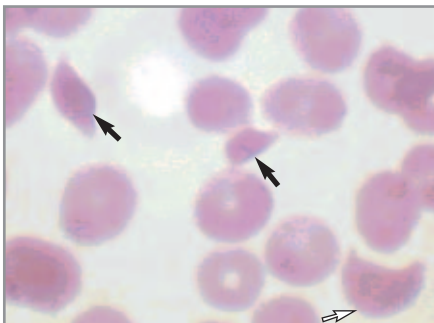


BIRD FLU - planning & preparation to prevent pandemic



Test and Teach Case

Indicative but not diagnostic of a serious condition

A 47-year-old male presented with suprapubic pain, mild fever, abdominal pain and urinary retention following two weeks of malaise, myalgia, fever with sweating, but no diarrhoea. PR revealed an enlarged, boggy and tender prostate. Urine microscopy showed >100 white cells/cmm but no organisms. He improved initially on IV ceftriaxone and gentamicin for prostatitis. FBC on admission: Hb 154, WCC 11.24, Plt 248, LFT and UEC normal. On day five he developed jaundice and acute renal failure. Pathology: Hb 87, WCC 21.7, Plt 54, reticulocyte count 55, EUC 128/3.2/93/24/13.7/195; LFT - Bili 181, ALT 217, AST 172, GGT 241, LDH 1366. Coombs test negative. Blood film on day five is shown above.

Question

What morphological changes are present in the blood film and what is the differential diagnosis in this situation?

Answers page 3

Influenza is a highly contagious, respiratory disease which kills approximately 1200 Australians every year, people who might otherwise have survived if they were vaccinated. Avian influenza is spread from birds when they come into close contact with people. The concern with Avian influenza is that if the virus spreads from birds to humans, subsequently changes (via recombination with human influenza viruses), and is able to spread from person to person, then pandemic (worldwide) influenza might result. During the most severe pandemic of the twentieth century, 1918-1919, between 10 and 30 million people died. It has now been 32 years since the last pandemic. Community concern about the potential for a new pandemic is high.

Influenza is infection of the nose, throat, and more rarely the lungs, heart and brain with influenza virus – typically type A, less commonly type B. Avian influenza presents with similar symptoms to those of human influenza (fever, cough, rigors, rapid onset) but has a much more abrupt course, with rapid deterioration and sometimes death from overwhelming infection and pneumonia.

Type A H5N1 influenza has infected many birds throughout South East Asia, but predominantly caused human infection and death in Vietnam and Thailand. A total of 34 human cases have occurred (compared with millions of bird infections), and 23 people have died since 1 January 2004 – eight in Thailand and 15 in Vietnam. Avian influenza is unusual in that most cases were young (median age 15.5 years) perhaps reflecting that young people without previous exposure to influenza viruses (Avian or human) are

immunologically naïve and more at risk of rapid, overwhelming infection. Diagnosis of influenza is relatively straightforward during the peak season (June to August in NSW) on the basis of typical symptoms, and a throat swab, nose swab or nasopharyngeal aspirate showing the presence of virus. Such rapid tests are available through the SEALS Virology Diagnostic Laboratory the same day when specimens are received before midday. Where new strains of influenza arise (antigenic shift), then new reagents may be needed. In the case of Avian Influenza, H5N1 specific tests have had to be developed – utilising RT-PCR with specific primers (to detect virus) or tests for antibody in infected humans, using WHO derived virus.

Prevention of pandemic influenza involves preparedness (there are State and Commonwealth pandemic planning teams involving members of SEALS and South East Health), public health measures, vaccination and treatment of suspected cases.

Continued page 2

In this issue...

- > Avian flu: a preventable pandemic?
- > Assess blood film for diagnosis
- > Viewpoint: review of public pathology
- > STR & iron deficiency anaemia
- > Are you passing the first page test?
- > DNA tests for fragile X
- > Roger Crouch earns a break
- > Laboratory Science Week
- > Playing it Safe
- > Noticeboard

The WHO has an Avian flu vaccine created by reverse genetics (a new technique of inserting immunogenic parts of the virus into a non fatal virus backbone) that should be available to manufacturers by mid April 2004 (The Scientist 17 March 04, www.news.yahoo.com 26 Feb 04). Information is available from government agencies via information

lines (1800 004599), from the WHO (http://www.who.int/csr/disease/avian_influenza), and through reference laboratories in NSW - SEALS on 9382 9050. Treatment with the neuraminidase inhibitors (Tamiflu - oseltamivir, or Relenza - zanamivir) is available to reduce the more severe symptoms of human influenza (A & B), and appears to be useful in Avian

influenza of humans if given within 30 hours of developing symptoms. Continuing preparedness is the key - in terms of surveillance, pandemic planning, availability of vaccine production facilities and antiviral drugs. ■

A/Prof Bill Rawlinson
Medical Virologist

STR and iron deficiency anaemia

Determination of serum iron, transferrin, transferrin saturation and ferritin are widely used as tests of iron status. However, these tests are considerably influenced by acute phase responses arising from infection, inflammation or malignancy.

