



## LAB CONNECTIONS

June 2011 / Issue #113

### IN THIS ISSUE:

- OHIP has restricted payment for Vitamin D testing unless required for certain medical conditions. Learn more about this in Dr. Cynthia Balion's update on Vitamin D testing.
- The Quality team elucidates the importance of good inventory in the Quality Snapshot.

### WHAT'S NEW?

**CARNITINE** (free and total) will now require biochemist approval before a sample is shipped to an outside lab. Acylcarnitine (fractionation) also reports free carnitine and is performed in-house. It requires no biochemist approval. Follow the link to learn more:

[Acylcarnitine memo](#) (Ctrl + Click to follow link)

#### **Coming soon to the HRLMP - Dabigatran Levels**

The HRLMP Special Coagulation laboratory will be offering Dabigatran levels soon.

Dabigatran (Pradax) is an oral direct thrombin inhibitor (DTI) that has been recently approved by Health Canada for use in patients with atrial fibrillation (A-Fib) for the prevention of strokes, and there are numerous randomized clinical trials to determine dabigatran's efficacy for the treatment of venous thromboembolism (VTE).

A benefit of dabigatran is that routine laboratory monitoring is not required; however, a clinician may require a dabigatran level in cases of bleeding or if there is a concern of accumulation of the drug due to renal insufficiency or other medical conditions.

The principle of this automated clot-based thrombin inhibition assay for dabigatran involves the dilution of the patient's plasma in normal plasma. After the addition of purified human thrombin, the clotting time (in seconds) is directly proportional to the dabigatran plasma concentration. The sample type is platelet poor sodium citrate plasma (collected from a 3.2% sodium citrate blue vacutainer). Once the test is live, samples are to be processed and sent to the Special Coagulation Laboratory, McMaster site.

The assay is a quantification of dabigatran and the results will be reported in  $\mu\text{g/mL}$ . There is no therapeutic range for dabigatran; therefore, the following comment will attach to all dabigatran results:

"A therapeutic range for dabigatran has not been established and normal plasma contains  $<0.04 \mu\text{g}$  dabigatran/mL. Trough levels ranging from  $<0.04 \mu\text{g/mL}$  to  $0.29 \mu\text{g/mL}$  have been observed in tests from 20 patients on 110 – 150 mg dabigatran twice daily. Although the patient's plasma is tested after dilution with added normal plasma, there is potential for false positive results in individuals on heparin or with acquired and inherited defects of fibrin polymerization."

The addition of dabigatran complements our current anticoagulant assays for antithrombotic agents, including fondaparinux, rivaroxaban (fall 2011), low molecular weight heparin, heparin and warfarin.

If you have any questions regarding this new assay or any other coagulation laboratory issue, please contact Karen Moffat, Technical Specialist, Coagulation, at 905-521-2100 ext. 73124 or you may e-mail Karen at [moffat@hhsc.ca](mailto:moffat@hhsc.ca).

### YOUR FEEDBACK IS VALUED!

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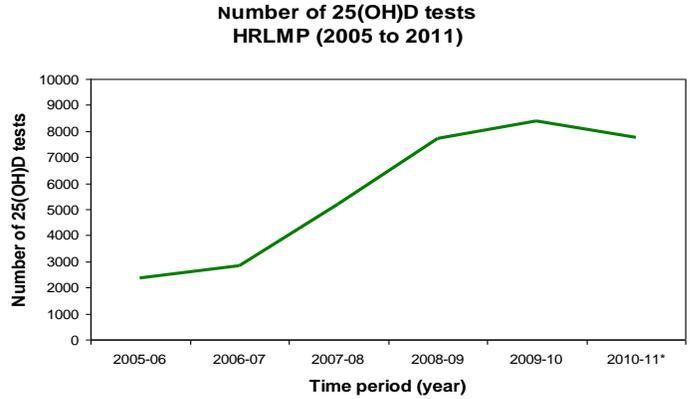
**Your feedback, suggestions and new ideas are most welcome!**

## Vitamin D: Update 2011

Over the last several years vitamin D has received an enormous amount of attention. Numerous studies have and continue to be published examining the relation between vitamin D and disease beyond bone health. These studies have resulted in an exponential rise in vitamin D testing.

