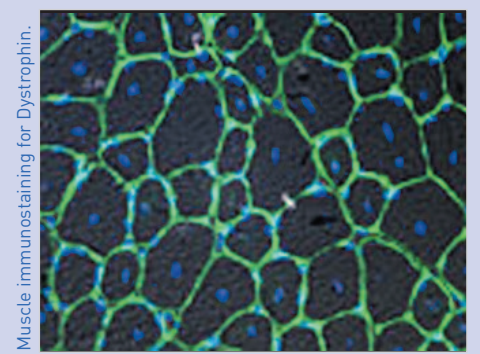
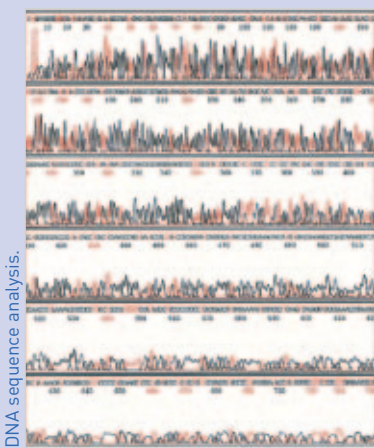


DMD CARRIER TEST REDUCES SURVEILLANCE



in 36 families whose carrier status was uncertain were investigated. Of these, eight women were confirmed to be carriers of the mutation and 37 were shown not to be carriers. The exclusion of the carrier state in these 37 women has major implications as some carriers of a DMD mutation can exhibit late onset of cardiomyopathy. Only carriers now need cardiac surveillance.

In addition, at risk women no longer need to be worried about invasive prenatal diagnosis to detect DMD. This new testing thus has the potential to significantly reduce the anxiety of female relatives of patients with DMD and to reduce unnecessary demands on the health system for expensive and limited resources such as cardiac catheterisation. For each woman in whom DMD carrier status has been excluded, another five female relatives, on average, can be excused from active surveillance.

Continued page 2



Fig. 1, Low power H&E, mass lesion.

Test and Teach Case

BENIGN OR MALIGNANT?

An 87-year-old female presented with a subcutaneous mass located on the ulnar aspect of her left wrist. The lesion was surgically removed and sent for histology with a clinical request to determine if the lesion was benign or malignant. No other history was available. The specimen macroscopically consisted of a skin ellipse 16x7mm with central ulcer and a separate "fibrous" piece of tissue 14x10x7mm. Figure 1 shows an H&E stained section of the mass at low power.

Questions

1. Is the mass benign or malignant?
2. What is the diagnosis?

Answers page 2

Duchenne muscular dystrophy (DMD) is severe, progressive and fatal. The inherited X-linked muscle disease is transmitted through carrier females and affects approximately 1:3,000 boys.

In South East Health the diagnosis and care of children and families with DMD rests on two pillars. The first is clinical assessment by a team of specialist neurologists, geneticists, surgeons, social workers and genetic counsellors at the muscle disease clinic at Sydney Children's Hospital. The second is the coordinated pathology assessment of patient samples involving the SEALS Clinical Chemistry, Immunopathology, Anatomic Pathology and Genetics laboratories.

The SEALS Genetics Laboratories are the NSW state reference centre for the genetic diagnosis of DMD and offer one of the most comprehensive suites of laboratory tests for this disorder anywhere in the world. Recently the laboratory has introduced carrier testing for the most common form of mutation in the Dystrophin gene. Glenda Mullan, who has received a SEALS Award of Excellence in part for this work, developed the test. SEALS is the first pathology service in Australasia and the South East Asian region to offer carrier testing for Duchenne muscular dystrophy.

The importance of carrier testing for families is illustrated by the results of a small pilot study. A total of 45 women

In this issue...

- > SEALS offers DMD carrier testing
- > Viewpoint - Area mergers won't change service
- > Plasma metanephrines detect tumours
- > New slip for Pap smears
- > Pathology requests - a matter of form
- > The blended life of Dennis Wakefield
- > Comings and goings
- > Breath test detects *H. pylori*

The SEALS genetics laboratories are continuing to develop a comprehensive screen for all classes of mutations in families with DMD. Our aim is that within two years we will be able to rapidly diagnose the mutational basis of every family with this condition and accurately

work out who are carriers and non-carriers of the mutated gene.

