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Laboratory

Test Referral Guidelines

2013

Document Control

Title	Version	Date	Summary of changes
Laboratory Test Referral Guidelines	V1.0	4 October 2013	N/A

LABORATORY TEST REFERRAL GUIDELINES

Table of Contents

TEST NAME	Amino acids	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	13 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	For investigation and monitoring of genetic biochemical disorders (inborn errors) of amino acid metabolism.
Indications / referral criteria	The test **is not indicated** for the evaluation of general nutritional status or mood disorders.
Collection information	
Frequency of Testing	There are no specific restrictions at this time, but clinical details are expected and the request may or may not be approved based on clinical background.
Links to further information	
References	

TEST NAME	Anti-neutrophil cytoplasmic antibody	CODE		OWNER	Chair, Immunology Laboratory Schedule Subgroup
OTHER NAMES	ANCA	VERSION	11.1	DATE	21 December 2011

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	Indicated for the evaluation of: 1. Glomerulonephritis (especially RPGN) 2. Pulmonary haemorrhage (especially pulmonary renal syndrome) 3. Cutaneous vasculitis with systemic features, multiple lung nodules 4. Chronic destructive disease of the upper airways 5. Longstanding sinusitis or otitis 6. Subglottic tracheal stenosis 7. Mononeuritis multiplex or other peripheral neuropathy 8. Retro-orbital masses 9. Monitoring response to treatment (more controversial)
Collection information	
Frequency of Testing	N/A
Links to further information	
References	1. J. Savige et al, Am J Clin Pathol. 1999; 111:507-513.

TEST NAME	Androstenedione	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	A4, ASD	VERSION	12.1	DATE	13 December 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Endocrinologist - Paediatrician - O&G specialist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Less than 10% of patients with hirsutism due to PCOS have isolated raised androstenedione, but data is limited. This may reflect difficulties in reference range derivation. US Endocrine Society guidelines are for testosterone as first line measurement in patients with moderate or worse hirsutism. Other androgens such as DHEAS and androstenedione add little, if any, value in most situations, especially where testosterone is normal. They do not generally change management, which is with oral contraceptives and anti-androgens. Androstenedione may be raised in late onset congenital adrenal hyperplasia, but is not specific for this condition and 17-hydroxyprogesterone is a better test.
Indications / referral criteria	For patients under specialist evaluation and management of hirsutism or other disorders such as premature adrenarche.
Collection information	
Frequency of Testing	N/A
Links to further information	
References	1. Endocrine Society Guidelines, Martin, KA et al. J. Clin. Endocrinol. Metab. 2008; 93: 1105-20.

TEST NAME	Apolipoprotein A1 and B	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	APO-A1, APO-B	VERSION	12.1	DATE	13 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Apolipoprotein B (apo B) and Apolipoprotein A1 (apo A1) give an indication of concentration of different classes of lipid particles: - Apo B - concentration of LDL, and related precursor VLDL and IDL particles - Apo A1 – concentration of HDL particles Some large studies (e.g. INTERHEART) show these measurements are useful for stratifying CVD risk. However, they are more expensive than cholesterol measurements, which are well established, and the added value of measuring them is unproven for the general population. Reference ranges and international calibration/measurement are not as well established as for lipids. Situations where they are most likely to be of relevance include: - assessing patients at 'intermediate risk', especially with mildly raised triglyceride and other possible features of the metabolic syndrome - patients with early personal or family history of CVD but lipid measurements within reference limits - assessing residual risk in patients on aggressive statin treatment - evaluation of a suspected genetic cause for very low LDL and/or HDL levels
Indications / referral criteria	Currently no specific indications or referral criteria are required (this may change depending on future studies or requesting patterns)
Collection information	Fasting is not necessary
Frequency of Testing	
Links to further information	
References	.

TEST NAME	Apolipoprotein E (apoE) genotyping	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: – Specialist lipid clinic - Neurologist - Psychiatrist - Geriatrician - Geneticist - Cardiologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	This test is indicated in the diagnostic work-up of certain uncommon hyperlipidemias: the homozygous e2 genotype is associated with type III hyperlipidemia. The e4 alelle is associated with Alzheimer disease (AD). However, the predictive value of apoE genotyping is too low to be useful in the diagnosis of AD in symptomatic patients[1]. ApoE genotype analysis has the potential to cause harm and should not be performed in asymptomatic individuals. This ethical position is supported by a number of consensus statements.[2] The majority of requests for this test in NZ have been based on the theory that apoE genotype is a susceptibility marker for subclinical mercury toxicity. This is not supported by scientific evidence. Requests for apoE genotyping as an adjunct to chelation therapy are not indicated.
Collection information	
Frequency of Testing	
Links to further information	GHSNZ – Genetic Health Service NZ www.genetichealthservice.org.nz
References	1. Liddell MB, Lovestone S, Owen MJ. Genetic risk of Alzheimer's disease: advising relatives. Br J Psychiatry. 2001;178:7-11. 2. Panegyres PK, Goldblatt J, Walpole I et al. Genetic testing for Alzheimer's disease. Med J Aust. 2000;172:339-343.

TEST NAME	BNP and NT-ProBNP	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Natriuretic peptides	VERSION	12.1	DATE	13 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	These natriuretic peptides are extremely useful for evaluation patients with non-specific symptoms of early chronic heart failure. In particular, the strong negative predictive value of a normal result is very useful and enables evaluation and treatment to be directed elsewhere. A clearly high result supports heart failure, although in most acute cases this is clinically obvious through other means and measurement adds little to management or prognosis. Mild-moderate elevation is not specific and may be due to a wide range of other causes besides, or in addition to, mild heart failure. A high level also carries adverse prognosis, independent of other variables. However, while aiding management, these tests do not completely avoid the need for echocardiography, which also provides other important information, such as cardiac valve anatomy and cardiac function. Value is much less well established for guiding ongoing anti-failure treatment, and at present they have a secondary role only. NICE guidelines (UK) recommend their use for this purpose be restricted to difficult patients under specialist management. NHF/NZGG guidelines do not specifically restrict their use in this setting but have not encouraged it.
Indications / referral criteria	Exclusion of heart failure as a cause of unexplained breathlessness and other non-specific symptoms. Management of anti-failure therapy (secondary role only, usually for difficult patients).
Collection information	
Frequency of Testing	For cardiologists - unrestricted For others there are no formal restrictions but recommend: – no more than four tests/year per patient (more frequent need than this suggests excessive use or need for specialist involvement) – no sooner than 2 weeks between tests (it takes at least this time for the level to re-stablise after a change in anti-failure treatment)
Links to further information	
References	

TEST NAME	Bordetella pertussis	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES	B. pertussis	VERSION	12.1	DATE	16 March 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	Polymerase chain reaction (PCR) is the most sensitive test for diagnosing *B. pertussis* in the 3 weeks after the onset of a cough. It is especially useful in infants and young children, and in health care and early child care centre workers (discuss the testing of this group with the Medical Officer of Health). Culture may be required to determine antimicrobial susceptibility and serotype (some funding and a surveillance strategy are required for this). *B. pertussis* serology may occasionally be useful in older children and adults who have had the cough for >21 days. Bordetella IgA is the most appropriate serological test, and those using mixed antigens are unreliable. Test results can be affected if patient has been vaccinated in the past (refs: Riffelmann, Guiso).
Collection information	The preferred sample is a nasopharyngeal swab or aspirate.
Frequency of Testing	
Links to further information	
References	1. Public Health Laboratory Network (Australia) Laboratory case definition *Bordetella pertussis* 18 April 2011. http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phlncd-pertussis.htm 2. CDC Vaccines and Immunizations. Chapter 10: Pertussis. http://www.cdc.gov/vaccines/pubs/surv-manual/chpt10-pertussis.html 3. Wei SC, Tatti K, Cushing K, et al. Effectiveness of adolescent and adult Tetanus, Reduced-Dose Diphtheria, and Acellular Pertussis Vaccine against Pertussis, Clinical Infectious Diseases 2010;51(3):315-321. 4. Riffelmann M, Thiel K, et al Performance of Commercial Enzyme-linked Immunosorbent Assays for detection of antibodies to *Bordetella pertussis* Journal of Clinical Microbiology 2010;48(12):4459-4463 5. Guiso N, Berbers G, Fry NK et al What to do and what not to do in the serological diagnosis of pertussis: recommendations from EU reference laboratories Eur J Clin Microbiology Inf Dis 2011;30:307-312

TEST NAME	CA 125	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Carbohydrate Antigen 125 Cancer Antigen 125	VERSION	12.1	DATE	1 February 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	CA 125 is elevated in patients with a wide range of malignancies including ovarian, pancreatic, lung, breast, endometrial, non Hodgkin's Lymphoma and hepatocellular. It is also elevated in non malignant disorders such as acute and chronic liver diseases, acute and chronic pancreatitis, Rheumatoid Arthritis, ulcerative colitis, endometriosis, menstruation, non malignant ascites and pleural effusions, and SLE. It is most widely used in monitoring serous epithelial ovarian cancer and it may provide prognostic information. Its role in screening is still under evaluation but it may be useful in diagnosis in patients with high probability of ovarian cancer at presentation.
Indications / referral criteria	**INDICATED FOR:** – Patients with symptoms or signs associated with high suspicion of ovarian cancer: Persistent continuous or worsening unexplained abdominal or urinary symptoms. Pelvic mass. – Case detection in patients at high risk of familial ovarian cancer. – At diagnosis of ovarian cancer to provide prognostic information – After treatment to monitor response and detect relapse **IT IS NOT INDICATED FOR:** – Screening of asymptomatic low risk population – Investigation of non specific symptoms, when probability of malignancy is low – Investigation of other suspected malignancies
Collection information	
Frequency of Testing	Minimum repeat interval two weeks.
Links to further information	**BPAC** www.bpac.org.nz **National Comprehensive Cancer Network** www.nccn.org **European Group on Tumour Markers** www.egtm.eu
References	1. www.bmj.com/contents/339/bmj.b3527 Clinical Review Serum tumour markers : how to order and interpret them CM Sturgeon, LC Lai, MJ Duffy 2. Sturgeon CM et al. National Academy of Clinical Biochemistry laboratory medicine guidelines for use of tumor markers in testicular, prostate, colorectal, breast and ovarian cancers. Clin Chem 2008;54(12):11-79

TEST NAME	CA 15-3	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Carbohydrate Antigen 15-3 Cancer Antigen 15-3	VERSION	12.1	DATE	1 February 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	CA 15-3 is elevated in patients with a wide range of malignancies including breast, pancreatic, colorectal, lung, endometrial, liver and ovarian. It is also elevated in non malignant disorders such as cirrhosis, benign breast disease and gynaecological disorders and pregnancy. It is most widely used in monitoring breast cancer patients after treatment although evidence this improves outcomes is weak. It does not have the required sensitivity or specificity to be used as a screening or diagnostic test. At diagnosis of breast cancer the level of CA 15-3 can provide information about the likelihood of metastases.
Indications / referral criteria	**INDICATED FOR:** – At diagnosis of breast cancer to provide prognostic information – After treatment to monitor response and detect relapse **IT IS NOT INDICATED FOR:** – Screening of asymptomatic low risk population – Investigation of non specific symptoms, when probability of malignancy is low – Investigation of other suspected malignancies
Collection information	
Frequency of Testing	Minimum repeat interval two weeks.
Links to further information	**BPAC** www.bpac.org.nz **National Comprehensive Cancer Network** www.nccn.org **European Group on Tumour Markers** www.egtm.eu
References	1. Molina R et al. Tumor Markers in Breast Cancer - European Group on Tumor Markers Recommendations Tumor Biol 2005;26:281-293 2. Sturgeon CM et al. National Academy of Clinical Biochemistry laboratory medicine guidelines for use of tumor markers in testicular, prostate, colorectal, breast and ovarian cancers. Clin Chem 2008;54(12):11-79

