HMCL223
Clinical Diagnostic Techniques

Session 2: Screening
blood tests part II,
Inflammation
Session Objectives

**Screening Blood Tests Part II**
- Cholesterol panel
- Homocysteine

**Inflammation**
- C-Reactive Protein
- Erythrocyte Sedimentation Rate (ESR)
Cholesterol Panel
Cholesterol Panel

(Nuclear Medical Media 2014, Hyperlipidmia (high cholesterol) – medical animation ANH13104 viewed 13/07/2015
Cholesterol

Cholesterol has a number of important & useful functions:
- Building and maintaining cell membranes
- May act as an antioxidant
- Aids in the manufacture of bile
- Metabolism of fat soluble vitamins
- Major precursor for the synthesis of vitamin D and of the various steroid hormones (cortisol, aldosterone, progesterone, oestrogens, testosterone and derivatives of these).
- Implicated in cell signalling processes
- Important for mental health – increased suicide risk and depression seen in patients with low serum cholesterol
Cholesterol

• The liver metabolizes the cholesterol to its free form, and cholesterol is transported in the blood-stream by lipoproteins
• Nearly 75% of the cholesterol is bound to low-density lipoproteins (LDL - bad cholesterol) and 25% is bound to high-density lipoproteins (HDLs – good cholesterol)
• Cholesterol is the main component of LDL and only a minimal component of HDL and very-low-density lipoprotein (VLDL)
# Cholesterol

## Cholesterol and Lipid Profile

<table>
<thead>
<tr>
<th>Serum</th>
<th>A group of tests that measure total cholesterol, lipoprotein fractions and ratios, and triglycerides. Commonly used to determine cardiovascular risk. Performed after 12 hour fast.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reference Ranges (Adult)</strong></td>
<td><strong>Components: (Adult Values)</strong></td>
</tr>
<tr>
<td></td>
<td>• <strong>Total Cholesterol</strong> - &lt;5.20mmol/L</td>
</tr>
<tr>
<td></td>
<td>• <strong>High Density Lipoprotein (HDL)</strong> – [M] &gt;45mg/dL [F] &gt;55mg/dL</td>
</tr>
<tr>
<td></td>
<td>• <strong>Low Density Lipoprotein (LDL)</strong> - &lt;130mg/dL</td>
</tr>
<tr>
<td></td>
<td>• Very Low Density Lipoprotein (VLDL) – 7-32mg/dL</td>
</tr>
<tr>
<td></td>
<td>• <strong>Triglycerides</strong> – [M] 40-160mg/dL [F] 35-135mg/dL</td>
</tr>
</tbody>
</table>
Cardiac Society of Australia and New Zealand: suggested target cholesterol levels in high risk populations are:

Total cholesterol < 4.0 mmol/L
HDL cholesterol > 1.0 mmol/L
LDL cholesterol < 1.8 mmol/L
Triglycerides < 2.0 mmol/L

(http://www.fatfreekitchen.com/cholesterol/cholesterol-ldl-hdl-ratio.html)
Cholesterol

• Pregnancy, oophorectomy (surgical removal of ovaries) & postmenopausal status are associated with increased levels. A recumbent position decreases levels.

• Drugs implicated in increasing levels include: ACTH, anabolic steroids, β-adrenergic blockers, corticosteroids, epinephrine, OCP, phenytoin, sulfonamides, thiazide diuretics, cyclosporine, and Vitamin D.

• Drugs implicated in reducing levels include: allopurinol, androgens, bile salt-binding agents, captopril, chlorpropamide, clofibrate, colchicine, colestipol, erythromycin, isoniazid, liothyronine, lovastatin, monoamine oxidase inhibitors, neomycin (oral), niacin, and nitrates.
# Cholesterol: Interpreting the Results

