



# PATHCENTRE

## NEWS

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## DRINK SPIKING

PathCentre's Toxicology Laboratory, with its expertise in assays for pharmacological agents and drugs of abuse is increasingly involved in testing for drink spiking.

This topic has received much coverage in the media recently and, even though the crime dates back to the nineteenth century, its prevalence is thought to be increasing with the growing popularity of the club and rave scene.

The motive behind the crime may be drug facilitated sexual assault (DFSA), or the dangerous practice of 'pranking'.

There are many drugs available that can be used for DFSA but investigations in Australia and overseas suggest that the most common drugs used are alcohol (ethanol), gamma-hydroxy butyrate (GHB), ketamine and benzodiazepines. These compounds produce relaxation and sedation, and the common observation in a victim is that they suddenly appear very drunk, despite having consumed little or no alcohol. Both women and men may be targets.

The WA Police Service has reported increases in allegations of drink spiking and been proactive in warning patrons about the problem and how it may be avoided.

A new advertising campaign to inform potential victims and deter possible offenders was launched in November 2002.



*Drink spiking advertisement as part of the WA Police Service's awareness campaign.*

Nevertheless, information on the drugs used locally and on the exact extent of the problem is anecdotal. To gather information and to assist victims in having their concerns dealt with in a positive manner, the Sir Charles Gairdner Hospital Emergency Department (SCGH ED), together with the WA Police, the Sexual Assault Referral Centre (SARC) and PathCentre, will study the effects on 100 victims of drink spiking.

People who suspect they have had their drinks spiked can attend the SCGH ED to receive confidential assessment and advice. Assessment within 12 hours of the incident is optimal as it offers the best chance of detecting the offending drugs.

In situations where this criterion is met, urine will be tested for the drugs mentioned above, and blood will be tested for alcohol. These samples will be taken under a strict 'chain-of-custody' procedure so that they may be used as forensic evidence at a later date if required.

Results will be confidential and reports remain separate from medical records. Victims will be informed of any drugs detected and encouraged to report the matter to the Police.

General Practitioners who see victims of drink spiking should consider the following course of action after an initial assessment of the victim's immediate needs and treatment:

1. Immediate referral to SCGH ED if the victim is in the metropolitan area and if within 12 hours of the alleged drink spiking incident. Further assessment and testing will be done through the research project, with or without Police involvement and at no cost to the victim;

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2. Immediate referral to the WA Police service if the victim agrees and wishes to press charges. The Police can arrange testing of samples at no cost to the victim. Contact 9222 1111 (country 131 444); and
3. The victim should be advised that because these drugs have short half-lives, there is a high probability that the urine testing will return negative results. This is particularly true if the first urine is not collected within 12 hours of the alleged incident. However, negative results should not discourage the victim

from reporting the incident to the Police.

In situations that fall outside of 1 and 2, the Toxicology Laboratory, by prior arrangement, can perform testing on urine and blood (heparinised) samples. However, Medicare does not cover this type of non-clinical request and all costs involved will need to be paid prior to testing.

The SCGH ED or the Police can refer the victim to other agencies such as SARC.

**For further information contact  
Mr Leon Dusci or Mr Peter Hackett,  
PathCentre Toxicology on 9346 3743.**

## TRANSFUSION BLOOD SPECIMEN LABELLING

For safety reasons the Australasian Society of Blood Transfusion (ASBT), Royal College of Pathologists of Australasia (RCPA) and the National Association of Testing Authorities (NATA) have required that samples for all Transfusion Medicine testing are legibly labelled with:

1. Patient's surname, given name in full, and hospital record number or date of birth where no hospital record number has been assigned; and
2. Date and time of collection.

In addition, it is now required that if a pre-printed patient label is used the signature or initials of the collector must appear on the sample tube label.

Therefore, samples for Transfusion Medicine testing cannot be accepted if they do not meet the above criteria.

**For further information contact  
Ms Dianne Grey, Medical Scientist,  
PathCentre on 9346 2778.**

## PROTHROMBINEX HT

### Background

Prothrombinex HT is a concentrate of human blood coagulation Factors II, IX and X prepared from pooled heat treated plasma. It is screened and negative for HIV, Hepatitis B and C. Each vial contains 500IU of Factor IX, 550IU of Factor II and approximately 600IU of Factor X. The Prothrombinex is supplied as a freeze-dried powder and is reconstituted immediately prior to use with the supplied sterile 20mL distilled water.

### Indications

1. Treatment of Haemophilia B (when MonoFIX-VF unavailable or not indicated, such as surgery).
2. Treatment of overdose with one of the phenindone group of anticoagulants (e.g. Warfarin).

## PATHCENTRE VISITING LECTURER

PathCentre welcomed Professor Dennis Lo during September as its 2002 visiting lecturer.

