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From our management team



As well as clinical updates from our pathology team, this third issue of The Scope includes important operational information for practitioners. We'll continue to use this newsletter to communicate both clinical updates and housekeeping matters as they arise.

It's been a busy time over the past couple of months with the International Accreditation New Zealand (IANZ) team on site here at Labtests. We'd like to extend our warmest thanks to the Labtests scientists and medical staff for all their hard work throughout the accreditation process.

Full accreditation was awarded on 13 May 2010, following a comprehensive assessment of our laboratory operations. This accreditation means

a great deal to us, acknowledging as it does our commitment to quality and best practice in the laboratory.

Pathology updates and CME

Members of the Labtests pathology team, including Drs Richard Lloyd, Arlo Upton, Andre Simmance and Jeff Barron, were pleased to present at the Goodfellow Symposium at the end of March. The Symposium was well attended and positively received by GPs, and we look forward to attending next year's event.

The next Labtests pathology update meetings, scheduled for 2 June and 9 June, will focus on immunopathology. They will be presented by Professor Ban-Hock Toh, who is consulting to Labtests from Gribbles Pathology in Melbourne.

Despite our efforts to gain full registration from the RNZCGP, the College has advised that it can only offer credits for these meetings in the APDA (Additional Professional Development Activities) category. These are worth one credit per hour and

count towards the minimum 150 credits required over the current MOPS triennium.

Labtests remains committed to providing practitioners with ongoing medical education in the community pathology field, and we will be meeting with Auckland PHOs in June to discuss the best ways of delivering this. Dr Arlo Upton has been appointed Labtests' CME coordinator to help facilitate the process.

Pathologist recruitment complete

We are very pleased to announce the appointment of laboratory haematologist Dr Fransisca de Silva to our pathology team. Fransisca is a Fellow of the RCPA and is expected to join our haematology team in June. Her appointment marks the completion of Labtests' pathologist recruitment programme.

Please don't hesitate to bring your clinical questions to our pathology team. We would also welcome hearing from you directly should you have any questions or concerns.

Dr Richard Lloyd & Dr Craig Marshall

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MEET THE TEAM

Eric Oudyn

HOD Haematology

My background

I was born in Amsterdam and brought up in The Netherlands, Sri Lanka and Australia before moving to New Zealand while I was still a teenager.

I commenced laboratory work at the Princess Alexandra Hospital in Brisbane, before moving to Auckland where I worked for the Laboratory Diagnostic Service for three years. I next moved to Medlab Hamilton, where I completed my training. I was HOD of Haematology from 1992 until the laboratory ceased operations in January 2008.

I then spent a year as manager of the Tokoroa

Hospital Laboratory. I took up my present position at Labtests in February 2009.

My role at Labtests

As HOD Haematology, my role is to oversee a team of 30 (20 scientists, nine technicians and one laboratory assistant) and to ensure the efficient running of the department. The automation and equipment we operate is state of the art and essential for processing the huge daily workload.

Highlights of the job

The highlight of the role has been the opportunity to be involved in setting up such a large laboratory from scratch, something the pundits said was impossible. It was certainly a rare opportunity and very challenging in the political climate at the time.

It was very rewarding to be responsible for interviewing and employing a great team of



scientists and technicians from a very diverse group of people. They come from 10 different countries and work very well together.

Where you'll find me outside work

Usually you will find me at home with my family. I used to be a keen bridge player and play golf socially. My other interests include occasional fishing, gardening and reading. I keep fit with recreational walking, which I especially enjoy at the beach and around rivers and lakes.

PRACTITIONER UPDATES

Fasting glucose test results

There is a perception among some referrers that Labtests' fasting serum glucose results are too high. We are doing a number of things to address these concerns.

Siemens, the supplier of our test reagents, has re-standardised the calibration of our serum glucose analysers. This is to provide better alignment with external proficiency programmes and better comparisons with other manufacturers' glucose assays.

Preliminary data show that this recalibration has resulted in a slight reduction in fasting serum glucose levels and better alignment with the current plasma glucose method.

We are also evaluating the differences between serum glucose test results (specimens received from Labtests collection rooms) and plasma glucose test results (specimens received from home visits and doctor collections). We will keep you informed of our progress.