TEST NAME	CA 19-9	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Carbohydrate Antigen 19-9 Cancer Antigen 19-9	VERSION	12.1	DATE	1 February 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	CA 19-9 is elevated in patients with a wide range of malignancies including pancreatic, gastric, colorectal, hepatic and ovarian. It is also elevated in non malignant disorders such as acute and chronic liver disease, acute and chronic pancreatitis, biliary diseases, diabetes and irritable bowel syndrome. It is most widely used in monitoring pancreatic cancer but is not sufficiently sensitive to be used in screening and not selective enough to be used in diagnosis. It may provide prognostic information at time of diagnosis.
Indications / referral criteria	**INDICATED FOR:** – Patients with symptoms or signs associated with high suspicion of pancreatic cancer: Progressive obstructive jaundice with weight loss and/or pain in the abdomen or mid back – At diagnosis of pancreatic cancer to provide prognostic information – After treatment of pancreatic cancer to monitor response and detect relapse **IT IS NOT INDICATED FOR:** – Screening – Investigation of non specific symptoms, when probability of malignancy is low – Investigation of other suspected malignancies
Collection information	
Frequency of Testing	Minimum repeat interval two weeks.
Links to further information	**BPAC** www.bpac.org.nz **National Comprehensive Cancer Network** www.nccn.org **European Group on Tumour Markers** www.egtm.eu
References	1. www.bmj.com/contents/339/bmj.b3527 Clinical Review Serum tumour markers: how to order and interpret them CM Sturgeon, LC Lai, MJ Duffy 2. Duffy MJ et al Tumor Markers in pancreatic cancer: A European Group on Tumor Markers (EGTM) status report. Ann Onc 2010;21:441-447

TEST NAME	CA 72-4	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Cancer Antigen 72-4	VERSION	12.1	DATE	1 February 2012

CATEGORY	NOT FUNDED
REFERRAL CRITERIA	Not applicable

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	CA 72-4 is raised in a wide range of malignancies and in many non malignant disorders. However it is not recommended as a useful marker in any of the guidelines issued by NACB, ETMG, NCCN or ESMO. It has not so far been proven to be superior to the established markers such as CEA, CA 125, CA 15-3 and CA 19-9 in patient follow up. Like other tumour markers it is not suitable to be used as a screening test or in confirming diagnosis, and does not appear to offer any useful prognostic information. On current evidence there is no role for this marker in routine clinical practice.
Indications / referral criteria	None. This tumour marker should only be provided in the setting of a controlled clinical trial.
Collection information	N/A
Frequency of Testing	N/A
Links to further information	**BPAC** www.bpac.org.nz **National Comprehensive Cancer Network** www.nccn.org **European Group on Tumour Markers** www.egtm.eu
References	

TEST NAME	CEA	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Carcinoembryonic Antigen	VERSION	12.1	DATE	1 February 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	CEA is elevated in patients with a wide range of malignancies including colorectal, gastric, pancreatic, lung, breast, and medullary thyroid cancer. It is also elevated in non malignant disorders such as ulcerative colitis, pancreatitis, cirrhosis, pleural inflammation, chronic renal failure and in smokers. It is most widely used in monitoring colorectal cancer (CRC) but is not sufficiently sensitive to be used in screening and not selective enough to be used in diagnosis. It may provide prognostic information in CRC. The European Group on Tumor Markers also advise CEA as an adjunct to CA 15-3 in Breast cancer monitoring.
Indications / referral criteria	**INDICATED FOR:** – Patients with symptoms or signs associated with high suspicion of CRC - Intermittent abdominal pain, nausea, vomiting or bleeding; palpable abdominal mass. – At diagnosis of CRC (to provide prognostic information) – After treatment of CRC (to monitor response and detect relapse) – In some cases of breast cancer to monitor response after treatment and detect relapse **IT IS NOT INDICATED FOR:** – Screening – Investigation of non specific symptoms, when probability of malignancy is low – Investigation of other suspected malignancies
Collection information	
Frequency of Testing	Minimum repeat interval two weeks.
Links to further information	**BPAC** www.bpac.org.nz **National Comprehensive Cancer Network** www.nccn.org **European Group on Tumor Markers** www.egtm.eu
References	1. www.bmj.com/contents/339/bmj.b3527 Clinical Review Serum tumour markers: how to order and interpret them CM Sturgeon, LC Lai, MJ Duffy 2. Sturgeon CM et al. National Academy of Clinical Biochemistry laboratory medicine guidelines for use of tumor markers in testicular, prostate, colorectal, breast and ovarian cancers. Clin Chem 2008;54(12):11-79 3. Molina R et al. Tumor Markers in Breast Cancer - European Group on Tumor Markers Recommendations Tumor Biol 2005;26:281-293.

TEST NAME	Chronic Lymphocytic Leukaemia (CLL) testing	CODE		OWNER	Chair, Haematology Laboratory Schedule Subgroup
OTHER NAMES	Chronic Lymphoid Leukaemia testing	VERSION	12.1	DATE	10 June 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Early B cell lymphocytic leukaemia is the most common type of adult leukaemia. It mainly affects those aged over 50 (median 65 years) and is asymptomatic in the early stages with the only feature being a peripheral lymphocytosis. **Diagnosis** Consider CLL or other lymphoproliferative disorders if persistent lymphocytosis of >5 for more than 3months. 1. *Discuss with a haematologist* if cell marker studies are required for persistent unexplained lymphocytosis. 2. *Refer to the Haematology Outpatients Department* if the referral criteria below are met. Otherwise regular monitoring in general practice is indicated.
Indications / referral criteria	***Treatment is not offered to CLL patients unless there is evidence of advanced or progressive disease. General practitioners can manage patients with early stage CLL by reviewing regularly (3-6 monthly). Consider referral for Haematology assessment if the patient:*** – is young (<55 years) with progressive disease as they may be candidates for innovative treatment strategies e.g. bone marrow transplant. – has significant symptoms e.g. night sweats, significant weight loss, extreme fatigue after excluding other causes such as infection. – develops Binet Stage B or C disease (or Rai Stage II or III) ○ Stage A (0-I)– 0-2 areas of organ enlargement – prognosis is >12+ years ○ Stage B(II) – 3-5 areas of organ enlargement – prognosis is 7 years ○ Stage C (III-IV)– HB <100 g/L, or platelets <100 x 10^9/L (unless due to immune mechanisms) – prognosis is 2 years – has disfiguring lymphadenopathy or hepatosplenomegaly – has recurrent infections – develops haemolytic anaemia OR - the lymphocyte count doubles in less than 6 months and is greater than 30x109/L.
Collection information	**Laboratory testing** a. Cell marker studies (immunophenotyping) of peripheral blood lymphocytes using a CLL/Lymphoproliferative panel, if referral

	criteria are met. This will confirm that a lymphoproliferative disorder is present and define the subtype. b. Direct Coombs test c. Immunoglobulins Bone marrow examination is not usually necessary.
Frequency of Testing	**Follow up / Monitoring** 1. Assess six monthly for the first year, then yearly if stable or slow, asymptomatic progression. 2. Arrange yearly bloods with a CBC. The rise of WBCs is less important than the development of any cytopenias, night sweats or weight loss. (The absolute lymphocyte count can rise to >200 x 10^9 /L, and is not a reason in itself to start treatment). 3. Ask about a history of infections, weight loss, fatigue, night sweats, enlarged lymph nodes. 4. Check weight and examine for lymphadenopathy and hepatosplenomegaly. 5. Offer and recall for annual flu vaccination. 6. Consider pneumovax if the patient has a co-existent chronic respiratory disorder. 7. Serum immunoglobulins undertaken if there are recurrent infections 8. Educate about presenting early if there is any infection, including shingles. 9. Consider other malignancies as CLL patients have an increased risk. Non-melanoma skin cancers can progress rapidly. Consider age-appropriate screening for breast, prostate and colon cancer, and offer smoking cessation advice.
Links to further information	
References	1. Chronic Lymphocytic Leukaemia Primary Care Management Guideline, Waikato DHB. 2. B-Cell Chronic Lymphocytic Leukaemia Health Pathway, Canterbury DHB.

TEST NAME	CoQ10	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Coenzyme Q10	VERSION	12.1	DATE	9 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Cardiologist - Neurologist - Paediatrician OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	The primary value of CoQ10 measurement is for the investigation of inborn metabolic errors, where there may be primary CoQ10 deficiency. This includes patients with suspected mitochondrial disorders, especially with features of encephalopathy or nephritic syndrome. This test has also been suggested to be useful for the following situations: a) Statin-induced myopathy b) Cardiac failure c) Parkinsons disease However, the evidence for a benefit of measuring CoQ10 in these conditions is preliminary and the clinical usefulness of this test will depend upon the emergence of further evidence. The use of CoQ10 in chronic fatigue syndrome is not evidence-based.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Ogasahara S, Engel AG, Frens D, Mack D. Muscle coenzyme Q deficiency in familial mitochondrial encephalomyopathy. Proc Natl Acad Sci U S A 1989;86:2379-82. 2. Rötig A, Appelkvist E-L, Geromel V, et al. Quinone-responsive multiple respiratory-chain dysfunction due to widespread coenzyme Q10 deficiency. Lancet 2000;356:391-5. 3. Molyneux SL, Young JM, Florkowski CM, Lever M, George PM. Coenzyme Q10: is there a clinical role and a case for measurement? Clin Biochem Rev 2008; 29(2):71-82.

TEST NAME	Cortisol-binding globulin	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	CBG	VERSION	12.1	DATE	9 January 2012

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: - Endocrinologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Total, rather than free, cortisol is measured when assessing adrenal status. Cortisol levels can therefore be influenced by the serum concentration of cortisol binding globulin (CBG). However, there are very few indications for measuring levels of CBG itself.
Indications / referral criteria	This test is only indicated in very rare situations where cortisol levels are anomalous or unexplained.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Cortisol, urinary free	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Urinary free cortisol (UFC)	VERSION	12.1	DATE	9 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	**Indicated** The only established clinical indication for the UFC test is in the diagnosis of Cushing's syndrome. UFC is not regarded as a useful test for diagnosing primary or secondary hypoadrenalism. **Not Indicated** Many requests for UFC are made in the belief that adrenal insufficiency is a cause for chronic fatigue syndrome (CFS), and are being used to justify prescription of hydrocortisone therapy. The use of hydrocortisone in CFS is not supported by RCT evidence [1, 2], and both UK[3] and Australasian guidelines[4] specifically state that hydrocortisone should not be used in CFS. Urine cortisol testing does not help identify CFS patients who are more likely to respond to hydrocortisone.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Van Den Eede F, Moorkens G, Van Houdenhove B et al. Hypothalamic-pituitary-adrenal axis function in chronic fatigue syndrome. Neuropsychobiology. 2007;55:112-120. 2. Blockmans D, Persoons P, Van Houdenhove B et al. Combination therapy with hydrocortisone and fludrocortisone does not improve symptoms in chronic fatigue syndrome: a randomized, placebo-controlled, double-blind, crossover study. Am J Med. 2003;114:736-741. 3. NICE clinical guideline 53. Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): diagnosis and management of CFS/ME in adults and children. National Institute for Health and Clinical Excellence. www.nice.org.uk. 2007. 4. Chronic fatigue syndrome. Clinical practice guidelines--2002. Med J Aust. 2002;176 Suppl:S23-56.

