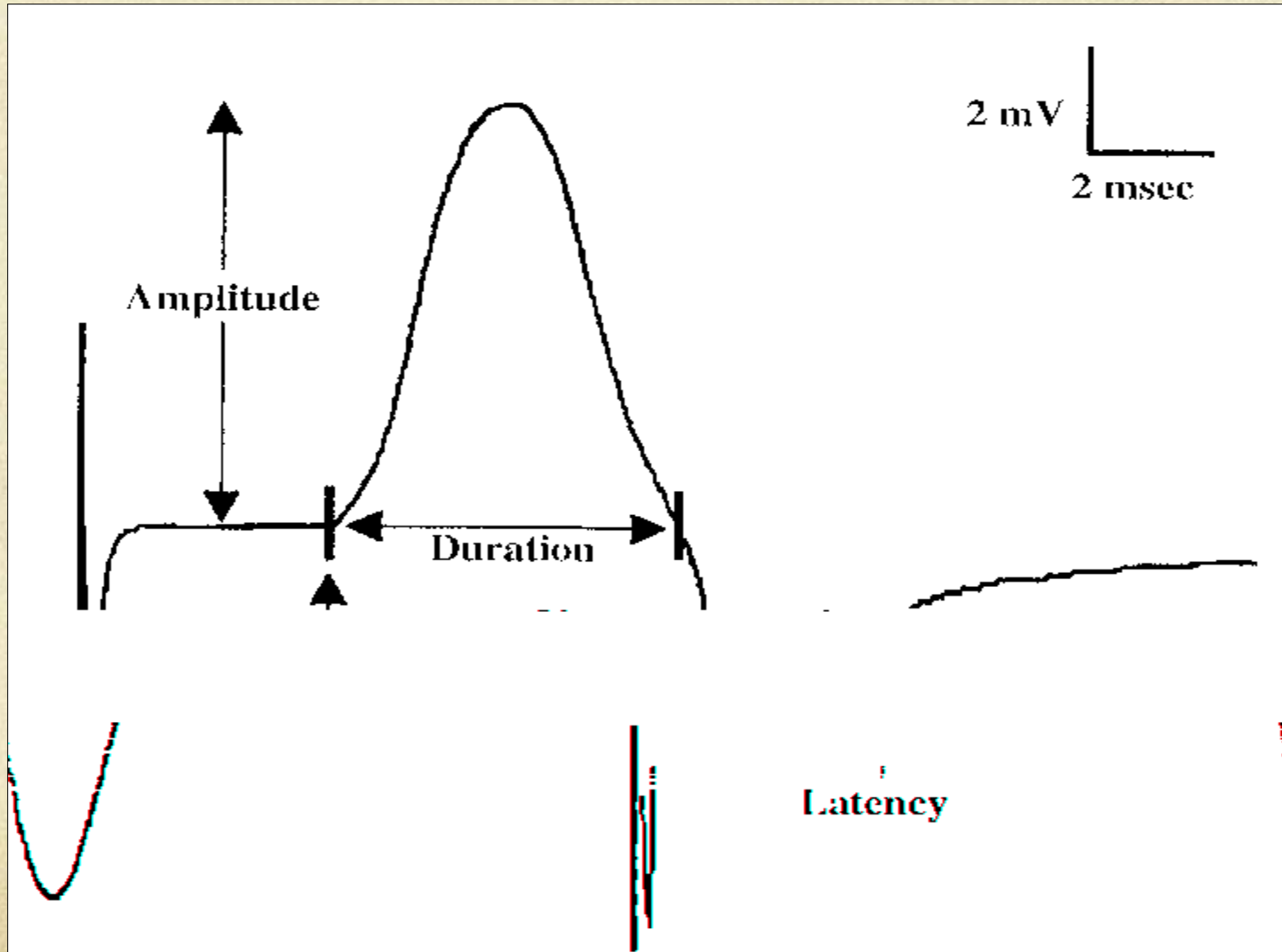
- Electrodes (active, reference & ground)
- Stimulator
- Preamplifier
- Amplifier
- Loudspeaker
- Digital Display
- Electrode gel



What a Study Looks Like...



CMAP



Autonomic Function Tests

❖ Screening tests to evaluate the autonomic nervous system

Sudomotor Quantitative Sudomotor Axon Reflex Test (QSART)

Cardiovagagal

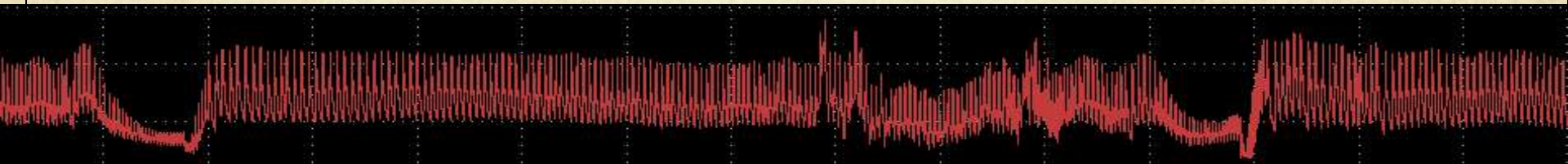
○ Heart Rate Response to Deep Breathing (HR_{DB})

○ Heart Rate Response to Valsalva Maneuver (VM)
Valsalva Ratio (VR)

Adrenergic

○ Beat to Beat Blood Pressure Changes to VM

○ Beat to Beat Blood Pressure Changes to Tilt-Up



○ Questions?