ANS1 : Sudopath & TM Oxi

- Assessment of:
  - Autonomic Nervous System
  - Cardiovascular System
  - Sudomotor Function
  - Endothelial Function

- Clinical Applications:
  - Early Detection of risk for Peripheral Small Fiber Neuropathy*
  - Detection of risk for Cardiac Autonomic Neuropathy (CAN)
  - Early detection of risk for Cardiovascular disease & Endothelial Dysfunction*
  - Cardio-Metabolic Risk Markers*
  - Adjunct in Diabetes treatment management

* Off label use
ANS1 : SudoPath & TM Oxi

TECHNOLOGIES:

• **Sudomotor Function Test** (*SudoPath*):
  • Galvanic Skin Response

• **Autonomic Nervous System & Cardiovascular Test** (*TM Oxi*):
  • Photoplethysmography / Pulse Wave Analysis
  • Heart Rate Variability (HRV)
  • Beat to Beat Blood Pressure
The Benefits To a Physician’s Practice

• Tests are non-invasive and easily performed by any member of the staff. Training is quick & easy, and devices are simple to learn.
• 7 minutes per test
• Easy Data Interpretation
• New source of revenue!
• Attractive Insurance Reimbursement!!
• FDA 510K Clearance on all of our devices.
• Clinical Studies on our products conducted at the University of Miami, University of Campinas (Brazil) and other institutions around the globe.
What patients require ANS Testing?

Patients with diseases and symptoms suggesting Autonomic Neuropathy

Autonomic neuropathy is a nerve disorder and is often associated with the following diseases:

• Diabetes
• Liver disease
• Thyroid disease
• Kidney disease
• Autoimmune disease
• HIV

• Certain medications could be responsible for autonomic neuropathy

Symptoms associated with Autonomic neuropathy:

- Pain, numbness, tingling or burning in the feet or hands,
- Headaches, fatigue,
- Nausea, constipation, or diarrhea,
- Dizziness, syncope, Headaches
- Exercise intolerance
ANS1 Tests

ANS Testing is used to detect ANS nerve damage of 3 functions:

1) Sudanmotor 2) Adrenergic (sympathetic system) 3) Cardiovagal (parasympathetic system)

ANS Testing System

• **SUDOMOTOR test** is based on Galvanic Skin Response and measures: 1) C-Fiber Condition 2) Micro-Circulation 3) Sweat Gland Function
  • **ASSESSMENT OF RISK FOR PERIPHERAL DISTAL NEUROPATHY**

• **SYMPATHETIC System, adrenergic function, test** comprises the analysis of 3 items: 1) Beat to beat systolic pressure response during Valsalva maneuver in phase 2 (SPRV2), 2) Beat to beat systolic pressure response to Valsalva maneuver in phase 4 (SPRV4), and 3) Systolic pressure response to standing.
  • **ASSESSMENT OF RISK FOR CARDIAC AUTONOMIC NEUROPATHY**

• **PARASYMPATHETIC System, cardiovagal function, test** comprises the analysis of 3 items: 1. Heart rate response to standing (K30/15) 2. Heart rate response to deep breathing (E/I ratio) and 3. Heart rate response to Valsalva maneuver (Valsalva ratio)
  • **ASSESSMENT OF RISK FOR CARDIAC AUTONOMIC NEUROPATHY**
What is Sudomotor Function?

• The Sudomotor, which is controlled by a division of the sympathetic system, is related to the nerve fibers controlling the activity of the sweat glands (post sympathetic cholinergic fiber or C-fibers). **Sudomotor dysfunction (sweat dysfunction) is an early indicator of possible autonomic neuropathy.**

• Traditional neurophysiologic measurements of sudomotor function include thermoregulatory sweat testing (TST), quantitative sudomotor axon reflex testing (QSART), silicone impressions, and **galvanic skin response (GSR).**

• The **GSR** method uses 2 pairs of tactile large electrodes. It is performed by the electrical stimulation of the skin, and the contralateral electrical stimulation of the cholinergic nerve fibers (C-fibers). This is low voltage current and not painful.

