Session 2: **Screening**

*blood tests part II, Inflammation*
Session Objectives

Screening Blood Tests Part II
• Blood lipids (Cholesterol, triglycerides, LDL and HDL)
• Homocysteine

Inflammation
• C-Reactive Protein
• Erythrocyte Sedimentation Rate (ESR)
Cholesterol Panel
Clinical Presentation

- A client may present with the following likely presenting complaints:
  - Personal concerns for poor dietary concerns
  - Past lifestyle factors increasing risk eg: sedentary
  - Past smoker
  - Familial history of Cardiovascular Disease (CVD)
  - Concern for stress levels and needs relaxation guidance
  - Fatigue
  - Referred by medical practitioner to make changes
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).
• 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)

(Pagana et al. 2015)
# 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>
</table>
| Reference Ranges (Adult) | Components: (Adult Values)  
  - **Total Cholesterol** - <5.20mmol/L  
  - **High Density Lipoprotein (HDL)** – [M] >45mg/dL [F] >55mg/dL  
  - **Low Density Lipoprotein (LDL)** - <130mg/dL  
  - Very Low Density Lipoprotein (VLDL) – 7-32mg/dL  
  - **Triglycerides** – [M] 40-160mg/dL [F] 35-135mg/dL |

(Pagana et al. 2015; RCPA manual, 2015)
Australian absolute cardiovascular disease risk calculator is useful for analysing the potential clinical implications (in the context of other health factors) of total cholesterol and HDL cholesterol levels.
Cholesterol

- Pregnancy, oophorectomy (surgical removal of ovaries) & postmenopausal status are associated with increased levels. A recumbent position decreases levels.
- Certain drugs can elevate or lower depending on their action within the body.

(Pagana et al. 2015)
# Cholesterol: Interpreting the Results

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

(Pagana et al. 2015; Labtests online Australasia, 2018)
Homocysteine
Clinical Presentation

- A client may present with the following likely presenting complaints:
  - Concerns for a genetic history of Cardiovascular Disease
  - Learning difficulties or a concern for cognitive decline
  - Curious about B12 or folate deficiencies & fatigued
  - Concerned about development of psychiatric developments such as anxiety or mood changes
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.

(Pagana et al. 2015)
# Homocysteine

## 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>

<table>
<thead>
<tr>
<th>Reference Ranges (Adult)</th>
<th>Components: (Adult Values)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Homocysteine – 4-14µmol/L</td>
</tr>
</tbody>
</table>

(Pagana et al. 2015; RCPA manual, 2015)
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
  (Pagana et al. 2015; RCPA manual, 2015)
# 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 |

(Pagana et al. 2015; RCPA manual, 2015)
Inflammation: C-Reactive Protein
Clinical Presentation

- A client may present with the following likely presenting complaints:

  - Pain and inflammation in a specific joint
  - Fatigue
  - Concerns for age related decline
  - Concern for infection
  - Generally feeling unwell with low vitality
What Is C-Reactive Protein (CRP)

CRP is a non-specific acute-phase reactant protein that indicates:

- Inflammatory illness
- Chronic inflammation
- Bacterial infectious disease
- Cardiovascular Disease
Testing For CRP

- The CRP test is an extremely nonspecific test. CRP levels can be elevated in any inflammatory condition.

- **C-reactive protein (CRP)** is a blood test marker for inflammation in the body.

- **CRP** is produced in the liver and its level is measured by testing the blood.

- **CRP** is classified as an acute phase reactant, which means that its levels will rise in response to inflammation.
C-Reactive Protein Testing

• CRP interacts with the complement system and serves as an opsonin (enhances phagocytosis) for some microorganisms

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

| Reference Ranges (Adult)  | CRP: <1.0 mg/dL = normal                                                                                                                   |
|                           | hsCRP: <1.0 mg/dL = low risk                                                                                                                |
|                           | 1.0 – 3.0 mg/dL = average risk                                                                                                              |
|                           | >3.0 mg/dL = high risk                                                                                                                     |

(Pagana et al. 2015; RCPA manual, 2015)
CRP/hs-CRP: Risk Factors

CRP levels showing cardiac risk and diseases

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.

(Pagana et al. 2015; RCPA manual, 2015)
CRP: Interpreting the Results

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

(Pagana et al. 2015; RCPA manual, 2015)
Inflammation: Erythrocyte Sedimentation Rate
Clinical Presentation

- A client may present with the following likely presenting complaints:
  - Pain, inflammation and joint stiffness
  - Nerve pain
  - Headaches, neck and shoulder pain
  - Concerns for genetic history of Polymyalgia rheumatica, or rheumatoid arthritis
  - Pelvic pain
  - Anemia, poor appetite, unexplained weight loss,
Erythrocyte Sedimentation Rate (ESR)

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

(Pagana et al. 2015; RCPA manual, 2015)
# Erythrocyte Sedimentation Rate (ESR)

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)

<table>
<thead>
<tr>
<th>Component</th>
<th>Male – up to 15mm/hr = normal</th>
<th>Female – up to 20mm/hr = normal</th>
</tr>
</thead>
</table>

(Pagana et al. 2015; RCPA manual, 2015)
# Erythrocyte Sedimentation Rate (ESR)

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

(Pagana et al. 2015; RCPA manual, 2015)
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)
Case Study

- Describe how clinical characteristics correlate with the findings of pathology reports for cholesterol blood lipids and inflammation.

- Discuss implications for test results/reports.
References


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