

## PROVIDER RESOURCE SERIES

# The CardioMetabolic Profile in Dried Blood Spot



### **The Problem**

The incidence of cardiovascular disease (CVD), obesity and type 2 diabetes mellitus (DM2) is rising at an alarming rate. CVD is the leading cause of mortality for both men and women in the United States; obesity, insulin resistance and DM2 significantly predispose individuals to developing CVD, yet these conditions are potentially avoidable. If we are to make an impact on the serious health and economic consequences of these diseases, we need to identify risk early enough for people to make lifestyle modifications or seek medical help, and avoid becoming a part of the rising statistics.

### **What is CardioMetabolic Risk?**

Cardio-metabolic risk has been defined as “the cluster of modifiable risk factors and markers that identify individuals at increased risk for cardiovascular disease (myocardial infarction, stroke, peripheral arterial disease) and type 2 diabetes<sup>1</sup>.” The National Cholesterol Education Program (NCEP)’s Adult Treatment Panel III (ATP III) has identified the metabolic syndrome/insulin resistance syndrome as a major risk factor for CVD<sup>2</sup>. The National Heart, Lung and Blood Institute and the American Heart Association in a 2003 conference<sup>3</sup> agreed that CVD is the primary clinical outcome of metabolic syndrome; when the Framingham Heart Study investigators analyzed their data according to the NCEP-ATP III criteria for the conference, the metabolic syndrome predicted about 25% of all new-onset CVD and the presence of metabolic syndrome was highly predictive of new-onset DM2. NCEP-ATP III criteria for identifying metabolic syndrome include:

- hypertension/elevated blood pressure
- abdominal obesity
- atherogenic dyslipidemia (low HDL cholesterol, elevated triglycerides, elevated LDL cholesterol)
- prothrombotic/pro-inflammatory state
- insulin resistance/glucose intolerance

### **Which Biomarkers are Included in the Profile**

#### **High Sensitivity C-Reactive Protein (hs-CRP)**

C-reactive protein (CRP) is an established marker of inflammation and has recently been suggested to be an important contributor to pro-inflammatory and pro-thrombotic elements of CVD risk. Extremely high CRP levels are seen in acute inflammatory states, but the small elevations that are indicative of the pro-inflammatory and pro-thrombotic states implicated in the metabolic syndrome require high sensitivity assays, and are thus referred to as hs-CRP levels. These high sensitivity assays have recently been developed for use with blood spots<sup>4,5,6</sup>.

- Overweight, obese, insulin resistant and diabetic individuals typically have elevated CRP levels<sup>7</sup>
- Studies have shown correlations between elevated CRP and increased risk of future heart attacks, ischemic stroke, and peripheral arterial disease<sup>8,9,10,11</sup>
- Elevated CRP levels have been found to predict the development of DM2<sup>12</sup>
- Increased CRP levels, which correlate inversely with insulin sensitivity, have been found in individuals with polycystic ovarian syndrome and may be a marker of early cardiovascular risk in these patients<sup>13,14</sup>
- Lifestyle changes such as aerobic exercise, weight loss and smoking cessation have been known to lower CRP
- Medications like aspirin and statins can lower CRP levels<sup>11,15</sup>
- Levels below 3.0 mg/L are considered to be normal; 3.1 to 10 mg/L is elevated, in the context of CVD risk, and above 10 mg/L is very high, more likely indicating an acute inflammatory event due to infection or trauma

#### **Insulin**

Dried blood spot technology has effectively been used for measurement of insulin levels<sup>16,17,18</sup>. The requirement to measure fasting insulin makes convenient blood spot collection at home especially advantageous to patients.

- High fasting insulin levels are a good indicator of insulin resistance, which occurs when the cellular response to the presence of insulin is impaired resulting in a reduced ability of tissues to take up glucose for energy production. Chronically high insulin levels are seen as the body attempts to normalize blood sugar levels
- High fasting insulin indicates the presence of insulin resistance whether or not the patient shows glucose intolerance
- The normal range for fasting insulin is 1 – 15  $\mu$ IU/mL, but levels between 2 and 6  $\mu$ IU/mL are optimal

(over)

## Hemoglobin A1c (HbA1c)

HbA1c is a measure of red blood cell hemoglobin glycation, indicating mean glycemia over the previous 3 months, which is the lifespan of circulating red blood cells. It can therefore indicate impaired glucose tolerance even when occasional fasting plasma glucose measurements are normal<sup>19</sup>.

- The American Diabetes Association's recommendation is to measure HbA1c every 3-6 months; normal levels are 4 – 6%
- Levels of HbA1c above 6% in diabetics are associated with an increased risk of developing complications such as eye disease, kidney disease, nerve damage, heart disease, and stroke, therefore treatment should aim to keep levels below 7%<sup>20</sup>
- An HbA1c of more than 6% can predict CVD and DM2 in high-risk individuals<sup>21,22,23</sup>

## Triglycerides

Hypertriglyceridemia, a triglyceride level >150 mg/dL, is an established indicator of atherogenic dyslipidemia and is often found in untreated DM2 and obesity.

- Studies have shown that levels above 200 mg/dL indicate an increased risk of heart disease and stroke<sup>24,25</sup>
- Some studies have shown that fasting triglyceride levels lower than 100 mg/dL should be considered as a more optimal cutoff in coronary heart disease risk assessment<sup>26</sup>
- The NCEP-ATP III defines levels of 150 mg/dL or above as one of the diagnostic criteria for metabolic syndrome

## Advantages of a Simple Blood Spot Test to Assess CardioMetabolic Risk

- A simple, almost painless finger prick provides the few drops of blood required, which are collected on the filter paper provided
- Convenient sample collection at home – no phlebotomist required
- Easy shipment of samples by regular mail for analysis – samples are stable for several weeks at room temperature
- Dried blood spots carry no infection risk – infectious agents are inactivated when dry
- Excellent correlation with serum/plasma and whole blood assays

## Clinical Utility

The blood spot cardiometabolic risk assessment panel allows early detection of major indicators associated with metabolic/insulin resistance syndrome. Used as a screening panel this can allow clinicians to recommend appropriate treatments to reduce the overall risk and potentially avoid the onset of DM2 and CVD. Regular testing can also be used for risk assessment and monitoring in patients being treated for DM2. Screening along with clinical assessment can be of reliable predictive value for determining the overall cardiometabolic risk.

## References

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