• **The Sudomotor function evaluation** is performed using Galvanic Skin Response to detect skin blood flow (microcirculation), C-fiber condition, Sweat Gland function for the early detection (first stages) of peripheral small fiber neuropathy in populations at high risk, such as diabetic patients.
The Sudomotor function evaluation is performed to detect skin blood flow (microcirculation), C-fiber (cholinergic nerve fiber) density, and sweat gland function (sweat output response) for the early detection of peripheral small fiber neuropathy in populations at high risk, such as diabetic patients.

- **Skin Blood Flow**
  - (Micro-circulation)

- **Sweat Gland Nerve Density**
  - (C-Fibers)

- **Sweat Gland Function**
  - (Sweat Output Response)

- Characteristics of C-Fiber:
  - Small Fiber: thin and unmyelinated, thus easily damaged.
  - Long Fiber: from spine to soles of feet and sensitive to length-dependent damage.
- Sweat dysfunction is the first detectable damage to the small fibers (C-Fiber) of the peripheral nervous system, before any clinical signs or symptoms.
- Damage to small nerve fibers is reversible, unlike most damage to large myelinated fibers.
As an early detection modality for sudomotor dysfunction and peripheral distal neuropathy, Sudopath should be the “go to” solution for physicians desiring to help their patients.
SUDOPATH PATENTED PROCESS:
Galvanic Skin Response

1. The device sends low voltage electric current through the sweat ducts (1.28 Volts)
2. This procedure electrically stimulates the nerve fiber (c-fiber)
3. The stimulation produces a sweat response
4. The device receives electrical conductance readings on the passive electrode
5. The electrochemical reading is comprised of the markers: ESRNO (Microcirculation), ESRL (C-Fiber Velocity), PEAK C (Sweat Output).
Autonomic Nervous System (ANS) Evaluation
ANS Testing Comprises:

1. BASELINE EVALUATION
   - Heart rate variability (HRV)

2. CARDIAC AUTONOMIC REFLEX TESTS (CARTs)
   - Adrenergic Function (Sympathetic)
   - Cardio Vagal Function (Parasympathetic)
ANS Testing is Performed using:

1. Finger Probe or Oximeter for:
   Photoplethysmography
2. Blood Pressure Device for:
   Beat to Beat Blood Pressure Analysis
Photoplethysmography (PTG)

- PTG is an optical measurement technique using red and infrared light to measure peripheral blood volume obtained with the finger probe or oximeter.
- Reflective of blood movement in cutaneous vessels and synchronous cardiovascular events.
- The Signal contains information regarding **heart rate** and **variability**, **vessel dilation** and **contraction**.

R-R Interval = time between A and B
- Instantaneous Heart Rate
ANS BASELINE EVALUATION

• Heart Rate Variability
Heart Rate Variability (HRV)

**Heart rate variability (HRV)**
- The physiological phenomenon of variation in the time interval between heartbeats. It is measured by the variation in the beat-to-beat interval. It’s measured in milliseconds.
- The Autonomic Nervous System plays a central role in HRV.
- Depressed or reduced HRV primarily means that the heart rate is monotonously regular, and it means a lowered ability of the ANS regulatory function and ability to keep homeostasis, cope with internal and external stressors (stress provoking agents), and resist disease or recover in proper time.
HRV ANALYSIS

Time domain Analysis + Frequency domain analysis

ANS Activity + ANS Balance
CARDIAC AUTONOMIC REFLEX TESTS (CART)

• Sympathetic System - Adrenergic Function
• Parasympathetic System - Cardio Vagal Function
1. **Cardiovagal (Parasympathetic) evaluation with Valsalva ratio**: Essentially a measure of vagal function. We are evaluating the Heart Rate Response during this challenge. *(GREEN DOTTED LINE)*

2. **Adrenergic (Sympathetic) evaluation with Beat-to-beat blood pressure response to the Valsalva maneuver**: We are measuring blood pressure response during the challenge (or adrenergic function of norepinephrine and epinephrine response in blood pressure). *(BLACK LINE)*
Cardiac Autonomic Reflex Test (CART) 2: Deep Breathing