Barcodes invalid on request forms

A large number of practices are still using barcode labels on their test request forms. Please note these labels were originally for collection centre use and are no longer valid for use on request forms. No barcodes are now

required on practitioner requests.

Any questions about the use of barcodes can be addressed to your regional medical liaison officer (see below).

COLLECTION CENTRES

Queen's Birthday opening hours

Saturday 5 June 2010

All centres usually open on Saturday will open 8am-12 noon as usual

Sunday 6 June 2010

Mt Wellington

37-41 Carbine Road
8am-12 noon

Monday 7 June 2010

(Queen's Birthday holiday)

Mt Wellington

37-41 Carbine Road
8am-12 noon

Mt Roskill

223 Stoddard Road
8am-12 noon

Mairangi Bay

Apollo Health & Wellness Centre
119 Apollo Drive
8am-12 noon

Henderson

51 Lincoln Road
8am-12 noon

Papakura

132A Great South Road
8am-12 noon

Synacthen special test bookings

From Monday 31 May 2010 all synacthen testing will be conducted at our Greenlane Collection Centre at 641 Manukau Road. This specialised service will be available on Thursday mornings.

Bookings for synacthen tests can be made through our Labtests freephone number, 0508 522 837, by selecting option 4, special test bookings.

Urine drug screens for clinical use

Labtests is able to provide sample collection for urine drug screening for clinical management purposes. This is where results are not intended for legal or evidential purposes and proof of patient identity or specimen chain of custody is not required. Examples include drug overdose or abuse, poisoning or detoxification cases.

Urine drug screening for evidential purposes must be handled with strict chain-of-custody procedures. Cases may include pre-employment screening, occupational health screening,

workplace or other accident investigation, visa applications, family court requests, probationary service requests, drug rehabilitation programmes and school drug testing.

For testing of this kind, patients should be referred to LabPLUS specimen collection services at Auckland City Hospital (Monday to Friday 7.30am to 4.30pm, see Specimen Collection Service at www.labplus.co.nz under 'Patient Services') or White Cross centres.

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Laboratory diagnosis of coeliac disease



Coeliac disease affects 1% of Caucasians but remains largely undiagnosed. It no longer presents with classic full-blown malabsorption syndrome.

Instead it masquerades as a wide variety of conditions including irritable bowel syndrome, asymptomatic osteoporosis and iron deficiency anaemia of unknown cause.

IgA antibody to tissue transglutaminase

Tissue transglutaminase is the molecular target of endomysium antibody. IgA antibody to tissue transglutaminase is the optimal first-line screening assay because it identifies up to 97% of patients with coeliac disease. Endomysium antibody is a useful confirmatory assay because, while it is less sensitive than the tissue transglutaminase assay, it is almost 100% specific for the disease.

IgG antibody to deamidated gliadin

Gliadin is derived from gluten. For gliadin to be pathogenic it must first be deamidated by tissue transglutaminase. This finding has led to the generation of the relatively new assay of IgG antibody to deamidated gliadin. The value of this antibody reportedly lies in the identification of the small proportion of patients with coeliac disease who test negative for tissue transglutaminase antibody.

It is also reported to be useful for the

identification of patients with coeliac disease who are IgA deficient, given that IgA deficiency affects about 2% of patients with coeliac disease. Early findings suggest it may also be useful for the identification of children with coeliac disease.

Standard screening at Labtests

Based on the above, Labtests' standard antibody screening assay for coeliac disease is to test for IgA antibody to tissue transglutaminase coupled with IgG antibody to deamidated gliadin, with endomysium antibody as confirmatory backup.

Genetic testing for HLA-DQ2/DQ8

HLA-DQ2/DQ8 is present in about 40% of Caucasians. While almost all patients with coeliac disease have this genotype, they make up only about 3% of the Caucasian population. The implication of these observations is that while the presence of this genotype is consistent with coeliac disease, it is not diagnostic. On the other hand the absence of this genotype virtually excludes coeliac disease.

Genotyping should therefore not be used as a first-line test. Instead, it should be reserved for patients who refuse to take a gluten-containing diet or who, despite a high clinical suspicion of disease, test negative for tissue transglutaminase antibody or who have a normal small biopsy.

