# Laboratory tests for Weight Management in General Practice

The following bloods should be ordered:

Blood test	< 25 Years	≥ 25 years
Full Blood Count (FBC)	~	~
Erythrocyte Sedimentation Rate (ESR)		~
Liver Functions Tests (LFT)-		
Alanine transferase (ALT)	✓	$\checkmark$
Bilirubin	√	✓
Aspartate transferase (AST)	~	√
Gamma glutaryl transferase (GGT)	~	✓
Alkaline phosphatase, (Alk Phos)	~	✓
HbA1C	√	✓
Random Glucose	✓	✓
Lipids (Total Cholesterol(TC), Triglycerides(TAG), High and Low Density Lipoprotein – cholesterol, H & LDL, , TC/HDL Ratio),)	√	×
Iron Studies (serum iron, transferrin, and transferrin saturation or serum iron, iron saturation, iron binding capacity) if the lab will allow/can afford otherwise just order <b>morning transferrin saturation</b> is ok.	✓ ✓	· · · · ·
B12 & Folate	✓	✓
Thyroid Stimulating Hormone (TSH)		✓
Uric Acid		✓
eGFR, Urea and Electrolytes		✓
Albumin/Creatinine Ratio (urine)		✓

Those with suspected Anorexia, Bulimia, and Polycystic Ovary Syndrome need special test.

Go to the "Weight Management" Pathway "Referrals" node <u>http://baynav.bopdhb.govt.nz/pathways</u> for Eating Disorders Services in the Bay of Plenty.

# **Explanatory notes on blood tests**

#### Introduction

Metabolic syndrome, the main medical reasons for reduced healthy life expectancy, is determined by laboratory tests (lipids, glucose, as well as uric acid, HbA<sub>1c</sub>, LFTs), and anthropometry (waist and blood pressure). Most of the major diagnoses are made and monitored by blood tests. Primary clinicians must keep as up-to-date as possible with laboratory indicators as although many tests have remained the same the *interpretation* has changed, as we understand more about metabolism.

## **Nutritional Tests**

*Haemoglobin, Red Cell Count:* Haemoglobin and red cell count: these indicate iron levels and other haematinics (Folate/ B12 and probably many proteins and nutrients). Haemoglobin (Hb) and cell concentrations (MCH), red blood cell (RBC) parameters: These measures can show late stage changes in iron deficiency (check for low dietary iron, menstrual/ haemorrhoidal blood loss. Beware faecal loss (tumour) and anaemia of chronic disease, both of which can be seen more often in metabolic syndrome (e.g. kidney failure with later stage Type 2 DM, cancer).

*Iron Studies*: Ideally full iron studies are performed; serum iron, transferrin and transferrin saturation (or iron binding) plus ferritin.

**Transferrin**: Morning transferrin saturation is an essential test of iron stores for people of any weight, and less sensitive to inflammatory stressors than Ferritin. If only one iron store test is done, chose transferrin saturation and not ferritin (see later). Even in young males, iron stores can be low, as plain red meat and fish consumption may be replaced by other low iron protein sources (battery chicken/ processed sausages).

If the transferrin is low then encourage an increase haem iron foods such as red meat, and other iron rich foods such as eggs (together with vegetables and fruit). Beans, nuts and figs also contain non haem iron. Iron treatment may be offered when you are sure of iron deficient anaemia and cannot increase dietary iron and there are no red flags.

**Ferritin**: With central overweight, high ferritin is a marker of oxidative/ inflammatory stress and possible early fibrosis of the liver, which can become irreversible and progress to cirrhosis. Recently, there has been a move to just use Ferritin for iron stores, but this comes at the wrong time as more and more people are overweight from high energy/low micronutrient (e.g. iron) diets.

This strategy of using transferrin saturation instead of ferritin was agreed with Tauranga and Auckland biochemists for the Weight Management Programme Pilot in the Western Bay of Plenty.

Do further tests for haemochromatosis (e.g. gene probes) if the ferritin is very high and/or iron binding or saturation or transferrin saturation is high.

### **Other Haematinics & Nutrients**

**Folate**: This is a very important nutritional test. Folate is one of the only measures of fresh vegetable and fruit intake (although some fermenting organisms synthesise folate (1). Although RBC folate may be a better test of function, at this screening stage, serum folate will increase as a marker of dietary change. Good folate intake is particularly important in women who are planning to become pregnant as this reduces the risk of neural tube defects and is good for general foetal health, as well as reducing risk of later heart disease risk through raised homocysteine levels. Homocysteine is a metabolite that accumulates if dietary folate is low, and is not corrected by folic acid supplements) (2).