The SEALS genetics laboratories gratefully acknowledge the support of the Muscular Dystrophy Association of New South Wales. ■



Dr Michael Buckley
Director SEALS Genetics

Plasma metanephrines detect pheochromocytoma

Pheochromocytomas are rare tumours that can be life threatening. They are characterised by excessive production of catecholamines, frequently leading to increased blood pressure. Though rare, pheochromocytomas must be considered in many patients with hypertension, who account for nearly a quarter of the adult population of western countries.

Diagnosis of pheochromocytoma is critically dependent on the demonstration of excessive amounts of catecholamines. However, this approach is fraught with difficulties. Vanillylmandelic acid (VMA) estimation in urine has been shown to produce false-negative results. Measurement of fractionated urinary catecholamines or metanephrines has long been the preferred route, but false-positive results may arise and can be troublesome. The collection of a complete 24 hour urine sample can also present difficulties.

Advances in HPLC technology mean measurement of plasma metanephrines is now possible. In recent studies, plasma metanephrines appear to have the highest sensitivity for the diagnosis of pheochromocytoma.

The superiority of plasma metanephrines is based on three factors. First, they are produced continuously by catecholamine metabolism within tumour cells. This contrasts with catecholamine secretion which is episodic. Secondly, sympathoadrenal excitation leads to large increases in catecholamine release whereas plasma-free metanephrines remain largely unaffected. Thirdly, urinary metanephrines and VMA are different metabolites from the free metanephrines in plasma and are produced in different parts of the body by metabolic processes not directly related to the tumour.

Therefore, plasma metanephrines is currently the best test for excluding pheochromocytoma. A fasting whole blood sample collected in an lithium heparin tube on ice is required. SEALS Department of Clinical Chemistry is the only laboratory currently offering this service in NSW. ■

Reference: Lenders JWM, Pacak K, McClellan MW et al. Biochemical Diagnosis of Pheochromocytoma: Which test is best? JAMA Mar 20, 2002. Vol 287, No 11, p1427-1434.

Dilo Pillai & Peter Day
SEALS Clinical Chemistry

Test and Teach answers

1. Benign
2. Foreign material with dematiaceous fungal infection consistent with phaeohyphomycosis.

MICROSCOPIC DESCRIPTION

Microscopy showed an inflammatory infiltrate (Fig. 2) with a granulomatous reaction around a piece of foreign vegetable matter (Fig. 3). Within granulomas there were brown fungal hyphae and occasional spores, which were highlighted with PAS staining (Fig. 4).

Fig. 4, PAS high power showing hyphae. Phaeohyphomycosis is used to describe a diverse group of pigmented fungal infections characterized by hyphae. The most common lesion is a circumscribed cyst or abscess within the lower dermis or subcutis.



Fig. 2, H&E high power, inflammatory infiltrate.



Fig. 3, H&E foreign body (vegetable matter).



Fig. 4, PAS high power showing hyphae.

COMMENT

Pigmented fungi (black moulds, dematiaceous) are a heterogeneous group common in the environment, which may occasionally cause infections in humans. The range of human infections includes mycetomas, chromoblastomycosis, sinusitis and phaeohyphomycosis. The usual mechanism of infection is via a penetrating injury with exposure to contaminated material e.g. decaying wood or plants. Infection is also possible by inhalation of spores, oral ingestion and nosocomial acquisition e.g. IV insertion.

Dematiaceous fungi are usually considered to have a relatively low virulence and host factors determine clinical presentation. Invasive disease is more frequent in immunocompromised individuals especially those with impaired cell-mediated immunity. Treatment usually consists of complete surgical excision plus an antifungal agent such as itraconazole.

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Dr Colin Arnold, Registrar in
Anatomical Pathology, SEALS Kogarah

EDITORIAL

Inside Insight is the quarterly clinician newsletter of the South East Area Laboratory Service (SEALS).

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Borders no barrier to service

The much-anticipated changes to the structure and management of NSW public health care services have just been announced. As expected, Area Health Services have amalgamated. The current 17 areas are being reduced to eight. Of particular relevance to SEALS is the merger of the former South East and Illawarra Health Areas.



