



Haemochromatosis Testing: GENETIC PREDISPOSITION DOESN'T EQUAL DISEASE

Dr Nigel Brown

Chemical Pathologist - Biochemistry Department

- Increasingly cases are found before dangerous iron accumulation has occurred
- Earlier detection calls for a longer term management view
- Life time follow-up will be part of the plan but may be low intensity
- Treat the patient not the genetics

Factors in iron accumulation

Haemochromatosis mutation genetic testing has been available for many years. As a result a significant number of cases are now found before iron accumulation has reached levels that result in clinical haemochromatosis. This means more treating doctors will be managing patients with a genetic predisposition to haemochromatosis rather than the fully expressed disease. These genetically predisposed patients are those that have two haemochromatosis mutations but have not accumulated dangerous amounts of iron in their body.

Genetic factors

Different mutations of the haemochromatosis gene (HFE) will have a different risk for iron accumulation. Patients homozygous for the classic haemochromatosis mutation C282Y (i.e. that have inherited two copies C282Y/C282Y) are at highest risk for clinically significant iron accumulation. Someone with one C282Y and one milder H63D mutation will have lower risk.

Other factors

Many factors in addition to their underlying genetic make-up go to determine how much iron a patient will accumulate over time. In females the blood losses associated with menstruation and pregnancies are a

natural 'protection' against iron accumulation, so many females with two haemochromatosis mutations still will not gain much iron until they are postmenopausal. In males dietary factors, and perhaps unrecognised genetic effects, may slow iron accumulation so that some may never need venesection or may only occasionally require venesections.

Long term management view

Taking a longer term view involves supporting dietary or other management plans, addressing the underlying life-long risk of iron accumulation and also ensuring that appropriate follow-up has been put in place. Notifying first-degree relatives regarding the desirability of their

continued inside...

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Dr Brown joined QML Pathology in May 1999 as Consultant Chemical Pathologist in the Biochemistry Department of the central laboratory. A graduate of the University of Queensland (1980), Dr Brown trained in pathology at the Royal Brisbane Hospital before obtaining his fellowship in chemical pathology in 1989. He remained at the Royal Brisbane Hospital for nearly a decade where, in addition to general chemical pathology, he explored his interests in genetics and errors of metabolism.

Special Interests

Use of Computers in Pathology Result Interpretation and Reporting
Legal Aspects of Drug Testing
Inborn Errors of Metabolism
Calcium Metabolism

Also in this issue:

Changes in Cytopathology Imaging Technology at QML Pathology

Position Statement on Lipid Management

Wesley Laboratory to Diagnose 24 Hours a Day- Seven Days a Week

being assessed for haemochromatosis is part of the long term management of the extended family group.

Phase 1: Removal of excess iron

Many new patients will meet the criteria for therapeutic venesection (see Table 1). With venesection serum ferritin should fall below 50 ug/L. This phase of management, including diagnosis and the role of liver biopsy, was covered in an earlier QML Newsletter (Identifying Haemochromatosis in your Practice, May 2003). If you would like to review this document please visit our website www.qml.com.au, or request a copy from your local Medical Liaison Officer.

Phase 2: Maintenance management

When a patient is not overloaded with iron, either due to therapeutic venesection or if found before iron has accumulated, the aim is to manage iron balance to prevent a toxic accumulation of iron. **If iron storage is controlled before development of cirrhosis then life expectancy is normal.**

There are a number of sources of management guidelines (for examples see references 1-3) that give a similar overall message:

- **Reduce exposure to excessive iron:**

Dietary iron is allowable but a moderate intake of sources high in iron, such as red meat and organ meats, should be recommended. Iron supplements, including multivitamins with iron added, should be avoided. Limitation of vitamin C supplements to less than 500mg per day has also been recommended.

- **Monitor and remove iron if accumulation does occur:**

If ferritin has not reached the threshold for venesection then prospective monitoring is indicated. Patients homozygous for C282Y should have annual assessment of iron studies. Some authorities also recommend lifetime annual iron studies for compound heterozygotes (e.g. C282Y/H63D) as well, while others allow longer periods between testing in this group.

