

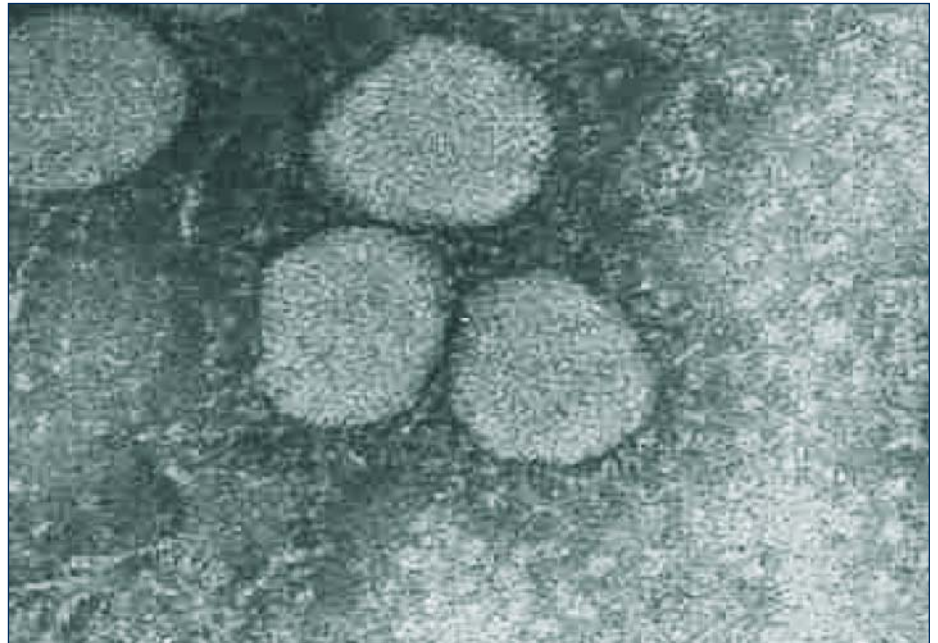


SEVERE ACUTE RESPIRATORY SYNDROME

Severe Acute Respiratory Syndrome (SARS) is believed to have appeared as a human infection in Southern China in November 2002. Global spread did not begin until the third week of February this year when an infected doctor carried the virus from Guangdong to a Hong Kong hotel, where several other guests were infected and subsequently spread the virus to Hanoi, Singapore, Vancouver, and Toronto. It was another week or two before it was realised that this was likely to be a new infectious disease.

In the absence of a known causal agent it was defined as a clinical syndrome to track the disease. It spread to many other countries, most of which were able to contain the infection, while Singapore, Hong Kong, mainland China, and Taiwan struggled with ongoing spread. The epidemic peaked in March and April followed by a steady decline over the following weeks. Taiwan was the final country to be officially declared free of ongoing transmission on 5th July. Over 8,000 cases had been identified and 1 in 10 of these people have died so far. In Australia, over 100 possible cases were investigated but none were shown to be infected with the new virus.

Within a matter of weeks the infectious agent had been identified and diagnostic tests had been developed. It has been convincingly shown that SARS is caused by a coronavirus new to humans, subsequently named SARS-CoV. Coronaviruses were already well known as a cause of mild illness in humans, usually the common cold, and as a cause of a range of animal diseases, but this virus was not like any of those already



An image of SARS-CoV, courtesy of the World Health Organisation

known. It is assumed that it does have an animal source but despite recent speculation about the role of civet cats, its animal origin and the method of entry into human populations has yet to be clarified.

The disease caused by SARS-CoV begins with a fever and myalgia, progressing to pneumonia and diarrhoea. About 20% of patients go on to a final phase of progressive deterioration of lung function usually leading to death. Overall the mortality is around 10-15%, but older adults are much more likely to succumb. Up to 90% of cases identified have been health care workers, and most of the remainder has been family contacts of cases. Health authorities realised that transmission required close contact with large respiratory droplets that usually spread only short distances of a metre or less. This was effectively stopped in health care facilities by the use of gloves, gowns, masks and handwashing. An unexpected mode of transmission occurred at the Amoy Gardens apartment complex outbreak in

Hong Kong, when problems with plumbing led to large amounts of virus contaminated aerosols being spread from the sewage system following the visit of an infected patient with diarrhoea. Strict application of infection control measures and traditional public health measures of outbreak investigation, contact tracing and isolation was the key to the successful control of the epidemic.

