Requirement for relevant clinical details for serum protein electrophoresis

Serum protein electrophoresis is a semi-manual test. It demands interpretation of findings on a result by result basis by skilled scientists, usually in conjunction with pathologists. It is therefore time consuming and requires significant expertise.

Indications for serum protein electrophoresis have been previously listed; please refer to Scope articles in Issue 15 (Serum Protein electrophoresis: indications and frequency of testing) and Issue 24 (Serum Protein electrophoresis requesting).

And include:
- Multiple myeloma
- Waldenstrom’s macroglobulinaemia
- Amyloidosis
- Myeloproliferative disorder
- Unexplained bone fracture
- Recurrent infections (assuming no other cause was found)
- Unexplained peripheral neuropathy
- Unexplained anaemia
- Rouleaux formation
- Unexplained high ESR (with normal CRP)
- Unexplained hypercalcaemia
- For renal transplant
- Unexplained renal impairment
- Proteinuria with no or minimal albuminuria
- Bence Jones proteins
- Abnormal ratio for serum free light chains
- Lytic lesions
- Unexplained osteopenia/osteoporosis

In support of efficient laboratory testing and evidence based clinical practices, and after consultation with clinical haematologists in the region, requests for serum protein electrophoresis will be vetted by chemical pathologists starting 1/12/2019.

All requests that include clinical information that is legible and relevant will be approved. The following comment will accompany all requests that have not been approved: “Serum protein electrophoresis has not been performed because either it is not indicated based on the clinical information provided or no relevant clinical information was provided. If still indicated, please call to discuss with the on-call chemical pathologist. The sample will be kept for 7 days.”

Dr Gary McAuliffe
Medical Director and Microbiologist
Labtests
Gary.mcauliiffe@labtests.co.nz
Important information regarding ‘Intermediate’ susceptibility interpretation and recommended antibiotic doses.

Key points

- The definition of ‘intermediate’, or ‘I’, has changed to mean ‘susceptible, increased exposure’. Organisms reported as intermediate to a given antibiotic can be effectively treated so long as increased exposure (e.g. through higher dosing) can be achieved. Intermediate susceptibility should not be considered the same as resistant, neither should the antibiotic automatically be avoided.
- Susceptibility results only apply if particular dosing regimens are used, as published in our laboratory clinical breakpoints document. If doses used are lower than the specific published recommendations, a susceptible result may not be valid.

‘Intermediate’ susceptibility – what does it mean and what should we do about it?

In the microbiology laboratory the most useful part of the reports we issue is often the susceptibility result. Whether or not a given organism is ‘S’ or ‘R’ to a given antibiotic in most instances will tell us which antibiotic to use (assuming infection is present of course!).

But what about ‘I’ (intermediate)? And does ‘I’ even matter?

The lab follows strict criteria, known as the clinical breakpoints, to determine how to interpret susceptibility test results. These clinical breakpoints are determined by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and are published every year (available here: [http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_9.0_Breakpoint_Tables.pdf](http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_9.0_Breakpoint_Tables.pdf)).

For microbiologists, 2019 saw some major changes to important aspects of susceptibility testing criteria and a shift in the way we view the ‘I’ category.

In line with the new EUCAST definitions our reports now display interpretation of results as follows:

- S = Susceptible, standard dose
- I = Susceptible, increased exposure
- R = Resistant

You will notice that ‘I’ organisms are now clearly placed in the susceptible group. Increased exposure of a given antibiotic may be achieved by using a higher dose, more frequent dosing or changing the mode of administration. Alternatively, if the antibiotic is already well concentrated at the site of action, for example trimethoprim for urinary tract infections, standard dosing should be sufficient. Intermediate should no longer be viewed as an uncertain result or lumped together with ‘R’ but, rather, the antibiotic dosing regimen optimised to ensure therapeutic success.

There are not very many situations where we will be reporting ‘I’ but should you see it and are unsure what to do, think about whether you can up the dose, up the frequency or whether the drug is already concentrated at the site where it’s needed. If you are still unsure, we invite you to discuss with a clinical microbiologist, available via your local microbiology laboratory or DHB hospital switchboard.