Data obtained through the Ontario Health Insurance Plan (OHIP) found testing for vitamin D has increased approximately 2500 percent since 2004. As a result of this increase and along with an evidenced-based review, OHIP restricted payment for vitamin D tests on December 1, 2010. This test will now only be covered for patients with osteoporosis, osteopenia, rickets, malabsorption syndrome, renal disease, or taking medications that affect vitamin D metabolism.

Test statistics for vitamin D from the Hamilton Regional Laboratory Medicine Program (HRLMP) are more modest than those from OHIP, but testing has increased by 250 percent.



\*Adjusted number based on test statistics from July 1, 2010 to May 31, 2011.

### Types of Vitamin D

There are two main types of vitamin D: 25-hydroxyvitamin D [calcidiol, 25(OH)D] and 1,25-dihydroxyvitamin D [calcitriol, 1,25(OH)<sub>2</sub>D]. UVB radiation (290-315 nm) of the skin converts provitamin D (7-dehydrocholesterol) to previtamin D (cholecalciferol or D<sub>3</sub>) followed by conversion by the enzyme 25-hydroxylase found in the liver to 25(OH)D. The second hydroxylation is carried out by 1 $\alpha$ -hydroxylase, primarily in the kidney.

The most abundant and useful form to assess adequacy is 25(OH)D. Although 1,25(OH)<sub>2</sub>D is the form that regulates calcium, it is present in circulation at only 0.1% of 25(OH)D concentration and has a half-life of only 0.25 days compared to 14-21 days for 25(OH)D. There is also no relationship between 25(OH)D and 1,25(OH)<sub>2</sub>D, except in obese persons.

### Factors associated with Vitamin D status

- |                   |  |
|-------------------|--|
| Sunlight exposure | <ul style="list-style-type: none"> <li>• Accounts for about 90% of 25(OH)D found in circulation.</li> <li>• People living in Canada will only receive sufficient radiation between 10 a.m. and 3 p.m. from April to September.</li> <li>• In the Canadian Health Measures Survey (CHMS), 25(OH)D concentration was approximately 10% lower in November-March than in April-October.</li> </ul> |
| Diet              | <ul style="list-style-type: none"> <li>• Sunscreen reduces conversion of cholecalciferol to 25(OH)D.</li> <li>• Natural, e.g., salmon, sardines, tuna, egg yolks.</li> <li>• Fortification, e.g., milk products.</li> </ul>  |
| Supplements       | <ul style="list-style-type: none"> <li>• D<sub>3</sub> (rarely D<sub>2</sub> in Canada).</li> <li>• 100 IU increases 25(OH)D by 2-3 nmol/L.</li> </ul>   |
| Skin pigmentation | <ul style="list-style-type: none"> <li>• 5-10 greater sun exposure time required with dark compared to light skin.</li> </ul>  |
| Older age         | <ul style="list-style-type: none"> <li>• Decrease in cutaneous synthesis (due to lower amounts of 7-dehydrocholesterol with increasing age).</li> </ul>  |

### Vitamin D Insufficiency

Epidemiological studies have shown relationships between vitamin D insufficiency and various health outcomes beyond skeletal effects, including cancer, rheumatoid arthritis, cardiovascular disease, diabetes mellitus, dementia, multiple sclerosis, tuberculosis, and falls. Vitamin D is an essential vitamin but exactly how much is required relative to various clinical outcomes is uncertain. The most reliable outcome evidence is on bone health.

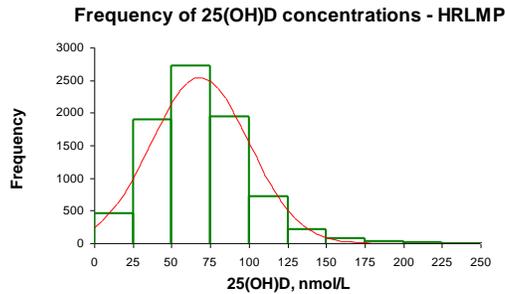
### Classification of Vitamin D status

The HRLMP will now provide new interpretive comments for 25(OH)D tests according to concentration group. This classification has been adapted from the guideline statement from Osteoporosis Canada (2010).