TEST NAME	Cortisol, saliva	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	27 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Salivary cortisol shows a similar diurnal cycle to plasma cortisol, with a peak on waking, and a trough at bedtime. In Cushing's syndrome, the bedtime salivary cortisol is typically increased due to loss of diurnal variation in cortisol secretion, and this is a useful screening test. The reference ranges and clinical value of salivary cortisol levels taken at other times are not established.
Indications / referral criteria	Screening for Cushings syndrome is the only established indication for this test.
Collection information	Only bedtime samples are acceptable.
Frequency of Testing	
Links to further information	
References	1. Papanicolau DA, Mullen N, Kyrou I. Night-time salivary cortisol: a useful test for the diagnosis of Cushing's syndrome. J Clin Endocrinol Metab 2002; 87: 4515-4521. 2. Raff H, Raff JL, Findling JW. Late-night salivary cortisol as a screening test for Cushing's syndrome. J Clin Endocrinol Metab 1998:83;2681-2686.

TEST NAME	C-peptide	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	27 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Internal medicine specialist - Paediatrician - Endocrinologist - Bariatric surgeon - Specialist lipid, metabolic or cardiovascular disease clinic OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	C-peptide (plasma or urine) measurement may be useful in determining whether hypoglycaemia is due to an insulinoma, exogenous insulin administration, or other cause. It may also be useful in classifying some indeterminate cases of diabetes, where there is uncertainty as to whether it is type 1 or type 2. Clinical utility of C-peptide for assessing insulin resistance is limited and it is not recommended for this purpose.
Indications / referral criteria	For investigation of insulinoma (for proper interpretation plasma glucose and insulin should always be collected simultaneously)
Collection information	Fasting status (time since last meal) should be defined. Serum glucose needs to be ordered concomitantly. For evaluation of insulinoma the sample should be taken during a spontaneous hypoglycaemic attack or a controlled fast, preferably under close supervision. Correlation with symptoms is critical.
Frequency of Testing	
Links to further information	
References	

TEST NAME	Creatine kinase - MB	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	CK-MB	VERSION	12.1	DATE	24 August 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Cardiologist - Internal medicine specialist OR prior approval by a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	CK-MB is an isoform of creatine kinase (CK). It is present in highest concentration in heart muscle, but is also widely distributed in skeletal muscle at lower concentrations. CKMB was the diagnostic test of choice for myocardial infarction prior to the wide availability of troponin tests. However, cardiac troponin tests (TnT or TnI) are far more sensitive and specific for myocardial injury. The 2000 Consensus definition of myocardial infarction, updated in 2007[1], identified the key diagnostic importance of a biochemical marker (rise and/or fall) in the appropriate clinical context in the large majority of situations. While CKMB was acceptable at that time, the guideline specifically stated that troponin testing (T or I) was preferred, where available. The continued improvement in sensitivity of troponin assays has enabled greater sensitivity and earlier detection of myocardial injury, generally before CKMB is increased. Troponin is also raised for much longer than CKMB after acute myocardial injury, enabling a much longer diagnostic window for up to 10-14 days post M.I. Troponin testing is now routine in New Zealand laboratories and the 2012 New Zealand Cardiac Society guidelines for management of patients presenting with symptoms of acute myocardial ischaemia in the previous 24 hours recommend troponin (T or I) as the marker of choice. They also recommend that CKMB no longer be measured.[2] CKMB has been advocated as giving a measure of infarct size, but repeated measurement (to gain an 'area under the time curve') is required. The magnitude of troponin elevation correlates consistently with the risk of death and the composite risk of death or nonfatal MI[3]. Troponin levels have been shown to be more powerful prognostic indicators than CKMB levels[4]. CKMB has also been suggested as helpful in identifying the occurrence of reinfarction in a patient with onset of new symptoms, signs or ECG changes. However, levels parallel troponin in most settings and total CK can also be measured in an inpatient coronary care setting[5]. CKMB may potentially be useful where a troponin result is considered unreliable (e.g. due to assay interferences), but an alternative troponin assay (e.g. TnI instead of TnT, or different TnI assay) can almost always be used instead when in doubt. Other diagnostic modalities (e.g. cardiac perfusion scintigraphy) can

	also be used to aid the diagnosis.
Indications / referral criteria	As per discretion of cardiologist
Collection information	Fasting is not necessary
Frequency of Testing	
Links to further information	
References	1. Thygesen K, Alpert JS, White HD, on behalf of the Joint ESC/ ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. Circulation. 2007;116(22):2634-2653. 2. Non ST-Elevation Acute Coronary Syndrome Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand. New Zealand 2012 guidelines for the management of non-ST elevation acute coronary syndromes. http://journal.nzma.org.nz/journal/125-1357/5245/ 3. Newby LK, et al. Value of serial troponin T measures for early and late risk stratification in patients with acute coronary syndromes. Circulation 1998;98:1853–1859. 4. Panteghini M, et al. Single-point cardiac troponin T at coronary care unit discharge after myocardial infarction correlates with infarct size and ejection fraction. Clin Chem. 2002;48(9):1432-1436. 5. Apple FS, Murakami MM. Cardiac troponin and creatine kinase MB monitoring during in-hospital myocardial reinfarction. Clin Chem. 2005;51(2):460-463.

TEST NAME	DHEAS	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Dehydroepiandrosterone Sulphate	VERSION	12.1	DATE	9 January 2012

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: - Endocrinologist - Paediatrician - O&G specialist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	DHEAS is an androgenic steroid, mainly of adrenal origin. Its main diagnostic use is to exclude an adrenal tumour in the investigation of hirsutism, virilisation or hyperandrogenism in women[1]. Minor elevations of DHEAS are common in polycystic ovary syndrome and idiopathic hirsutism, but its measurement is of little diagnostic value in these conditions. In this context the key androgen to measure is testosterone and a normal testosterone level effectively excludes an adrenal tumour. DHEAS is also used in the investigation of ambiguous genitalia and congenital adrenal hyperplasia, and may be helpful in differentiating between different types of Cushing's syndrome and in the evaluation of the HPA axis.[2] DHEAS levels peak in early adulthood and decrease thereafter. This has led to the concept of DHEAS 'deficiency' or 'andropause' in the middle-aged and elderly, which is promoted by manufacturers of DHEA supplements and alternative medicine practitioners. There is no good evidence that a low DHEAS level constitutes a deficiency state, or that DHEA supplementation has any benefits, except in patients with proven adrenal insufficiency (Addison's disease or hypopituitarism).
Indications / referral criteria	This test is indicated in the following: - Investigation of ambiguous genitalia or congenital adrenal hyperplasia - Females with high testosterone level - A suspected adrenal tumour with symptoms such as rapid onset of hirsuitism and hyperandrogenism Requests should provide the appropriate clinical indications for the test.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Martin KA, Chang RJ, Ehrmann DA et al. Evaluation and treatment of hirsutism in premenopausal women: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2008;93:1105-1120. 2. Fischli S, Jenni S, Allemann S et al. Dehydroepiandrosterone sulfate in the assessment of the hypothalamic-pituitary-adrenal axis. J Clin Endocrinol Metab. 2008;93:539-542.

TEST NAME	Dihydrotestosterone	CODE		OWNER	Chair, Chemical Laboratory Schedule Subgroup
OTHER NAMES	DHT	VERSION	12.1	DATE	9 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Endocrinologist - Paediatrician - O&G specialist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	Measurement of DHT is used to diagnose 5-alpha-reductase deficiency and is only indicated in the investigation of ambiguous genitalia and sometimes lack of pubertal development. It has no role in the management of hirsutism or sexual dysfunction.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	ESR	CODE		OWNER	Chair, Haematology Laboratory Schedule Subgroup
OTHER NAMES	Erythrocyte Sedimentation Rate	VERSION	12.1	DATE	1 August 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	The ESR has a longstanding use in clinical medicine but has significant limitations in terms of measurement accuracy. In addition it is affected by numerous physiological variables and by factors other than inflammation such as haemoglobin and plasma protein levels.
Indications / referral criteria	The ESR may have some advantages in the assessment of the following conditions: – Systemic lupus erythematosis; – Rheumatoid arthritis; – Kawasaki Disease; – Rheumatic fever; – Hodgkin lymphoma; – Temporal arteritis; – Inflammatory bowel disease in children (initial assessment). The ESR should not be used to screen for plasma cell dyscrasias; if these conditions are suspected, protein electrophoresis and/or serum free light chains should be used. The CRP is the preferred investigation for the assessment of possible inflammatory or infective disorders. It is seldom appropriate for both an ESR and CRP to be performed on the same sample.
Collection information	An ESR cannot be performed if the sample is older than 12 hours.
Frequency of Testing	
Links to further information	
References	

TEST NAME	Essential Fatty Acids	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	30 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: – Specialist metabolic paediatrician – Paediatric gastroenterologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Testing for Essential Fatty Acids includes the differentiation of: Linoleic acid, oleic acid, stearic acid, arachidonic acid (AA), omega 6, omega 3, omega 9, docosapentaenoic acid, docosahexaenoic acid, and eicopentaenoic acid (EPA). This needs to be clearly differentiated from requests for determination of total free fatty acids or very long chain fatty acids (C24:0/C22:0 or C26:0/C22:0 ratios) which are of value in the diagnosis of peroxisomal biogenesis or beta-oxidation disorders.
Indications / referral criteria	– Essential Fatty Acids may reflect recent dietary intakes, although has not been conclusively demonstrated to leverage clinically important management decisions that other more accessible dietary data cannot influence. – The AA/EPA ratio has been promoted as indication of "cellular inflammation", although this is not evidence based. – In some instances it may be helpful to know essential fatty acid profiles when investigating inborn errors of metabolism or following hepatic transplantation, or in managing paediatric cholestatic liver disease or intestinal failure.
Collection information	
Frequency of Testing	N/A
Links to further information	
References	

TEST NAME	Faecal calprotectin	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	30 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Faecal calprotectin is a marker of intestinal mucosal inflammation that can be useful in differentiating between irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) in symptomatic patients. In IBD, levels correlate with disease activity and a concentration <50 µg/g is considered to be a good negative predictor (published negative predictive values 70-90%) and to help triage patients for colonoscopy. For patients with known inflammatory bowel disease in remission, faecal calprotectin >50 µg/g is associated with an increased risk of relapse over the next 12 months.
Indications / referral criteria	In patients presenting with diarrhoea, first line tests to exclude pathology may include CBC, CRP, ferritin, tTG, TFTs, stool culture and ova and parasites if travel history. Faecal calprotectin is a second line investigation if there is a concern about possible inflammatory bowel disease, although may be a first line investigation if there is a family history of IBD. It may be particularly helpful in paediatric IBD when other investigations may be normal. In the presence of "red flags" (e.g. unexplained iron deficiency anaemia, rectal bleeding, weight loss or family history of colon cancer), faecal calprotectin testing may incur unnecessary delay in referral to a gastroenterologist and especially where there is likely consideration for colonoscopy.
Collection information	
Frequency of Testing	
Links to further information	http://www.bpac.org.nz/resources/bt/2010/03_ibs.asp http://www.alphalabs.co.uk/asp/db/documents/cep09026_Calprotectin%20Evidence_Jan10.pdf Summary of evidence from NHS Centre for Evidence Based Purchasing
References	1. Van Rheenen PF et al. Faecal calprotectin for screening of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. BMJ 2010; 341:c3369.

