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Common Sense Pathology

A REGULAR CASE-BASED SERIES ON PRACTICAL PATHOLOGY FOR GPs

CONTENTS

- When to perform a diagnostic test
- Which test is appropriate
- Case studies



AVOIDING unnecessary laboratory tests

A JOINT INITIATIVE OF



Australian
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AVOIDING UNNECESSARY LABORATORY TESTS



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Introduction

Unnecessary laboratory tests may be defined as those that have a ‘vanishingly small’ chance of:

- revealing any unexpected pathological process.
- contributing to the diagnosis of the cause of a patient’s presenting symptoms.
- assisting in the monitoring of the progress of a known pathological process.
- helping to assess the management of a known disease process.

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“The millions of dollars spent on unnecessary tests are, in [doctors’] minds, balanced against the tens of millions involved in adverse court judgments.”

Unnecessary laboratory tests may not be harmless. Most test reference ranges include 95% of the population, so when multiple tests are performed there is a high probability that at least one will be flagged as outside the normal range. This often leads to patient and/or doctor anxiety, followed by more expensive or invasive follow-up tests, and even therapies that are not indicated. Unnecessary tests also increase costs.

However, with the increase in litigation, the perceived bias of the legal system against the doctor and the lack of an agreed definition of the term ‘vanishingly small’, many practitioners adopt a defensive strategy and test for whatever is convenient at each patient visit. The millions of dollars spent on unnecessary tests are, in their minds, balanced against the tens of millions involved in adverse court judgments.

Frequently patients have to travel or take time off work for medical appointments, and the convenience of having all tests performed on one occasion may also be a significant factor.

The following five common case scenarios aim to assist GPs when making the decision to order relevant laboratory investigations.

Case study 1

QC, 61, comes for a check up before going on a trip overseas. She is in good health and has no relevant history. She has travelled overseas several times before with no problems.

Should you perform a thyroid test, and if so, which one?

About 5% of the female population in Australia will develop some degree of asymptomatic hypothyroidism, most over the age of 50. So, it is reasonable to check QC’s thyroid function if it has not been done (that is, you have no record and she has no memory of such a test) within the past five years. The current expert recommendation for such a patient is not more frequently than every five years, because it is unlikely that significant thyroid disease will develop more rapidly at this age.

The Royal College of Pathologists of Australasia recommendation and Medicare policy is to only measure thyroid-stimulating hormone (TSH) and then follow with further tests if it is outside the reference range of 0.4-4.0 mU/L. If the patient has a moderate-to-severe acute illness, which this patient does not, then following up a modestly low TSH value is not worthwhile until the patient has



“Glucose and ketones on urinary dipstick in a symptomatic child mandate urgent referral which should not be delayed by confirmatory tests.”



completely recovered, as illness may temporarily suppress the pituitary thyrotrophs.

What advice should be given about travel and venous thrombosis?

Despite extensive coverage in the lay press, the association between prolonged air or land travel and venous thrombosis remains controversial. The studies performed do not show any consistent additional risk factors that may help predict the occurrence of DVT during or after air travel. Thrombophilia testing should not be routinely performed if there is no personal or family history of thrombosis because 5% of people of European descent will have genetic polymorphisms for thrombophilia but will never have a thrombotic event. Avoiding constrictive clothing around lower extremities or waist, keeping well hydrated and frequently stretching calf muscles have been recommended as the steps for long-distance travellers (ie, flights of more than six hours) to prevent thrombosis occurring. Currently, there is no evidence to support the use of compression stockings to prevent DVT.

The following tests are not generally recommended:

- TSH, in the absence of symptoms, in males or females younger than 50 years of age.
- Free-thyroid hormones: TSH is the recommended screening test for symptomatic thyroid disease. If

TSH is elevated, suggest FT4 level only. If TSH is low, FT3 and FT4 are recommended.

- Thrombotic screen in the absence of any symptoms or signs of thrombosis.

Case study 2

DL, a child aged 10, has a short history of thirst and weight loss and has relapsed into bed wetting at night. Urine dipstick shows 3+ glycosuria and a trace of ketones.

Should you request a glucose tolerance test (GTT) to confirm diabetes? If yes, what dose of glucose is appropriate?

