The New Zealand Laboratory Schedule and Test Guidelines: haematology tests

The New Zealand Laboratory Schedule has been created to provide consistent guidance and ensure uniform availability of tests across all District Health Boards (DHBs). The new Schedule divides tests into Tier 1 and Tier 2 to indicate whether all referrers can order the test, i.e. Tier 1, or whether a test must be ordered in conjunction with another health professional with a particular area of expertise, i.e. Tier 2. In addition, clinical guidelines are provided on the use of some tests. In this article we focus on the haematology tests in the schedule.

It is estimated that 85% of clinical decisions involve laboratory investigations. The objective of the New Zealand Laboratory Schedule is to make the most relevant tests available, and to provide guidelines on their optimal use.

The schedule was created by an overall steering group, managed by DHB Shared Services, with subgroups formed for each area of clinical speciality. The haematology subgroup is led by Dr Stephen May and made up of clinical and laboratory haematologists, with representation from around the country. The subgroup continues to meet to consider new investigations available as well as reviewing indications for older tests.

The haematology tests are ranked in Tier 1 and Tier 2 tests

Tier 1 tests may be requested by any registered medical practitioner as well as other practitioners who are able to request investigations, e.g. midwives.

Tier 2 tests are specialist tests whereby the referrer needs appropriate vocational registration or credentialing to order the test. Tier 2 test are also able to be ordered by General Practitioners on the advice of a relevant specialist.

Guidelines on selected haematology tests

Erythrocyte sedimentation rate (ESR) (Tier 1)

ESR has historically been used in clinical medicine as a measure of inflammation. However, it has significant limitations in terms of measurement accuracy. In addition, ESR is affected by numerous physiological variables and by factors other than inflammation, such as haemoglobin and plasma protein levels.

Despite its limitations, ESR may have some advantages in the assessment of the following conditions:

- Systematic lupus erythematosis
- Rheumatoid arthritis
- Kawasaki disease
- Rheumatic fever
- Hodgkin lymphoma
- Temporal arteritis
- Inflammatory bowel disease in children (initial assessment)

ESR should not be used to screen for plasma cell dyscrasias. If these conditions are suspected, protein electrophoresis and immunofixation or serum free light chain assays (see below) should be used.

C-reactive protein (CRP) is the preferred investigation for the assessment for a possible inflammatory or infective disorder. It is seldom appropriate for both ESR and CRP to be requested together.

While ESR and CRP are no longer routinely requested together for most conditions, either marker (or both) can be raised in giant cell arteritis (temporal arteritis) and given the significant potential for morbidity in people with giant cell arteritis, it is recommended that both are requested in the initial presentation. For further information see: "Giant cell arteritis: Always keep it in your head", BPJ 53 (Jun, 2013).

Serum free light chains (Tier 2)

The symptoms of multiple myeloma may be classical (e.g. bone pain) or non-specific. If multiple myeloma is suspected, a practical approach is to first request serum protein electrophoresis. If an increase in immunoglobulins is found, or the test is normal, but clinical suspicion remains, the need for further testing should be discussed with a Haematologist or other relevant specialist.

Serum free light chain assays can detect elevated levels of light chains (of immunoglobulin) in the blood, even when those levels are undetectable by serum protein electrophoresis. In a serum free light chain assay, both free kappa (κ) and lambda (λ) chains are measured and the ratio is calculated. Excessive free κ or λ increases the likelihood a of monoclonal plasma cell disorder.

The International Myeloma Working Group guidelines suggest that a serum free light chain assay is used for prognostic purposes in all patients with:

- Monoclonal gammopathy of unknown significance (MGUS)
- Smouldering multiple myeloma
- Active multiple myeloma
- Amyloidosis

The test is also indicated for patients with:

- Suspected myeloma, MGUS or amyloidosis
- Unexplained renal impairment
- Unexplained proteinuria
- Unexplained peripheral neuropathy

Follow-up testing is recommended no more frequently than every three months, unless the patient is on active chemotherapy.

