BiophysicalPre-D™

QUICK REFERENCE GUIDE

Version 1.0 | Revision 1

BiophysicalPre-D™

Biomarker	Clinical Relevance
GLUCOSE	Diabetes mellitus, insulin resistance, pre-diabetes
HEMOGLOBIN A1C	Reflects the average plasma glucose level over the past 30-120 days. A high level reflects poor glucose control over time. HemA1c levels may not be accurate in patients with conditions that affect rbcs such as anemia, recent blood loss, high rbc turnover, recent transfusion, erythropoetin treatment, chronic kidney disease, chronic liver disease.
C-PEPTIDE	High levels are seen with insulin resistance and pre-diabetes. Portal vein insulin levels are 2-10 times higher than peripheral circulation (insulin is extracted by the liver). C-Peptide is secreted in a 1:1 ratio with insulin, therefore, peripheral levels are a better indication of endogenous insulin production.
INSULIN	Diabetes mellitus, impaired glucose metabolism, insulin resistance. Levels increase with increasing insulin resistance.
PRO-INSULIN, TOTAL	Prohormone made in the pancreas that splits to form insulin and C-peptide. Increased levels indicate pancreatic exhaustion and risk for faster progression to type II diabetes.

Action

Exercise –exercise even without dietary change or weight loss has positive effects on insulin dynamics.

- 150 minutes (30 minutes 5 times per week) of moderate intensity aerobic exercise. Moderate intensity is defined as any activity that raises the heart rate above the resting heart rate.
- Weight-bearing exercises – 30 minutes 2-3 times per week.

Diet – several diets have proven effective.

- **Mediterranean Diet** – As recommended by the ADA
- **Low carbohydrate calorie restricted diet**
  i. For people with high triglyceride levels
  ii. May control blood sugar better for people with diabetes
- **Low fat calorie restricted diet** – for people with normal triglycerides and elevated LDL cholesterol.
- **Paleolithic Diet** (also known as the hunter-gatherer diet) – includes foods that can be hunted (or fished) and gathered.
- **Increase fiber to 14 g/1,000 kcal**.
  i. Slows the passage of food through the gastrointestinal track thereby slowing the absorption of sugar into the bloodstream.
  ii. Two types of fiber: soluble and insoluble. Soluble fiber is particularly helpful for the prevention of type 2 diabetes.
- All diets should avoid simple sugars, fructose, soft drinks and trans-fats.

Weight loss/correction

- 5-7% weight loss, then reassess Pre-D biomarkers.
- Additional weight loss until at goal
- Aim for BMI of 18-25

Medications

- Conservative Approach – as suggested by the ADA
  i. Metformin – most successful for patients with a BMI over 35 kg/m2 and under the age of 60. Can be considered for patients for whom lifestyle changes have been ineffective or for patients with very high risk (strong family history, long standing pre-diabetes).
- Progressive Approach – triple therapy – as suggested by Defronzo
  i. Metformin
  ii. Thiazolidinedione
  iii. GLP-1 receptor agonist - exenatide

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Biomarker	Clinical Relevance
ADIPONECTIN	Produced by adipose tissue, but production decreases with increasing adiposity. Regulates glucose and fatty acid catabolism, and is protective of endothelium. Low levels are a risk for CVD, type 2 diabetes and metabolic syndrome. Low levels affect insulin sensitivity.
LEPTIN	Levels increase with obesity. Levels in women are about 3 times those in men. Low levels associated with hunger, high levels should be associated with satiation, however, some obese people become "leptin resistant" after prolonged exposure to high leptin levels.
SEX HORMONE BINDING GLOBULIN	Binds to testosterone and estradiol, inhibiting their function. Production of SHBG is inhibited by high levels of insulin, insulin-like growth factor (IGF-1), androgens and transcortin. Levels decrease with polycystic ovarian disease (PCOS), diabetes, hypothyroidism, and increase with pregnancy, hyperthyroidism, and anorexia nervosa.
RESISTIN	Released by adipose cells. Adipose cells of central obesity are more active, causing increased resistin levels. Directly linked to type II diabetes.
TESTOSTERONE	Levels decrease with increasing obesity in men. Levels increase with increasing obesity in women, specifically women with polycystic ovarian disease (PCOS).

Action

Diet – Can include:

- Mediterranean
- Low fat calorie restricted
- Low carbohydrate calorie restricted
- Paleolithic

Exercise

- 150 minutes of moderate intensity physical activity per week.
- 60-90 minutes of weight bearing exercise per week.
- Increase activity level by 15 minutes per day if additional weight loss is desired.

Weight loss/correction

- 5-7% weight loss, then reassess Pre-D biomarkers.
- Additional weight loss until at goal
- Aim for BMI of 18-25

Consider surgery

- Bariatric surgery for adults with BMI >35
  i. Gastric banding
  ii. Roux-en-Y
  iii. Gastric sleeve
  iv. Omentectomy plus adjustable gastric banding

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Biomarker	Clinical Relevance
INTERLEUKIN 6	Increased production by hypertrophied adipose cells. Increased levels are consistent with increased risk for insulin resistance and CVD. Can be increased in other inflammatory conditions.
INTERLEUKIN 8	Increased production by hypertrophied adipose cells. Increased levels are consistent with increased risk for insulin resistance and CVD. Can be increased in other inflammatory conditions.
PLASMINOGEN ACTIVATOR INHIBITOR (PAI-1)	PAI-1 blocks tissue plasminogen activator (TPA), Increased PAI-1 levels are associated with increased thrombosis risk, and increased CVD risk.
TUMOR NECROSIS FACTOR ALPHA (TNF ALPHA)	Increased production by hypertrophied adipose cells. Increase consistent with increased risk for insulin resistance and CVD. May be elevated in other inflammatory conditions.
HIGH SENSITIVITY C-REACTIVE PROTEIN (hsCRP)	Synthesized by the liver in response to adipocytes. Small amounts also produced by the cells lining the blood vessels. CRP is an acute phase reactant, indicating inflammation. Chronic low level hsCRP is indicated in the progression of type 2 diabetes and CVD.

Action

Diet – Can include Mediterranean, Low fat calorie restricted , Low carbohydrate calorie restricted or Paleolithic

- Always eat breakfast
- Eat the majority of calories in the first half of the day
- Eat nothing after dinner
- Fiber – AHA recommends 25-30 grams per day. Should be both soluble and insoluble.

Exercise

- 150 minutes of moderate intensity physical activity per week.
- 60-90 minutes of weight bearing exercise per week.
- Increase activity level by 15 minutes per day if additional weight loss is desired.

Smoking cessation

- **Cold Turkey**
  - i. Abrupt cessation
  - ii. Gradual cutting back
- **Antidepressant**
  - i. Bupropion
- **Nicotine receptor partial agonists**
  - i. Cytisine
  - ii. Varenicline
- **Nicotine Replacement Therapy (NRT)**
  - i. Patch
  - ii. Gum
  - iii. Lozenge
  - iv. Spray
  - v. Inhaler

Medications

- Consider:
  - i. Low dose ASA (81 mg/day)
  - ii. Statins for patients with cardiovascular risk factors
  - iii. Omega-3 supplementation
  - iv. Curcumin (found in turmeric)
  - v. Catechins (found in green tea)