Small fiber Neuropathy and Testing (QSWEAT)

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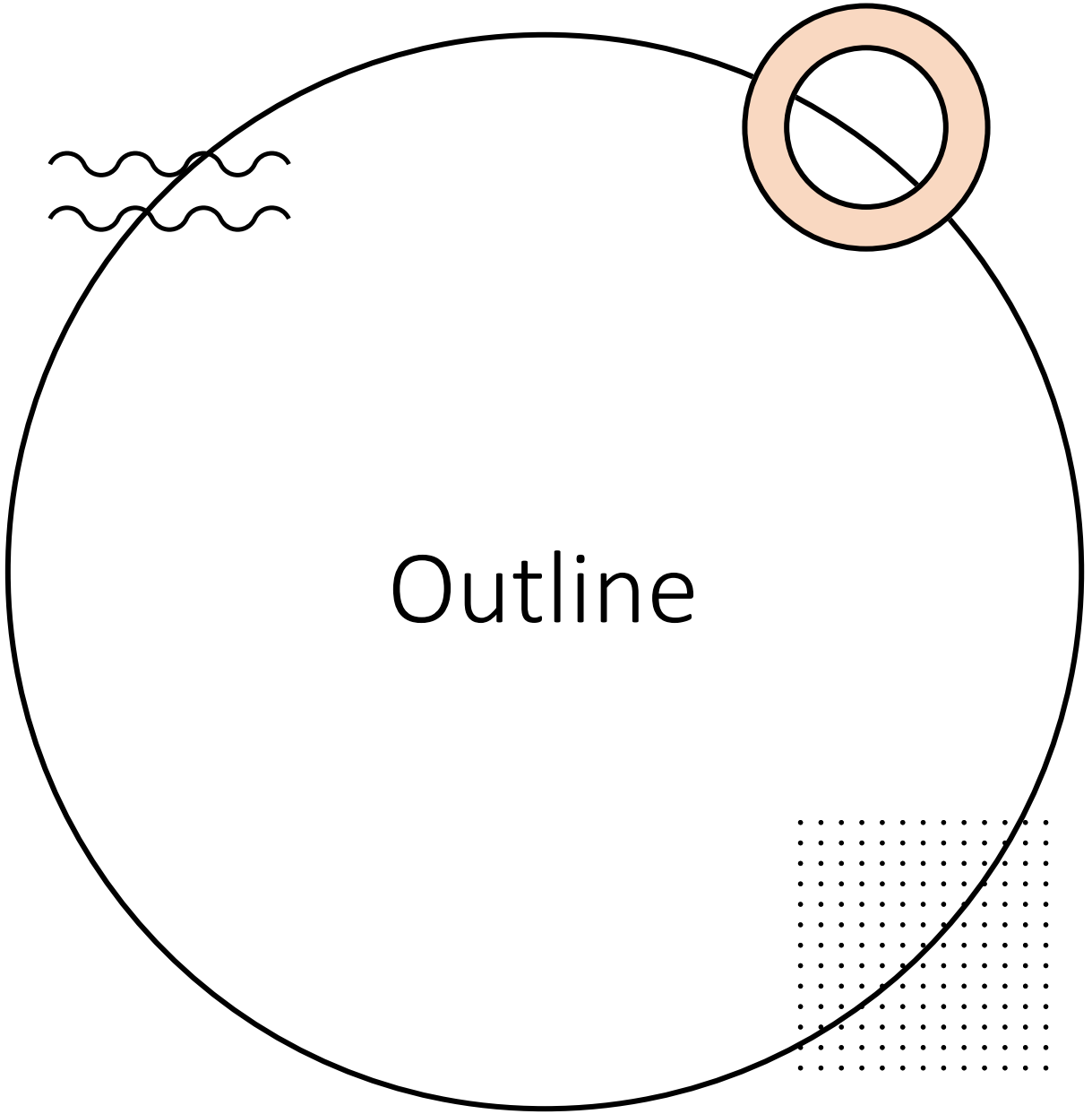
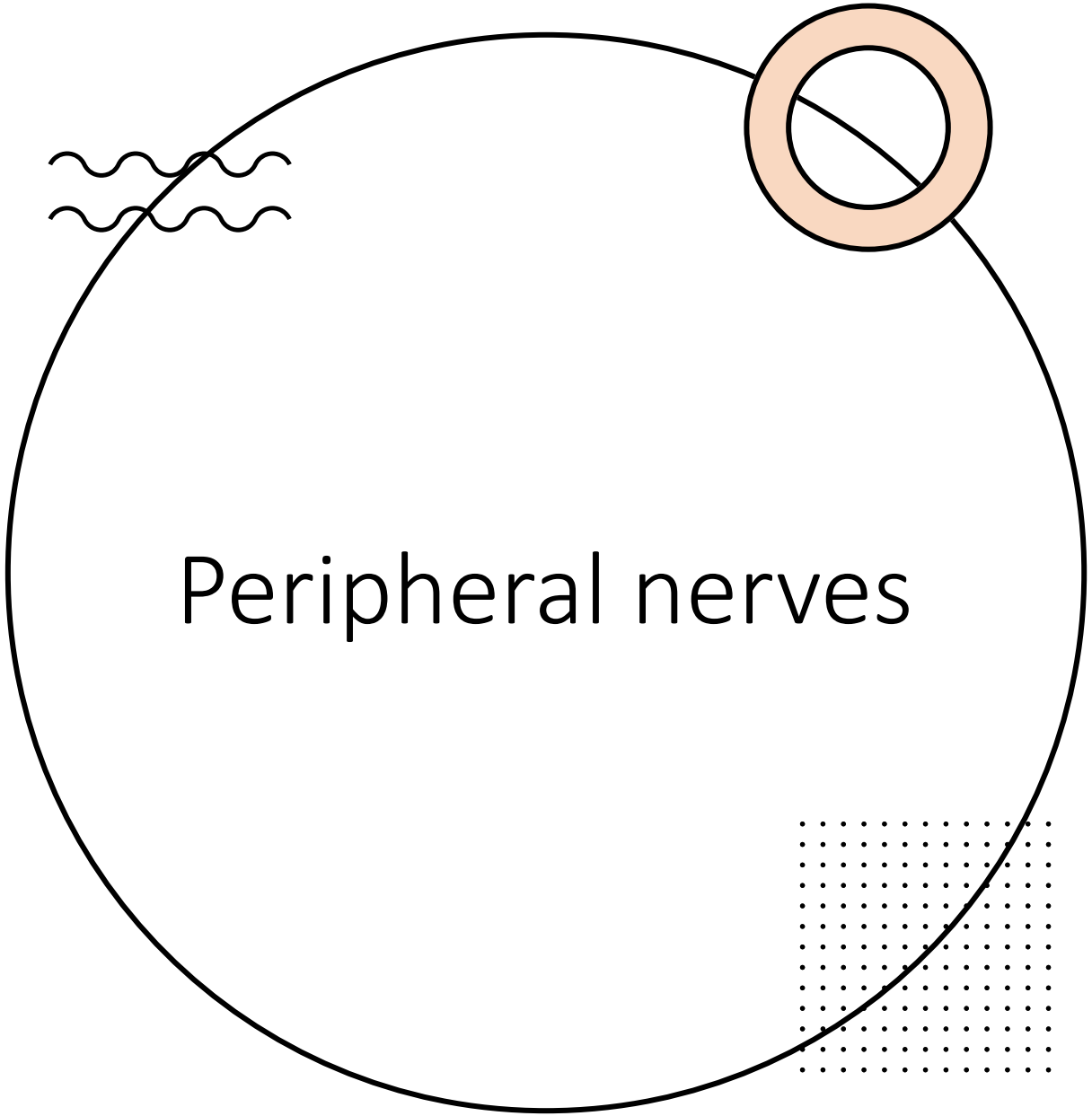
- No COI with today’s presentation.