No, you should not order a GTT for this patient. Glucose and ketones on urinary dipstick in this symptomatic child mandate urgent referral which should not be delayed by confirmatory tests. In general, never do a GTT in a child before first measuring a fasting or random blood glucose. In this patient, a hypertonic glucose load (the glucose drink is about 1400 mOsm/L) will further increase the blood sugar and lead to a more intense glycosuria with the potential to further dehydrate the child. This risk is greater in children but also present in adults. In general, diabetes is confirmed by the finding of raised fasting blood glucose of 7.0mmol/L or more on two occasions. In a symptomatic child, a random plasma glucose of more than 11.1mmol/L or a fasting blood glucose of more than 7.0mmol/L confirms the diagnosis.



Urgent insulin treatment is necessary, if there are signs of significant ketoacidosis ($\geq 2+$ ketonuria) such as hyperpnoea, hypotension, low bicarbonate or excessively high blood sugar on the first sample.

This child, whose initial blood glucose level was found to be 25mmol/L, certainly warranted inpatient observation and care.

Should you request a HbA1c at the initial visit to confirm diabetes?

No. The Medicare recommendations are that this test is applicable only in a patient with established diabetes, that is with two fasting blood glucose levels more than 7.0mmol/L, or in an older patient with fasting glucose in the impaired glycaemic control region (6.1-7.0mmol/L) and GTT results of a fasting blood glucose ≥ 7.0 mmol/L or two-hourly blood glucose ≥ 11.1 mmol/L.

This patient is so ill that the diagnosis could be made at the initial consultation and the HbA1c would be justified, but the result may be difficult to interpret as the history is so short and the lifetime of the red cell is three months.

Having established the diagnosis of diabetes, should the HbA1c be measured at every visit?

Probably not. Initially visits are likely to be more frequent than the three-monthly measurement permitted by Medicare — this is in keeping with the lifetime of the red cell.

Key points:

- Screening tests are not indicated when the diagnosis is clear.
- HbA1c is not recommended as a diagnostic test for diabetes.
- The ordering of tests should be evidence-based and should comply with Medicare rules.
- Any test with potential for harm should be avoided.

Case study 3

FS, 61, has been feeling mildly unwell for about a month with some anorexia, and has had an unintentional weight loss of 4kg. Physical examination is normal.

Should you order a set of tumour markers (such as carcinoembryonic antigen, carbohydrate antigen 19.9, human chorionic gonadotropin, alpha-fetoprotein)?

This is not a recommended strategy. Tumour markers are not very sensitive. In more than 50% of cancers, they are not raised, especially early in the disease. Also, at slightly elevated levels they are not very specific because they can be secreted by organs involved in other pathological processes. For example, a moderate increase in one or more of these markers may occur in chronic liver disease, either non-alcoholic steatorrhoeic hepatitis or cirrhosis. Therefore, no increase does not exclude a malignancy and a moderate increase can lead to a false diagnosis or a false expectation by the patient regardless of the doctor's opinion.

The major value of such markers is for monitoring recurrence or persistence of tumours after treatment of a hormone-secreting tumour. The jury is still out on the role of PSA.

Summary of inappropriate use of tumour markers:

- A test with low sensitivity does not exclude a diagnosis and leads to false reassurance.
- A test with low specificity can lead to misdiagnosis with subsequent morbidity and mortality.
- When used appropriately, tumour markers can help to monitor a disease.

Case study 4

GR, 47, complains of crushing chest pain radiating down his left arm for one hour, with sweating and a feeling of weakness. On examination, his blood pressure is 110/60mmHg (normally 140/85mmHg) and ECG shows 3mm elevation of the ST segments in V3-V6 leads.

Should you immediately measure troponin and 'cardiac enzymes' (such as creatine kinase [CK], aspartate aminotransferase [AST], lactate dehydrogenase [LD]) to assist in the diagnosis of MI, before commencing anticoagulant or thrombolytic therapy?

No. There is evidence of an extensive anterolateral infarct (symptoms in the presence of hypotension



and four chest leads with ST elevation) and therapy should be commenced as soon as possible because “time is muscle”. The delay involved in waiting for test results will extend the area of muscle death.

With the availability of the highly specific cardiac marker troponin, AST and LD should no longer be used as markers of MI because they are not specific to cardiac events. It is important to remember that neither troponin or CK begins to rise until at least 4-5 hours after an MI.

Would knowledge of a baseline level of troponin and CK (at the time of the infarct) be of any value in assessing the degree of damage?

Baseline CK may be of value, as there is always some present in plasma. The increase above this level at 24 hours post-infarct is moderately well correlated with the mass of infarcted tissue, although the relationship changes if the patient has been thrombolysed.