Professor Lo, is the Professor of Chemical Pathology at the Chinese University of Hong Kong and has an international reputation for his work on the biological and diagnostic implications of circulating plasma DNA.

During his visit, Professor Lo gave four lectures on topics related to the diagnostic use of plasma DNA and RNA, and participated in two sessions of clinical case presentations and many discussions with PathCentre staff interested in molecular biology. Research workers outside of PathCentre also had the opportunity to discuss their projects with Professor Lo.

Although DNA is an intracellular molecule it is not widely appreciated that in certain circumstances it 'leaks' from cells into the blood. Professor Lo is at the forefront of investigating this new field. He spoke on the biology and diagnostic applications of prenatal



*PathCentre's 2002 Visiting Lecturer, Professor Dennis Lo.*

genetic analysis from maternal blood, the use of plasma DNA for tumour detection and monitoring, the applications of plasma DNA to emergency medicine, early detection of organ transplantation rejection and new frontiers in circulating nucleic acid research. Professor Lo highlighted the importance of this emerging scientific area to clinical management and diagnosis of disease.

Professor Lo's presentations were of the highest quality and provided stimulus for the investigation of a number of new laboratory advances in PathCentre.

**For further information contact Dr  
John Beilby, Senior Biochemist,  
PathCentre on 9346 2368.**

## Contraindications

Prothrombinex is contraindicated in patients' showing clinical signs of thrombosis or disseminated intravascular coagulation (DIC).

## Warfarin Reversal In The Bleeding Patient: Management Guidelines

Life threatening bleeding requires rapid and complete reversal of the anticoagulation due to Warfarin. The PathCentre recommended approach to reversing the anticoagulation is as follows:

### 1. Cease Warfarin

Omitting Warfarin does not have an immediate effect and does not have a significant role in the emergency situation. Discontinuation of Warfarin reverses the anticoagulation only slowly;

### 2. Administer Vitamin K

Give 5mg intravenous (IV) Vitamin K by slow injection. Do not mix with other solutions as anaphylaxis can occur. IV Vitamin K has a significant effect on the INR within 4-6 hours; and

### 3. Transfuse Coagulation Factors

The deficient clotting factors II, VII, IX and X should be replaced as rapidly as possible by therapy with:

#### i. Prothrombinex HT

Each vial of **Prothrombinex HT** contains factors **II, IX and X** (500-600 IU of each). One vial of Prothrombinex is recommended to reverse the anticoagulation due to Warfarin in a patient with life threatening bleeding.

Note: 1 vial of Prothrombinex approximately equates to 2 units of FFP.

#### ii. Fresh Frozen Plasma (FFP)

FFP contains all coagulation factors **but** is not immediately available. FFP must be blood group compatible and takes 30 minutes to thaw. The

## Profile

### DR CLAYTON GOLLEDGE

Dr Clay Golledge is a Senior Consultant in Clinical Microbiology and Infectious Diseases at PathCentre.

He has a wide clinical and laboratory experience with special clinical interests in tropical and travel medicine, respiratory tract infection and infectious diarrhoea.

He has authored or co-authored over 100 scientific papers and case reports and is on the Editorial Board of four medical journals. He has won two



*Dr Clayton Golledge, Senior Consultant, Microbiology and Infectious Diseases.*

teaching awards and is also the Honorary Medical Director of the Meningococcal Foundation of Australia.

recommended dose of FFP to reverse Warfarin anticoagulation is 15mL/kg body weight.

**FFP is not the optimal method to replace coagulation factors in anti-coagulated patients because:**

1. Large volumes are required (e.g. 800-1000mL from 3 - 4 units FFP);
2. The blood group must be compatible; the patient's blood group must be known;
3. FFP is not available in all PathCentre laboratories;
4. FFP takes 30 minutes to thaw; and
5. It takes 1-2 hours to administer the FFP required to reverse the anticoagulation.

## Management Recommendation

1. Cease Warfarin;
2. Administer IV Vitamin K (5 mg); and
3. Transfuse Prothrombinex HT (1 vial).

Approval for Prothrombinex use must be obtained from the PathCentre Haematologist. The Duty Haematologist can be contacted on 9346 2890 between 0800-1700 hours or 9346 2783 between 1700-0800 hours.

## FINE NEEDLE ASPIRATION OF THE LIVER

Fine Needle Aspiration (FNA) of the liver is usually performed for a localised mass lesion or 'tumour'. It has a limited role in diffuse disease such as viral hepatitis and cirrhosis.

Liver masses usually present in one of several ways:

1. In the setting of chronic liver disease, where the differential diagnosis is hepatocellular carcinoma (HCC) versus macro-regenerative nodule or metastatic malignancy; or
2. As an incidental radiological finding during imaging for an unrelated reason where the differential diagnosis may be focal nodular hyperplasia versus hepatocellular adenoma versus HCC; or
3. In the setting of a known primary malignancy elsewhere in the body where the differential diagnosis is metastatic disease versus a primary liver neoplasm, either benign or malignant (HCC or cholangiocarcinoma).