### Does dosing matter?

Did you know that the laboratory clinical breakpoints, which determine whether we report ‘S’, ‘I’ or ‘R’, are only valid if a particular dose of an antibiotic is being used? Dosing tables are provided at the end of the EUCAST breakpoints document we use in the microbiology lab to determine susceptibility test results (available here: [http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_9.0_Breakpoint_Tables.pdf](http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_9.0_Breakpoint_Tables.pdf)).

These recommended dosing regimens are published following careful consideration of a number of factors, including the minimum inhibitory concentration (MIC) of the organism, the pharmacokinetics and pharmodynamics (PK/PD) of the antibiotic, as well as clinical (in vivo), laboratory (in vitro) and predictive modelling studies.

Worth a particular mention are *Haemophilus influenzae* and *Pseudomonas aeruginosa* where a higher dose should always be used. Therapeutic failure is not always due to bacterial resistance – dose optimisation has an extremely important part to play. See the table below for some common antibiotic doses published by EUCAST:

*Skin and soft tissue infections require 1g whereas urinary tract infections may respond to lower dosing regimens due to concentration of the antibiotic within the urinary tract.*

Where we report ‘I’ (see section above) it will be important to use the higher dose listed.

It is timely to review the current dosing recommendations available from the various different sources such as BPAC, NZF and Health-Pathways, to ensure they align with what EUCAST require us to report in the laboratory.

**Dr Juliet Elvy, Microbiologist, Medlab South**

<table>
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<tr>
<th>Antibiotic</th>
<th>Standard dose</th>
<th>High dose</th>
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<tr>
<td>Flucloxacillin</td>
<td>1g TDS</td>
<td>1g QID</td>
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<tr>
<td>Amoxicillin</td>
<td>500mg TDS</td>
<td>0.75-1g TDS</td>
<td><em>Haemophilus influenzae</em> high dose only</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>625mg TDS</td>
<td>1g TDS</td>
<td><em>Haemophilus influenzae</em> high dose only</td>
</tr>
<tr>
<td>Cefalexin</td>
<td>250mg to 1g BD or TDS*</td>
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<td>Depends on species and/or type of infection</td>
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<tr>
<td>Doxycycline</td>
<td>100mg OD</td>
<td>200mg OD</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacillin</td>
<td>500mg BD</td>
<td>750mg BD</td>
<td><em>Pseudomonas</em> high dose only</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>960mg BD</td>
<td>960mg TDS or 1.44g BD</td>
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Does your patient have adrenal insufficiency?

Synacthen testing is the preferred diagnostic test in the evaluation of possible primary or secondary adrenal insufficiency (hypoadrenalism). The test is effectively a ‘stress test’ of the ability of the adrenals to respond to very strong ACTH stimulation by showing a rapid increase in cortisol. The ACTH is given as a shortened 24 amino acid form of the natural 39 amino acid hormone.

While various protocols have been used for performance and interpretation of the test over the years, the method used locally involves a very large 250ug dose of ACTH1-24 (synacthen) given intravenously, with measurement of baseline plasma cortisol at 30 minutes through an indwelling cannula.

Intramuscular injection of synacthen can also be used, but this is much less convenient for the patient (requiring three needle-sticks rather than one) and the overall interpretation is similar.

Synacthen injection (IV or IM) carries an extremely low risk of allergic reaction. Occasional patients describe a sensation of warmth, and mild flushing. A few may say they feel slightly nauseated, but this is also mild.

Labtests and Northland Pathology Laboratory phlebotomists are trained and accredited to collect blood, but are not accredited to give drugs. Even though the risk of an adverse reaction is extremely low staff and facilities should also be available should there be any problems.

For these reasons, for some time Labtests has not provided this service and referrals need to be made for an appointment to the endocrinology service in the Auckland region. (Phone 09 307 4949 extension 26854, 26855 or 26871 for booking). In Northland, Northland Pathology Laboratory can no longer provide the synacthen test, and the dosing regimen should be recorded on the request to Endocrinology at Whangarei hospital.

Whom to refer for a Synacthen Test?