- **Deep breathing tests cardiac parasympathetic functions.**
  
  Because the heart responses to deep breathing are mediated by the vagal nerve, the test is also referred to as cardiovagal testing. During inspiration, intra thoracic pressure is reduced, which will decrease venous return from the pulmonary circulation to the left atrium of the heart and decrease preload; heart rate will therefore increase slightly to compensate and maintain the same cardiac output. The opposite happens during expiration; intra thoracic pressure rises, increasing pulmonary venous return (and therefore preload), so heart rate will decrease to maintain constant cardiac output. The results is expressed as E/I Ratio (Expiration/Inspiration Ratio).
Cardiac Autonomic Reflex Test (CART) 3: Change in Posture

- **Cardiovagal (parasympathetic) evaluation** with K30/15: At the standing position, the **heart rate** increased during the first 15 seconds and then decreased and stabilized at 30 seconds.

- **Adrenergic (sympathetic) evaluation** with **systolic pressure response** to standing (BPRS). At the standing position, the blood pressure should increase and should be greater than 10 mmHg compared to the blood pressure lying or sitting position.
Significance of Cardiac Autonomic Neuropathy (CAN)

- Studies demonstrate that Cardiac Autonomic Neuropathy (CAN) increases the risk of cardiovascular events by 2 or 3 fold

- A recent study proved that diabetic patients with CAN have an increased risk of severe hypoglycemia

(* Diabetes Care 2014: “Cardiovascular autonomic Dysfunction Predicts Severe Hypoglycemia in Patients with T2DM: A 10 year Follow Up Study)
Endothelial Function Evaluation
Endothelial Function

• The endothelium is the thin layer of cells that line the interior surface of all blood vessels. Because of inflammation, fatty foods, or exposure to toxins, the endothelium can be easily damaged. This attracts white blood cells to the site, and these cells and low-density lipoprotein (LDL) cholesterol enter the inner surface of the artery.

• The endothelium’s main job is to defend the blood vessels from attack from microbes, pollutants, and other assailants by mounting an appropriate inflammatory response. Over time, however, prolonged irritation from smoking, salt- and fat-laden foods, and lack of exercise can deplete its anti-inflammatory reserve, opening the door to endothelial damage.

• The endothelial function is related to 1) the ability of the blood vessels to dilate when necessary - vasodilation control, 2) cell walls ability to protect the vessels from outside intruders, such white blood cells, cholesterol, etc.
Endothelial Dysfunction

• Endothelial dysfunction or damage is characterized by reduction of the bioavailability of nitric oxide (NO) which upsets the balance between vasoconstriction and vasodilation and initiates a number of processes that promote hypertension. In addition, Endothelial damage includes increased endothelial permeability, platelet aggregation, pro-inflammatory and pro-coagulatory states and monocytes migration from the blood into the subendothelial intima and transformation into macrophages, which accumulate lipids to form the lipid core of the atherosclerotic plaque.

• Plaque rupture can cause continued development of the atherosclerotic lesion by inducing further thrombus formation and release of more inflammatory mediators, resulting in continued luminal narrowing.

• Endothelial dysfunction has been recognized as the critical junction between risk factors and clinical disease.

• Endothelial dysfunction and arterial stiffness are associated with insulin resistance in type 2 diabetes mellitus.

• Endothelial dysfunction is the earliest detectable stage of cardiovascular disease. Unlike the atherosclerotic plaque which it causes, endothelial dysfunction is reversible.
What are the causes of Endothelial Dysfunction?

Main Cause: Diabetes

- Diabetes disrupts endothelial integrity through increased oxidative stress. Recent evidence indicates that there is a strong interaction between diabetes, the secretory proteins of adipocytes, called adipokines, and the endothelium.
- Endothelial dysfunction may precede the development of overt DM, and a prolonged and repeated exposure to postprandial hyperglycemia may play an important role in the development of atherosclerosis, even in those who have normal fasting plasma glucose levels.

Other Causes:

- High blood pressure
- High cholesterol
- Smoking
How is endothelial function measured by TM OXI?