TEST NAME	Free T3	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	FT3	VERSION	12.1	DATE	10 January 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	TSH is the most biologically sensitive and useful marker of both hypo- and hyperthyroidism, and is recommended as the first line test for evaluation of thyroid function in the large majority of situations. Free T3 rises early in hyperthyroidism, but free T4 is also usually elevated and TSH is almost always below reference limits (except in very early cases and very rare situations such as TSH producing tumours). Free T3 only falls late in hypothyroidism and is an insensitive marker. It is also often affected (sometimes acutely) by factors such as illness and fasting. Free T3 measurement is useful only in specific clinical settings: 1. Evaluation of possible or established hyperthyroidism. It can identify the severity and also patients with low TSH but FT4 within reference limits (either 'T3 toxicosis' or early recurrence) 2. Monitoring of patients on thyroid replacement in two specific circumstances (measurement is not indicated in the context of replacement for other reasons except by approval of an endocrinologist or chemical pathologist): – patients with hypopituitarism, sometimes as an adjunct to measurement of free T4 (especially in the setting of growth hormone deficiency). TSH is typically unreliable in such patients. – sometimes in the monitoring of patients on suppressive treatment for thyroid cancer 3. Rare clinical settings of TSH secreting pituitary tumours or defects in thyroid hormone metabolism or action (e.g. congenital deiodinase deficiency, thyroid hormone resistance)
Indications / referral criteria	- Clinical details of hyperthyroidism (possible or known) OR hypopituitarism OR thyroid cancer - Other tests by prior approval of an endocrinologist or chemical pathologist
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Fructosamine	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	1 February 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Fructosamine is a measure of glycated protein, mainly glycated albumin. Historically fructosamine has been used as a measure of short to medium glycaemic control [previous 10-20 days] in subjects with diabetes. In particular it had a use in monitoring glycaemic control in pregnancy in those women with either established or gestational diabetes. The advent of high quality measurement of haemoglobin A1c for general assessment of glycaemic control and the use of intensive home monitoring of blood glucose for directing treatment [especially in diabetic pregnancy] means that there is now no routine indication for fructosamine. A further disadvantage of the test is that results have no clear linkage to long term complications of diabetes nor does it have a role in diagnosis of diabetes. It is now not offered by most laboratories. The only recognised use is when HbA1c is invalid and an indication of glycaemic control is required.
Indications / referral criteria	Fructosamine should be measured when there is clear evidence that HbA1c is invalid. In general this will require evidence of an interfering haemoglobinopathy or condition in which red cell turnover is shortened.
Collection information	
Frequency of Testing	No more than monthly testing.
Links to further information	
References	

TEST NAME	Growth Hormone	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	16 July 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	GPs may order this test when there is a clinical suspicion of acromegaly. However, IGF-1 is a much better first line screen and is recommended as the first choice.
Indications / referral criteria	**INDICATED FOR:** 1. Known or suspected acromegaly 1. Pituitary disease or short stature in children 2. Suspected GH deficiency in adults with known pituitary disease. **NOT INDICATED FOR:** Fatigue or routine screening are *not* valid indications for testing.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Haemoglobinopathy Investigations	CODE		OWNER	Chair, Haematology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	1 February 2012

CATEGORY	**Tier One Test**
REFERRAL CRITERIA	**Not available - Discussion with a Haematologist is recommended.**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Currently no formal haemoglobinopathy screening is undertaken in New Zealand. Investigations are undertaken on an ad hoc basis for: 1. Investigation of hypochromic microcytic blood pattern when iron deficiency has been excluded. 2. High risk ethnic groups. 3. Follow-up of family studies. 4. Investigation of abnormal haemoglobins during other investigation e.g. haemoglobin A1C screening for diabetes. The most clinically significant haemoglobinopathies/thalassaemias are sickle cell disease, beta thalassaemia and alpha thalassaemia ('Cis' inheritance pattern).
Indications / referral criteria	Investigation is indicated for: – Urgent pre-operative screening for sickle cell disease in appropriate ethnic groups. – Antenatal screening of an unexplained blood pattern, or a family history of thalassaemia. – People with an unexplained hypochromic microcytic blood pattern when iron deficiency has been excluded, especially in women of child bearing age. – Partners / spouses of affected women planning a pregnancy or very early in pregnancy
Collection information	
Frequency of Testing	Once only[1].
Links to further information	GHSNZ – Genetic Health Service NZ www.genetichealthservice.org.nz
References	1. Family Origin Questionnaire *British Journal of Haematology* 149 35-49. 2. *Blood Reviews*, Barbara Bain 25 (2011) 205-213. 3. Significant Haemoglobinopathies: Guidelines for Screening and Diagnosis. Kate Ryan et el. *British Journal of Haematology* 149,p 35-49, 2010.

[1] The test may be repeated if the result is not accessible or available.

TEST NAME	Hepatitis testing (viral)	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	26 April 2012

CATEGORY	Tier One and Two Test (depending on the test)
REFERRAL CRITERIA	Referral criteria available for some tests

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	There have been a number of developments that are starting to have a wider impact on primary and secondary care. The starting point is always serology and measurement of transaminases, which provide most of the information required to identify and diagnose viral hepatitis, but molecular tests for viral nucleic acid are central to the active management of hepatitis B and C. There is a new standard of care around identifying pregnant women with high HBV viral loads, in whom antiviral therapy is now recommended to reduce transmission to the newborn.
Indications / referral criteria	**Serological diagnosis** ***Hepatitis A and E*** These are the simplest to diagnose: the IgM is almost always positive at the time the transaminases are raised. The IgG is used to determine immunity, or to show seroconversion if the IgM results are inconclusive. Both are self-limited disease which can be serious in adults, but children are usually asymptomatic. They occur as a result of contact overseas, and in local outbreaks. ***Hepatitis B*** HBsAg is present in almost all actively infected persons with HBV and is the first test that should be requested if HBV infection is suspected. All who are positive should have a care and monitoring plan developed, particularly women who are pregnant or about to become so. The surface antibody is a test that should really only be ordered for adults in occupational health settings, preferably within a few months of the final dose of vaccine: those who develop a clear response will be protected for life. The e antigen predicts high titres of virus, but its absence does not exclude high viral loads, especially in adults who were infected in childhood. See **Hepatatis B in pregnancy** (below). ***Hepatitis C*** Anti-HCV antibody is present in almost all those infected with HCV, but depending on the age and sex at acquisition, only 70-80% will have active viral replication. Like HIV, the antibodies are non neutralising, ie do not control infection.

Managing the patient

Persons with chronic HBV and HCV are usually asymptomatic until the ongoing liver inflammation results in fibrosis, cirrhosis, hepatic failure or hepatocellular carcinoma. There are large numbers (up to 8% in some Pacific Peoples) of either undiagnosed or diagnosed, but not followed, persons in the community. It is essential to monitor and/or treat to prevent these severe outcomes. The Hepatitis Foundation provides a great deal of help with monitoring and motivating patients with chronic viral hepatitis.

Hepatitis B

Hepatitis B is a very complicated condition and thoughts regarding ideal management are constantly changing. Spontaneous or treatment-induced clearance of virus is uncommon, so the expectation is that long term follow-up and treatment will be required, unless interferon-based therapy is used. Unfortunately, many of those infected with viral hepatitis have financial and other barriers to accessing health care.

The highest priority patients for referral to specialists (gastroenterology or infectious diseases) are those with raised ALT, especially if over the age of 45. HBV DNA measurement is an essential part of assessment and management:

- To assess risk of progression and eligibility for antiviral treatment (risk increases from 10^4IU/ml)
- To assess treatment adherence and monitor development of resistance (usually 3-6 monthly on treatment)
- To identify mothers who should receive antiviral therapy in the second and third trimesters of pregnancy (if > 10^7IU/l)

Hepatitis B in pregnancy

As described in the PHARMAC schedule and the 2011 Immunisation Handbook, pregnant women who are surface antigen-positive should have their HBV viral load measured in the first trimester. Those with high viral loads may still transmit the infection to the baby (usually prenatally) despite neonatal immunoglobulin and vaccination. The rate of transmission with viral loads > 10^8IU/ml is over 5%, and is dramatically reduced with the use of antiviral therapy in pregnancy.

The PHARMAC schedule is somewhat ambiguous, so it would be wise to discuss all HBsAg-positive pregnant women with a gastroenterologist or infectious diseases physician.

Babies born to HBsAg-positive mothers are a special group and should be tested at 5 months of age (along with HBsAg) to ensure that they are protected and have not become infected after delivery and neonatal immunisation.

Hepatitis C

In contrast to HBV, HCV the aim of treatment is to cure rather than control. There is a state of flux around treatment of HCV, with several new drugs in the pipeline, but it is not possible to identify when they will be available and funded in NZ. The new direct acting antivirals appear to have either fewer side effects or higher rates of cure than interferon-ribavirin.

The current emphasis is to identify and refer patients with raised ALT who are keen to engage in treatment. It is likely that the new expensive drugs will be only available for patients with gentoypes 1 and 4, which do not respond so well

	to current regimens. This means a viral load test is needed to identify actively infected patients, and once referred, engaged patients will have a genotype test so that those with the favourable genotypes 2 and 3 can be treated sooner rather than later. Those with higher risk of liver fibrosis (older, with longer duration of infection) should also be actively considered for referral. No matter what genotype, once on treatment, the viral load is used to identify those doing well and those who are not responding. In practice this means serial viral load measurements at 4 and 12 weeks, and a test of cure after stopping therapy. **Other tests used in the advanced management of viral hepatitis** – Liver biopsy: still recommended in many cases of HBV to determine need for therapy, and to determine if treatment can be delayed in HCV – Fibroscan: used to avoid liver biopsy when there are clear results, but not available in the region yet – Ultrasound: mainly used to detect portal hypertension and hepatocellular carcinoma, and to guide liver biopsy – IL28B gene polymorphisms: to identify people more likely to respond to interferon in HCV therapy – Alpha fetoprotein: used to monitor and detect hepatocellular carcinoma in those with liver fibrosis **Summary** – Clinicians should be looking to particularly identify patients with raised LFTs due to chronic viral hepatitis. – All HBsAg-positive pregnant women should have their HBV viral load measured. – There is somewhat of a hiatus in treating HCV infection, pending the availability of newer agents, but all HCV PCR-positive patients should be referred to a specialist for assessment and planning. – Many HBsAg-positive patients are not being properly followed up or referred, and stand the risk of developing preventable liver disease.
Collection information	
Frequency of Testing	
Links to further information	The Hepatitis Foundation http://www.hepfoundation.org.nz/
References	1. PHARMAC schedule http://www.pharmac.govt.nz/2011/12/01/SA1047.pdf 2. Immunisation Handbook, 2011 http://www.health.govt.nz/publication/immunisation-handbook-2011 3. Hepatitis B management guidelines http://www.nzsg.org.nz/uploads///Documents/HepBClinical.pdf

TEST NAME	Hepatitis C confirmatory immunoblot	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 February 2012

CATEGORY	NOT FUNDED
REFERRAL CRITERIA	Not applicable

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	Hepatitis C immunoblots are no longer recommended for the serological confirmation of hepatitis C exposure or infection. This is because it is an expensive test which does not determine the infectious state of the individual. Recommended algorithms include a screening EIA, with the option to perform a second EIA on low level positive/indeterminate results. NAAT testing (RT-PCR) to detect RNA in selected patients may be used to select patients for referral or to determine infectivity.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Homocysteine	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: – Specialist lipid, metabolic or cardiovascular disease clinic - Paediatrician - Cardiologist - Vascular surgeon - Haematologist - Ophthalmologist - Neurologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Classical Homocystinuria is a rare genetic condition associated with premature vascular disease, lens dislocation, and very high homocysteine levels (> 50 umol/L). Plasma homocysteine may be elevated in vitamin B12 or folate deficiency, or genetic defects of B12 or folate metabolic pathways. In the general population, raised homocysteine levels are associated with increased risk of cardiovascular disease and stroke. However, homocysteine-lowering interventions (e.g. folate and vitamin B6 supplementation) do **not** modify cardiovascular risk, despite the fact that they lower homocysteine levels.[1,2] This suggests that homocysteine does not have a causative role in vascular disease. Routine homocysteine testing is not recommended as part of cardiovascular risk assessment.[3]
Indications / referral criteria	The test is indicated for the diagnosis of genetic classical homocystinuria. Clinical details should state "?homocystinuria", "premature vascular disease", "thrombophilia", "thrombotic tendency" or similar.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Marti-Carvajal AJ, Sola I, Lathyris D, Salanti G. Homocysteine lowering interventions for preventing cardiovascular events. Cochrane Database Syst Rev. 2009:CD006612. 2. Miller ER, 3rd, Juraschek S, Pastor-Barriuso R et al. Meta-analysis of folic acid supplementation trials on risk of cardiovascular disease and risk interaction with baseline homocysteine levels. Am J Cardiol;106:517-527. 3. Assessing cardiovascular risk: what the experts think. . Best Practice Journal (www.BPAC.org.nz):10-21.