Virus detection by PCR became available at PathCentre in late March and serological tests more recently. Unfortunately neither the PCR or serological tests reliably detect early

(continued on page 2)

INSIDE THIS ISSUE

Lipase assay	Page 2
Cardiac enzymes	Page 2
Profile: Leanne Negus	Page 3
Risperidone	Page 3
Notifiable infections	Page 3
Onychomycosis	Page 4

(continued from page 1)

infection, so patients need to be managed based on the clinical syndrome until it is certain they were not infected with SARS-CoV. Guidelines for the investigation of cases are available from the Public Health Laboratory Network (www.health.gov.au/sars/pdf/specimen.pdf).

Although SARS-CoV is now controlled, we need more information before we know what the future holds. Assuming there is an animal reservoir for the virus, then it is unlikely we will ever be able to eliminate it, and we need to determine how we prevent it spreading to humans again. Also it is possible that the virus is now established in human populations and will re-emerge in the next Northern Hemisphere winter. We need to know whether it will continue to change and perhaps enhance its ability to be transmitted, and we need to understand the host immune responses if we are to develop effective vaccines. No antiviral agents have yet been shown to be useful, and work needs to continue on this. Perhaps most importantly we need to use this experience to build better systems for detecting and controlling newly emerging infectious diseases.

Further general information about SARS can be obtained from World Health Organization web site (www.who.int/csr/sars/en/), including a review of the outbreak evolution (Severe acute respiratory syndrome (SARS): Status of the outbreak and lessons for the immediate future. World Health Organization 2003 www.who.int/csr/media/sars_wha.pdf). An on line text is also available (SARS Reference, 2nd ed, www.sarsreference.com/). Information about infection control precautions and travel advice are available through the Department of Health and Ageing (www.health.gov.au/sars/index.htm).

For further information contact
Dr David Smith, Clinical Director,
Microbiology & Infectious Diseases,
PathCentre on 9346 2164.

ACUTE PANCREATITIS: LIPASE INSTEAD OF AMYLASE

Amylase has traditionally been used in the diagnosis of acute pancreatitis. It usually becomes elevated within 6-24 hours after the onset of acute pancreatitis, peaks at 48 hours and normalizes over 5-7 days. Its half-life is 2 hours. However, it may also be increased in other conditions, such as perforated peptic ulcer, bowel obstruction, hepatitis, ruptured ectopic pregnancy, renal failure and diabetic ketoacidosis. Thus, the amylase test has a low diagnostic specificity. Furthermore, it may be normal in up to 32% of patients with acute alcoholic pancreatitis.

Lipase is another pancreatic enzyme that is used for the diagnosis of acute pancreatitis. It increases within 4-8 hours, peaks at 24 hours and normalizes over 8-14 days after the event. Its half-life ranges from 7 to 14 hours. Lipase like amylase, is raised in other conditions but it is slightly more specific.

Lipase is more sensitive than amylase for the diagnosis of acute alcoholic pancreatitis and in patients who present late after the onset of acute pancreatitis, since it is elevated for a longer period. Lipase is also more sensitive than amylase in acute-on-chronic pancreatitis, since the remaining lipase activity in the pancreas is reduced to a lesser degree than amylase - by 26 % as against 91 % for amylase. Until recently assays for lipase have been technically difficult and laborious. Now lipase can be measured as easily and quickly as amylase and is no more costly. In view of this, it has been decided to replace amylase with lipase for the diagnosis of acute pancreatitis.

Neither lipase nor amylase levels are an indication to the severity or prognosis of acute pancreatitis. Plasma C-reactive protein at 48 hours is the best available marker for the severity of acute pancreatitis.

The upper limit of normal (ULN) for lipase depends on the method of analysis. At PathCentre Nedlands, the ULN is <60 U/L whereas at all the other PathCentre branches it is <300 U/L because of different methods being used. Lipase levels greater than twice the ULN are suggestive of acute pancreatitis. When an amylase test is requested PathCentre will automatically do a lipase assay.

For further information contact
Dr Chotoo Bhagat, Clinical Director,
Clinical Biochemistry, PathCentre on
9346 2670.

CARDIAC ENZYMES AND TROPONIN T

Troponin T is a highly sensitive marker for the detection of myocardial necrosis. It is used to detect myocardial damage in the acute coronary syndromes ranging from unstable angina to myocardial infarction. Troponin T should be determined at presentation and if negative, and the clinical suspicion is high for myocardial damage, a second blood sample should be taken at 6 to 9 hours after the onset of chest pain. Once myocardial necrosis has been confirmed by a positive troponin T, thereafter only CK measurements are used to monitor infarct size and possible re-infarctions.