Outline



- Nerve fiber classification.
- Assessment of Small fiber neuropathy
- Sympathetic Skin response (SSR)
- Thermoregulatory Skin testing (TST)
- Quantitative SWEAT response (QSART)
- Skin Biopsy and microscopy
- Summary

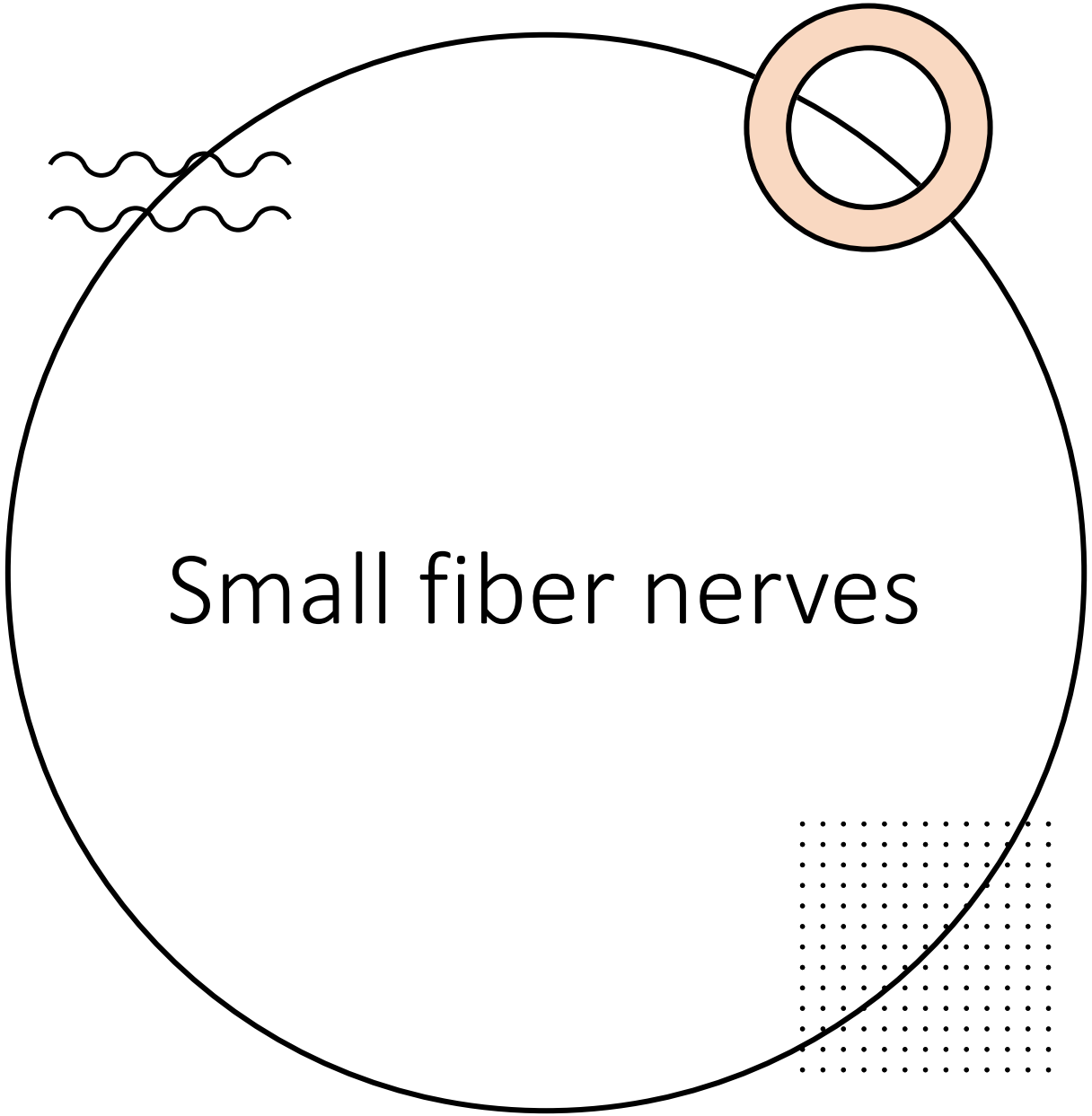
Peripheral nerves



1. Somatic motor nerves (A- alpha and gamma)
2. Somatic sensory nerves (A-beta and delta)
3. Unmyelinated C fibers (Somatic and sympathetic)

- Myelinated- 29%
- Unmyelinated- 71%, Somatic-sympathetic ratio 2:1

Small fiber nerves



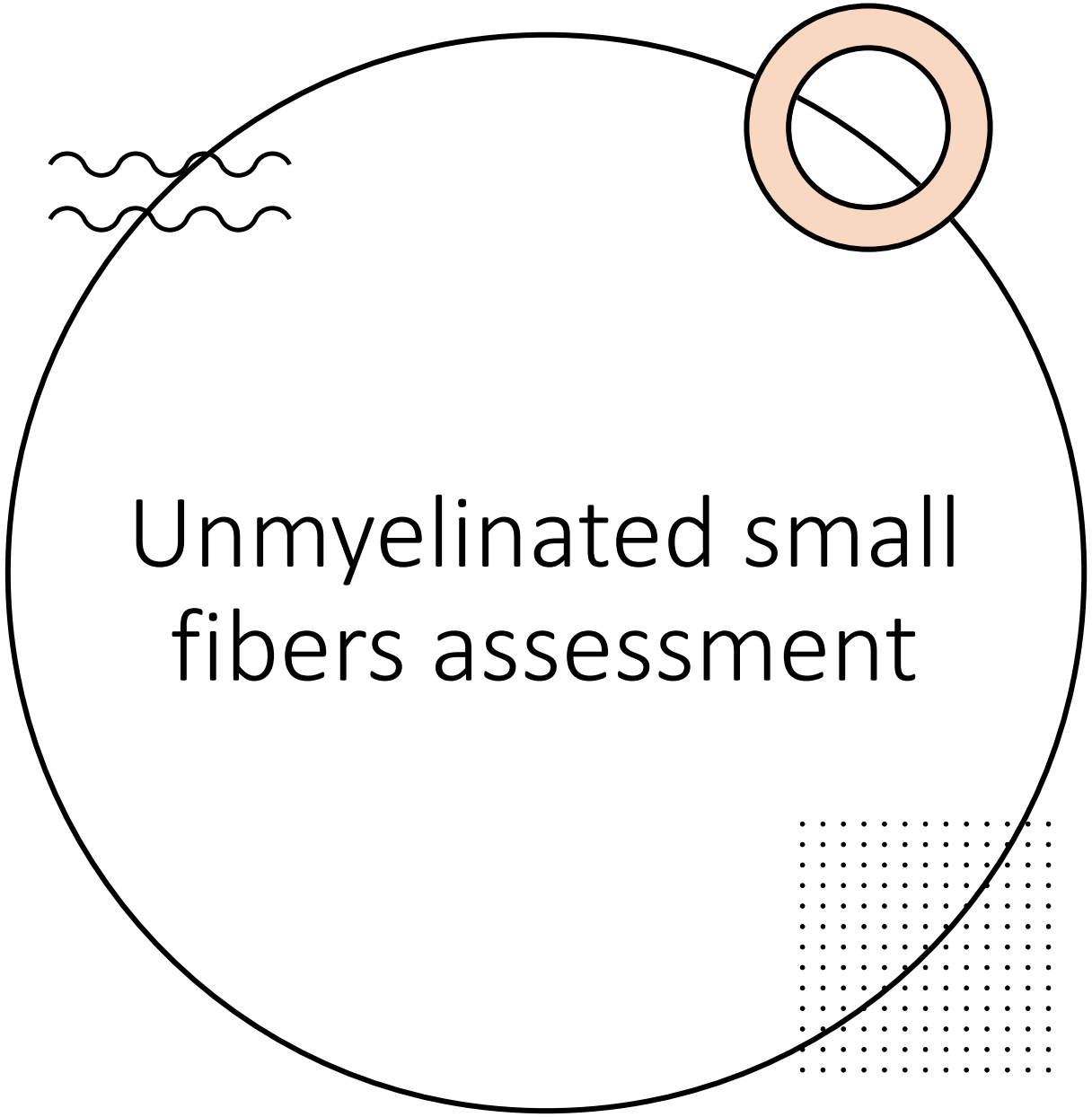
- A-delta and C- fibers
- Distributed throughout skin, peripheral nerves and organs.
- Mediate pain, temperature sensation and autonomic functions.
- Pattern of distribution.
  - Length dependent.
  - Non-length dependent.
  - Autonomic distribution