Professor Ban-Hock Toh

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Reproductive hormone testing

To potentially allow additional tests to be initiated, practitioners should provide the reason for the request on the request form.

Presentation: Suspected polycystic ovarian syndrome (especially in patients with hirsutism), anovulatory infertility, oligomenorrhoea, hirsutism, acne.

Request: Testosterone, preferably in the follicular phase (days 2-5). Testosterone is only increased in 70% of PCOS. Raised testosterone fulfils one of three criteria for diagnosis of PCOS, the others being ultrasound PCO; oligo- and/or anovulation. LH and FSH have no discrimination in the diagnosis of PCOS and are not indicated in diagnosis of PCOS.

Presentation: Suspected perimenopause or menopause/ovarian failure, e.g. hot flushes together with oligo-/polymenorrhoea.

Request: FSH, LH, in follicular phase if possible. If the FSH is raised and higher than LH, this is indicative of failing ovaries. FSH levels may fluctuate markedly. During the reproductive years LH is higher than FSH.

Presentation: A-/oligo-/polymenorrhoea and no menopausal symptoms.

Request: FSH, LH, oestradiol, prolactin, testosterone, consider TSH.

Presentation: Amenorrhoea.

Consider pregnancy, weight loss, severe illness, then request: FSH, LH, oestradiol, prolactin, testosterone, consider TSH.

Presentation: Infertility/sub-fertility.

Monitor the pituitary-ovarian axis; request: Midluteal progesterone on day 21 of a 28-day cycle.

If >30 nmol/L, then probably ovulating; no further hormone tests required.

If <30 nmol/L, then repeat twice.

If <30 nmol/L at third cycle, make further test request: Day 5 FSH, LH, oestradiol, prolactin, testosterone.

Presentation: Galactorrhoea.

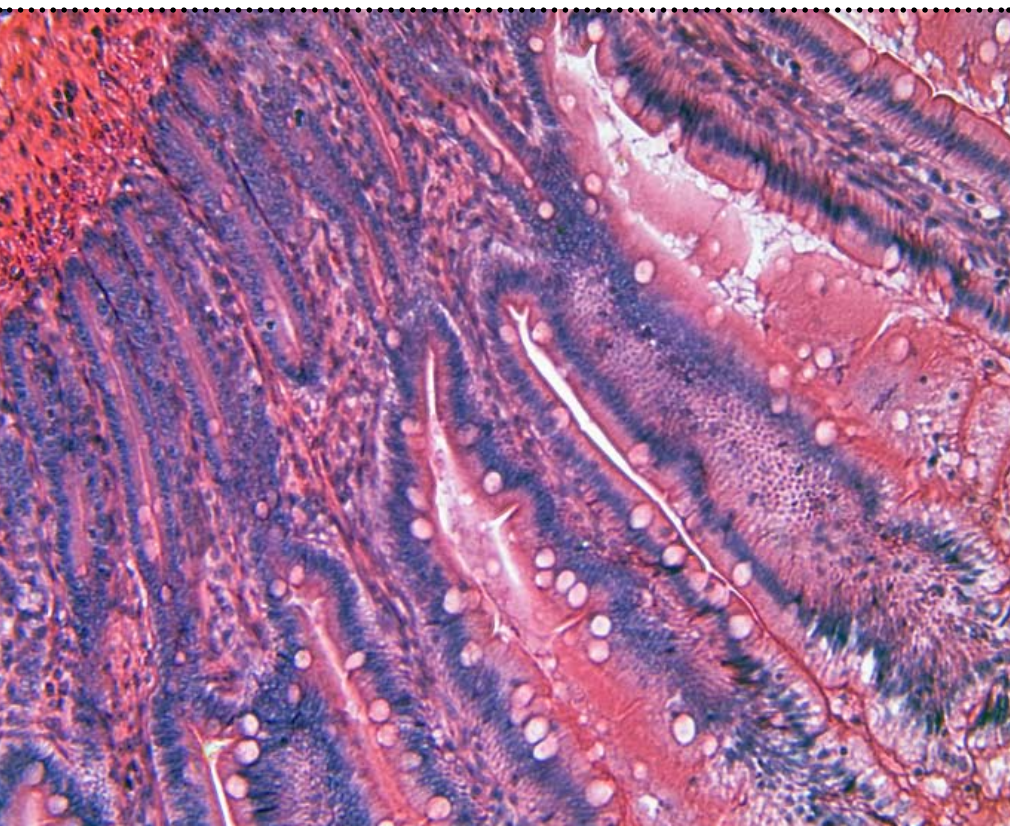
Request: Prolactin, with sample collected after midday in follicular phase (if menses present). Prolactin has a diurnal rhythm and is higher in the morning. Raised prolactin occurs in pregnancy, hypothyroidism and on neuroleptics and other drugs.