The impact of Area restructuring on the distribution of public pathology services and the recommendations of the recent Paxton's report into public pathology are not yet clear. However, SEALS, by whatever name, will adapt to any new structures required. These changes will create new opportunities to improve diagnostic services to the state's public hospitals where the most serious, complex and difficult medical problems are usually managed, and to our referring clinicians.

SEALS' charter is to deliver diagnostic services and expert opinion for direct patient care. A close watch will be needed to ensure that changes do not diminish the quality, timeliness and effectiveness of public pathology provided by a committed staff.

We look to our clinical colleagues for support and for their insistence that pathology is retained as an essential element in clinical service planning for the new structures and is not separated from clinical management into an environment where its role and importance is less well understood. ■

Dr Roger Wilson
Executive Director, SEALS

Innovations

NEW PAP SLIPS

SEALS Cytology has introduced a Pap smear result notification slip as a new service to clinicians for their patients.

The slip is only provided for negative results and is attached to the back of the Pap smear report. The slip displays the patient's name and address with the negative result. It is designed to be cut off and to fit into a standard windowed envelope for mailing.

Space is provided for the clinician/nurse practitioner's signature to indicate they have sighted the result. A recommended time for the patient's next smear can also be included.

The slip is an easy way to notify patients of their normal smear results. It reduces clerical work and provides a record that the patient has been notified. Currently, it is available to all clinicians in the POWPH L7 consulting suites, the Royal Hospital for Women, Prince of Wales Hospital, Sutherland Hospital and selected St George Hospital clinics.

We hope that this new service will be of value to our clinicians, their clinics and administrative staff.

Please direct all enquiries to the Cytology section, Anatomical Pathology Department, SEALS Randwick.
Tel: 9382 9128 Fax: 9382 9037. ■

PATHOLOGY REQUESTS - a matter of form

Pathology [testing] is essentially communication between clinicians and laboratories regarding a sample from a patient. Most of SEALS' business is transacted in response to written requests on forms, which must be approved by the Health Insurance Commission (HIC). While changes to the request form are not always popular with clinicians, they are considered necessary in a testing environment which is experiencing technological and regulatory change.

The new general pathology request form, approved by the HIC, was determined by competing factors - inpatient/outpatient/emergency, public/private/billable, changing patient locations and shared medical care, ethnicity, urgency, PAP registry. Not all spaces apply to all requests, however multiple tests collected at one service episode can be accommodated using a single form.

Blood Bank/Transfusion requests should be made on the separate request forms which are available at all SEALS sites

Even with around two million tests a year, every patient sample is as precious to SEALS as to the requesting clinician. The content and timeliness of the final laboratory report is often determined by the quality of the request and the tests selected initially - if there are questions about a particular test request, SEALS is always happy to assist. Errors at the beginning are only compounded in analysis.

Good communication underlies quality healthcare - there is no magic. SEALS will continue to ask for legible and relevant clinical information or a diagnosis with each request, however obvious it may seem to you, the user. This is the most cost effective and time efficient solution. In computer-speak, "Garbage in = garbage out".

Using request forms thoughtfully will improve SEALS' service to your patients. On request, personalised forms can be prepared. Phone the Call Centre (1800 0 SEALS). ■

Ron Begg, Campus Operations Manager
Ivy Fong, SEALS Quality Manager

Blending practise and passion

Economist reader, father of three and a recent grandfather, Professor Denis Wakefield manages to blend work and play into a full programme that still allows time for a daily run and theoretically, a weekly game of golf. Sadly, something has to give and although a speed-reader, the Prof regrets he can't squeeze in his historical literary interests in conflict and warfare.



And with such a busy life, it's hardly surprising. Prof Wakefield is Head of School of Medical Sciences and Professor of Pathology at UNSW. He was sub Dean (Education) in the planning stages of the new undergraduate curriculum. For the last 15 years Prof Wakefield has been Clinical Director of Immunology in SEALS, now situated in the Sutherland Centre for Immunology (SCI). He consults at Sutherland Hospital and the Randwick Campus. He is the chairman of Academic Pathology in the RCPA.