25(OH)D, nmol/L	Interpretation
< 25	Vitamin D deficiency
25 – 75	Suboptimal vitamin D status
> 75	Desirable vitamin D status
> 250	Potential adverse effects

### Vitamin D status of Canadians

Data from the CHMS (2007-2009) found the mean concentration of 25(OH)D to be 67.7 nmol/L. The CHMS survey found 65% of individuals aged 6 to 79 did not have a desirable vitamin D status (> 75 nmol/L). This percent is similar to concentrations found in samples tested by the HRLMP (63%). The distribution of 25(OH)D in the CHMS exhibited a U-shaped curve with higher concentrations in the young and elderly.



### Vitamin D test methods

The HRLMP uses the automated DiaSorin Liaison 25(OH)D method which detects both the natural form (D3) and plant form (ergocalciferol, D2) of 25(OH)D. It is the most widely used method in the clinical laboratory setting (approximately 85% of laboratories use this method). Overall, this method agrees well with the DiaSorin RIA manual method, on which the interpretation cut points are based, but individual test results may differ by up to  $\pm 14$  nmol/L. Vitamin D method standardization is coming, but currently different methods will yield different values potentially leading to misclassification with the use of common cut points.

### When to measure Vitamin D

Single or repeated measurements of 25(OH)D have limited value because of the various factors associated with its presence in the blood, differences between test methods, and only putative evidence for protection in diseases other than bone health.

Best practice for vitamin D testing is limited to patients who have decreased bone density, have a medical condition reducing vitamin D absorption or synthesis, or are taking medications that reduce the absorption or metabolism of vitamin D.

### References:

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2. Chung M, Balk EM, Brendel M, Ip S, Lau J, Lee J, Lichtenstein A, Patel K, Raman G, Tatsioni A, Terasawa T, Trikalinos TA. Vitamin D and Calcium: A Systematic Review of Health Outcomes. *Evid Rep Technol Assess (Full Rep)*. 2009 Aug;(183):1-420.
3. Langlois K, Greene-Finestone L, Little J, Hidirglou N, Whiting S. Vitamin D status of Canadians as measured in the 2007 to 2009 Canadian Health Measures Survey. *Health Rep* 2010;21:47-55.
4. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, Hanley DA, Hodsmann A, Jamal SA, Kaiser SM, Kvern B, Siminoski K, Leslie WD; Scientific Advisory Council of Osteoporosis Canada. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. *CMAJ*. 2010 Nov 23;182:1864-73.

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## Quality Snapshot:

### Purchasing and Inventory

*Have you ever made it home after grocery shopping and realized that you purchased milk that expired last week or you added cream to your morning coffee and realized it had lumps in it?*

What did you do? Why did it happen? What could have happened if you didn't notice?

Manufacturers of products provide expiry dates and lot numbers to help manage their inventory and to help us manage it once we purchase it. You have probably heard of "**FIFO**".

**F**irst In, **F**irst **O**ut is a standard in inventory control systems. The goal is to use the oldest product first so that it does not expire while still in your inventory, thus preventing waste. This seems simple but tracking product use can save time later. Here's a scenario....

In the laboratory setting, tracking when a particular lot number of reagent is placed into use is a very important step in order to know which patient results were produced using that lot number. We recently encountered a situation where our Microbiology Laboratory received notification from the manufacturer that a specific lot number of blood culture specimen containers had been recalled. The recall notice indicated there was a quality issue with specific lot numbers and, therefore, test results produced using these lot numbers could be compromised and possibly affect patient care.

The laboratory worked with our clinical partners to recall the affected inventory from the units but discovered that much of the affected lot number had already been used. As a result, the laboratory could not prevent this from affecting patient care and we, therefore, had to inform our physicians of the potentially compromised test results during the affected time period. We suggested that they re-evaluate their patient's clinical situation with this information in mind.

In order to provide accurate, reproducible and clinically relevant test results, the laboratory manages its inventory of reagents, supplies and services to ensure that supplies are adequate and acceptable for use.

*Next time you go to the grocery store for milk, check the expiry dates and see if your grocer uses the FIFO method!*

**Cathie McCallum, Quality Manager, HRLMP, and  
Tom Dorland, Quality Specialist, HRLMP**

## EDUCATION:

### Training Programs:

Congratulations to our residents who succeeded in their Royal College exams! Resident Research day held on May 12, 2011 was a success. Read about these accomplishments and other information on the training program by following the link: <http://www.fhs.mcmaster.ca/pathres/news/index.html>

Information on the postdoctoral fellowship training program can be obtained by following the link: <http://fhs.mcmaster.ca/pathology/education/postdoctoralfellowshiptraining.html>