Note: In the case of post-pill amenorrhoea, weight loss and hypopituitarism, LH, FSH and oestradiol are usually all low.

Dr Jeffrey Barron & Dr Charles Ng

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Appropriate use of D-dimer testing



D-dimer is a fibrin degradation product, a marker of fibrinolysis. It is typically elevated in patients with disseminated intravascular coagulation (DIC). With

the introduction of more sensitive assays, it is also detectable in patients with venous thromboembolism (VTE).

However, the specificity of a positive D-dimer to indicate VTE is poor. D-dimer can also be raised in patients without a clot, such as those who have had recent surgery, as well as in malignancy, normal pregnancy and severe infection.

Elevated levels can occur in patients over 70, or those already on anticoagulant therapy. An activated blood sample from a difficult or problematic venepuncture can also be a source of a false positive D-dimer.

Good negative predictive value

The strength of D-dimer testing lies with its good negative predictive value, in patients who present with a low likelihood of having VTE based on pre-test probability scoring.

Clinical models, such as Wells' Criteria, help evaluate possible deep venous thrombosis (DVT) by stratifying patients into low, intermediate or high probability categories, depending on their clinical presentation (table 1).

Patients with an intermediate or high probability of DVT (Wells score 1 or higher) should *not* have D-dimer testing, and instead proceed to ultrasound. Patients with a low probability (Wells score 0 or less) can have D-dimer testing. If the D-dimer is negative, DVT is unlikely and ultrasound is not required. A positive D-dimer in this situation should prompt an ultrasound to exclude DVT, especially if no other reason for the presentation is apparent.

D-dimer and pulmonary embolism

For patients presenting with chest symptoms, the Modified Wells' Criteria model (table 2) is useful for clinically establishing the possibility of pulmonary embolism (PE).

For those with a low probability of PE (Wells score 4 or less), an initial D-dimer can be helpful, because a negative D-dimer can exclude PE. Patients with a positive D-dimer in this situation, or those with likely PE based on a probability score of more than 4 points, should have appropriate radiological investigation.

The purpose of using these clinical algorithms is to avoid ordering unnecessary imaging tests on low-probability patients who are found to have a

normal D-dimer result.

D-dimer should therefore be requested only on low-probability patients, during assessment for VTE. Intermediate or high-probability groups – those already with risk factors or signs of VTE –

are best investigated next with radiology, without delaying for D-dimer testing.

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Table 1. Wells' Criteria: A nine-point clinical model for determining likelihood of DVT

| | Score |
|---|-------|
| Active cancer (treatment ongoing or within previous six months or palliative) | 1 |
| Paralysis, paresis or recent plaster immobilisation of the lower extremities | 1 |
| Recently bedridden for more than three days or major surgery within four weeks | 1 |
| Localised tenderness along the distribution of the deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swelling 3cm more than asymptomatic side (measured 10cm below tibial tuberosity) | 1 |
| Pitting oedema confined to the symptomatic leg | 1 |
| Collateral superficial veins (non varicose) | 1 |
| Alternative diagnosis as likely or greater than that of DVT | -2 |

In patients with symptoms in both legs, the more symptomatic leg should be used. Pre-test probability is calculated as the total score. High: 3 or more points. Moderate: 1-2 points. Low: 0 points or less.