- The photoplethysmography (PTG) of the pulse waveform using both derivate to measure the contour wave form and spectral analysis allows the accurate measurement of endothelial function.
- Pulse wave analysis
  - “[An] approach to derive information about cardiovascular properties from the pulse wave is based on analysis of an optically derived finger or digital volume pulse (DVP). [T]his approach deserves further consideration, not least because of its simplicity and ease of use. The technique has the potential to provide an estimate of large artery stiffness. Stiffening of large arteries is an inevitable consequence of ageing, and the ability to identify premature vascular stiffening may be of considerable value in the prevention of cardiovascular disease.”
TEST PROCEDURE

Testing is performed in **roughly 7 minutes** and is completely **non invasive**. The recordings include a base line phase where the patient is relaxed, and a testing phase where the patient is asked to perform basic breathing exercises and one active postural change. Scores are calculated based on several recorded parameters, and it allows for a fast and intuitive interpretation of the color coded results.
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
</table>
| 95921 | TESTING OF AUTONOMIC NERVOUS SYSTEM FUNCTION; CARDIOVAGAL INNERVATION (PARASYMPATHETIC FUNCTION), INCLUDING 2 OR MORE OF THE FOLLOWING: HEART RATE RESPONSE TO DEEP BREATHING WITH RECORDED R-R INTERVAL, VALSALVA RATIO, AND 30:15 RATIO

**Parasympathetic Test**

<table>
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<tr>
<th>Code</th>
<th>Description</th>
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| 95923 | TESTING OF AUTONOMIC NERVOUS SYSTEM FUNCTION; SUDOMOTOR, INCLUDING 1 OR MORE OF THE FOLLOWING: QUANTITATIVE SUDOMOTOR AXON REFLEX TEST (QSART), SILASTIC SWEAT IMPRINT, THERMOREGULATORY SWEAT TEST, AND CHANGES IN SYMPATHETIC SKIN POTENTIAL

**Sudomotor Test**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
</table>
| 95943 | This code has been established to report when an autonomic function testing does not include beat-to-beat recording, or for testing without the use of a tilt table. This is a simpler, automated procedure compared to the other autonomic codes. Simultaneous, independent, quantitative measures of both parasympathetic function and sympathetic function, based on time-frequency analysis of heart rate variability concurrent with time-frequency analysis of continuous respiratory activity, with mean heart rate and blood pressure measures, during rest, paced (deep) breathing, Valsalva maneuvers, and head-up postural change.

**Sympathetic Test & Parasympathetic Test**
<table>
<thead>
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<th>Code</th>
<th>Description</th>
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<tr>
<td>250.6-250.63</td>
<td>DIABETES WITH NEUROLOGICAL MANIFESTATIONS, TYPE II OR UNSPECIFIED TYPE, NOT STATED AS UNCONTROLLED - DIABETES WITH NEUROLOGICAL MANIFESTATIONS, TYPE I [JUVENILE TYPE], UNCONTROLLED</td>
</tr>
<tr>
<td>277.30-277.39</td>
<td>AMYLOIDOSIS, UNSPECIFIED - OTHER AMYLOIDOSIS</td>
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<td>333.0</td>
<td>OTHER DEGENERATIVE DISEASES OF THE BASAL GANGLIA</td>
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<td>337.00</td>
<td>IDIOPATHIC PERIPHERAL AUTONOMIC NEUROPATHY, UNSPECIFIED</td>
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<td>337.09</td>
<td>OTHER IDIOPATHIC PERIPHERAL AUTONOMIC NEUROPATHY</td>
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<td>REFLEX SYMPATHETIC DYSTROPHY UNSPECIFIED - REFLEX SYMPATHETIC DYSTROPHY OF OTHER SPECIFIED SITE</td>
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<td>356.4</td>
<td>IDIOPATHIC PROGRESSIVE POLYNEUROPATHY</td>
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<td>356.8</td>
<td>OTHER SPECIFIED IDIOPATHIC PERIPHERAL NEUROPATHY</td>
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<tr>
<td>356.9</td>
<td>UNSPECIFIED IDIOPATHIC PERIPHERAL NEUROPATHY</td>
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<td>458.0</td>
<td>ORTHOSTATIC HYPOTENSION</td>
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<tr>
<td>780.2</td>
<td>SYNCOPE AND COLLAPSE</td>
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<td>780.8</td>
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<tr>
<td>785.0</td>
<td>TACHYCARDIA UNSPECIFIED</td>
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Contact Affordable Cancer Screenings at 901-264-0332

Visit our website www.affordablecancerscreenings.com To apply