Transferrin is the major transport protein of iron in the blood. The iron-carrying transferrin binds to cell surfaces through a specific transferrin receptor (TfR). The transferrin-receptor complex is internalised into the cell and the iron released. Virtually all cells have transferrin receptors on their surface but about 80% of cellular receptors are in the erythroid marrow.

The transferrin receptor number on the cell surface reflects the iron requirement, and iron deprivation has been shown to result in the prompt induction of transferrin receptor synthesis.

A form of the transferrin receptor exists in the blood circulation. This soluble transferrin receptor (sTfR) has been shown to be a truncated form of the cell surface receptor and is derived from proteolysis of the cell membrane. The soluble transferrin receptor concentration reflects the number of cellular receptors and their concentration increases in states of iron deficiency. Unlike iron, transferrin and ferritin, the soluble transferrin receptor is not an acute phase protein and therefore can be used to differentiate iron deficient anaemia from the anaemia of chronic disease. ■

Table 1: LEVELS OF STFR IN NORMAL AND DISEASE STATES

Non-disease levels	Adult level: 0.8 – 2.3mg/L Neonates: Increased. Adult levels reached by about 17 years of age. Pregnancy: Increases with gestational age and returns to non-pregnant values by about 12 weeks post delivery.
Increased in disease	Increased erythroid proliferation (b-thalassaemia, autoimmune haemolytic anaemia, polycythaemia, sickle cell disease).
Normal in disease	Most leukaemias (chronic lymphocytic leukaemia and myelodysplastic diseases may show increased levels). Haemochromatosis may show normal to decreased levels.
Decreased in disease	Chronic renal failure, aplastic anaemia, post-bone marrow transplantation.

The measurement of sTfR is included in the iron studies panel at the Clinical Chemistry Laboratory at Randwick, on a trial basis.

Peter Day & Mary Moriatis
SEALS Clinical Chemistry

Play it safe

In this age of litigation and liability, SEALS cannot afford to leave the management of workplace safety to chance.

With new OH&S legislation, regulations, codes of practice, national guidelines and Australian Standards, not to mention severe penalties for non-compliance, there is no reason why any workplace should not have a risk management program in place.

An effective risk management approach at the workplace can result in reduced workplace injury claims, reduced insurance premiums and improved staff morale and productivity.

SEALS recognises that the very real benefits of strong risk management policy flow not only to its staff, but to its referring clinicians and their patients as well.

Laboratories which have suffered the disruption and workload pressures of having highly skilled and valuable staff away injured or ill, well know that protecting staff is essential for morale, quality management and ultimately, customer service.

As well as benefiting from SEALS safety procedures, clinicians have an important role to play in minimising the risk to staff from exposure to patient specimens.

Although universal precautions are taken when handling all specimens, we are reminded by the SARS experience that special cases require special procedures – specimens from patients with highly infectious conditions or who are on cytotoxic drug therapy, need to be appropriately labelled and identified to protect those who handle them and to permit additional measures to be taken. Workplace safety is everyone's concern. ■

Melinda Tan
SEALS OH&S Manager

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

Editorial team: Peter Taylor, Stuart Purvis-Smith, Sue Acland, Anne-Maree McDougall, Desiree Berry.

Copy editor: Kath O'Sullivan, Active Voice www.activevoice.net.au

Design: Garry McArthur, Design Unit, SESAHS

Please send your comments and contributions to taylorp@sesahs.nsw.gov.au

Deadline for Issue 4: Friday July 2, 2004.

© SEALS

Review of NSW Public Pathology Services

Consultants to NSW Health have recommended that the 17 NSW area-based Public Pathology Services be merged into three large entities. The business case for such a change is being audited. The impact on clinician users and university partners of public pathology also needs to be identified and debated. It is vital that any decisions made will advance the quality and effectiveness of public pathology in all its important roles in patient care, biomedical research, teaching and public health, and not be solely a cost-cutting measure.