TEST NAME	hs-CRP	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	1 February 2012

CATEGORY	Tier Two Test
	Referred or preauthorised by: - Cardiologist - Internal medicine specialist - Specialist lipid, metabolic or cardiovascular disease clinic OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	High sensitivity CRP [hs-CRP] refers to CRP found in the general asymptomatic population at levels below those traditionally associated with infection or inflammation. There is evidence that these lower levels of CRP have a graded association with cardiovascular risk and may have a use in refining cardiovascular risk assessment. These levels of CRP, mainly in the range 0-5mg/L, are not measured reliably with routine assays and require a special application with high sensitivity. Recently, some routine assays for CRP have been enhanced to allow sensitivity to near 1mg/L but they are not as sensitive or reproducible as the high sensitivity applications. The evidence around cardiovascular risk stratification was not developed with these routine assays and it is not clear if they are valid for this purpose. The original data suggested that levels < 1mg/L are associated with low relative risk for CVD, 1.0-2.9 with intermediate risk and levels > 3mg/L with high risk. Calculators are available which incorporate this data, together with that from traditional risk factors, into calculations of absolute risk. Although there is a reasonable body of epidemiological evidence linking levels of CRP with levels of cardiovascular risk, the more recent data has suggested that the risk is not as strong as originally stated. Nor is there a clear causal link of hs-CRP with cardiovascular disease. No current guideline recommends that it should be used as part of routine risk assessment. It is suggested by some guidelines that measurement of hs-CRP has a use in refining the absolute risk score in people rated at intermediate risk with the traditional risk factors. The American Heart Association suggests that this use be at the physician's discretion, especially in the context of deciding whether or not to prescribe a statin. Very recent data has suggested has suggested that this is not a cost effective strategy. Furthermore, using the value for hs-CRP in the Reynolds modification of the Framingham equation does not change risk sufficiently in those at intermediate risk to enhance the accuracy of the risk prediction. As well, there is heated debate about the validity of the main intervention trial that has been quoted to support the use of stratification by CRP to guide treatment with statins. Neither NZGG nor bpac recommend routine use of hs-CRP in cardiovascular risk assessment.

	The current risk calculator used in New Zealand does not allow data for hs-CRP to be used.
Indications /referral criteria	Very limited indication for use in the context of only some patients at intermediate cardiovascular risk and in whom the decision to use pharmacological treatment may be difficult. Specialist approval required. There is no indication for using this test in low risk subjects or in those already known to be at high risk.
Collection information	
Frequency of Testing	Not indicated for monitoring therapy. Maximum frequency keyed to guidelines for cardiovascular risk assessment. In general this will be at intervals of 1-5 years and the limited indications also apply.
Links to further information	bpac: assessment of cardiovascular risk. http://www.bpac.org.nz/magazine/2010/december/cvra.asp NZGG cardiovascular guideline 2012. http://nzgg.org.nz/library_resources/92_primary_care_handbook
References	1. Lee K, Cipriano L, et al. Cost-effectiveness of using high sensitivity C-Reactive Protein to identify intermediate and low cardiovascular risk individuals for statin therapy. Circulation 2010 122: 1478-1487. 2. Associated editorial – page 1446.

TEST NAME	IGF-1	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	16 July 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Referral criteria available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Medical practitioners working in general practice may order this test when there is a clinical suspicion of acromegaly.
Indications / referral criteria	**INDICATED FOR:** 1. Known or suspected acromegaly 2. Pituitary disease or short stature in children 3. Suspected GH deficiency in adults with known pituitary disease. **NOT INDICATED FOR:** Fatigue or routine screening are *not* valid indications for testing.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	IGF-BP3	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	3 August 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Endocrinologist / Paediatric endocrinologist OR prior approval of a chemical pathologist
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Of the six different binding proteins for IGF-1, IGF-BP3 is the major carrier (about 75%). IGF-BP3 levels are responsive to growth hormone status, being higher in conditions of growth hormone excess and lower in deficiency states. For most clinical indications IGF-1 levels are sufficient as a screening marker for acromegaly and possible growth hormone deficiency. There are few indications for IGF-BP3 measurement. IGF-BP3 is reportedly less influenced by nutritional status and illness than IGF-1 when there is concern over possible growth hormone deficiency, particularly in young children and in the context of other illness. However, other hormones, such as testosterone, estrogen, and thyroxine, also regulate IGFBP-3 synthesis. Deficiency of one or more of these hormones lowers IGF-BP3 levels similarly to IGF-1. Like IGF-1, the reference interval varies by age, sex and pubertal (sex hormone) status. In patients with growth hormone (GH) insensitivity circulating levels of growth hormone are raised whereas IGF-BP3 and IGF-1 levels are low.
Indications / referral criteria	For the evaluation of growth hormone status where IGF-1 results are considered potentially unreliable.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Bhala A, et al. Insulin-like growth factor axis parameters in sick hospitalized neonates. J. Paed. Endocrinol. Metab. 1998 11(3): 451. 2. Hasegawa Y, et al. Comparison between insulin-like growth factor-I (IGF-I) and IGF binding protein-3 (IGFBP-3) measurement in the diagnosis of growth hormone deficiency. Endocr. J. 1993;40(2):185. 3. Nunez SB, et al. Insulin-like growth factor I (IGF-I) and IGF-binding protein-3 concentrations compared to stimulated and night growth hormone in the evaluation of short children--a clinical research center study. J Clin Endocrinol Metab. 1996;81(5):1927.

TEST NAME	IgG - Testing for IgG antibodies in infants under 12 months	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 February 2012

CATEGORY	Tier One and Tier Two Test
	Medical practitioners working in general practice may order a post-vaccination Hepatitis B antibody / antigen test of infants born to surface antigen positive mothers. A paediatrician must refer for all other antibody testing.
REFERRAL CRITERIA	**Aside from post-vaccination Hepatitis B antibody / antigen tests of infants born to surface antigen positive mothers, the requirement for the test is determined by the specialist referrer.**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	Serological testing of children under the age of 18 months is difficult because of passive acquisition of maternal IgG class antibodies. If testing is indicated, it is preferred to test the mother, from whom it will be easier to obtain blood. For these reasons only requests by paediatricians (preferably before blood collection) for serological testing of children is indicated. The exception to this rule is post-vaccination testing for hepatitis B antibody and antigen of infants born to surface antigen positive mothers at age 5 months.
Collection information	
Frequency of Testing	N/A
Links to further information	
References	1. Ministry of Health (2011) Immunisation Handbook, pp96-99.

TEST NAME	Infectious Diarrhoea - investigation	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	11 September 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE /SUPPORTING INFORMATION	
Overview	Diarrhoea is an increase in the number of stools passed in a day but also relates to a change in consistency of stools. (They take on the shape of the container in which they are placed). Specific investigations are not routinely required in the majority of patients with acute diarrhoea i.e. up to 14 days duration. Enteric pathogens may not be amenable to treatment, however in some situations they pose a public health risk.
Indications / referral criteria	A laboratory diagnosis is useful for people who: - may have an infection that could benefit from specific therapy; - are at risk of severe complications e.g. have intestinal failure and short bowel syndrome[2]; - are at risk of spreading infection; or - are involved in an outbreak and may have a common source of infection.
Collection information	Refer to: Table 1 (below) – What samples are required? Table 2 (below) – Tests to request for specific risk factors
Frequency of Testing	None of the tests are 100% sensitive. A repeat test is justified if a particular pathogen is suspected, the test is negative, and the patient has on-going symptoms. In this situation, discussing the case with an infectious disease physician / clinical microbiologist is helpful for on-going management.
Links to further information	
References	1. BPAC. 2008. Laboratory Investigation of Infectious Diarrhoea. January.

[2] Prone to enteric infection and bacterial translocation to the blood as a result of intestinal mucosal inflammation and leak. They are very vulnerable if they acquire gut pathogens.

Table 1 – What samples are required?

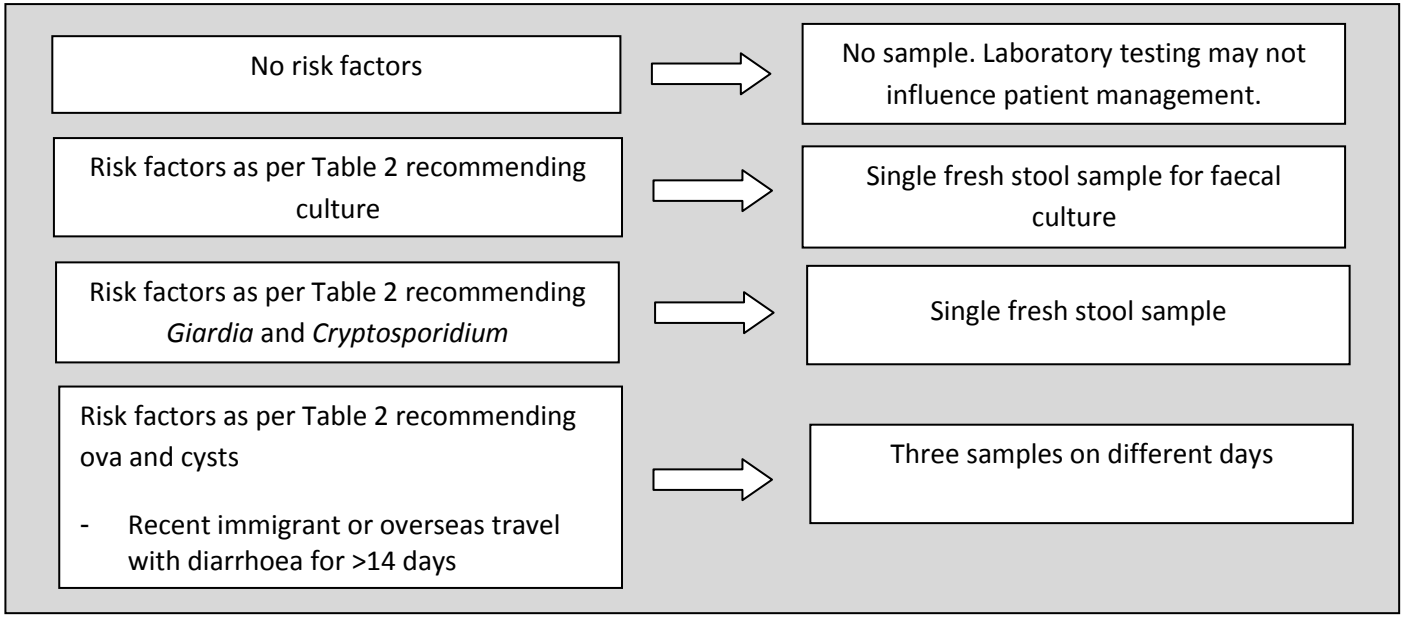

Table 2 – Tests to request for specific risk factors

Risk Factors	What boxes to tick?				Notes
	Culture	Giardia Crypto	Ova and cysts	C. difficile	
	What sample to collect?				
	Fresh stool	Fresh stool	Stool in faecal fixative	Fresh stool	
	Number of samples to collect?				
	Single sample	Single sample	1-3 stool samples	1-3 stool samples	
Diarrhoea, no risk factors	No tests				Manage symptomatically
Food handler	√				
<5 years of age	√				Consider Rotavirus, but testing is not routinely required. Combined tests sometimes include enteric adenovirus
Child care attendance	√	√			
Rural	√	√			
Raw seafood	√				Provide clinical details to the laboratory
Bloody diarrhoea	√				Provide clinical details to the laboratory
Recent antibiotics or chemotherapy				√	
Recent hospitalisation				√	
Age > 70 years	√			√	
Immuno-compromised	√	√	√		
Overseas travel, immigrant	√	√	√		
Persistent diarrhoea	√	√	√		

From BPAC. 2008. Laboratory Investigation of Infectious Diarrhoea. January.
NB When there is an outbreak of acute gastroenteritis, specialists may suggest testing some cases for norovirus infection.

