PD2i Frequently Asked Questions

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- **What is Autonomic Dysfunction?**

The autonomic nervous system (ANS) is the part of the nervous system that runs autonomously (i.e., by itself, without conscious awareness or input). It controls a wide variety of body functions automatically, such as heart rate, blood pressure, respiration, digestion, urination, sweating, sexual function, etc. If there is ANS dysfunction, then those systems will not function properly and the patient will experience symptoms from one or more of those systems.

- **What are the symptoms of Autonomic Dysfunction?**

Symptoms can include slow heart beats, low blood pressure, dizziness, constipation, incontinence, impotence, etc. ANS dysfunction can affect the sympathetic branch of the ANS, the parasympathetic branch, or both. Note that many things can cause these symptoms, some of which have nothing to do with the ANS (e.g., an infection or psychological issues). Assessing the ANS can help a physician decide whether the symptoms are, indeed, due to autonomic dysfunction.

- **How do we assess the ANS/test for ANS dysfunction?**

The ANS has multiple "sensory-motor loops" (SMLs) which consist of an input – i.e., a blood pressure sensor – and one or more outputs – i.e., one that constricts arterial blood vessels, another that raises heart rate. The SML processes the input and decides on what the output(s) should be. In our example, if the blood pressure were low, the outputs might be to (1) constrict the blood vessels to the legs and (2) raise the heart rate. When a patient has Autonomic Dysfunction, the SMLs don't function properly; one of the manifestations will be an abnormal heart beat pattern, even at rest.

- **How do we check the heart beat pattern?**

We know of at least 6 SMLs that affect heart rate: temperature, blood pH, baroreceptor reflex (involves blood pressure), respiratory variation, cerebral defense system, and intrinsic cardiac nervous system (chemo- and stretch reflexes). The competition between these 6 SMLs is what causes heart rate variability (HRV) and, in health, these SMLs are allowed to act relatively independently. We measure that degree of independence (which can also be expressed in the opposite way – the co-operativity) of these systems at rest and during maneuvers that stress the ANS ((Ewing maneuvers).

- **What causes the SMLs to behave differently from normal?**

If the patient has a disease process that affects the ANS – either the inputs (sensors) to the SMLs or the outputs from them – then the SMLs either react to incorrect information (inputs) or cannot react properly (outputs) so the body will be adversely affected. Since one of the outputs is heart rate, the heart rate pattern will look abnormal – that's what we look at.

•What do we look for in the PD2i?

In health, when the SMLs are allowed to act more independently, the minimum PD2i value will be higher. Under the stress of chronic (e.g., heart failure, autonomic dysfunction) or acute (e.g., trauma) illness, the SMLs will act with more co-operativity, so the values will fall. This is the normal function of the ANS.

•Why is there a resting portion and Ewing maneuvers in the PD2i test protocol?

We look at the HRV pattern under two sets of conditions: resting and stressed. The three Ewing maneuvers are designed to stress the ANS in specific ways: (1) metronomic breathing (2) Valsalva maneuver, and (3) orthostatic (gravity) stress of going from sitting to standing. By assessing the PD2i results from baseline and stress we can make statements about the ANS which can – in conjunction with other patient data such as the history, physical exam, and lab results - help a physician make a diagnosis.

•What is autonomic neuropathy?

The autonomic nervous system's function may appear different than normal for at least 3 reasons: (1) a normal ANS reacting to an abnormal situation/stressor – e.g., acute illness or trauma; (2) a normal ANS affected by medications; (3) the ANS is itself diseased (as noted above). Autonomic neuropathy is a form of #3 - the ANS itself is actually damaged. This can be the result of chronic disease (such as diabetes or Parkinson's), toxic exposures, genetic defects, infection, etc. It may or may not be reversible. The symptoms would be those described above. Patients with autonomic neuropathy will likely manifest symptoms of autonomic dysfunction at some point.

•What is Diabetic autonomic neuropathy (DAN)?

DAN is simply autonomic neuropathy due to the ravages of diabetes on the ANS. It is the most common cause of autonomic neuropathy.

•What is cardiac autonomic neuropathy (CAN)?

CAN is a form of ANS dysfunction that mostly affects the heart. The heart has rich autonomic innervation. Patients with CAN are at elevated (2x) risk for adverse cardiac events such as heart attacks and sudden death. This may be due to the ANS's effects on blood vessel (endothelial) function, platelet function, and the clotting system, cholesterol plaque rupture, among others. Heart rate variability is considered the earliest indicator and most frequent finding in symptomatic cardiovascular autonomic dysfunction.

•What are the specific symptoms of CAN?

1. Reduced cardiac ejection fraction: with systolic dysfunction and decreased diastolic filling.
2. Limited exercise tolerance: due to impaired sympathetic and parasympathetic responses that normally augment cardiac output and redirect peripheral blood flow to skeletal muscles. Exercise tolerance is also reduced by a reduced ejection fraction, systolic dysfunction, and decreased diastolic filling.
3. Arrhythmias: A prolonged corrected QT interval and QT dispersion (the difference between the longest and shortest QT interval) indicates an imbalance between right and left sympathetic innervation. Diabetic patients with a regional sympathetic imbalance and QT interval prolongation may be at greater risk for arrhythmias. Regional myocardial autonomic denervation and altered vascular responsiveness in diabetic autonomic neuropathy may predispose to malignant arrhythmogenesis and sudden cardiac death.
4. Diabetic patients have a high rate of coronary heart disease, which may be asymptomatic owing to autonomic neuropathy.
5. Silent ischemia in diabetic patients is significantly more frequent in patients with autonomic neuropathy than in those without autonomic neuropathy (38% versus 5%). The cause of silent myocardial ischemia in diabetic patients is controversial. It is clear, however, that a reduced appreciation for ischemic pain can impair timely recognition of myocardial ischemia or infarction and thereby delay appropriate therapy.
6. Higher mortality rates after a myocardial infarction for diabetic patients than for nondiabetic patients. This may be due to autonomic insufficiency, increasing the tendency for development of ventricular arrhythmias and cardiovascular events after infarction.
7. Orthostatic hypotension: a fall in systolic blood pressure of greater than 30 mm Hg upon standing. Patients with orthostatic hypotension typically present with lightheadedness and/or fainting (syncope). Symptoms such as dizziness, weakness, fatigue, visual blurring, and neck pain also may be due to orthostatic hypotension. Many patients, however, remain asymptomatic despite significant falls in blood pressure