The status of pathology as a critical clinical service has been subjugated by its bureaucratic designation as a corporate support service and commodity. It is mostly those who neither use nor provide pathology services who use this language. Whether unwitting or not, their lack of insight devalues the medical contribution of pathology and isolates it from the clinical management process in which it is so vitally important.

Pathology teaching is vanishing from undergraduate medicine, resulting in declining knowledge about test selection and interpretation and the inherent limitations of laboratory medicine investigations. Declining interest in pathology as a career choice compounds an evolving medical workforce crisis. If these very worrying trends continue unchecked, any expectation that future models of pathology services will improve clinical care of hospital based patients, particularly those needing the support of our major public teaching hospitals, may prove soundly misplaced. ■

Dr Roger Wilson
Executive Director, SEALS

Innovations

DNA TESTS MORE SENSITIVE THAN FRAGILE X SCORES

Fragile X syndrome is the most common inherited cause of intellectual disability but is no longer defined by the chromosomal fragility for which it is named.



Identification of the amplified or expanded triplet repeat which inhibits the FMR1 gene function in this disorder has led to DNA testing which is more sensitive and specific than the previous cytogenetic scoring of "fragile" X chromosomes.

DNA testing is now the standard method for fragile X diagnosis. SEALS Genetics, which has provided this service since 1990, is the only laboratory in NSW providing comprehensive patient diagnosis and prenatal fragile X testing. If the aetiology of the mental impairment is unknown, both the fragile X DNA test and routine cytogenetics should be considered as part of a comprehensive genetic evaluation.

As an inherited disorder, the diagnosis of fragile X syndrome has implications for the patient's family and it is important that relatives of an affected individual be offered genetic counselling. ■

Peter Taylor
Molecular & Cytogenetics Unit

Test and Teach answers

This blood film showed significant red cell fragments. The two dense staining ones (solid arrow) near centre field are characteristic of microangiopathic haemolytic anaemia (MAHA). The 'helmet' cell (block arrow) is more typical of renal failure.

CLINICAL PROGRESS

A diagnosis of haemolytic-uraemic syndrome (HUS) was made, possibly related to infection (?prostatitis). Other investigations: no heparin dependent Abs, D-dimer 6.05, Fibrinogen 6.2. Urine and blood cultures were negative. Special stool culture for E. coli (O157:H7) serotype was subsequently requested.

He was infused with plasma (20ml/kg/day) over three days (total 23 units) and transfused with two units of packed cells. Renal function stabilized and after an additional five units of plasma his creatinine peaked at 196 umol/L and returned to normal after seven days (corresponding bilirubin and LDH were 32 and 290 respectively).

LESSONS FROM THIS CASE

1. Adequate history will lead the laboratory to look for presence of the characteristic red cell fragments and communicate with the clinical team.
2. Special stool culture is required to isolate E. coli strains responsible for cases of HUS. Again, appropriate clinical information on the request form is crucial.

REFERENCE

George JN et al. Thrombotic thrombocytopenic purpura-haemolytic uremic syndrome: diagnosis and management. J Clin Apheresis 1998; 13:120-5.

Dr Y L Kwan, Director
Haematology SEALS Kogarah

Heroes and villains of the first page

Readers of the Sydney Morning Herald literary pages may be familiar with "The First Page Test", a weekly column which examines the success or otherwise of a book's first page in which heroes and villains are introduced, the plot glimpsed and the reader enticed to read on...

The first page in pathology testing, the request form, is likewise critical to the success of the testing process. It introduces the main characters, states its aims and provides the context. A dysfunctional first page can cause delays, frustration and confusion. This is unsatisfactory for the clinician, the patient and laboratory staff.

Quality management is designed to ensure integrity of the testing process but does not extend to the quality of the request form – that is in the hands of clinicians. Audits of request forms show that many fail the first page test because they are unsigned, illegible or missing important details such as consultant's name (and initials), DOB or MRN, location (in patients) and private patient address, or most importantly why the test was requested.

SEALS staff expend considerable time and energy chasing up problem request forms. We need more "first page heroes" to provide a quality start to our testing. Tell us what the specimen is, where it came from and what questions you want answered then leave the rest to SEALS. ■

Stuart Purvis-Smith, Lab Manager, SEALS Genetics
Ivy Fong, SEALS Quality Manager

Crouching pathologist, (not so) hidden legacy

After 36 years in one institution, Roger Crouch has earned a break. On 2 July he will retire as Director, Anatomical Pathology, SEALS.