In the past, cardiac enzymes (CE) have been used as a requesting profile, and CK and AST were measured. The CK/AST ratio gave some indication of whether the raised CK was of cardiac or skeletal muscle origin. In view of troponin T being a specific marker for myocardial damage, there is no need for the measurement of AST.

In conclusion, when ordering cardiac markers in a patient suspected of myocardial necrosis, the tests to request are CK and troponin T. Once troponin T is positive only CK is used to monitor infarct size and possible re-infarctions.

For further information contact
Dr John Beilby, Senior Scientist on
9346 2368 or Dr Chotoo Bhagat,
Clinical Director, Clinical Biochemistry,
PathCentre on 9346 2670.

RISPERIDONE REVISITED

Risperidone (Risperdal®) is an atypical antipsychotic drug belonging to the benzisoxazole class. It is a selective monoaminergic antagonist with high affinity for serotonergic 5HT₂ and dopaminergic D₂ receptors. It has been in clinical use since 1990 with usual oral doses starting at 1-2 mg/day and titrated up to approximately 6 mg/day, according to the patient's needs. A depot preparation Risperdal-Consta® has recently become available, but its use is limited to special circumstances only.

Peak plasma concentrations occur about 1-2 hours after an oral dose. Risperidone is extensively metabolized in the liver, but only the 9-hydroxyrisperidone metabolite is pharmacologically active, being equipotent with risperidone itself. Risperidone has an elimination half-life of between 3 and 19 hours, depending on

whether the patient is an extensive or poor CYP2D6 metaboliser. The elimination half-life of 9-hydroxyrisperidone is approximately 24 hours. The overall elimination half-life of Risperidone and 9-hydroxyrisperidone may be increased by up to 30% in the elderly and those with moderate renal dysfunction. It is unaffected by hepatic dysfunction.

A number of drugs can interact with risperidone by altering its metabolism. For example, co-medication with the mood-stabiliser carbamazepine induces metabolism of risperidone, with trough risperidone and 9-hydroxyrisperidone levels being reduced by approximately 53% and 77%, respectively.

Although there is no recognised therapeutic range for risperidone and 9-hydroxyrisperidone, measurement of levels can be very useful in assessing compliance, and in dealing with drug

interactions. Our experience in the laboratory shows that trough concentrations of Risperidone plus its metabolite (expressed in micrograms/litre) are around ten times the mg/day dose. A minimum of 2 ml of plasma is required for the assay. Heparinised plasma tubes should be used for sample collection (gel separators are unsuitable as they adsorb the drug) and co-medications should be listed on the request form.

The WA Drug and Therapeutics Committee Antipsychotic Drug Guidelines for the best-practice use of risperidone and other similar agents can be found at www.wadtc.org.au/pdsc/guidelines.cfm

For further information contact Mr Peter Hackett, Research Scientist at Clinical Pharmacology and Toxicology on 9346 2441.

Profile

MS LEANNE NEGUS, PATHCENTRE NARROGIN

Ms Leanne Negus graduated with a Bachelor of Applied Science (Medical Science) from the Western Australian Institute of Technology (WAIT) in 1981. She started work in the State Health (now PathCentre) Enteric Laboratory in 1982. A year later Leanne joined the laboratory relief staff and travelled the state working in many of PathCentre's country laboratories. In this position Leanne fulfilled her aim of being a Medical Scientist and working in the country. Her time in a number of laboratories gave her a solid grounding to become the Laboratory Manager in Broome. She then moved to Merredin where she was Laboratory Manager for the next ten years.

Late in 1995 Leanne was appointed as the inaugural laboratory manager in Narrogin. She packed up and moved to a newly purchased home in February



Ms Leanne Negus

1996, after fond farewells to close friends in Merredin. Leanne is still managing the Narrogin laboratory and now feels as much a part of the Narrogin community as she did in Merredin.

In her years working in the country (often as an only scientist), Leanne has attended many state and national AIMS (Australian Institute of Medical Scientists) conferences. This led to her joining the WA committee of AIMS last year. She hopes by being a member of this committee to be able to represent the views of the scientists who work outside of the major hospitals in smaller laboratories.

NOTIFIABLE INFECTIONS

In January 2001, the Western Australia Department of Health added a number of infectious diseases to the list of notifiable diseases, making a total of 63 conditions. Leaving aside HIV/AIDS, sexually transmitted diseases and adverse events following immunisation, for which there are separate arrangements, there are now 56 notifiable infections that require formal notification. The full list is provided on the Department of Health's notification form, which indicates the 23 conditions that should be notified by telephone. The others can all be notified by posting or faxing the form to the Communicable Disease Branch.