For further information see: "Making sense of serum protein bands", Best Tests (Jul, 2011).

Chronic lymphocytic leukaemia (CLL) investigations (Tier 1)

Early B-cell chronic lymphocytic leukaemia is the most common type of adult leukaemia. It mainly affects people aged over 50 years (median 65 years), and patients are asymptomatic in the early stages with the only feature being a peripheral lymphocytosis. Diagnosis of chronic lymphocytic leukaemia (CLL) is based on cell marker studies (flow cytometry), along with clinical assessment.

Consider CLL or other lymphoproliferative disorders if the patient has persistent lymphocytosis of $> 5 \times 10^9$/L for more than three months.

1. Discuss with the Haematologist if cell marker studies are required for persistent unexplained lymphocytosis
2. Refer to the Haematology Outpatient Department if the referral criteria are met (see below); this usually signals advanced or progressive disease. Otherwise, regular monitoring (full blood count) in general practice is indicated; initially every three to six months, then yearly if stable or slow.

Referral criteria are outlined in full in the Laboratory Test Guidelines. The criteria include:

- Age < 55 years, with progressive disease
- Significant symptoms, e.g. significant weight loss, fatigue, night sweats
- Advanced stage of disease
- Disfiguring lymphadenopathy or hepatosplenomegaly
- Recurrent infections
- Haemolytic anaemia
- Lymphocyte count which has doubled in less than six months and is $> 30 \times 10^9$/L

Haemoglobinopathy investigations (Tier 1)

The most significant haemoglobinopathies/thalassaemias are: sickle cell disease, beta thalassaemia and alpha thalassaemia ("CIS" inheritance pattern). Although there are currently no specific referral criteria on the laboratory schedule for patients suspected of having one of these conditions, discussion with a Haematologist is recommended.

There is no formal haemoglobinopathy screening currently undertaken in New Zealand, therefore investigations are done on an *ad hoc* basis (as a once only investigation) for:

1. Investigations of hypochromic microcytic blood pattern when iron deficiency has been excluded
2. High risk ethnic groups, e.g. Middle Eastern, African, Pacific peoples
3. Follow up of family studies
4. Investigations of abnormal haemoglobins during other investigations, e.g. an abnormal haemoglobin found incidentally while testing HbA_{1c} for diabetes

For further information on investigating haemoglobinopathies/thalassaemias in patients with microcytic anaemia, see: "Anaemia on full blood count: investigating beyond the pale", Best Tests (Sep, 2013).

Inherited thrombophilia testing (Tier 1 and 2)

Thrombophilia testing is of limited utility and should not be used as a screening test. However, it is indicated in the following situations:

- Idiopathic venous thromboembolism in patients aged less than 45 years
- Warfarin induced skin necrosis
- Children presenting with purpura fulminans
- Siblings of patients with homozygous factor V Leiden
- Homozygous PT20210A or compound heterozygotes for these mutations
- Thrombosis in unusual sites, e.g. cerebral, mesenteric or portal

In all other situations testing should only be undertaken after consultation with a Haematologist or as part of a clinical trial.

The need for any investigation is dependent on the usefulness of the result and if there will be no change in clinical management as a result of the investigation, then it is not indicated.

For further information, see: Baglin T, Gray E, Greaves M, *et al*. Clinical guidelines for testing for heritable thrombophilia. British Journal of Haematology 2010;149:209-20.

Additional considerations for testing

Any testing should be requested as a result of, or to provide evidence of, a clinical condition, or to monitor chronic conditions or exclude clinically significant differential diagnoses.

Tests on the Laboratory Schedule should not be used for screening purposes outside a formal screening programme. Pre-employment screening is excluded from funding, as is testing for immigration purposes, or tests required prior to travel, although these tests can be purchased from an IANZ accredited laboratory.

The Laboratory Test Schedule and Laboratory Test Guidelines are available from: **www.dhbsharedservices.health.nz/Site/Laboratory/Default.aspx**

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