TEST NAME	Iodide (urine)	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	11.1	DATE	13 December 2011

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Endocrinologist - Internal medicine specialist OR prior approval of a chemical pathologist
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Urine iodine levels are highly variable from day to day in a given patient, only reflect recent iodine intake, and have a low predictive value for iodine deficiency.[1,2] The median urine iodide level in a population can be used as an index of iodine status of that population. However, the WHO guidelines for population medians do not apply to individual subjects and will grossly over-diagnose iodine deficiency if misapplied in this way. The most sensitive index of iodine deficiency is a rise in TSH, and the only reliable way to diagnose iodine deficiency in an individual is to demonstrate a raised TSH level which decreases following iodine supplementation. Iodine supplementation, but not testing, is recommended in pregnancy.[3] There is no evidence that routine urine iodide testing leads to any beneficial outcomes in patients who are appropriately monitored for hypothyroidism and appropriately supplemented in pregnancy. Routine urine iodine testing has no established role in general practice.
Indications / referral criteria	– For assessment of iodine status at the time of therapeutic radioiodine administration – As part of the investigation of some cases of mild hyperthyroidism
Collection information	Creatinine should also be measured to determine concentration and (on a 24hr sample) collection adequacy.
Frequency of testing	
Links to further information	
References	1. Davidson, JS. An epidemic of non-existent iodine deficiency due to inappropriate urine iodide testing and reference ranges. N.Z. Med. J. 2009; 122: 109. 2. Rasmussen, LB et al. Day to day and within day variation in urine iodide excretion. Eur. J. Clin. Nutr. 1999; 53: 401-7. **3.** BPAC Guideline. www.bpac.org.nz/magazine/2008/december/pregnancy.asp (2008).

TEST NAME	Insulin	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	11.1	DATE	13 December 2011

CATEGORY	Tier One and Tier Two Test
	Referred or pre-authorised by: - Paediatrician - Endocrinologist - Hepatologist - GI surgeon OR prior approval of a chemical pathologist. Post-bariatric surgery - able to be ordered by other medical practitioners and relevant clinicians if this is stated on the form.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Serum insulin measurement is important in determining whether hypoglycaemia is due to an insulinoma, exogenous insulin administration, or other cause. It may also be useful in classifying some unusual cases of diabetes. Calculation of the HOMA index of insulin resistance may be useful in assessing the probability of non-alcoholic steatohepatitis (NASH) and the need for liver biopsy or bariatric surgery. Clinical utility of fasting insulin for assessing insulin resistance is otherwise limited and it is not recommended for this purpose.
Indications / referral criteria	For investigation of insulinoma (for proper interpretation plasma glucose should always be collected simultaneously).
Collection information	Fasting status (time since last meal) should be defined. Serum glucose needs to be ordered concomitantly. For evaluation of insulinoma the sample should be taken during a spontaneous hypoglycaemic attack or a controlled fast, preferably under close supervision. Correlation with symptoms is critical.
Frequency of Testing	
Links to further information	
References	1. Samaras, K. et al. Insulin levels in insulin resistance; phantom of the metabolic opera? Med. J. Aust. 2006; 185: 159-161.

TEST NAME	Lipoprotein(a)	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: – Specialist lipid, metabolic or cardiovascular disease clinic - Cardiologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Lipoprotein (a) is an atherogenic lipoprotein and is a modest independent risk factor for premature coronary artery disease. It is thought to have pro-thrombotic effects. Lp(a) levels are mainly genetically determined, change little over time, and are poorly responsive to diet or to lipid-lowering drugs.[2] Because Lp(a) levels are difficult to alter, there are no clinical trials that have adequately tested whether Lp(a) reduction reduces the incidence of cardiovascular events. Routine measurement of lipoprotein (a) is not indicated as part of a cardiovascular risk assessment in primary care[1, 2]. If the clinical approach is otherwise clear based on other risk factors, then measuring Lp(a) has little additional value. In borderline cases, where a decision on management is not clear from other risk factors, Lp(a) measurement (once only) may be indicated.
Indications / referral criteria	Repeat testing is not indicated.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Assessing cardiovascular risk: what the experts think. Best Practice Journal (www.BPAC.org.nz):10-21. 2. G.R. Cooper PWFW, G.L. Myers, S.M. Grundy, Labarthe DR. Lipoprotein (a) and Cardiovascular Disease Risk. Emerging Biomarkers for Primary Prevention of Cardiovascular Disease and Stroke. AACC Press, 2009.

TEST NAME	Lipoprotein electrophoresis	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	Lipid EPP	VERSION	12.1	DATE	24 August 2012

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: - Cardiologist - Endocrinologist/metabolic specialist - Internal medicine specialist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Lipoprotein electrophoresis was used historically to classify patients with likely familial dyslipidaemias using the Frederickson classification. Interpretation is based on the staining pattern and intensity of different lipid fractions as they migrate differently: - Chylomicrons - Pre-beta (VLDL, VLDL remnants, IDL) - Beta (LDL) - Alpha (HDL) The Frederickson classification is seldom used nowadays and electrophoresis is seldom needed. There are other clinical and laboratory means of recognising primary lipid disorders (e.g. apolipoprotein measurements, genetic tests). Today the major remaining application of electrophoresis is when considering a possible diagnosis of type III dysbetalipoproteinaemia ('broad beta' or remnant removal disease). Such patients have increased concentrations of apoB-containing remnant particles (VLDL remnants, IDL), and typically have similar molar increases in cholesterol and triglyceride on their routine lipid profile. Lipoprotein electrophoresis may also occasionally be helpful in identifying the presence of chylomicrons which are not in sufficient numbers to be noted as a creamy layer. One such situation is in the evaluation of a possible chylous fistula in a sample of pleural fluid. This will almost always be in an inpatient setting.
Indications / referral criteria	For evaluation of possible genetic disorders as cause of dyslipidaemia, as per discretion of specialist
Collection information	Fasting is usually preferred but not essential
Frequency of Testing	
Links to further information	
References	

TEST NAME	Prostatic acid phosphatase	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	PAP	VERSION	12.1	DATE	24 August 2012

CATEGORY	Tier Two Test
	Referred or pre-authorised by: - Urologist - Internal medicine specialist - Paediatrician - Haematologist OR by prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Prostatic acid phosphatase (PAP) is a lysosomal enzyme and one of the major proteins secreted by prostatic epithelial cells. While phosphatases are widely distributed throughout the body, the prostatic enzyme had optimal activity below pH 7.0, hence its name. The prostate form is also inhibited by tartrate, which can aid in distinguishing it from the other tissue forms. PAP is expressed in >95% of primary prostate adenocarcinomas and stains for PAP are used when identifying prostate as a possible source of an unknown cancer. However, the sensitivity of serum PAP for detecting and diagnosing early prostate cancer is poor compared with PSA, and serum PAP is likely to be raised only in advanced stage disease. PSA is also almost entirely prostate-specific, whereas acid phosphatase is also found in tissues such as bone, liver, erythrocytes and leukocytes. Neither test can completely distinguish between benign and malignant prostate disease. PSA therefore has equal or superior clinical utility compared with PAP in almost all clinical situations for both diagnosis and monitoring. PAP may be helpful in rare prostate cancer patients where the tumour does not secrete PSA and some recent studies have suggested PAP as a prognostic factor in patients with intermediate- and high-risk prostate cancer. However, its value for this purpose is unclear and is currently largely confined to research settings. The US National Academy of Clinical Biochemistry[1], the European Group on Tumor Markers[2], and the Canadian Society of Clinical Chemists[3] all have declined to recommend the use of prostatic acid phosphate, stating that the marker provides no clinical benefit in addition to that of PSA. Tartrate-resistant acid phosphatase is also characteristically raised in Gaucher's disease, and sometimes in other rare storage disorders. It may be used for diagnosis and monitoring in this setting, along with other markers such as angiotensin converting enzyme (ACE) and chitotriosidase.
Indications / referral criteria	As per discretion of specialist
Collection information	Prior arrangement is needed. The sample must be separated promptly. Special preservative tubes are supplied by the Specialist Lab. Samples should NOT be taken after prostate manipulation (including DRE) which may cause false elevation.

Frequency of Testing	
Links to further information	
References	1. Sturgeon CM, et al; National Academy of Clinical Biochemistry. National Academy of Clinical Biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers. Clin Chem. 2008;54(12):e11-e79. 2. Tumour markers in prostate cancer: EGTM recommendations. European Group on Tumour Markers. Anticancer Res. 1999;19(4A):2799- 2801. 3. Bunting PS. Is there still a role for prostatic acid phosphatase? CSCC Position Statement. Canadian Society of Clinical Chemists. Clin Biochem. 1999;32(8):591-594.

TEST NAME	RBC magnesium	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	NOT FUNDED
REFERRAL CRITERIA	Not applicable

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Plasma Mg is adequate for assessment of Mg status for clinical purposes. Evidence linking chronic fatigue syndrome to Mg is unconvincing.[1,2] There is insufficient evidence to justify the additional expense of RBC Mg measurement and insufficient evidence to justify the use of this test for any clinical purpose.
Indications / referral criteria	
Collection information	
Frequency of Testing	
Links to further information	
References	1. Hinds G, Bell NP, McMaster D, McCluskey DR. Normal red cell magnesium concentrations and magnesium loading tests in patients with chronic fatigue syndrome. Ann Clin Biochem. 1994;31 (Pt 5):459-461. 2. Reid SF, Chalder T, Cleare A et al. Chronic fatigue syndrome. Clin Evid (Online). 2008.

