

Cost-effective utilisation of basic biochemical laboratory investigations in primary care

Cost-effective use of laboratory investigations is vital in primary care.

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The current burden of care imposed on all practising physicians by the four colliding epidemics (lifestyle diseases, tuberculosis, HIV and AIDS, and trauma) in resource-constrained and low- to middle-income countries in sub-Saharan Africa, has prompted the call for a paradigm shift in current medical practice. Unnecessary laboratory tests and consumer demand for certain tests have escalated in recent years, and have contributed to rising healthcare costs.

It is of paramount importance to understand the basic principles that govern the selection and ordering of the most cost-effective tests in specific patients.¹ Such an understanding will facilitate improved patient and illness outcomes and also contribute to sound professional practice. The patient's socio-environmental context must be integrated into the comprehensive (clinical, individual and contextual) assessment before any management or investigative plan is formulated.

This article provides general guidelines for the commonly requested chemical pathology investigations encountered in primary care when dealing with common

clinical situations. Full patient participation and due consideration must therefore be given to ethical issues such as autonomy, non-maleficence, beneficence and justice.²

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Changes in laboratory results

When trying to determine if a change in laboratory results is significant, one has to consider the effects of biological variation³ (refer to the article in this issue by F Omar). Furthermore, one needs to be aware of the different reference ranges that may be used by different laboratories.

Investigation of suspected anaemias

Typically, the full blood count (FBC) is the first investigation in most clinical situations

where laboratory assessment and diagnosis is required. One should first examine the FBC and pay particular attention to certain indices. With a progressive decrease in mean corpuscular volume (MCV), the

probability of iron deficiency anaemia increases.⁴ If the MCV is less than 75 fl there is a 38% chance of iron deficiency,⁵ but if it is greater than 95 fl the probability of iron deficiency is very low. Conversely, a raised MCV should alert one to the possibility of macrocytic anaemia, and vitamin B₁₂ and thyroid-stimulating hormone (TSH) levels should be assessed. Serum ferritin is the test of choice to confirm iron deficiency.^{4,6} If the serum ferritin level is less than 15 ng/ml the diagnosis is confirmed, but if the level is greater than 100 ng/ml the diagnosis can be ruled out. A level of 15 - 40 ng/ml is sufficient evidence to treat.⁶ It should be noted that ferritin is an acute-phase reactant and levels may be raised in acute inflammation in the presence of iron deficiency.

Blood glucose testing⁷

For blood glucose testing one can use random or fasting glucose for the first sample. Take a second fasting plasma glucose sample unless there are symptoms of hyperglycaemia. Whole blood/capillary blood glucose meters are not recommended for screening. Ideally, one should confirm a level with two plasma glucose measurements at different times. Urine testing is not recommended for the diagnosis of diabetes.

Glucometers are convenient for point-of-care testing, but there is often confusion with regard to the diagnostic criteria for diabetes mellitus (DM). There are also issues of quality control and the audit trail of quality assurance in the maintenance of the former. One should always try to confirm an abnormal point-of-care test (POCT) result using a laboratory test.

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HbA_{1c}

HbA_{1c} is currently used to assess glycaemia over the preceding 2 - 3 months in the absence of blood loss or haemolysis. The general guidelines are the following: patients who are well controlled should have their HbA_{1c} measured twice a year, and those who have their treatment adjusted and do not meet treatment goals should have it measured quarterly.⁸ Recently, there have been moves to use HbA_{1c} as a screening test to diagnose diabetes, and a cut-off level of 6.5% has been proposed. However, there is still much debate about its usefulness as a screening test in the African context.

Urea and electrolytes

Low serum sodium – if given a low serum osmolarity (below 270 mM) – should alert the physician to the possibility of the syndrome of inappropriate antidiuretic hormone (SIADH) secretion, especially against the background of a high prevalence of tuberculosis and HIV-related complications and co-morbidity. If the serum osmolarity is abnormal (less than 270 mM), then urine osmolarity and sodium should be assessed to exclude SIADH. In this scenario, the urine osmolarity is increased and the ratio of urine to serum is 2:1, with urine sodium greater than 30 mmol/l.

Urea, creatinine and estimated GFR (e-GFR) (when provided) are useful indicators of renal impairment or the degree of renal damage. In certain circumstances it may be necessary to repeat the urea and creatinine level

measurements to differentiate between pre-renal uraemia and actual renal impairment.