If folate is low, advise the person to eat more leafy greens.

Although folic acid supplements are advised for pregnant women to prevent neural tube defects, they are much less ideal than acquiring B12/folate and iodine and all other micronutrients nutrient from a good pre-pregnancy and post 12 week/morning sickness diet.

Folic acid should not be given if B12 is low. This needs to be based on clinical judgement.

**Vitamin B12**: True lack of intrinsic factor (usually autoimmune) is quite rare, but many people seem to either not consume much B12 or are generally poor absorbers (this is possibly worse if an individual is overweight). Intrinsic factor secretion decreases with age therefore decreasing B12 absorption. B12 is also a test of animal and certain microbe product intakes and can be low in vegetarians and especially vegans. A wide varied diet is helpful. A low B12 with high folate can have serious neurological effects, which is also why both are tested together.

Do not give B12 injections or other supplements unless B12 deficiency is confirmed, and then only bring into the normal range, not above, as this will upset the folate/B12 or haematinic balance.

In general terms a strong problem-solving effort should be made to encourage (spending on) whole foods for consumption. Purchase of highly advertised, costly supplements, unless a deficiency is shown, is not advised and can cause harm (3) <u>http://www.heart.org/HEARTORG/GettingHealthy/ NutritionCenter/Vitamin-and-Mineral-Supplements\_UCM\_306033\_Article.jsp</u>

**Oxidative stress/'metaflammatory' markers:** Oxidative stress is an early metabolic change seen in those with diets that are deficient in micronutrients – vitamins, minerals and myriads of (mainly plant) complex organic chemicals. Metabolic inflammation 'metaflammation' (4) is a mix of low grade inflammation related (or following on from) oxidative stress.

**Liver enzymes**: ALT is usually raised in central overweight related fatty liver. AST (often no longer done but useful – indicates early inflammation) & GGT (check alcohol also) indicates that fibrosis may be starting. The treatment required is an urgent increase in vegetable and fruit nutrients. NB: Bilirubin is a powerful 'in-house' antioxidant. Hereditary mild unconjugated hyperbilirubinemia (Gilbert syndrome) is beneficial for metabolic syndrome (5). People should know if they have this syndrome so that they (and GP's) are confident that there is no disease.

**Oxidant markers:** Hba1c, uric acid, LDL, TAG are all oxidant markers. All should improve with increased intake of vegetables, fruit and wholefoods high in antioxidant/phytochemicals. Some transitory effects/increases in glucose may be noted for the first 5 days or so of commencing higher fruit intake, but this effect settles, and fruit fibre and other nutrient effects are important in the long term. For people with diabetes a better source of carbohydrate would be from fruit as opposed to refined carbohydrates. Fruit is a better source of micronutrients and fibre (6-10).

Metformin helps decrease HbA1c by decreasing oxidative stress, and improving overall metabolism. It has been found to have 'super-vitamin' antioxidant biochemical type effects, and therefore confers weight losing properties (11-13).

**Inflammatory markers:** WBC and ESR, are the classic inflammatory markers and can all show low grade inflammation. These will improve as vegetable and fruit intake increases even if weight remains static. ESR is affected by many metabolic problems of overweight and can decrease with metabolic improvement. CRP is a very general inflammatory marker that is synthesised in the liver and many other cells, including adipose (14) and endothelium. It had been used with lipids for CVD prediction and obesity, but is so general, it is interfered with by other inflammatory diseases and does not add to interpretation. See change in Auckland laboratory LabPlus tests guide on use of C reactive protein for CVD risk prediction over time. http://testguide.adhb.govt.nz/eguidemob/?gm=206&gs=3

**Lipids**: HDL is adequate when >1mmol/L for men and >1.39mmol/L for women. HDL will usually increase with better nutrition and increased physical activity over time, and decrease in inflammation. If the HDL is high (above 1.5 - 2.2mmol/L) often LDL-C particle are big and fluffy (as opposed to small and dense), has a low oxidation state and

rises with HDL. In New Zealand there is no routine particle size testing, but if triglyceride levels are below 1mmol/L then small dense oxidised LDL-C is less likely (15). Triglycerides drop well/quickly with high vegetable (and nut) intake. A trial of increasing vegetable and fruit (to 5-9 portions a day) with reducing or stopping junk food is very important. Non pharmacological interventions particularly increasing vegetable and fruit should be first line interventions (16-18). Consider the Tot/HDL-C ratio before prescribing statins (especially in aged people), and consider the benefits to the particular individual.