If venesection is required, an ongoing plan of venesections 3 to 6 monthly with repeat serum ferritin monitoring every 1 to 2 years is a common protocol once the initial venesection is complete. Some individuals may not require ongoing venesection but monitoring should continue.

- **Monitor for complications and take preventive measures:**

Regular review will include monitoring for complications as appropriate for the individual patient. There is controversy regarding the role of liver ultrasound and serum alpha-fetoprotein testing in the follow-up of cirrhotic patients at risk of hepatocellular carcinoma. Decisions for such patients are best made by a supervising specialist.

If no liver damage has occurred then moderating alcohol intake is advised, but minimising use of alcohol is advisable if there is evidence of liver injury.

Table 1: Suggested serum ferritin levels at which therapeutic phlebotomy should be considered in individuals with hereditary haemochromatosis.

Patient	Serum Ferritin Level
Age under 18 years (both sexes)	200 ug/L or greater
Woman 18 years or older (menstruating)	200 ug/L or greater
Postmenopausal woman	300 ug/L or greater
Man 18 years or older	300 ug/L or greater

Summary

Effective management of haemochromatosis requires long term attention from both doctor and patient. Prospective management greatly improves the likelihood of a desirable outcome. For further queries regarding this information please contact one of our Chemical Pathologists on (07) 3840 4444.

References:

1. Fletcher LM, Halliday JW. Haemochromatosis: Understanding the mechanism of disease and implications for diagnosis and patient management following the recent cloning of novel genes involved in iron metabolism. *J Intern Med.* 2002 Mar;251(3):181-92.
2. Powell LW. Broadsheet number 54. Hereditary hemochromatosis. *Pathology.* 2000 Feb;32(1):24-36.
3. Barton JC, McDonnell SM, Adams PC, Brissot P, Powell LW, Edwards CQ, et al. Management of hemochromatosis. hemochromatosis management working group. *Ann Intern Med.* 1998 Dec 1;129(11):932-9.



Doctors' Notice Board

Dr Boon Kua would like to announce he is now a visiting Urologist at the Wesley Hospital. Dr Kua has a keen interest in urological malignancies. However he has been trained in all aspects of general urology including female urology, stone diseases, laparoscopic and prosthetic surgery and is happy to accept and manage adult patients with general urological problems. He does not see any paediatric urology patients.

For referrals please contact his secretary at the Wesley Medical Centre on (07) 3232 7686. For a quick opinion on a patient, he is happy to be contacted at all times via his mobile phone on 0402 449 039.

Dr Karan Chau, Psychogeriatrician, would like to announce she has opened a clinic in New Farm as of March 8, 2006.

Clinic details are:

22 Sargent St, New Farm

Appointments: (07) 3254 0639

Changes in Cytopathology Imaging Technology at QML Pathology

QML Pathology has an ongoing commitment to the introduction of new technologies, particularly in relation to gynaecological cytology. As a result of this commitment, we will be introducing Cytyc's ThinPrep Imaging System® which is designed to automatically scan ThinPrep slides.

Currently QML Pathology offers PAPNET as an automated screening system for detecting abnormalities not identified on conventional Pap smears. However, as a result of the introduction of the ThinPrep Imaging System® QML Pathology is no longer offering PAPNET as of Monday 13 March 2006.

As you are aware ThinPrep is a liquid based system that has proven effective in removing excessive blood, mucus and inflammatory exudate. Thus the screening of slides and detection of abnormalities that would otherwise have been obscured is easier with ThinPrep slides. Until now ThinPrep slides have been screened and reported manually. The new Imaging System scans the ThinPrep slide and measures the integrated optical density of

each cell's nucleus, identifying 22 'fields of view' (FOVs) which are likely to contain abnormal cells. These FOVs are reviewed by the cytotechnologist using a specially integrated Review Microscope. If abnormal cells are identified, the entire slide is re-screened. If no abnormal cells are identified, these slides are immediately archived and reported as negative.

With over 10 years experience in the interpretation and processing of ThinPrep slides, QML Pathology has developed a comprehensive ThinPrep training program and regularly compares results from ThinPrep with conventional cytology to ensure the highest testing integrity. In addition, data amassed in both Australia and abroad demonstrates the sensitivity and specificity of automated ThinPrep screening is equivalent to that achieved through manual ThinPrep screening. However, both methods show superiority to conventional screening.