High potassium levels

Firstly, one should identify patients at risk, such as those with chronic renal disease, on anti-hypertensives, with obstructive uropathy, with myopathy, elderly patients with urea greater than 8.9 mM, and with acute illness such as acute rheumatic fever (ARF) or diabetic ketoacidosis (DKA).⁹ Consider spurious hyperkalaemia if the above are absent. Check that the specimen was not haemolysed when received at the laboratory. Usually, the laboratory may insert a comment or the analysis will be cancelled if haemolysis is present. A true result should be assessed for urgency by considering the level: mild, moderate or severe; in the last case the level will be greater than 7. One should check for changes in creatinine and eGFR. Are there ECG changes and are the values increasing with time? If renal function tests and bicarbonate levels are normal, then these are likely to be spurious. Causes of spurious hyperkalaemia include inappropriate refrigeration of the sample, delays in separation, difficult venepuncture, haemolysis *in vitro*, raised WBCs and using the incorrect tube such as a K-EDTA tube or incorrect order of tube when drawing blood.

Low potassium levels⁹

Determine the underlying cause of low potassium levels: review medications and check nutrition. Consider 24-hour urinary potassium levels to check for renal loss.

Monitoring lithium therapy

Lithium levels should be measured at 3-monthly intervals and 12 hours after the last dose. Renal function should be checked annually and thyroid function should be assessed 6-monthly in the first two years and then annually thereafter. If the dose is changed the level should be checked 3 - 4 days later and again within 1 week. The target range for most adults is 0.6 - 1.0 mM, and for the elderly patient 0.4 - 0.8 mM.

Minor liver function test abnormalities¹⁰

If the alkaline phosphatase (ALP) is raised in isolation in an asymptomatic patient,

check liver and bone profiles. An isolated increase of about 20% above the upper limit may be normal. Check the gamma glutamyl transferase (GGT) level to determine if it is related to the bone profile. If the GGT is normal, it is likely. Check fasting corrected calcium and parathyroid hormone (PTH) and consider assessing vitamin D levels.

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A slightly raised bilirubin in an asymptomatic adult may be normal, e.g. a level of 20% above the range may be a statistical variation. If the level is greater than 50% above the range assess the level of conjugation, and if it is greater than 70% unconjugated consider the diagnosis of Gilbert's syndrome. Levels greater than 3-fold above the upper limit of normal are likely to be a sign of clinical disease.

Mildly elevated transaminases should be re-checked in 1 - 3 months. If the elevation is marked then secondary assessment by a specialist should be considered.

Abnormal isolated GGT¹⁰

GGT is useful for investigating the cause of a raised ALP and is not always due to alcohol abuse.

Prostate-specific antigen (PSA)

Please refer to the article in this issue by B Sedumedi. Measurement of the PSA should start at 50 years of age or earlier if there is a high risk.¹¹ Samples should be taken more than 48 hours after ejaculation or exercise, especially bike-riding, and before the rectal examination. In the patient who has been diagnosed with cancer, the measurement should be done every 3 months for the first 2 years or if symptoms develop.

Thyroid function testing

Please refer to the article in this issue by D Haarburger. The most sensitive test is TSH, which should be requested first. If abnormal, it should be followed by T4. If secondary hyperthyroidism is suspected then TSH and T4 should be measured. Testing should be done in high-risk patients, e.g. in cases of

goitre, nodules, infertility, dyslipidaemia, pregnancy, and type 1 DM.

Lipid testing

Ideally, fasting samples should be taken for accurate assessment of triglycerides (TGs). Total cholesterol (TC) and HDL cholesterol (HDL-C) form part of the lipid profile, with LDL cholesterol (LDL-C) calculated in the majority of laboratories, rather than measured directly. Laboratories can bill for this extra calculation and the clinician is able to calculate the LDL-C directly from the Friedewald equation $(TC-HDL-C-TG/2.2)$, i.e. all cholesterol not accounted for by HDL and TGs), providing TGs are measured after fasting and are less than 4.5 mmol/l.

When initiating treatment with statins, wait at least 4 weeks before assessing treatment. TC, HDL-C and LDL-C should be assessed at 8 (± 4)-week intervals. Consider the effect of biological variation when interpreting the effect of a statin on cholesterol levels. When changing the dose of a statin, wait at least 4 weeks before assessing the effect.

References available at www.cmej.org.za

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- Be cognizant of ethical considerations and the economic aspects of laboratory testing.
- Consider the FBC indices first to guide further testing.
- Diabetes mellitus should be diagnosed on the basis of a formal laboratory test, not a POCT, and should be confirmed on two occasions.
- HbA_{1c} should not be used in the African context to diagnose diabetes.
- Urea and electrolytes should be analysed carefully for electrolyte abnormalities, especially in the sick patient.
- In the setting of HIV and TB, keep a high index of suspicion for SIADH.
- When analysing liver function tests, take into account the level of the abnormality to guide further management.
- TSH is the best screening test for thyroid disease.
- Lipid profiles should preferably be taken from a fasting subject and one should wait 4 weeks before re-assessing the effect of treatment.