Skin sympathetic nerve activity

Four nerve types

- Vasoconstrictor
- Vasodilator
- Sudomotor
- Pilomotor

Unmyelinated small fibers assessment



- **Indirect**

-Sympathetic skin response

-Thermal Skin test

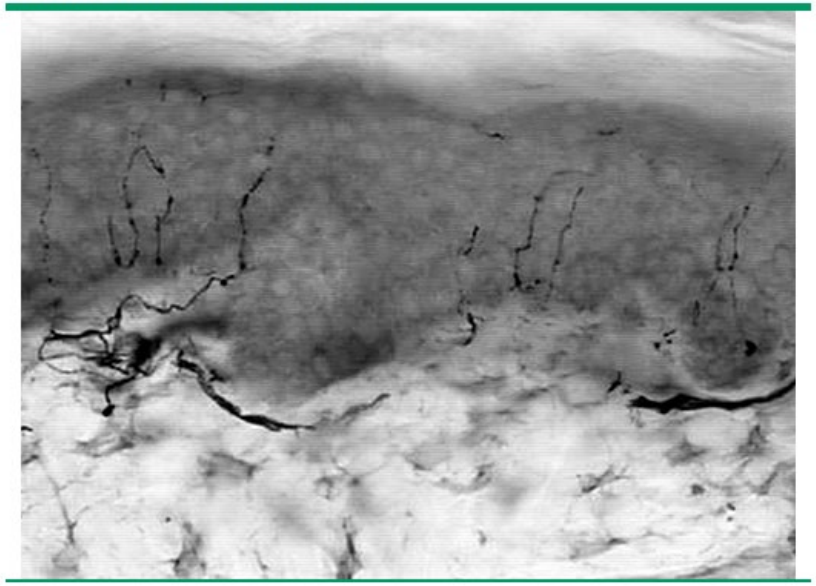
-Quantitative Sudomotor Axon reflex testing

- **Direct**

- Electron microscope- dense core particles, immuno-gold localization of tyrosine hydroxylase

- Fluorescence microscopy- glyoxylic acid, nerve nor-epinephrine content, dopamine hydroxylase measurement.

Unmyelinated sensory axons



Unmyelinated sensory axons are seen extending from the dermal-epidermal junction towards the surface in this biopsy from a normal subject (40x).

Courtesy of A. Gordon Smith, MD

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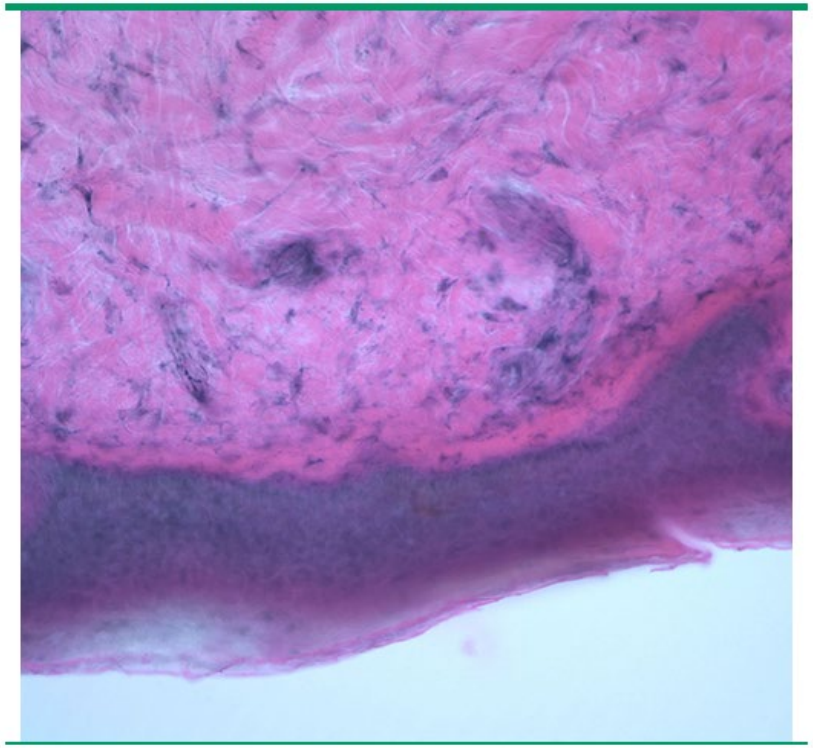
Reduced epidermal nerve fiber density



There is a reduction in the epidermal nerve fiber density in this biopsy from a patient with diabetic neuropathy.

Courtesy of A. Gordon Smith, MD

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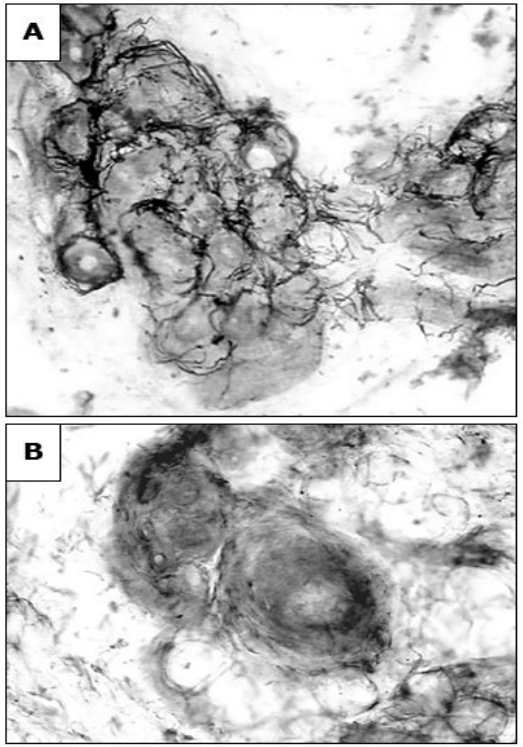
Sweat gland innervation