It is helpful to look at a few specific examples:

Meningococcal meningitis. The laboratory will communicate early results (e.g. Gram stain or preliminary culture result to the referring physician). PathCentre will notify the Department of Health of the definitive result automatically by electronic transfer of the laboratory report. A Clinical

Microbiologist will assist with telephone notification, particularly outside normal office hours.

Salmonella infection. *Salmonella typhi* and *paratyphi* require telephone notification. The more common *Salmonellas* are usually notified by post or fax, unless there is a cluster of two or more cases or a food handler is involved. PathCentre will notify the Department of Health by electronic transfer of results.

Tuberculosis. This is another infection that does not officially require telephone notification. Laboratory results are communicated electronically to the Department of Health for review by the Director of Tuberculosis Control.

Though the notification process may differ slightly for different infectious diseases, the common feature is a requirement to supply the Department of Health with timely information on selected infections in a way that does not impair the flow of diagnostic information to the requesting physician. Senior staff at the Division of Microbiology and Infectious Diseases at PathCentre will usually communicate significant new diagnostic information (e.g. meningococcal PCR or acid fast smear results) irrespective of their notifiable status, directly to the requesting doctor.

For further advice about laboratory aspects of notifiable diseases, contact a Clinical Microbiologist at PathCentre on 9346 3000. Copies of the notification form can be obtained by phoning 9388 4852.

DIAGNOSIS AND TREATMENT OF ONYCHOMYCOSIS

Onychomycosis is the cause of about half the cases of nail dystrophy. It is a very common condition increasing with age to a reported prevalence of 90% in the elderly. Most cases are caused by fungi known as dermatophytes that are

acquired when infected particles adhere onto skin or nail for sufficient time. More specifically termed *tinea unguium*, dermatophyte infection of the nail is commonly associated with *tinea pedis* either by infection at the same time or by spread from the initially infected site.

Non-dermatophyte onychomycosis occurs rarely when certain environmental fungi and yeasts gain opportunity to invade nail structures usually secondarily to other factors such as psoriasis or prolonged exposure to water. A recent example from PathCentre is of a patient whose usual practice was to soften her thick nails prior to cutting by soaking them in basin of water. In non-dermatophyte onychomycosis, the differentiation between saprophytic colonisation and active infection is a clinical one backed by laboratory data. It is recommended a repeat collection be performed to re-isolate the same environmental fungus and so give weight to its possible significance.

Investigation for onychomycosis and *tinea pedis* should initially include a clinical examination for general skin conditions including psoriasis. Laboratory investigation of the affected nails is essential, but also scrapings from the feet and toe spaces are routinely recommended because the associated *tinea pedis* may be asymptomatic.



An example of Tinea unguium

Good collection technique is of prime importance in obtaining a correct result. Adequate amounts of material must be obtained from the appropriate sites, which must be processed optimally to obtain accurate results. The PathCentre

collection centre at Nedlands has long had a reputation for its excellence in Mycology specimen collection. A continuous training programme throughout the PathCentre branch laboratories maintains skills at all PathCentre collection centres.

Treatment of *tinea unguium* under the PBS allows for the prescription of terbinafine by authority in "proximal or extensive (greater than 80%) onychomycosis due to dermatophyte infection where topical treatments have failed. The infection must be proven by microscopy or culture and confirmed by an approved pathology provider." During treatment the antifungal is incorporated into the nail, however it will take at least a further 6-12 months for the successfully treated nail to grow sufficiently to demonstrate cure. Mycological cure rates of 71-82% and clinical cure rates of 60-70% have been reported by this regime. In vitro resistance is extremely rare so treatment failure is usually due to patient factors such as the lack of absorption of the antifungal into the nail (related to circulatory function) and slow rate of growth of nails (related to age).

Treatment of non-dermatophyte onychomycosis is less clear cut, as the precipitating cause of the onychomycosis also needs to be addressed for a successful outcome. The primary option for treatment is with itraconazole, but success is somewhat dependent on the infecting organism.

For further information contact Dr Clay Golledge, Clinical Microbiologist on 9346 3625 or Mr Ian Arthur, Senior Scientist on 9346 4134.

Any comments or suggestions on the content of the PathCentre News should be addressed to:

Editor, Dr John Beilby
PathCentre
Locked Bag 2009
Nedlands, WA, 6909

or: John.Beilby@health.wa.gov.au.