In general there should be clinical suspicion of hypoadrenalism, PLUS a baseline cortisol that does not clearly rule in or rule out the diagnosis. Note that Synacthen testing is not the appropriate test if cortisol excess (Cushing’s syndrome) is suspected.

Reasons to suspect hypoadrenalism include symptoms such as unexplained fatigue, weight loss, pigmentation, salt craving. A background of pituitary disease, autoimmune disease or long-term steroid replacement also heighten suspicion.

If suspicion is high (e.g. classic symptoms or clear other evidence of pituitary or adrenal disease) an early morning cortisol below the reference limit, and especially below 100 nmol/L, makes the diagnosis highly likely. Treatment should not be delayed, and early review by an endocrinologist is strongly advised. An early morning plasma ACTH performed can help confirm primary, but not secondary, adrenal insufficiency.

A baseline early morning plasma cortisol above 350 nmol/L in either assay has high specificity in ruling out hypoadrenalism, unless the patient is acutely unwell or is taking steroids at the time; a synacthen test is not needed in this setting. In an acutely unwell patient a baseline cortisol over 400 nmol/L (the post-dose diagnostic threshold for the test) also rules out the diagnosis.

When a diagnosis of hypoadrenalism needs exclusion and baseline cortisol is unable to do so, a synacthen test can resolve the uncertainty, e.g. baseline morning cortisol in the following range:

- 180–350 nmol/L using Siemens Centaur assay (Labtests Auckland)
- 160–350 nmol/L using the Roche assay (LabPlus Auckland Hospital, Northland Pathology Whangarei)

Note that samples taken outside the early morning in normal patients will often have values below the early morning reference range, as cortisol has a pronounced diurnal variation.

Exogenous steroids both suppress endogenous cortisol production and can cross-react with the assay. If the patient has been taking steroids then the morning dose should be withheld on the day of the test, and the dosing regimen should be recorded on the request form.

Synacthen diagnostic thresholds are similar in men and women. However, oral oestrogens (OCP or HRT), or pregnancy, raise cortisol binding protein (CBG) and lead to significantly higher cortisol values. The above thresholds (both baseline and post-synacthen) do not apply in this setting.

Interpretation of Synacthen Results.

A peak cortisol over 400 nmol/L at 30 minutes post-dose (250ug) is regarded as an adequate response. While a baseline cortisol can be helpful, it is not critical to interpretation, nor is the degree of rise in cortisol post-synacthen. The test can be performed if necessary at any time of day, but a morning test is preferred.

This threshold of 400nmol/L applies only to the Roche Cobas assay in Northland Pathology and LabPlus Auckland Hospital. This assay is aligned to the gold standard LCMS assay and has very low cross-reaction with other steroids that may be increased after synacthen. Results from other assays (e.g. Labtests Siemens Centaur) are not transposable and are not used locally in synacthen testing.

Dr Cam Kyle

Chemical Pathologist, Labtests and LabPlus

References:

Sbardell E, et al. Baseline morning cortisol level as a predictor of pituitary–adrenal reserve: a comparison across three assays Clinical Endocrinology 2017; 86: 177-84
Clinically appropriate throat swabs: choosing wisely and avoiding unnecessary testing and antibiotics

“Most sore throats are due to viral infections, and antibiotics are of no use.”

Background

In the past decade, New Zealand’s diagnostic laboratories have been inundated with throat swabs. Over the same period, the number of amoxicillin prescriptions has steadily increased. Conversely, testing and treatment for group A Streptococcus (GAS) pharyngitis in other high income countries has reduced.

Much of the increased testing in NZ has been in response to attempts to reduce our rates of acute rheumatic fever (ARF), with an expected and dramatic increase in throat swabs from those New Zealanders considered at greater risk of ARF. However, laboratories have also seen significant increases in throat swabs coming from those not considered at risk.

There is a sharp divide in risk of ARF amongst New Zealanders with ARF rates highest for those of Pacific (75/100,000 people), and Maori ethnicity (19/100,000 people) whereas rates are logarithmically lower for those of European or other ethnicity (<1/100,000 people).