TEST NAME	Salivary progesterone	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	NOT FUNDED
REFERRAL CRITERIA	Not applicable

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	There is insufficient evidence to justify the use of this test for any clinical purpose.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Salivary testosterone	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	NOT FUNDED
REFERRAL CRITERIA	Not applicable

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	There is insufficient evidence to justify the use of this test for any clinical purpose.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Serotonin	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	10 January 2012

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: – Endocrinologist – Oncologist – General surgeon – GI surgeon OR prior approval of a chemical pathologist
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Diagnosis and monitoring of carcinoid syndrome constitutes the most important clinical scenario for the assay of blood serotonin (not all enterochromaffin tumours are able to metabolise serotonin to 5-HIAA – a more commonly used marker for carcinoid syndrome). Recent guidelines recommend the use of either 5-HIAA or another marker of enterochromaffin tissue – chromogranin A (CgA)[1]. However, others suggest that the better sensitivity of elevated blood serotonin concentration (particularly those involving the hind gut where 5-HIAA is not produced) make it a useful test for the presence of tumour[2]. As a tumour marker for carcinoid syndrome, blood serotonin concentration may be less useful as the platelet accumulation of serotonin is saturable and blood concentration may not reflect tumour burden. CgA or 5-HIAA may be of more use in these circumstances. It has been suggested that depression may be associated with low CSF levels of some neurotransmitters, including serotonin. There is no convincing evidence for this view. Even less evidence exists implicating low blood levels of serotonin with depressive illnesses[3]. In blood, highest concentrations of serotonin are found in the platelet fraction.
Indications / referral criteria	Tumour marker for carcinoid tumours in conjunction with other markers (e.g. CgA) where assay of 5-HIAA is known to be inappropriate or unhelpful (e.g. hind-gut carcinoid tumours). **Not indicated** in the investigation of depressive illness and low mood.
Collection information	A whole blood specimen is required (EDTA).
Frequency of Testing	
Links to further information	
References	1. Maroun J et al. (2006) Guidelines for the diagnosis and management of carcinoid tumours. Part 1: The gastrointestinal tract. A statement from a Canadian National Carcinoid Expert Group. Curr Oncol 13(2) 67-76 2. Lips CJM et al (2003) The spectrum of carcinoid tumours and carcinoid syndromes. Ann Clin Biochem 40(6) 612-27. 3. Lacasse J & Leo J (2005) Serotonin and Depression: A Disconnect between the Advertisements and the Scientific Literature. PLoS Medicine 2(12) e392 1211-16

TEST NAME	Serum Free Light Chains	CODE		OWNER	Chair, Haematology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	14 May 2012

CATEGORY	Tier Two Test
REFERRAL CRITERIA	The requirement for the test is determined by the specialist referrer

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	The International Myeloma Working Group guidelines (Dispenzieri et al, 2009) suggest that Serum Free Light Chains (SFLCs) is used for prognostic purposes in all patients with monoclonal gammopathy of unknown significance (MGUS) and also smouldering multiple myeloma, active multiple myeloma and amyloidosis.
Indications / referral criteria	The test is indicated if: – the patient has known or suspected myeloma or MGUS – the patient has known or suspected amyloidosis – the patient has unexplained renal impairment or proteinuria – the patient has unexplained peripheral neuropathy
Collection information	
Frequency of Testing	The test should only be performed with a maximal frequency of once every 4 weeks (levels don't change that quickly and 4 weekly monitoring is adequate). It is anticipated testing is needed no more frequently than every 3 months unless the patient is on active chemotherapy. To save costs, the Testing Laboratory should start the next test at the same dilution as the previous result.
Links to further information	
References	1. Dispenzieri A et al. International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders. Leukemia. 2009 Feb;23(2):215-24. Epub 2008 Nov 20.

TEST NAME	Sex Hormone Binding Globulin	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	SHBG	VERSION	12.1	DATE	10 January 2012

CATEGORY	**Tier Two Test** Referred or pre-authorised by: - Endocrinologist - O&G specialist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	SHBG is the major transport protein for testosterone in humans. It is synthesised in liver and in women, oestrogens (oral contraceptive pill, HRT, pregnancy) are important in determining plasma SHBG concentration. Hyperthyroidism and cirrhosis may also result in elevated levels. Because SHBG binds most of the testosterone in plasma, higher levels of SHBG are associated with higher levels of total testosterone (TT). Assay of SHBG allows calculation of Free Androgen Index (FAI) and Free Testosterone (FT) – thought to be better markers than TT of androgen exposure.
Indications / referral criteria	– For investigation of hirsutism / oligomenorrhoea and other features suggesting Polycystic Ovary Syndrome (PCOS) when assayed in conjunction with testosterone. – Investigation of some cases of male hypogonadism. – **The test is of limited value** when testosterone ≤1.3 or ≥5.0 in females or when testosterone ≤7.0 or ≥15.0 in males (1), as outside of these ranges the result is unlikely to add further diagnostic information. Refer to local guidelines on this range. – **The test is not indicated** in monitoring testosterone replacement / supplementation. (2)
Collection information	Samples should be taken 8-10am because of the diurnal variation in plasma testosterone concentration. Any current therapy with oestrogens or androgens should be noted on the form.
Frequency of Testing	
Links to further information	http://www.bpac.org.nz/resources/bt/2010/sept.asp?page=2#pcos
References	1. Assoc. Prof J Davidson, Auckland Hospital – *personal communication* 2. Bhasin S et al (2010); Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 95; 2536–2559

TEST NAME	Thrombophilia (Inherited)	CODE		OWNER	Chair, Haematology Laboratory Schedule Subgroup Chair, Genetics Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	13 May 2012

CATEGORY	Tier One and Tier Two Test
	Medical practitioners working in general practice may order a thrombophilia screen. If there is an index case in the family, individual genetic tests (e.g. Antithrombin, or Protein C) are restricted to a haematologist or clinical geneticist as counselling may be required prior to testing other family members.
REFERRAL CRITERIA	**Referral criteria available**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	The currently recognised conditions resulting in heritable thrombophilia are:- 1. Antithrombin deficiency 2. Protein C deficiency 3. Protein S deficiency 4. Factor V Leiden (FVL) 5. Prothrombin G20210A mutation (PT20210A) 6. Dysfibrinogenaemia 7. Inherited antiphospholipid syndrome Patients with deficiencies of the naturally occurring anticoagulants (antithrombin, protein C and protein S) in thrombosis-prone families have a severe thrombophilic tendency with a relative risk for venous thromboembolism (VTE) of approximately 10-20 fold compared to unaffected people. This compares to a relative risk of approximately 3-5 fold for people who are heterozygotes for FVL or PT20210A. People who are homozygous for FVL or PT20210A or double heterozygotes for these conditions are rarely seen but appear to have a particularly high risk of VTE, with a relative risk rate estimated at approximately 50-80 fold. The dysfibrinogenaemias are a heterogeneous group of extremely rare disorders associated with variable venous thrombotic risk. The inherited antiphospholipid syndrome is very rare but appears to be associated with a high venous and arterial thrombotic risk.
Indications / referral criteria	Testing is indicated in the following situations: – Idiopathic venous thrombo-embolism in young patients (<45 years) – Warfarin-induced skin necrosis ○ Patients should be tested for protein C deficiency and protein S deficiency one month after stopping vitamin K antagonist therapy if this can safely be discontinued. – Children presenting with purpura fulminans (they should be tested for protein C and protein S deficiency). – Siblings of patients with homozygous FVL, homozygous PT20210A or compound heterozygotes for these mutations (they will be offered testing for FVL and PT20210A as they have at least a 1 in 4 chance of

	being similarly affected by these severe thrombotic disorders). – Thrombosis in unusual sites (e.g. cerebral, mesenteric, portal). In all other situation testing should only be undertaken after consultation with a Haematologist or as part of a clinical trial. Testing is not indicated in the following: – Recurrent VTE – Recurrent VTE despite adequate therapeutic anticoagulation – VTE in the context of a family history of unprovoked VTE in a first degree relative – VTE in association with a history of thrombophlebitis – Arterial thrombosis (Lupus testing is indicated in this setting) – Women with a history of miscarriage, pre-eclampsia, abruption or intrauterine growth restriction (Lupus testing is indicated in this setting). Current British guidelines recommend avoidance of the combined oral contraceptive pill in women with a history of VTE in a first degree relative regardless of the thrombophilia results. Therefore, a thrombophilia screen will not be performed: – Prior to use of combined oral contraceptives in patients with a family history of VTE – In unselected women considering the use of the combined oral contraceptive pill Testing for heritable thrombophilia may assist counselling of selected women particularly if a high risk thrombophilia has been identified in the symptomatic relative. **Patient counselling** Testing for heritable thrombophilia may reveal the presence of a genetically determined disorder and patients should be counselled appropriately before testing is performed. Patients should also be advised that testing for heritable thrombophilia may affect their insurance risk and that their access to insurance policies may be changed, regardless of the result of the test result. **Genetic Testing** Index case sequencing (if initial testing has been negative) should only occur at the request of a haematologist.
Collection information	**Tests** The tests offered for heritable thrombophilia testing are:- – Antithrombin, protein C and protein S levels, FVL, PT20210A, fibrinogen, lupus anticoagulant, IgG anticardiolipin antibody. NB This excludes IgM antibody unless specifically requested. Wherever possible, thrombophilia testing should be avoided in the following settings as one or more of the laboratory tests may give misleading results:- – In people taking hormone replacement therapy – Acute thrombosis – During warfarin or other vitamin K antagonist therapy – During treatment with any form of heparin – During pregnancy and for 8 weeks post partum **Testing information** Testing will only be performed on samples accompanied by appropriate clinical details. Samples arriving in the laboratory without appropriate clinical details will not be tested but will be held for 28 days. Such samples will be tested if the requesting clinician subsequently provides appropriate clinical details.

	Where low levels of antithrombin, protein C or protein S are found a repeat sample will be requested to confirm the abnormal finding.
Frequency of Testing	Requests for repeat testing of normal results will not normally be accepted.
Links to further information	GHSNZ – Genetic Health Service NZ www.geneticheathservice.org.nz
References	1. Baglin T et al. Clinical Guidelines for testing for heritable thrombophilia. British Journal of Haematology 2010;149:209-220 2. Lijfering. Blood 2009;113(21):5314-5322

TEST NAME	TORCH Screening	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	8 January 2012

CATEGORY	NOT FUNDED
REFERRAL CRITERIA	Not applicable

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	The acronym TORCH leads to tests for serological testing for the following infections: - Toxoplasmosis - Other (syphilis) - Rubella - Cytomegalovirus (CMV) - Herpes simplex virus (HSV)
Indications / referral criteria	Requests for screening for specific pathogens should be requested in conjunction with details of clinical presentation. This approach will allow for screening tests to be targeted towards the most likely cause as well as reducing the amount of unnecessary screening tests. The following advice should be provided with a request for TORCH screening: "**TORCH screening is no longer funded. Please notify laboratory of tests required for specific pathogens related to clinical findings for this patient".**
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	**Trace Element Tests: Plasma zinc, copper, cobalt, chromium and selenium, blood and urine mercury**	**CODE**		**OWNER**	**Chair, Chemical Pathology Laboratory Schedule Subgroup**
OTHER NAMES		**VERSION**	**12.1**	**DATE**	**9 January 2012**

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: – Paediatrician – Haematologist – Dermatologist – Gastroenterologist – GI surgeon – Neurologist – Anaesthetist / Intensive Care Medicine Specialist – Oral and maxillofacial surgeon / Oral medicine specialist – Orthopaedic surgeon (cobalt and chromium) – Approved workplace monitoring scheme OR prior approval of a chemical pathologist
REFERRAL CRITERIA	**Referral criteria available**

REFERRAL GUIDELINE / SUPPORTING INFORMATON	
Overview	Deficiencies of zinc, copper and selenium can occur in the settings of malnutrition and malabsorption, and measurement of plasma levels may be useful in the management of patients with gastrointestinal disorders and especially in parenteral nutrition. Measurement of plasma and urine copper levels are also useful in the diagnosis and management of Wilson's Disease and in rare genetic disorders of copper metabolism. These tests are also of value in cases of Zn, Cu and Se poisoning. Measurement of whole blood and urine mercury are of value in monitoring workplace exposure and in cases of mercury poisoning. Any artificial joint that contains at least one component that is made from cobalt-chromium metal will increase serum metal ion levels and has the potential to result in metal toxicity if the device is faulty, such as a loose metal head on a stem.
Indications / referral criteria	For cobalt and chromium: – Patients with a worn or faulty prosthesis may present with localised symptoms or systemic illness due to metal ion toxicity or sensitivity reactions. This includes ○ Pain ○ Swelling, due to fluid collection and inflammatory reactions ○ Limping or trouble walking or moving the joint ○ Noise coming from the joint such as clunking or squeaking For Zinc, Selenium: - on TPN, malabsorption, short bowel syndrome, malnutrition, eating

	disorder, gastric bypass, cystic fibrosis - ? zinc poisoning - acrodermatitis enteropathica For Copper, as above plus: - Wilson's Disease, Menke's syndrome - abnormal liver function tests for investigation Cases of suspected poisoning are an indication for referral. Requests for serum or urine copper are indicated for investigation of suspected Wilson's Disease. Clinical details should state "?Wilson's Disease" or "raised LFTs". Unless there is a high pre-test probability of deficiency (i.e. a pre-disposing condition such as gastrointestinal disease), or toxicity (e.g. workplace exposure) it is rarely necessary to measure plasma copper, zinc, selenium or blood mercury in patients in general practice. There is no convincing evidence to justify the measurement of plasma zinc or the zinc/copper ratio in patients with depression, autism, other mental health disorders or chronic fatigue syndrome. Results of these tests are often misleading because low plasma zinc and raised copper levels are non-specific changes commonly seen in inflammatory states and chronic disease. The presence of amalgam dental fillings or symptoms of fatigue, depression, cognitive decline etc. are not sufficient indications for measurement of blood or urine mercury levels.[1,2] The major determinant of blood mercury is dietary fish intake, and amalgam fillings do not cause a significant increase in blood mercury levels.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Bates MN. Mercury amalgam dental fillings: an epidemiologic assessment. Int J Hyg Environ Health. 2006;209:309-316. 2. Barrett S. The "Mercury Toxicity" Scam: How Anti-Amalgamists Swindle People. www.quackwatch.org. 2010. 3. BPAC. Testing serum cobalt and chromium in people with metal-on-metal hip replacements. Best Tests, December 2012.