<table>
<thead>
<tr>
<th>CHOLESTEROL</th>
<th>HDL</th>
<th>LDL/VLDL</th>
<th>TRIGLYCERIDES</th>
</tr>
</thead>
</table>
| **HIGH**    | Familial ↑ Cholesterol  
Hypothyroidism  
Diabetes mellitus  
Poor diet  
Liver disease  
Nephrotic syndrome  
Familial ↑ HDL  
Excessive exercise | Familial ↑ LDL  
Hypothyroidism  
Alcohol  
Liver disease  
Cushings syndrome  
Nephrotic syndrome | Familial ↑ Tg  
Hyperlipidaemia  
Hypothyroidism  
Poor diet  
Nephrotic syndrome  
Chronic renal failure |
| **LOW**     | Malabsorption  
Malnutrition  
Advanced cancer  
Hyperthyroidism  
Anaemia  
Medication  
Metabolic syndrome  
Familial ↓ HDL  
Hepatocellular disease  
Nephrotic syndrome | Hypoproteinemia  
hyperthyroidism | Malabsorption syndrome  
Malnutrition  
hyperthyroidism |
Homocysteine
Homocysteine

- Homocysteine is an important predictor of coronary, cerebral, and peripheral vascular disease
- When a strong familial predisposition or early onset vascular disease is noted, homocysteine testing should be performed to determine if genetic or acquired homocysteine excess exists
- Because elevated homocysteine levels are associated with vitamin B12 or folate deficiency, this is a reasonable test to use for the detection and surveillance of malnutrition.
- Homocysteine is a naturally occurring sulfur-containing amino acid produced during catabolism of methionine, an essential amino acid
## Homocysteine

<table>
<thead>
<tr>
<th>Serum</th>
<th>Homocysteine: a non-protein forming intermediate amino acid formed during the metabolism of methionine. Indicates risk factor for cardio-vascular disease and is associated with B12 and folate deficiency</th>
</tr>
</thead>
</table>
| Reference Ranges (Adult) | Components: (Adult Values)  
- Homocysteine – 4-14µmol/L |
Homocysteine: Interfering/Risk Factors

• Levels may increase with age, renal impairment (poor excretion), lower B vitamin status, smoking & drugs (azaribine, cabamazepine, methotrexate, nitrous oxide, theophylline, and phenytoin)

• Men usually have higher levels of homocysteine than women do. This is most likely because of higher creatinine values and greater muscle mass

• Drugs that are associated with decreased levels include folic acid, oral contraceptives, and tamoxifen
## Homocysteine: Interpreting the Results

| HIGH                                      | Commonly associated with cardiovascular, cerebrovascular and peripheral vascular disease due to the effect of homocysteine to increase vascular endothelial inflammation and plaque formation  
|                                           | B12 deficiency  
|                                           | Folate deficiency  
|                                           | Pernicious anaemia  
|                                           | malnutrition  
|                                           | The above are related to the role of B12 and folate as cofactors for homocysteine metabolism  
| LOW                                      | Downs Syndrome  
|                                           | Hyperthyroidism |

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Inflammation: C-Reactive Protein
C-Reactive Protein

• Non-specific acute-phase reactant protein that indicates inflammatory illness, chronic inflammation and/or bacterial infectious disease.
• CRP interacts with the complement system and serves as an opsonin (enhances phagocytosis) for some microorganisms.
• Recently, a high sensitivity assay for CRP has enabled accurate assays at even low levels.
• Elevated CRP: linked with increased cardiovascular morbidity and mortality in patients with coronary artery disease, elevated when there is tissue necrosis, malignancies and autoimmune disorders.
• Independent marker for assessing likelihood of recurrent events, including death and myocardial Infarction.
# C-Reactive Protein

## C-Reactive Protein (CRP)

<table>
<thead>
<tr>
<th>Serum</th>
<th><strong>CRP</strong>: Non-specific acute-phase reactant protein used to diagnose bacterial infections and inflammatory disorders with associated tissue necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Sensitivity CRP</strong>:</td>
<td>measures lower CRP levels associates to estimated cardiovascular risk.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference Ranges (Adult)</th>
<th><strong>CRP</strong></th>
<th>&lt;1.0 mg/dL = normal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>hsCRP</strong></td>
<td>&lt;1.0 mg/dL = low risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0 – 3.0 mg/dL = average risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;3.0 mg/dL = high risk</td>
</tr>
</tbody>
</table>
CRP/hs-CRP: Risk Factors