The number of throat swabs taken and tested from individuals at low risk of ARF is concerning for a number of reasons:

- GAS causes only 20-30% of sore throats, with the rest having a viral aetiology.
- However, GAS colonises the oropharynx in 12-15% of the population, and therefore even in a patient with a sore throat isolation of GAS from a throat swab doesn’t necessarily indicate it is the cause of infection / disease.
- Prediction criteria or scoring systems do not differentiate between causes of pharyngitis as symptoms and signs of bacterial and viral infections overlap.
- Unless a patient is at high risk for ARF or requires hospitalisation for severe disease, throat swabbing and antibiotics are of marginal benefit. Antibiotics make little difference to how long symptoms last or the number of people whose symptoms improve. Withholding antibiotics is unlikely to lead to complications.
- Treating all positive throat swabs will result in excessive and unnecessary antibiotic prescription, which can cause patient harm such as drug intolerance or allergic reactions.
- We have had feedback from GPs who look after patients at low risk of ARF that they routinely collect throat swabs now, when they would not have ten years ago, and that patient expectation has driven some of this change in clinical practice.

As microbiologists we support the use of testing for symptomatic patients at risk of preventable sequelae i.e. ARF and severe disease e.g. abscess formation.

If patient is not at risk of rheumatic fever, throat swabs cannot be recommended as supportive care with analgesics and adequate fluid intake would be appropriate for most patients. Possible exceptions where throat swab +/- treatment could be indicated would be immunocompromised patients or those with severe symptoms e.g. pain not responding to simple analgesics or difficulty swallowing (refer to HealthPathways).

Who should have a throat swab?

Is the patient at epidemiological or person/family risk of rheumatic fever?

Presenting with a sore throat and two of the following:

- Maori or Pacific
- Aged 3-35 years
- Socioeconomic deprivation/overcrowding

Or presenting with a sore throat and:

- Personal or immediate family history of rheumatic fever

Sometimes public health will request throat swabbing as part of investigation around a case of acute rheumatic fever.

Other indications for throat swabbing include:

1. Possible scarlet fever
2. Public health investigation of case of acute rheumatic fever

Dr Gary McAuliffe
Microbiologist and Medical Director
Labtests

Dr Arlo Upton
Microbiologist, Dunedin Hospital

Tissue autoantibodies at Labtests

Why do I get a result I didn’t request?

One of the common calls I get is from requesters who have received an unexpected result after requesting a specific tissue autoantibody, e.g. ordering gastric parietal cell (GPC) antibodies in a patient with a low B12 and being notified of a positive antimitochondrial antibody (AMA). They are concerned firstly as to what this means, and secondly as to why they have received it.

Autoantibodies to specific tissues and organs are found in a number of autoimmune diseases. In many cases they are not thought to be directly pathogenic, but reflect underlying immune damage from other parts of the immune system such as antigen-specific T cells. Antibodies can be looked for by a number of different test methods; some of these, such as ELISA, will only detect a specific antibody, but other methods such as immunofluorescence can...
Tissue autoantibodies at Labtests Continued.....

reveal autoantibodies to a wide range of targets present in the cell or tissue studied.

For any requests for GPC, smooth muscle (SMA) and/or AMA auto-

antibodies at Labtests, serum from the patient will be added to a

slide containing rat kidney and stomach; antibodies to these tis-

sues are then detected via immunofluorescence. This means that

requesters may receive results that they did not specifically order - i.e., if gastric parietal cell autoantibodies are requested but the laboratory scientists see smooth muscle autoantibodies on the same tissue, this will also be reported. If an antinuclear antibody (ANA) pattern is seen it will also be reported even if not requested.

What does it mean?

In all cases we will report whether the autoantibody was positive or negative, and if positive what titre. We screen at a titre of 1:40.

GPC: Positive in >90% of patients with autoimmune pernicious anaemia. The target is the parietal cell enzyme, H+K+ ATPase. Can be seen in other gastric conditions such as atrophic gastritis and gastric ulcer, as well as in other endocrinological conditions and healthy adults. Increases in prevalence with age.

SMA: Associated with autoimmune liver disease but relatively non-specific; can also be found in viral hepatitis, connective tissue diseases, and chronic infection. Titres >1:160 are more likely to be significant.