TEST NAME	Tuberculosis / - Tests to diagnose latent tuberculosis infection (LTBI)	CODE		OWNER	Chair, Microbiology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	8 January 2012

CATEGORY	**Tier One Test**
REFERRAL CRITERIA	**Not available**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	There are two types of test to choose from: – the Mantoux or Heaf test – Tuberculin Skin Test (TST) – Interferon Gamma Release Assay (IGRA) - or Quantiferon TB Gold[3].
Indications/ referral criteria	**Contact screening for LTBI** Contacts aged 7 years and under: use a Mantoux test. Contacts aged over 7 years: use a Mantoux test or IGRA or a Mantoux test followed by IGRA (if the Mantoux is positive). **Healthcare worker screening for LTBI** Use IGRA to screen health care workers for LTBI **Refugee screening for LTBI** Refugee children aged 7 years and under: use a Mantoux test Refugee children aged 8- 15 years: use a Mantoux test or IGRA or a Mantoux followed by IGRA (if the Mantoux is positive) Refugees aged 16 and older: use either a Mantoux Test or IGRA **Screening for LTBI in immune-compromised people** – Use IGRA – In some situations a clinician may elect to use both a Mantoux test and IGRA An IGRA is particularly recommended in the following: – BCG vaccinated people – Immune-compromised people – When it is considered a high risk that the person will not return for the reading of their Mantoux test – When it is impractical for the person to make repeat visits for sequential testing
Collection information	
Frequency of Testing	

[3] The commercial name.

Links to further information	
References	1. Ministry of Health. (2010). Guidelines for Tuberculosis Control in New Zealand 2010. Wellington: Ministry of Health.

TEST NAME	Vitamin A & E, beta-carotene	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	3 August 2012

CATEGORY	Tier One Test
REFERRAL CRITERIA	Not available

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	These are all fat soluble vitamins. Vitamin E (tocopherol) is widely present in food and dietary causes of deficiency are uncommon. Vitamin A deficiency is common in third world countries and an important cause of eye and GI symptoms. Carotene is a precursor of vitamin A (provitamin A) and levels, usually measured together, are a surrogate marker of vitamin A absorption and nutritional status. In Western countries, deficiency of both vitamin A and E most often reflects fat malabsorption, with the severity of deficiency related to the degree and duration of steatorrhoea. Deficiency can also occur through other very uncommon mechanisms, e.g. abnormalities of vitamin E transport proteins or extremely low levels of plasma lipoproteins (e.g. abetalipoproteinaemia). Such patients can present with haematological (haemolysis, irregular cell shapes) and neuromuscular symptoms. Although an antioxidant, the evidence for benefit from vitamin E supplementation on reducing cardiovascular events is disappointing and large meta-analysis studies suggest it is more likely to cause harm[1]. It has no established role for this purpose. Other studies have shown no benefit from supplementation with vitamin A or beta-carotene[2]. Possible benefits on other diseases such as cancer, and Alzheimer's disease are not supported by current evidence and other studies have shown no evidence of benefit in reducing infection risk, even though vitamin E may have a role in immunity. Toxicity is very uncommon, but is a particular concern with vitamin A, from excessive vitamin supplements (formation of vitamin A from beta-carotene is tightly regulated and does not lead to toxicity). The measured plasma levels may be misleading as an index of tissue adequacy. Vitamin E is carried in the lipid fraction and levels are strongly influenced by plasma concentrations of cholesterol and triglyceride. Vitamin A is carried on retinol binding protein and variation in RBP can influence levels, e.g. falsely low with protein-calorie malnutrition or Zn deficiency, independent of vitamin A status.
Indications / referral criteria	The main reason for measurement is in the assessment of possible fat malabsorption due to disorders affecting the liver/biliary system, pancreas, or small bowel, e.g. cirrhosis, chronic pancreatitis with insufficiency, small intestinal bacterial overgrowth, Crohn's disease, celiac disease. Both vitamins may also uncommonly be requested where there is concern over possible toxicity.
Collection information	Lipids should also be measured to aid interpretation.

Frequency of Testing	
Links to further information	
References	1. Miller ER 3rd, et al. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality Ann Intern Med. 2005;142(1):37 2. Vivekananthan DP, et al. Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomised trials. Lancet. 2003;361(9374):2017

TEST NAME	Vitamins B1 (thiamine), B2 (riboflavin), and B6 (pyridoxine)	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	9 January 2012

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: - Paediatrician - Neurologist - Bariatric surgeon - Gastroenterologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	
Indications / referral criteria	In New Zealand, clinically significant deficiencies of vitamins B1 and B6 are seen almost exclusively in patients with malabsorption due to gastrointestinal disease, eating disorders and in alcoholics. In this type of setting B1, B2 and B6 deficiencies occur in combination with multiple other vitamin deficiencies (e.g. pantothenic acid, biotin, riboflavin etc.). It is rarely helpful to test blood levels of B1, B2 and B6, as the turnaround time is slow (several weeks), and the clinical response to vitamin therapy is usually more helpful in confirming the diagnosis than vitamin levels.
Collection information	
Frequency of Testing	
Links to further information	
References	

TEST NAME	Vitamin D	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES	25-hydroxy vitamin D	VERSION	12.1	DATE	9 January 2012

CATEGORY	**Tier One and Tier Two Test**
	A medical practitioner working in general practice may refer for the indications noted in referral criteria (below). Otherwise this test is referred or pre-authorised by: - Endocrinologist - Hepatologist - Rheumatologist - Nephrologist - Gastroenterologist - GI surgeon OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**Referral criteria available** The request form must clearly indicate a high risk of vitamin D/calcium abnormalities for investigation e.g. - rickets or osteomalacia, known osteoporosis, abnormalities of calcium/phosphate metabolism, raised ALP with likely bone cause - cystic fibrosis, special diets (e.g. PKU), renal transplant, anticonvulsant use - also, children (16 years and under), refugees, and prior to treatment with bisphosphonates for osteoporosis or interferon for hepatitis C ,

	REFERRAL GUIDELINE / SUPPORTING INFORMATION
Overview	Vitamin D tests were developed for investigation of rickets, osteomalacia and other metabolic bone disorders. In recent years the number of requests for vitamin D tests has increased dramatically. Most of these requests are unrelated to metabolic bone disease, and have arisen because of reported associations between various disorders (cancers, cardiovascular disease, diabetes, autoimmune disorders and infectious diseases) and lower vitamin D concentrations. However, a causal link with vitamin D has yet to be demonstrated for any of these conditions.[1-3] The Institute of Medicine, following an comprehensive review of the evidence, concluded that "For extraskeletal outcomes, including cancer, cardiovascular disease, diabetes, and autoimmune disorders, the evidence was inconsistent, inconclusive as to causality, and insufficient to inform nutritional requirements. Randomised clinical trial evidence for extraskeletal outcomes was limited and generally uninformative"[2] . A recent review aimed at general practitioners in New Zealand has been published by BPAC[4]. A recent comprehensive literature review for the Ontario Ministry of Health has concluded that there is little evidence that it is useful to test vitamin D concentrations in patients without symptoms of metabolic bone disease. [5] It is not necessary to routinely measure vitamin D in patients with low bone density. It is reasonable to routinely provide vitamin D supplements (1.25 mg or 50,000IU cholecalciferol per month) without testing vitamin D to frail housebound or institutionalized elderly people, or those in the community who practise sunlight avoidance for cultural or medical reasons.

	Recent advice indicates some hepatologists are seeking vitamin D levels on Hepatitis C patients before starting treatment. If patients are vitamin D deficient, vitamin D supplementation can make a difference to the efficacy of therapy.
Indications / referral criteria	The test in indicated in the following circumstances: – When ordered for specific high risk groups for rickets/osteomalacia (e.g. cystic fibrosis, proven malabsorption, post bariatric surgery) – When ordered for the investigation of rickets/osteomalacia, osteoporosis/osteopaenia, disorders of calcium and phosphate metabolism, elevated ALP, hepatitis C – Children (16 years or less) – Refugees – Patients on anticonvulsants Check with the local laboratory on the ability for the patient to pay for this test privately.
Collection information	
Frequency of Testing	
Links to further information	
References	1. Grey A, Bolland M. Vitamin D: a place in the sun? Arch Intern Med. 2010;170:1099-1100. 2. Ross AC, Manson JE, Abrams SA et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab. 2011;96:53-58. 3. Manson JE, Mayne ST, Clinton SK. Vitamin D and prevention of cancer--ready for prime time? N Engl J Med. 2011;364:1385-1387. 4. Vitamin D supplementation: navigating the debate. Best Practice Journal (BPAC). 2011:26-35. 5. Clinical utility of vitamin D testing: an evidence-based analysis. Ont Health Technol Assess Ser [Internet].www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_vitamin%20d_201002.pdf. Vol. 10: Medical Advisory Secretariat. , 2010:1-95.

TEST NAME	Vitamin K	CODE		OWNER	Chair, Chemical Pathology Laboratory Schedule Subgroup
OTHER NAMES		VERSION	12.1	DATE	10 January 2012

CATEGORY	**Tier Two Test**
	Referred or pre-authorised by: – Paediatrician – Haematologist – Gastroenterologist – Hepatologist OR prior approval of a chemical pathologist.
REFERRAL CRITERIA	**The requirement for the test is determined by the specialist referrer**

REFERRAL GUIDELINE / SUPPORTING INFORMATION	
Overview	Vitamin K is a fat-soluble vitamin. It is vital for the γ-carboxylation of glutamyl to γ-carboxyglutamyl (Gla) residues in a number of proteins – including the clotting factors II, VII, IX and X. Individuals at risk of vitamin K deficiency include those with fat malabsorbtion (chronic pancreatitis, cystic fibrosis, parenteral nutrition) and some neonates. The coagulation abnormalities caused by vitamin K deficiency are manifested as a prolonged prothrombin time (predominantly factor VII effect). If severe, both the PT and partial thromboplastin time may be affected. The recommended assessment of patients with clotting disorders due to vitamin K deficiency is the assessment of clotting status (prothrombin time, activated partial thromboplastin time) and, if required, individual clotting factors.[1] Echis ratio may also be helpful in some cases.[2]
Indications / referral criteria	Specialist investigation of coagulation disorders where routine testing has failed to provide a diagnosis. **Not indicated** in nutritional investigation in the absence of a coagulation disorder.
Collection information	At least 1 mL of plasma required for assay.
Frequency of Testing	
Links to further information	
References	1. Uptodate:http://www.uptodate.com/contents/overview-of-vitamin-k?source=search_result&search=vitamin+k+deficiency&selectedTitle=1%7E51 2. Dr Russell O'Neil – *personal communication*.