CRP levels showing cardiac risk and diseases

1. Low risk
2. Intermediate risk
3. High risk
4. Normal range
5. CRP assay range
6. hs CRP assay range
7. Full range CRP assay range
8. After surgery
9. Myocardial infarction
10. Viral infection
11. Rheumatoid arthritis


viewed 12/01/2010
CRP/hs-CRP: Interfering/Risk Factors

- Medications that may increase test results include oestrogen and progesterone.
- Medications that may decrease test results include fibrates, niacin and statins. Both aspirin and statins may help to reduce the inflammation linked to the atherosclerotic process.
- Other drugs, such as non-steroidal-anti-inflammatory drugs (for example ibuprofen) and glucocorticoid drugs, may also lower CRP levels.
CRP: Interpreting the Results

<table>
<thead>
<tr>
<th>CRP</th>
<th>hsCRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased test results</td>
<td>Moderate alcohol consumption, weight loss, increased activity or endurance exercise.</td>
</tr>
<tr>
<td>Elevated test results</td>
<td>Hypertension, elevated BMI, metabolic syndrome, diabetes mellitus, chronic infection, chronic inflammation, low high-density lipoprotein (HDL) and/or triglycerides</td>
</tr>
<tr>
<td>Elevated above 1.0mg/dL</td>
<td>Acute non-infectious inflammatory reactions, Collagen vascular diseases, Tissue infarction or damage, Bacterial infections, Malignant disease</td>
</tr>
</tbody>
</table>
Inflammation: Erythrocyte Sedimentation Rate
Erythrocyte Sedimentation Rate (ESR)

- In plasma RBCs usually settle slowly (<15mm/hr). However, in the presence of inflammation, infection or necrosis, there is an increase in plasma proteins (e.g. Fibrinogen) which cause the RBCs to aggregate (Rouleaux) and settle more rapidly.

- The ESR measures in millimeters how fast the RBCs settle over the period of 1 hour.

- Pregnancy (2nd-3rd Trimester), menstruation, OCP, Vitamin A and some medication can cause elevated levels while anti-inflammatory medications can result in lower ESR levels.
## Erythrocyte Sedimentation Rate (ESR)

### Serum

**ESR:** A measurement of the rate in which RBCs settle in plasma over the period of 1 hour. The ESR is a non-specific test used to detect illnesses associated with infection, inflammation, neoplasm and necrosis.

### Reference Ranges (Adult)

**Components:** (Adult Values)

- **ESR**
  - Male – up to 15mm/hr = normal
  - Female – up to 20mm/hr = normal
# Erythrocyte Sedimentation Rate

<table>
<thead>
<tr>
<th>ESR</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td></td>
<td>Malignant disease</td>
</tr>
<tr>
<td></td>
<td>Bacterial infection</td>
</tr>
<tr>
<td></td>
<td>Inflammatory disease</td>
</tr>
<tr>
<td></td>
<td>Necrotic disease</td>
</tr>
<tr>
<td></td>
<td>Increased serum proteins</td>
</tr>
<tr>
<td></td>
<td>Severe anaemia</td>
</tr>
<tr>
<td>LOW</td>
<td>Sickle cell anaemia</td>
</tr>
<tr>
<td>(False decrease)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spherocytosis</td>
</tr>
<tr>
<td></td>
<td>Polycythemia vera</td>
</tr>
<tr>
<td></td>
<td>Low serum fibrin levels</td>
</tr>
</tbody>
</table>
Inflammation: CRP & ESR
CRP & ESR

- ESR is a common initial test when inflammation is being explored due to the cost & complexity of the CRP test.
- Both are markers of inflammation:
  - ESR is a non-specific marker for inflammation whereas CRP is a sensitive indicator of acute phase responses & returns to normal levels quickly with improvement of disease resolution.
  - CRP is not affected by as many other factors as is ESR, making it a better marker of some types of inflammation

(RCPA Manual, 2015)
References

- Lord, RS & Bralley, JA (eds) 2012, Laboratory evaluations for integrative and functional medicine. 2nd edn, Metametrix institute, Duluth, Georgia
- Wians, FH 2009, Clinical laboratory tests: which, why and what do the results mean? Labmedicine, volume 40, number 2, pp. 105-113
- Weatherb D & Ferguson, S 2002, Blood chemistry & CBC analysis: clinical laboratory testing from a functional perspective, Bear Mountain publishing, Jacksonville, USA.
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