Having transferred to medicine from an undergraduate course in applied psychology, Prof Wakefield is no stranger to mixing disciplines. His career has been a blend of teaching, clinical work and research in immunology, especially of the eye. His proudest achievements include establishing SCI and developing and expanding the School of Pathology into the leading institution in Australia. The School has networked national centres of excellence in Vascular Research, Inflammation and Bone Metabolism.

"The recent explosion in knowledge of the nature of diseases is astounding. We now can teach pathology as a dynamic, clinically relevant discipline. Clinical teaching in the new curriculum starts from year one where pathology forms the basis of all medicine," said Wakefield.

"New tests are useful but without a thorough patient history and careful clinical examination they will be devalued. My mentors always took a history and examined their patients. They listened and thought about their patients' problems before using tests, thus maximising the value of pathology services," he commented.

"Practising medicine is a privilege and a passion. To be able to help patients and to be rewarded by their appreciation is wonderful; I would not want any other career."■

Urea Breath Test | SIMPLE, SAFE - SAME-DAY RESULTS

The urea breath test is a simple technique for both detecting *Helicobacter pylori* and assessing the success of eradication therapy. It is the only test, apart from endoscopy, which will give an answer regarding successful eradication therapy after completing therapy, as antibody levels take six to 12 months to decline.

H. pylori infection results in chronic gastritis and predisposes individuals to gastric ulcers (about 70% of cases) and duodenal ulcers (about 90% of cases). Breath tests are increasingly being used for identification because they are non-invasive, well tolerated and cheap in comparison to invasive procedures and can be performed easily as an outpatient service.

The test involves a minimum four-hour fast and takes less than an hour to perform. The patient must not have taken antibiotics or proton pump inhibitors (e.g. Losec or Zantac) for seven days prior to collection. These medications may suppress but not eliminate the bacteria.

A baseline breath sample is collected and the patient is given a drink containing ^{13}C urea. A second breath sample is collected 30 minutes later. If *H. pylori* is present the ^{13}C urea is split and $^{13}\text{CO}_2$ is produced and exhaled in the breath at much higher levels than in non-infected individuals.

^{13}C urea is non-radioactive and the test is therefore safe in children and during pregnancy.

Patients may be referred to SEALS Pathology Collection Centres at Sutherland, St George or Prince of Wales Hospitals for testing. All samples are sent to the laboratory for analysis and results are available on the same day.■

Peter Day and Ian Fraser
SEALS Clinical Chemistry

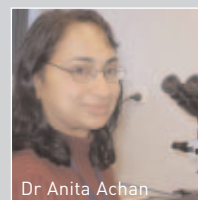
[NOTICEBOARD]

COMINGS & GOINGS

Overseas visitors are frequently found in our laboratories - a sign of the healthy regard in which SEALS is held in the wider world of laboratory medicine. **Henna Sunoko** from Semarang in Indonesia recently spent some weeks in both Clinical Chemistry and Molecular Genetics, furthering her interest in the role of polymorphisms of the *alaD* gene in lead toxicity.

While visiting Sydney, **Trudi McDevitt** of the National Centre for Medical Genetics, Dublin, has taken the opportunity to spend some days in the Molecular Genetics Laboratory to look at testing for hereditary breast cancer. This visit continues an established liaison between the two centres.

Karu Karunakaran, SEALS Director of Finance and Business Services, has accepted a secondment as Director of Finance and Business Development at Al Ahli Hospital in Qatar - a new private hospital under Australian management. Karu has made an enormous contribution to the financial management of SEALS over the last two and a half years and his steady hand will be greatly missed.



Dr Anita Achan

Three new pathologists have joined SEALS Randwick. In Anatomical Pathology **Dr Anita Achan** and **Dr Madhu Rao**, and in Haematology **Dr Carol Cheung** have been appointed staff specialists.



Dr Madhu Rao



Dr Carol Cheung

Dr Achan has relocated from John Hunter Hospital where she worked after completing post-graduate training at Geelong, Liverpool and John Hunter Hospitals. Dr Rao graduated from the University of Tasmania and completed his pathology training at Liverpool Hospital. Dr Cheung has recently completed her post-graduate training and PhD in the Haematology Department at SEALS Randwick and will be well known to many clinicians.■