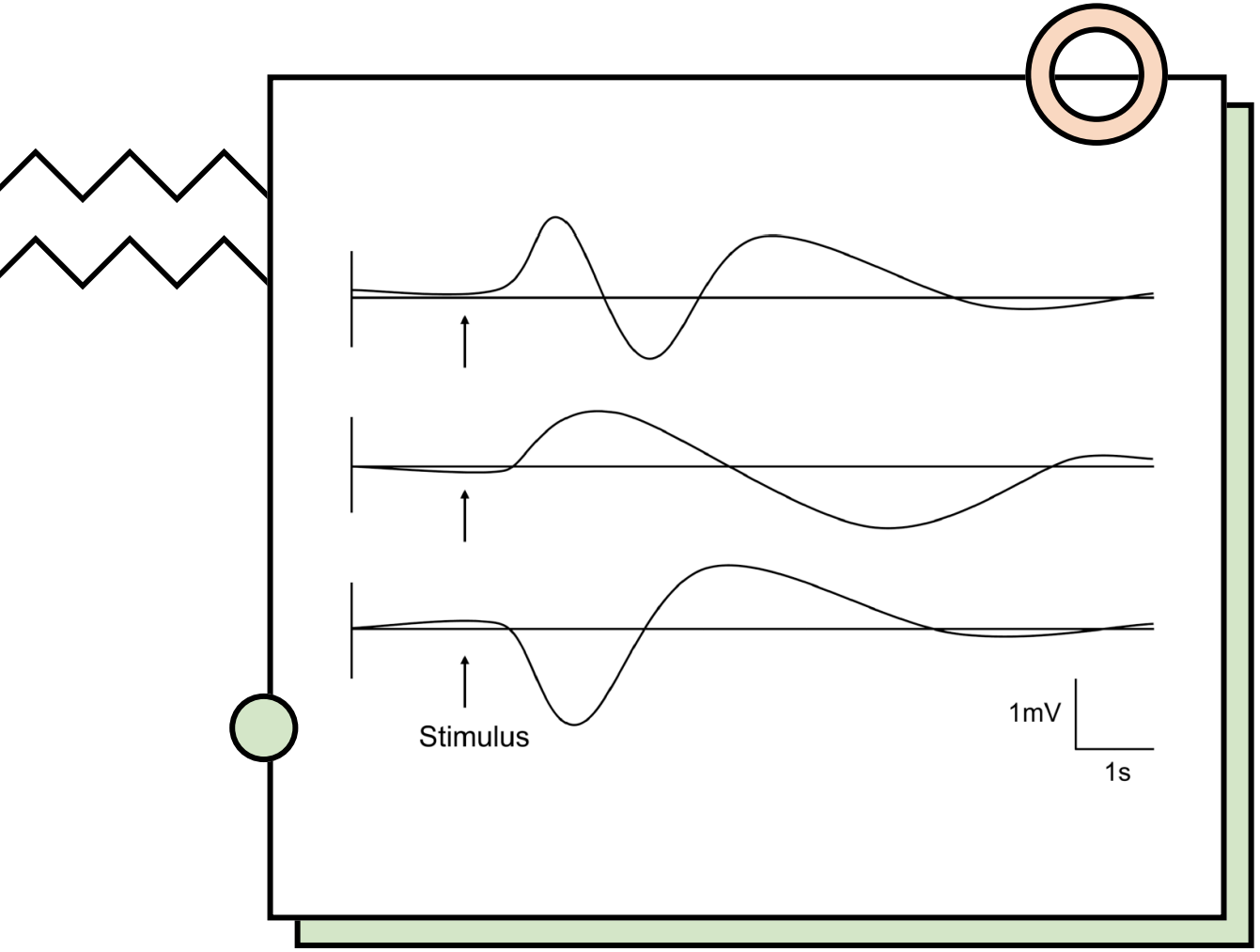


(A) Skin biopsy from a patient showing normal innervation of two sweat glands.

(B) Skin biopsy from a patient with congenital insensitivity to pain due to a mutation of the tyrosine kinase A receptor showing absent innervation of sweat glands.

Sympathetic skin response

- Tarchanoff 1890
- Electrical potential- Time locked wave form
- Eccrine sweat gland activity
- Both for central and peripheral nervous system



Waveform morphology

Clinical application

Peripheral nervous system

- Generalized peripheral neuropathy sec to DM (severity, prognosis and course of illness)
- Chronic alcoholism, leprosy and cryoglobulinemia
- Fabry disease, amyloidosis
- CIDP for assessment of autonomic involvement
- Carpal tunnel syndrome

Pain syndromes

- Complex regional pain syndrome
- Fibromyalgia
- Migraine headaches
- Erythromelalgia

Clinical application

Central nervous system

- Parkinson disease
- Multiple sclerosis
- Cerebral and brainstem stroke
- Chronic spinal cord injury