Table 2. Modified Wells' Criteria: To establish probability of pulmonary embolism

| | Score |
|---|-------|
| Clinical symptoms of DVT (leg swelling, pain with palpation) | 3.0 |
| Other diagnosis less likely than pulmonary embolism | 3.0 |
| Heart rate more than 100 | 1.5 |
| Immobilisation (three days or more) or surgery in the previous four weeks | 1.5 |
| Previous DVT/PE | 1.5 |
| Haemoptysis | 1.0 |
| Malignancy | 1.0 |

Clinical probability of pulmonary embolism: Likely: more than 4 points. Unlikely: 4 points or less.

References

How we diagnose and treat deep venous thrombosis. Hirsh J, Lee AY. *Blood*. 2002 May 1; 99(9): 3102-3110. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA*. 2006; 295: 172-179.

CASE STUDY

Hailey-Hailey disease

A family with a rare recurrent blistering skin disorder

A 55-year-old woman has had recurrent rashes around the sides and back of her neck since her mid-30s. Her father, brother and daughter have the same condition. The rashes recur about every three months and are usually multiple and asymmetrically distributed. They start as 20-30mm raised oval flat patches with a central blister. The blister ruptures and the lesion becomes a flat, excoriated papule, which resolves in one to two weeks.

A biopsy shows suprabasal acantholysis¹, parakeratosis², focal excoriation and crusting. The superficial dermis is oedematous and dermal blood vessels are congested. Neutrophils infiltrate the superficial dermis at sites of excoriation and crusting. Solar degeneration is present in the upper reticular dermis, together with abundant lymphocytes and a few eosinophils.

Case histology

The histology is that of a suprabasilar blistering disorder. The clinical progression of individual lesions from rash to blister to excoriated papule and the site and family history are typical of Hailey-Hailey disease (familial benign chronic pemphigus).

The histological pattern of suprabasal

acantholysis at different levels in the epidermis and the absence of dyskeratotic³ cells and hyperkeratosis favour this diagnosis over Darier's disease, another inherited blistering disorder. Further conditions in the differential diagnosis (pemphigus, Grover's disease and acantholytic actinic keratosis) are excluded by the clinical and histological findings.

Further characteristics

Hailey-Hailey disease was originally described by the Hailey brothers in 1939. It is sporadic in nearly one-third of cases or is inherited as an autosomal dominant condition with incomplete gene penetrance.

There is a widespread subclinical abnormality in keratinocyte adhesion and clinically apparent lesions may be induced by heat, UV light, perspiration or local infection. The neck is a typical site, as are the axillae, genitocrural, perianal and inframammary areas.

Management may be difficult and includes treatment of secondary infection, topical steroids for symptomatic disease and measures to reduce maceration and abrasion.

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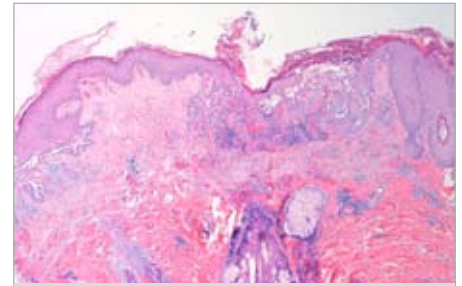


Figure 1. Low magnification

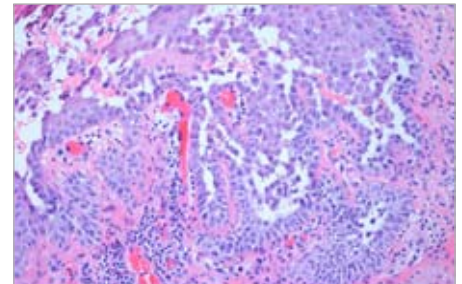


Figure 2. Higher magnification to show acantholysis

Footnotes

- ¹ Separation of epidermal cells from one another, above the basal layer
- ² Retention of nuclei in the keratinised cells of the stratum corneum
- ³ Abnormal keratinisation of individual keratinocytes (epidermal cells)

References

Weedon's *Skin Pathology*. David Weedon. Third edition, 2010. Churchill Livingstone.
Familial benign chronic pemphigus (Hailey-Hailey disease). Warycha M, Patel R, Meehan S, Merola JF. *Dermatol Online J*. 2009 Aug 15; 15(8): 15 (free article).

Acknowledgement

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