### **References:**

- **1.** Korhola, M., et al., *Production of folate in oat bran fermentation by yeasts isolated from barley and diverse foods.* J Appl Microbiol, 2014. **117**(3): p. 679-89.
- **2.** Catena, C., et al., *Elevated Homocysteine Levels Are Associated With the Metabolic Syndrome and Cardiovascular Events in Hypertensive Patients.* Am J Hypertens, 2014.
- **3.** Pearson, T.A., et al., *American Heart Association Guide for Improving Cardiovascular Health at the Community Level, 2013 update: a scientific statement for public health practitioners, healthcare providers, and health policy makers.* Circulation, 2013. **127**(16): p. 1730-53.
- **4.** Hummasti, S. and G. Hotamisligil, *Endoplasmic reticulum stress and inflammation in obesity and diabetes.* Circulation Research, 2010. **107**(5): p. 579-91.
- 5. Choi, S.H., K.E. Yun, and H.J. Choi, *Relationships between serum total bilirubin levels and metabolic syndrome in Korean adults*. Nutrition Metabolism & Cardiovascular Diseases, 2013. **23**(1): p. 31-7.
- **6.** Johnson, R.J., et al., *Theodore E. Woodward award. The evolution of obesity: insights from the mid-Miocene.* Trans Am Clin Climatol Assoc, 2010. **121**: p. 295-305; discussion 305-8.
- **7.** Esfahani, A., J. Lam, and C.W. Kendall, *Acute effects of raisin consumption on glucose and insulin reponses in healthy individuals.* J Nutr Sci, 2014. **3**: p. e1.
- **8.** Breen, C., et al., *High saturated-fat and low-fibre intake: a comparative analysis of nutrient intake in individuals with and without type 2 diabetes.* Nutr Diabetes, 2014. **4**: p. e104.
- **9.** Hettiaratchi, U.P., S. Ekanayake, and J. Welihinda, *Nutritional assessment of a jackfruit (Artocarpus heterophyllus) meal.* Ceylon Med J, 2011. **56**(2): p. 54-8.
- **10.** Spence, M., M.C. McKinley, and S.J. Hunter, *Session 4: CVD, diabetes and cancer: Diet, insulin resistance and diabetes: the right (pro)portions.* Proc Nutr Soc, 2010. **69**(1): p. 61-9.
- Watson, J., Oxidants, antioxidants and the current incurability of metastatic cancers. Open Biology, 2013.
  3(1).
- **12.** Esteghamati, A., et al., *Effects of metformin on markers of oxidative stress and antioxidant reserve in patients with newly diagnosed type 2 diabetes: A randomized clinical trial.* Clinical Nutrition, 2012.
- **13.** Formoso, G., et al., *Decreased 'in vivo' oxidative stress and decreased platelet activation following metformin treatment in newly diagnosed type 2 diabetic subjects.* Diabetes Metab Res Rev, 2008. **24**(3): p. 231-237.
- **14.** Anty, R., et al., *The inflammatory C-reactive protein is increased in both liver and adipose tissue in severely obese patients independently from metabolic syndrome, Type 2 diabetes, and NASH.* American Journal of Gastroenterology, 2006. **101**: p. 1-10.
- **15.** Aronis, K.N. and C.S. Mantzoros, *Novel concepts in lipoprotein particle metabolism and regulation.* Metabolism, 2014. **63**(1): p. 1-4.
- **16.** Garcia-Fernandez, E., et al., *Mediterranean diet and cardiodiabesity: a review.* Nutrients, 2014. **6**(9): p. 3474-500.
- **17.** Estruch, R., et al., *Primary Prevention of Cardiovascular Disease with a Mediterranean Diet.* New England Journal of Medicine, 2013. **DOI: 10.1056/NEJMoa1200303**.
- **18.** Escurriol, V., et al., Serum sterol responses to increasing plant sterol intake from natural foods in the Mediterranean diet. Eur J Nutr, 2009. **48**(6): p. 373-82.