Baseline troponin is of no value, as it would be close to zero. However, if previous infarction in the past week or two is suspected, it is worth measuring because it may be elevated. The increase in troponin at 24 hours is correlated with the infarct size in the absence of thrombolysis, but after this procedure there is such a rapid and variable washout that the correlation is quite poor.

Should you repeat the troponin measurement daily to observe progress? Will it help predict cardiac rupture or later failure?

As troponin levels decline with a half life of 2-3 days, there would seem to be no point in observing this process. Some cardiologists believe that it provides evidence for repeated infarction after the first episode, but as CK levels drop much more quickly this enzyme is probably a better marker for re-infarction, and new ECG changes may be even better. There is no evidence that troponin levels help predict rupture or failure, except in so far as the larger the infarct the greater the chance of later cardiac failure.

What is the role, if any, of CK-MB now that troponin is available?

CK-MB has a slightly shorter half life than CK itself, and much shorter than troponin. However,

its measurement is more difficult, especially in low concentrations, and many laboratories have largely discarded this test. It may be a better indicator for reinfarction, but the delay in obtaining results when the test needs to be sent away limits its usefulness.

Key points:

- Do not delay diagnosis and therapy of MI when the diagnosis is clear.
- Do not waste resources on baseline tests that have unhelpful results.
- Do not repeat tests when the diagnosis is well established if they have no real role in monitoring progress.

Case study 5

AC, 55, attends her doctor for the first time in three years for a general checkup, because she finds she has less energy and is considering giving up her part-time secretarial job. She had two uncomplicated pregnancies (at age 24 and 27) and has had no significant health problems. She has gained 3kg in the past five years, does not smoke and drinks one or two glasses of wine each night. Her diet is reasonably balanced apart from an almost total avoidance of red meat.

She takes no regular medications (HRT was used for two years and stopped three years ago) and no over-the-counter medications apart from occasional paracetamol for headaches. Examination is normal apart from a blood pressure of 160/90mmHg, which settles to 145/90mmHg after 10 minutes. Urine dipstick analysis is negative.

Which of the following investigations can you justify on this initial visit?

- FBC; iron studies and ferritin;
- coagulation screen
- electrolytes, urea and creatinine
- liver function tests; glucose HbA1c;
- lipid studies; thyroid tests
- urine or blood catecholamines; cortisol
- faecal occult blood test
- calcium, phosphate, magnesium and vitamin D
- tumour markers
- arterial blood gas



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You are investigating this patient for a possible physical cause to explain her loss of energy. The differential diagnosis includes: anaemia, hypertension, early renal impairment, excess alcohol intake, a psychological problem or any one of many rare conditions.

A FBC is essential and may rule out anaemia or reflect a major systemic illness given the range of pathophysiological conditions in which it may be abnormal. For example, microcytic hypochromic anaemia may indicate a nutritional deficiency (which may be relevant in this woman who avoids red meat) or a blood loss anaemia (occult gastrointestinal malignancy). Routine iron studies may not provide any additional useful information unless it is part of follow up of a low haemoglobin or treatment monitoring. The serum ferritin can be raised in a variety of inflammatory conditions and serum iron is not a reliable marker of iron stores. Given the lack of specificity of the iron studies, a normal study does not exclude iron deficiency.

Serum B₁₂ and red cell folate levels are useful screening tests in this setting. Serum B₁₂ (in the context of meat avoidance) or red cell folate could

be low and can, albeit uncommonly, cause neurological symptoms without anaemia. It is recommended that a serum red cell folate is ordered rather than serum folate alone as the latter does not accurately reflect folate stores in the body.