Limitations

Non-neural factors

1. Type and frequency of stimulus
2. Characteristics of skin hydration
3. Distracting stimuli

Neural factors

1. Level of consciousness
2. Cognitive activity
3. Emotional state

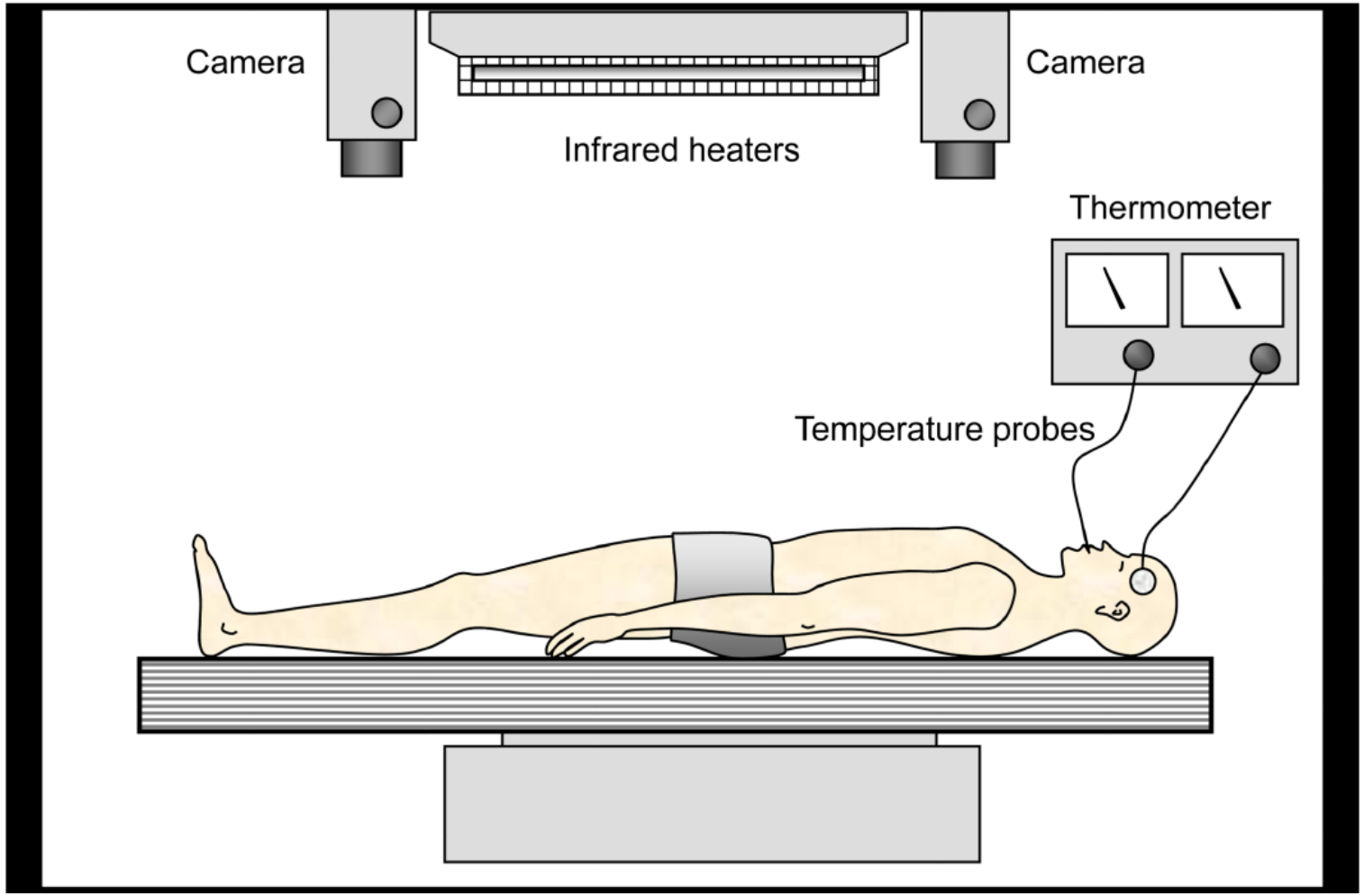
Limitations

- Intact reflex arc
- Normal eccrine glands
- Abnormal adrenergic sympathetic system may produce normal SSR
- Abnormalities in sensory system may produce abnormal SSR

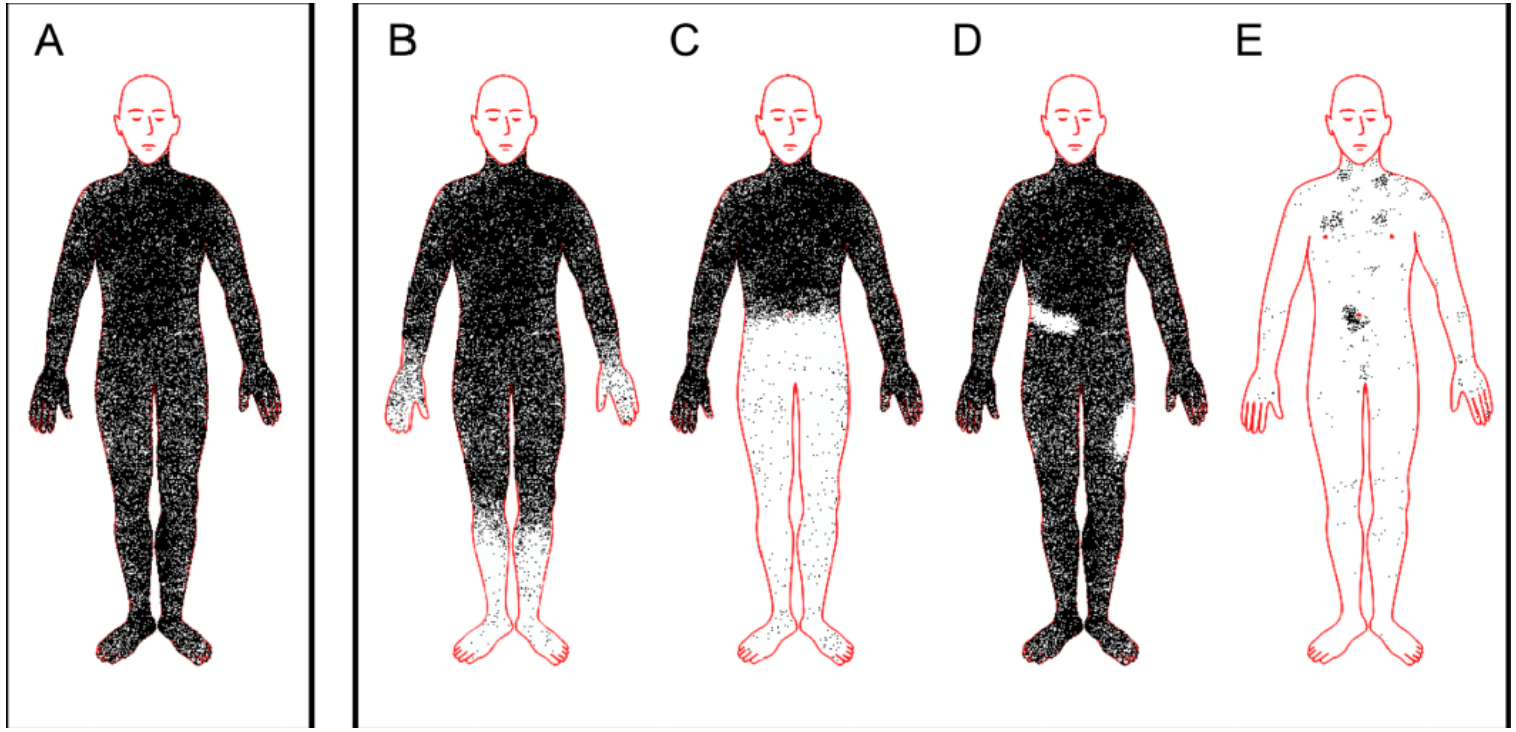
Thermoregulatory skin testing

- Temperature 45-50 C
- Humidity- 35-40%
- Indicator dye– Alizarin red powder, Iodine corn starch.
- Skin and oral temperature probes.
- Mean body temperature- 38.5-39.5 C
- Max time- 70 minutes