Roger commenced as a Pathology Registrar at Prince Henry Hospital in 1968. He was appointed Staff Specialist in Anatomical Pathology at Prince of Wales Hospital in 1973 and progressed to Senior Staff Specialist 1981, Head of Department 1984 and Director, Anatomical Pathology, SEALS 1996.

Roger has seen many changes to the practice of anatomical pathology over his career. Among them has been the development of fine needle aspiration cytology and immunohistochemistry in tumour diagnosis; a marked decline in autopsies (from 330/year in 1978 to less than 20/year now); and the growing role of cytogenetics/molecular genetics in diagnosis.

In 1973, long before continuing professional development programs became mandatory, Roger initiated a monthly slide seminar for pathology colleagues. More than 30 years later, it is still going strong.

More than 50 registrars have benefited from Roger's wisdom and experience. It has been a great pleasure to him to see most become practising anatomical pathologists.

In 1997 he orchestrated the amalgamation of five laboratories - Prince of Wales, Prince Henry, Sydney Children's, Sydney/Sydney Eye Hospitals and Royal Hospital for Women - into one functional unit.

"My memories of SEALS will be of the many dedicated staff, medical/laboratory/clerical, that I have worked with, the many clinicians I have both served and learned from, and bright young registrars that have stimulated me and kept me on my toes," Roger said.

"I have two lovely young granddaughters who are a great joy in my life. I am looking forward to having more time for my family, play a bit more golf and have time to travel."

Roger will be remembered for his good humour, patience and quiet leadership as a teacher and clinical pathologist through times of vigorous and often disruptive change.■

Kath O'Sullivan
Editorial Consultant for Inside Insight



[NOTICEBOARD]

NEW TEST FOR COELIAC DISEASE (CD)

Coeliac disease is found in three to seven per thousand of the general population when improved diagnostic testing is employed.

In 1997 tissue transglutaminase (tTg) was identified as the target of the endomysium specific autoantibodies in CD. The tTG converts glutamine into glutamic acid in gluten-derived peptides. These peptides bind with high affinity to the disease-associated HLA-DQ2 or HLA-DQ8 molecules and stimulate inflammatory T cell responses. tTG is involved in both humoral and cellular immune response to cereal (gluten) toxicity.

Human tTG is the target antigen source for the enzyme-linked immunosorbent assay for anti-endomysial antibodies (EMA). Anti-tTG IgA antibody is the preferred diagnostic test for patient screening and management of CD although anti-tTG IgG is an alternative assay in IgA deficiency, which is 10 to 15-fold more common in CD.

Anti-gliadin antibody testing for CD has been used in the past but the assay lacks the sensitivity and specificity of the newer tissue transglutaminase (tTG) assay. The anti-gliadin antibody assay is still available when specifically requested.■

NEW NHMRC GRANTS

Craniofacial genetic testing

2004, \$20,000, Michael Buckley with Tony Roscioli. "Testing of families with craniosynostosis." The collaborating groups: Anne Turner, Medical Genetics, SCH; Mark Gianoutsos, Plastic Surgery, SCH.■

Grant from the Muscular Dystrophy Association of NSW

2004, \$54,000, Michael Buckley, Molecular Genetics. The collaborating group: David Mowat, Medical Genetics, SCH. "Development of a sequence based testing system for families with Duchenne Muscular Dystrophy."■

Talking up medical science

From Marie Curie to modern medications, some of the greatest achievements in the history of medicine are delivered to us through the work of medical laboratory scientists.

Whether it's helping to prevent the spread of SARS or malaria, conducting laboratory tests that assist in transplant surgery, analysing tissue samples, supplying blood for transfusion, or determining how research results can be translated into new treatments, medical scientists help to save lives and improve care for millions of Australians.

Medical scientists usually specialise in the following disciplines: Histopathology; Microbiology; Virology; Cytology; Genetics; Haematology; Blood transfusion; Immunology; and Biochemistry.

Because much of the work of medical scientists is carried out behind the scenes and out of the public eye, there is a general lack of awareness about the profession.

In response to this, the Australian Institute of Medical Scientists (AIMS) organised National Medical Laboratory Science Week (NMLSW) from 10 to 16 May 2004. AIMS plans to host the week annually.■

For more information, visit www.aims.org.au/nmlsw