The Imaging System has the potential to greatly improve work-flow in the laboratory and more importantly, it allows the cytotechnologist to focus on accurate interpretation, which will result in increased screening productivity and improved diagnostic performance.

Training of staff in the use of the ThinPrep Imaging system has already commenced and it is anticipated full implementation will occur in the near future. We will endeavour to notify you as soon as possible once this technology is fully operational.

For further information please contact the Cytology Department on (07) 3840 4485.

Wesley Laboratory To Diagnose 24 Hours / 7 Days

It is with pleasure that QML Pathology announces the opening of our Wesley Laboratory in Auchenflower as a 24 hour, 7 day a week facility with a comprehensive blood bank service. This is an exciting step in our relocation plans and one which will give us the opportunity to increase after-hours service for Specialists and General Practitioners within this region.

With our impending move to a new state of the art facility at Murarrie in April, it has been necessary to move our Blood Bank to an area practical for servicing major Private Hospitals within the Brisbane CBD. With the introduction of the Blood Bank, our Wesley Laboratory will commence operation on a twenty-four hour, seven day a week basis. This will allow us to continue delivering a comprehensive inner-city pathology service, with particular attention on time efficient processing of specimens from late and emergency surgical procedures. It also ensures that the processing of urgent specimens continue to meet the standard our referrers have come to expect from the West End Laboratory.

For further information please do not hesitate to contact your Medical Liaison Officer.



Position Statement on Lipid Management – 2005

National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand

At the end of 2005, the above working party issued a revised position statement with respect to lipid management in Australia and New Zealand. The full statement is available for downloading from the Heart Foundation website - www.heartfoundation.com.au (please go to the Health & Lifestyle / Professional link). To assist you in receiving this information we have written an abbreviated form which will be distributed in the very near future.

In the meantime, we have outlined below several of the main points in the guidelines:

- There is an increased focus on the patient's absolute risk of CVD and a moving away from addressing the lipid picture (or other selected risk factors) in isolation.

- All references to a total cholesterol value as a target for lipid treatment have been removed and replaced with specific LDL and HDL cholesterol targets.
- Special high risk groups including patients with chronic kidney disease, Aboriginal and Torres Strait Islanders, and those in low socioeconomic positions are identified although the additional risk which they bear is difficult to quantify.
- Specific guidance with respect to lipid-lowering drug therapy is given and their safety issues discussed.
- The "gap" between evidence and long term compliance is discussed.

Dr Charles Appleton
Pathologist in Charge - Biochemistry

New Central Laboratory

It has been two years in the making and the time has almost arrived for our relocation to a new state-of-the-art Central Laboratory in Murarrie. Moving to one of the largest purpose built laboratories in the Southern Hemisphere is both an exciting and challenging prospect, but we can say with confidence it is one of the most momentous occasions in QML Pathology's 80 year history and an event we intend to do well.



The new laboratory boasts an open-plan architecture, built specifically to make processing more methodical and focused with equipment more extensive. With one of the biggest testing ranges offered in Queensland this is incredibly important if we are to offer a better level of service to the medical community.

The move will happen over a scheduled period just prior to and during the Easter Holiday weekend, due to the historically low demand we experience over this time. In the weeks preceding the move from West End you will be receiving specific information in regards to our service arrangements over this period.

If you would like to discuss any queries regarding the relocation, please don't hesitate to contact your local Medical Liaison Officer.

This newsletter has been prepared and published by QML Pathology for the information of referring doctors. Although every effort has been made to ensure that the newsletter is free from error or omission, readers are advised that the newsletter is not a substitute for detailed professional advice.

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 **QML Pathology.**



COLLECTION CENTRE NEWS

For the convenience of our doctors and patients, we have listed the latest changes to QML Pathology's network of clinics:

CLINIC CHANGES

Ashmore(07) 5564 9572 Miami (07) 5537 4162

Ashmore Plaza Shopping Centre, 130 Cotlew St
M - F 7.30am - 1.00pm
2.00pm - 4.00pm

Miami Family Medical Ctr, 1922 Gold Coast Hwy
M - F 8.00am - 1.30pm
2.00pm - 4.00pm

Please contact your local branch for further information.