Thermoregulatory skin testing



Staining Patterns

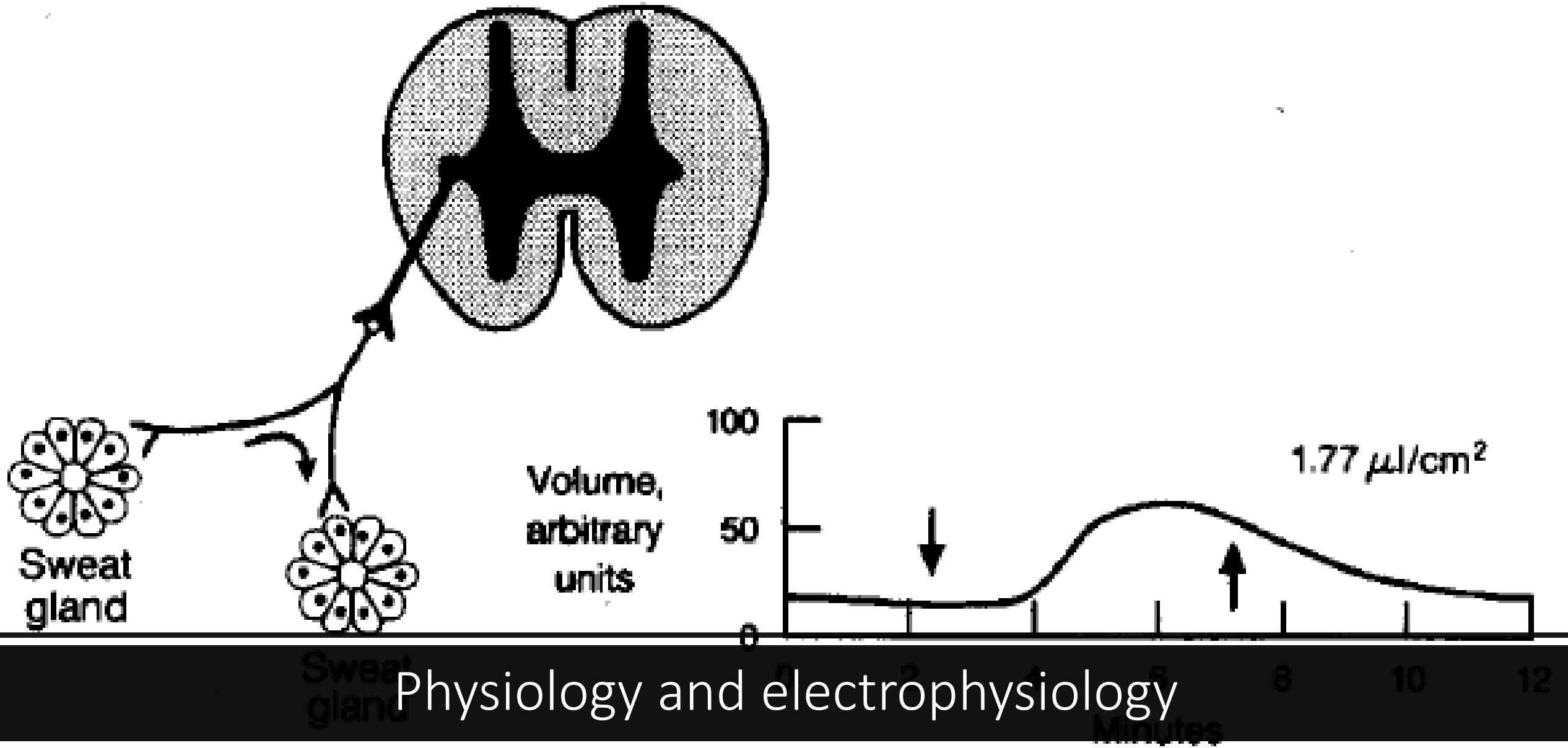


Quantitative Sudomotor Axon reflex test- QSART/QSWEAT

- Axon reflex mediated by postganglionic sympathetic sudomotor axon
- Stimulus: Ach, pilocarpine and Carbachol.

Apparatus

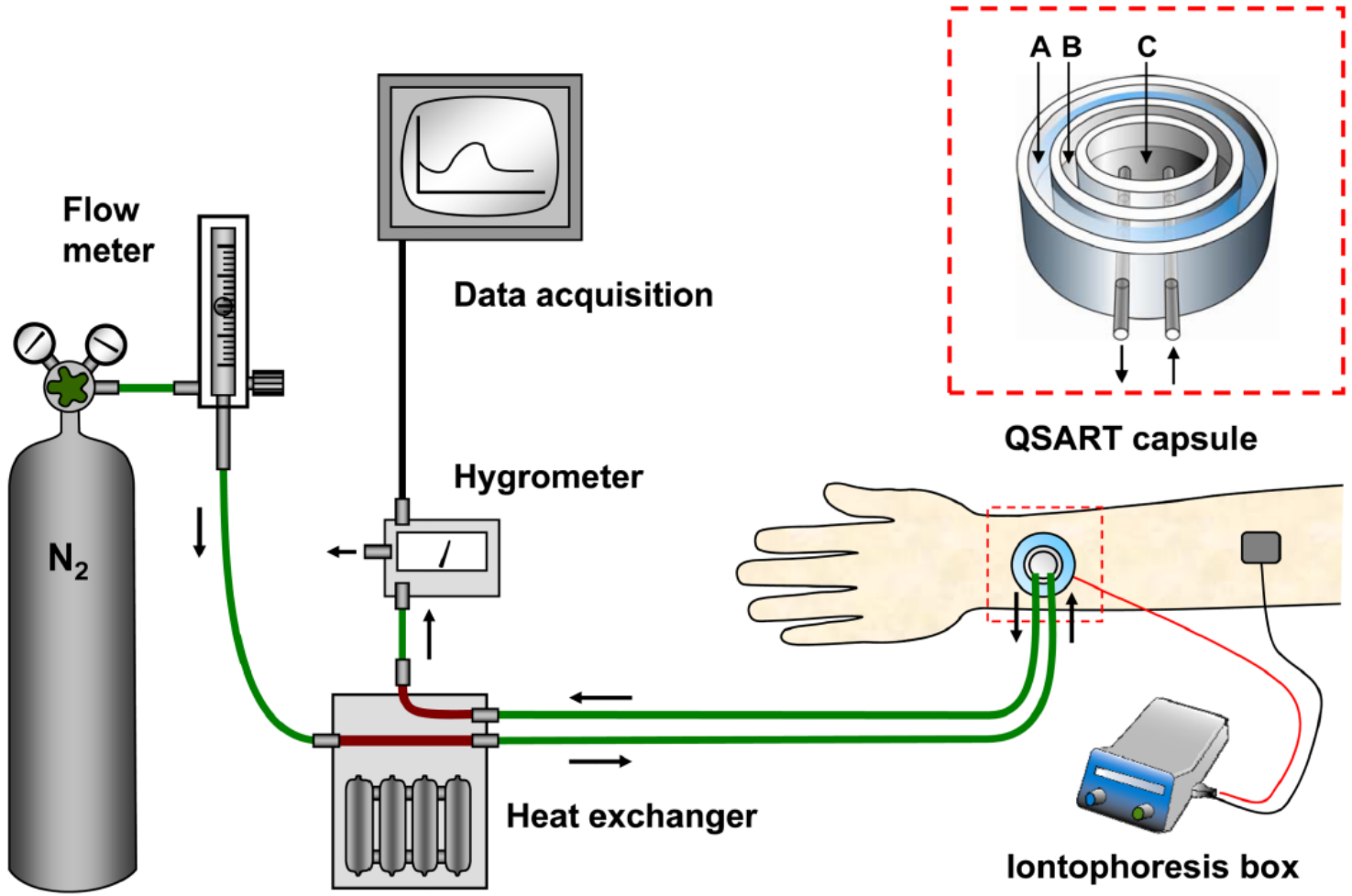
- Multi-compartment sweat cell
- Constant current stimulator- 2mA for 5 min