A FNA is usually 'directed' by a radiologist using Ultrasound or CT imaging guidance to ensure correct

needle placement. Optimally a pathologist attends for rapid review to confirm diagnostic material has been obtained and to triage the material for ancillary tests. As well as smears, the cytopathologist may collect material for a cell block to perform special stains and immunohistochemistry, flow cytometry (lymphomas), microbiology and electron microscopy as required.

Advantages of FNA over conventional core biopsy are that it is less invasive with fewer complications (haemorrhage, peritonitis, seeding by tumours) and that it samples over a wider area. The disadvantages are that it obtains material with limited architectural information and it requires a skilled radiologist and cytopathologist. Bleeding disorders are a contraindication to both procedures.

Accurate interpretation requires: knowledge of past history and current clinical history, the radiological appearance, the site of the sample and familiarity with what is normal for that site.

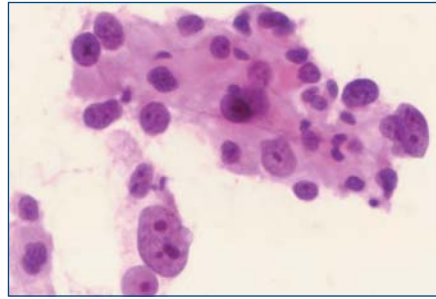
Pitfalls include picking up cells from other structures on the way to the liver e.g. mesothelium, which may not be representative of the lesion and that the clinical history or radiological appearance of a mass may be misleading.

Most lesions are readily diagnosed on FNA cytology. Typical diagnostic features are well described in textbooks and the literature. Metastases usually show the characteristic morphology and staining profile of the primary tumour.

Difficulty in the cytodiagnosis of HCC arises at both ends of the malignant spectrum:

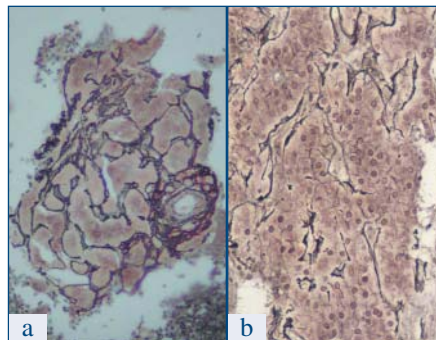
1. Distinguishing well-differentiated HCC from benign hepatocellular lesions, e.g. macro-regenerative nodule in the setting of cirrhosis or focal nodular hyperplasia and hepatocellular adenoma in a patient without chronic liver disease; and

Figure 1:



A cluster of hepatocellular carcinoma cells in a smear obtained by fine needle aspiration.

Figure 2:



a) A normal reticulin pattern in cell block material denoting a benign hepatocellular lesion.

b) Fragmentation and reduction of the normal reticulin pattern in cell block material supporting a diagnosis of hepatocellular carcinoma.

2. Separating poorly differentiated HCC from metastatic malignancies or other unusual primary tumours.

### Well differentiated HCC

At PathCentre we have investigated several ancillary techniques reported as useful in separating benign from malignant hepatocellular lesions. Most effective was a reticulin stain, which highlighted loss of a normal sinusoidal architecture with a reduction or total absence of reticulin. Less effective was immunohistochemical staining for CD34 antigen, which highlighted the 'capillarisation' of the hepatic sinusoids in HCCs, by staining the endothelial cells. This does not occur in normal liver but we found some overlap between smaller, well differentiated HCCs and benign hepatocellular lesions. We also

looked at the proliferation marker, 'proliferating cell nuclear antigen' but this did not distinguish between benign and malignant lesions.

### Poorly differentiated HCC

At the other end of the spectrum we are currently looking at several markers of hepatocellular differentiation as well as one adenocarcinoma marker to differentiate between poorly differentiated HCC, where there has been loss of architectural and cytological features of hepatocellular differentiation, and metastatic adenocarcinoma.

Immunoperoxidase staining for alpha-fetoprotein as a marker of hepatocellular differentiation has a sensitivity of around 50% in tissue sections and cell block material (no better than tossing a coin). Using a recently developed hepatocyte-specific antibody Hep Par 1 (hepatocyte paraffin 1), we have shown a sensitivity of 85%, with 100% specificity, a marked improvement. We are also looking at several other markers.

It should be noted that clinical investigations do not often provide the answer although a significantly raised serum alpha-fetoprotein is diagnostic of hepatocellular carcinoma.

In the process of retrospectively reviewing all of our liver FNA's and researching the utility of these ancillary techniques, we have better defined our diagnostic criteria and improved the sensitivity and specificity of our diagnoses.

**For further information contact  
Dr Bastiaan de Boer, Pathologist,  
PathCentre on 9346 4107.**

*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.