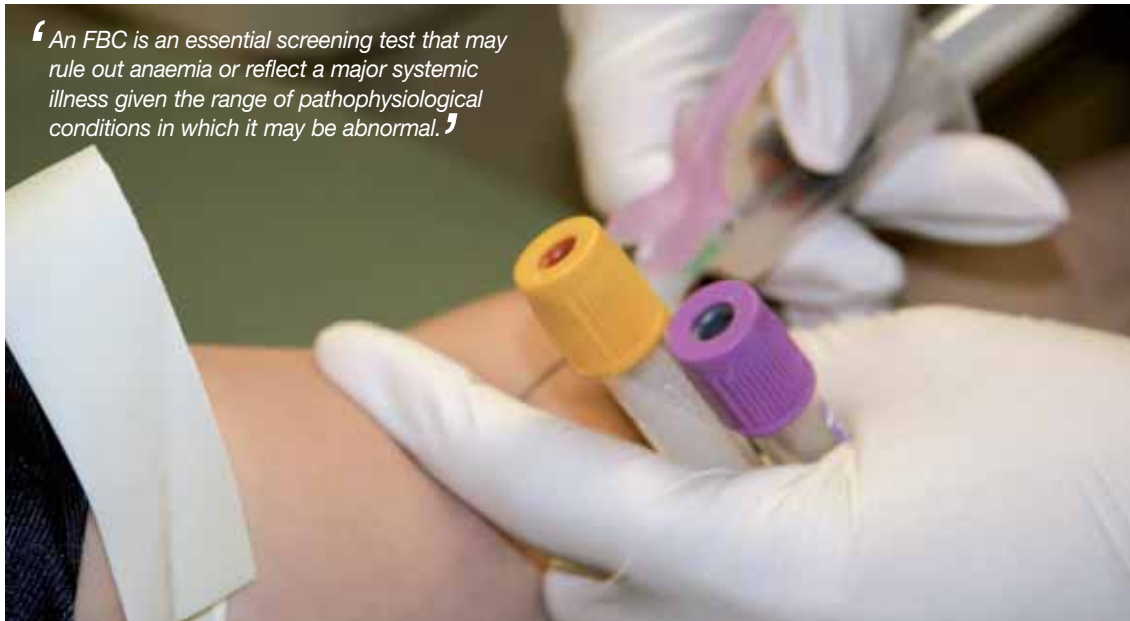
Coagulation testing is not routinely recommended. It could only be justified if the patient is on an oral anticoagulant or has a specific bruising/bleeding complaint. Mild prolongation of coagulation profiles due to technical issues associated with collection and testing is not uncommon and leads to unnecessary and expensive repeat testing or investigations. Unless a specific question from the history or examination is being addressed these tests should not be routinely performed.

Testing urea, creatinine and electrolytes can be justified as this patient is mildly hypertensive and these tests will give a measure of renal function and allow calculation of her estimated GFR, as well as pointing to any electrolyte disturbance.

Liver function tests are appropriate to exclude excessive alcohol intake. Gamma glutamyltransferase rises in about 40% of such patients even in the absence of transaminase increases. Albumin will



“An FBC is an essential screening test that may rule out anaemia or reflect a major systemic illness given the range of pathophysiological conditions in which it may be abnormal.”



decrease if nutrition has been chronically poor. Hepatitis is unlikely, but if she had received a blood transfusion before hepatitis screening of blood was available then it could have been acquired.

Diabetes is common and often symptomless so a fasting blood glucose test is justified, even in the absence of glycosuria. As mild hypertension and diabetes (or even impaired glycaemic control) are risk factors for coronary vascular disease, it may be reasonable to measure low-density and high-density lipoprotein cholesterol or total cholesterol and fasting triglycerides.

There are good arguments for adding calcium and phosphate to the electrolyte screen, at least occasionally, as there is no other way to exclude hyperparathyroidism. Vitamin D levels are not worth doing in an ambulatory patient of this age unless they have very limited exposure to sunlight. There is mounting evidence that there is a substantial group in the population who have limited sun exposure and, subsequently, low vitamin D levels, and those people should be intermittently checked. Of course, these tests are of no value in diagnosing or monitoring osteoporosis.

The National Bowel Cancer Screening Program involves faecal occult blood testing for all adults reaching the ages of 55 or 65 during 2006-08 with follow-up colonoscopy if positive. It is anticipated

that the program will be extended to all in these age groups as resources for the follow ups become available. At present, for those who don't come under the screening program, such testing can be done at the patient's own expense.

Catecholamines are not justified in this patient, as the hypertension is mild, not episodic and phaeochromocytoma is rare. Arterial blood gas is inappropriate and is reserved for significantly sick patients in hospital.

See discussion of Case study 1 (thyroid tests), Case study 2 (HbA1c) and Case study 3 (tumour markers).

Summary of recommended tests in this case:

- FBC, serum electrolytes and creatinine, liver function tests, fasting glucose, calcium, phosphate, fasting cholesterol and triglyceride, serum B₁₂ and red cell folate levels.
- Other tests are to be guided by symptoms and history taking.

Further reading

Dunstan R (ed). *Abnormal Laboratory Results*. McGraw-Hill, Sydney, 2005.