Physiology and electrophysiology

Sudomotor axon reflex

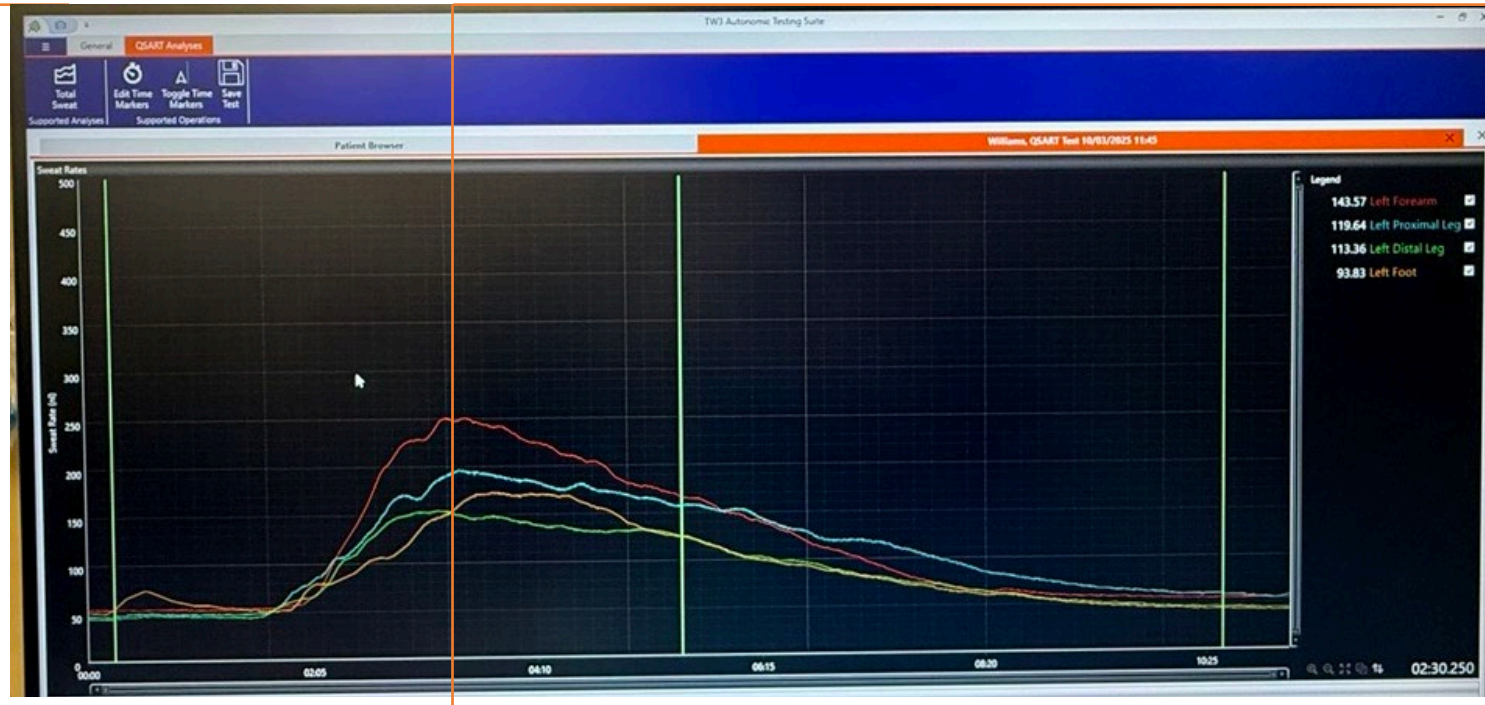
Apparatus


A B C
QSART capsule
Flow meter
Data acquisition
Hygrometer
N_2
Heat exchanger
Iontophoresis box