AMA: Positive in 90% of patients with primary biliary cholangitis (PBC), usually at titres of >1:160; the M2 autoantibody (tested via immunoblot) is more specific for PBC and will also be reported. Low titres can precede the development of disease but can also be found in other autoimmune liver diseases, connective tissue diseases and chronic infections. If mitochondrial antibodies are seen it is not possible to tell if GPC autoantibodies are also present.

Dr Miriam Hurst, Immunopathologist, Labtests
Miriam.hurst@labtests.co.nz

References:
ASCIA Consensus Guidelines on Anti-Intrinsic Factor Autoantibody Testing
Euroimmun Rat stomach kidney slide kit insert
SouthTees.nhs.uk Pathology

Serum urate testing, hyperuricaemia and gout: new research in the Auckland region

Urate is a degradation product of purine metabolism. Elevated serum urate concentration (hyperuricaemia) is associated with a number of clinical problems. Gout occurs in response to monosodium urate (MSU) crystals in the joints, which form when urate levels increase above saturation levels. Not all people with hyperuricaemia develop gout. Hyperuricaemia is also associated with increased risk of cardiovascular disease, hypertension, and renal disease. Hyperuricaemia and gout are becoming increasingly frequent throughout the world, with very high rates of gout reported in New Zealand (affecting up to one third of older Māori and Pacific men).

A number of factors contribute to elevated serum urate concentrations. These include non-modifiable factors such as increasing age, male sex, and genetic factors. Medical problems such as kidney disease, metabolic syndrome, and drugs such as diuretics and cyclosporine can also increase serum concentrations.

At present, drug treatment for asymptomatic hyperuricaemia is not recommended. Modifiable contributors to hyperuricaemia should be addressed in these patients. However, in patients with gout, urate-lowering drugs (usually allopurinol) are effective in reducing gout flares and reducing tophi. For patients taking urate-lowering drugs, serum urate should be monitored regularly, with the goal of maintaining the serum urate long-term below 0.36mmol/L.

Researchers at the University of Auckland and University of Otago are currently undertaking several studies in hyperuricaemia and gout. One is a longitudinal observational study of people with hyperuricaemia but no history of gout. The other study is a randomized controlled trial of low dose colchicine for people with gout who are starting allopurinol.

Labtests is assisting with recruitment of study participants, by writing to people with elevated serum urate concentrations of 0.50mmol/L or above to provide details about the study. If people are interested, they will contact the study coordinators for further information. No personal information will be shared by Labtests with the researchers. The studies have been funded by the Health Research Council, and are approved by the Multi Region Ethics Committee.

The contact details of the research leaders are: Professor Nicola Dalbeth, Department of Medicine, University of Auckland, 85 Park Rd, Grafton, Auckland, and Professor Lisa Stamp, Department of Medicine, University of Otago, Christchurch, PO Box 4345, Christchurch.

Professor Nicola Dalbeth, Department of Medicine, University of Auckland
# Labtests Key Contacts

**Labtests Services** | (09) 574 7399
---|---
Results | Press ‘1’  24 hours/7 days per week
Courier | Press ‘2’  24 hours/7 days per week

**Home Visits**

<table>
<thead>
<tr>
<th>Email to <a href="mailto:auk.home.visits@labtests.co.nz">auk.home.visits@labtests.co.nz</a> (preferred) Or fax the request form for the test/s to  (09) 574 7383. If the home visit cannot be booked for the date requested Home Visits staff will contact the referrer to arrange an alternative date.</th>
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**Special Test Bookings**

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**Other Enquiries**

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<td>Sat-Sun 8:00am to 7:00pm</td>
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**Add on tests**

To add test/s to an existing patient request form, Press ‘1’ to speak to our call centre staff.