QSWEAT

Result interpretation

- Reduced
- Absent
- Excessive
- Hung up response

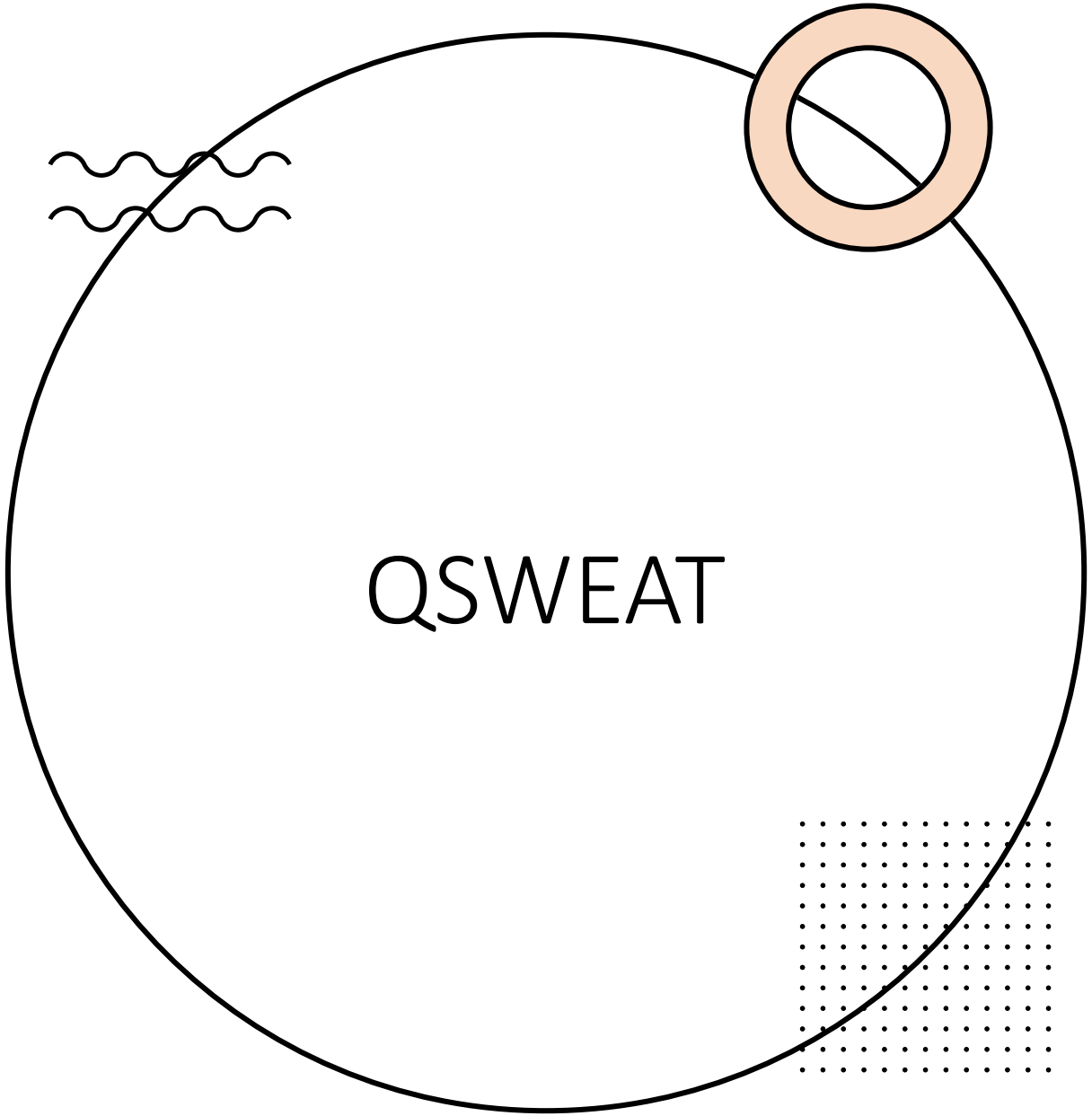



Adult
cnap


Position control
lonto4

Apparatus

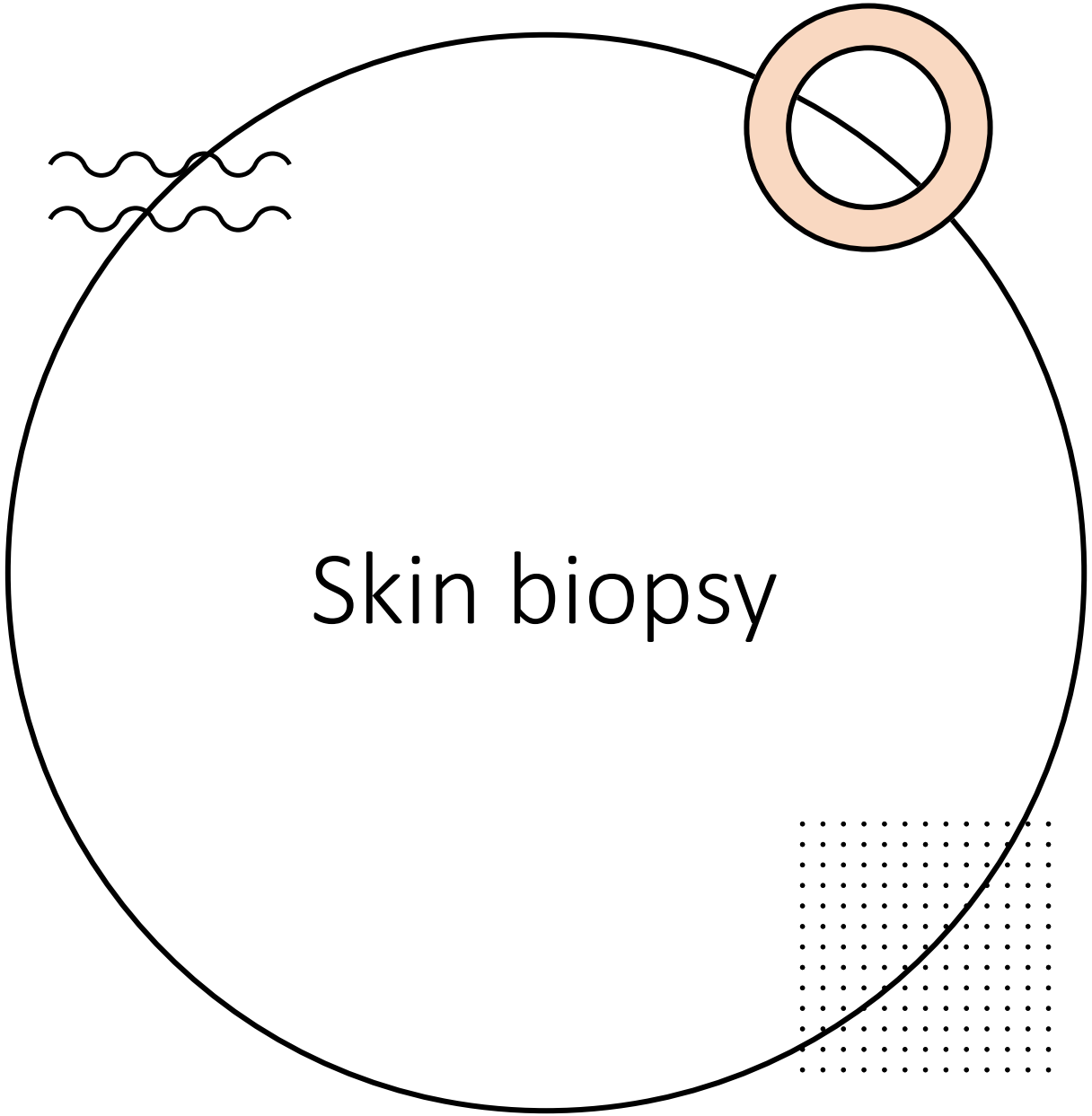

POWER
Q-Sweat
Quantitative Sweat Measurement System
CHANNEL 1
CHANNEL 2
CHANNEL 3
CHANNEL 4



- In preganglionic and central disorders- QSART is unimpaired
- Anhidrosis on thermoregulatory skin test- QSART normal

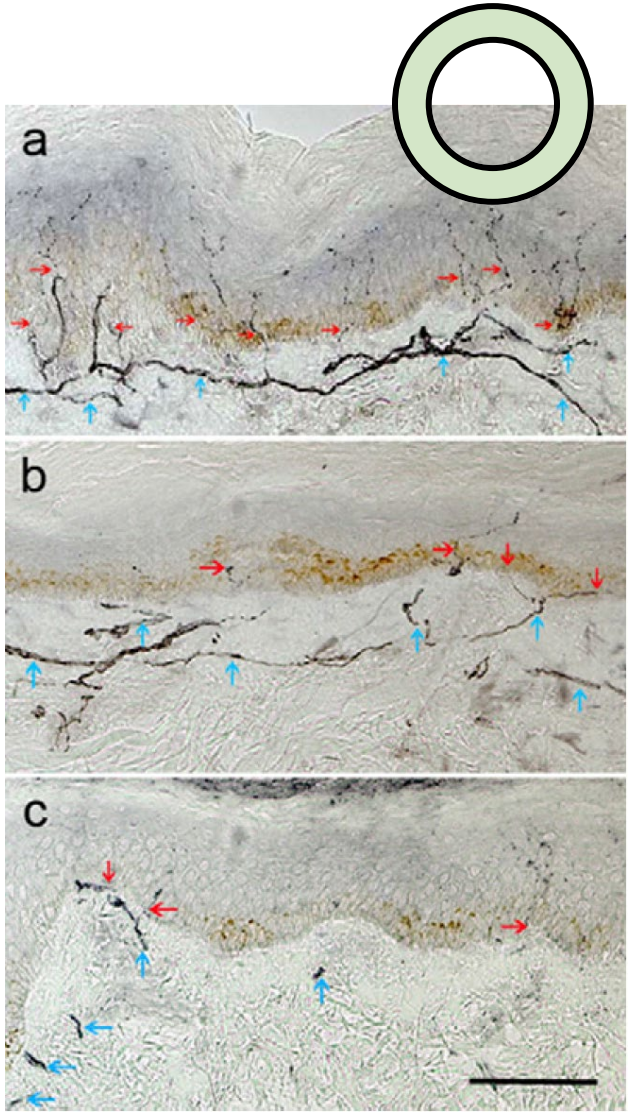
- QSART- Abnormal, TST- Abnormal→ Postganglionic
- QSART- normal, TST- Abnormal→ Pre-ganglionic

- Small fiber neuropathy- QSART is abnormal in 80% of cases
- Complex regional pain syndrome has altered sympathetic vasomotor and sudomotor tone.



- Protein gene product (PGP)- 9.5 antibody
- Calcitonin gene related peptide
- Vasoactive intestinal polypeptide
- Synaptophysin

Corneal confocal microscopy with intra-epidermal small fiber density

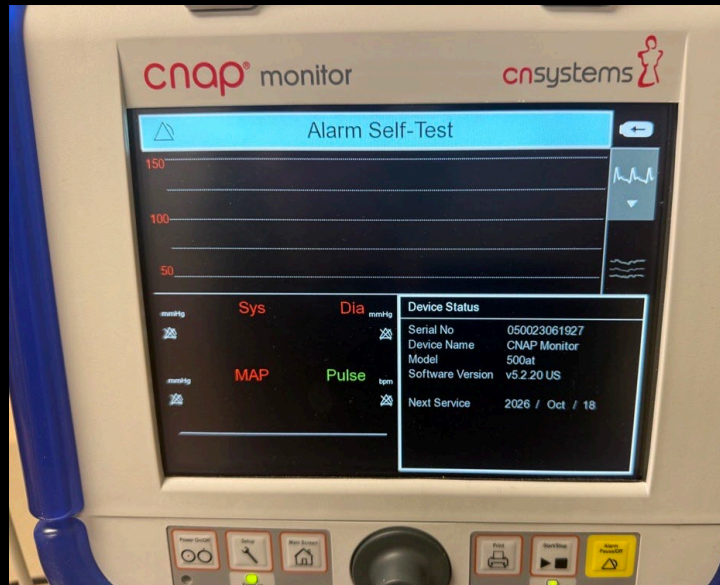


Summary

- Skin is a big organ system with it’s innervation by Sympathetic nervous system.
- Small fiber involvement is common.
- Sympathetic Cholinergic division can be assessed by SSR, QSART, TST
- SSR is easy to perform in lab and need no special equipment.
- QSART and TST are specialized tests and require special equipment.
- Skin biopsy is gold standard for assessment of small fiber testing

Thank you

Any questions?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cnsystems
Alarm Self-Test
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Sys
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MAP
Pulse
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