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<td>Note: some add on tests may require pathologists approval.</td>
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**eOrders Helpline**

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<thead>
<tr>
<th>Email: <a href="mailto:helpdesk@eorder.co.nz">helpdesk@eorder.co.nz</a></th>
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<td>0508 37 37 83</td>
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**Dedicated line for practitioners to access all results (24/7)**

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<th>(09) 574 7398</th>
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<td>Press ‘5’</td>
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<td>Mon-Fri 07:00am to 3:30pm</td>
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**Labtests Pathologists—phone 574 7399**

<table>
<thead>
<tr>
<th>Medical Director: Dr Gary McAuliffe 021 0215 7069 <a href="mailto:gary.mcauliffe@labtests.co.nz">gary.mcauliffe@labtests.co.nz</a></th>
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<tbody>
<tr>
<td><strong>Chemical Pathologists</strong></td>
</tr>
<tr>
<td>Dr Charles Ng <a href="mailto:charles.ng@labtests.co.nz">charles.ng@labtests.co.nz</a></td>
</tr>
<tr>
<td>Dr Cam Kyle <a href="mailto:cam.kyle@labtests.co.nz">cam.kyle@labtests.co.nz</a></td>
</tr>
<tr>
<td>Dr Samarina Musaad <a href="mailto:samarina.musaad@labtests.co.nz">samarina.musaad@labtests.co.nz</a></td>
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<tr>
<td>Dr Melissa Yssel <a href="mailto:melissa.yssel@labtests.co.nz">melissa.yssel@labtests.co.nz</a></td>
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<tr>
<td>Dr Gary McAuliffe <a href="mailto:gary.mcauliffe@labtests.co.nz">gary.mcauliffe@labtests.co.nz</a></td>
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<tr>
<td>Dr Matt Blakiston <a href="mailto:matthew.blakiston@labtests.co.nz">matthew.blakiston@labtests.co.nz</a></td>
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<tr>
<td>Dr Max Bloomfield <a href="mailto:maxim.bloomfield@ccdhb.org.nz">maxim.bloomfield@ccdhb.org.nz</a></td>
</tr>
<tr>
<td><strong>Microbiology:</strong> Fax: 09 574 7344</td>
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<tr>
<td>Dr James Liang <a href="mailto:james.liang@labtests.co.nz">james.liang@labtests.co.nz</a></td>
</tr>
<tr>
<td><strong>Haematologists</strong></td>
</tr>
<tr>
<td>Dr Fransisca De Silva <a href="mailto:fransisca.desilva@labtests.co.nz">fransisca.desilva@labtests.co.nz</a></td>
</tr>
<tr>
<td>Dr George Chan <a href="mailto:george.chan@labtests.co.nz">george.chan@labtests.co.nz</a></td>
</tr>
<tr>
<td>Dr Lesley Overend <a href="mailto:lesley.overend@labtests.co.nz">lesley.overend@labtests.co.nz</a></td>
</tr>
<tr>
<td>Dr Lochie Teague <a href="mailto:lochie.teague@labtests.co.nz">lochie.teague@labtests.co.nz</a></td>
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<tr>
<td><strong>Immunopathologist</strong></td>
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<tr>
<td>Dr Gary McAuliffe <a href="mailto:gary.mcauliffe@labtests.co.nz">gary.mcauliffe@labtests.co.nz</a></td>
</tr>
<tr>
<td>Dr Miriam Hurst <a href="mailto:miriam.hurst@labtests.co.nz">miriam.hurst@labtests.co.nz</a></td>
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<tr>
<td><strong>Department contact numbers</strong></td>
</tr>
<tr>
<td>Duty Scientist: DDI: 09 574 7382 // Fax: 09 574 7308</td>
</tr>
<tr>
<td>Haematology: Fax: 09 574 7308</td>
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<tr>
<td><strong>Biochemistry:</strong></td>
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<tr>
<td>Fax: 09 574 7308</td>
</tr>
<tr>
<td><strong>General enquiries:</strong> <a href="mailto:lta.clientservices@labtests.co.nz">lta.clientservices@labtests.co.nz</a></td>
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**Client Services**

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<tbody>
<tr>
<td>Mala Govender (09) 574 7306// 021 407 300 <a href="mailto:Mala.govender@labtests.co.nz">Mala.govender@labtests.co.nz</a></td>
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The contact numbers for all enquiries related to Anatomic Pathology

Mt Wellington are:  
**Phone (09) 302 0516**  
**Fax: (09) 302 0517**  

Updated: 11/11/19