Lab Updates

August 2008

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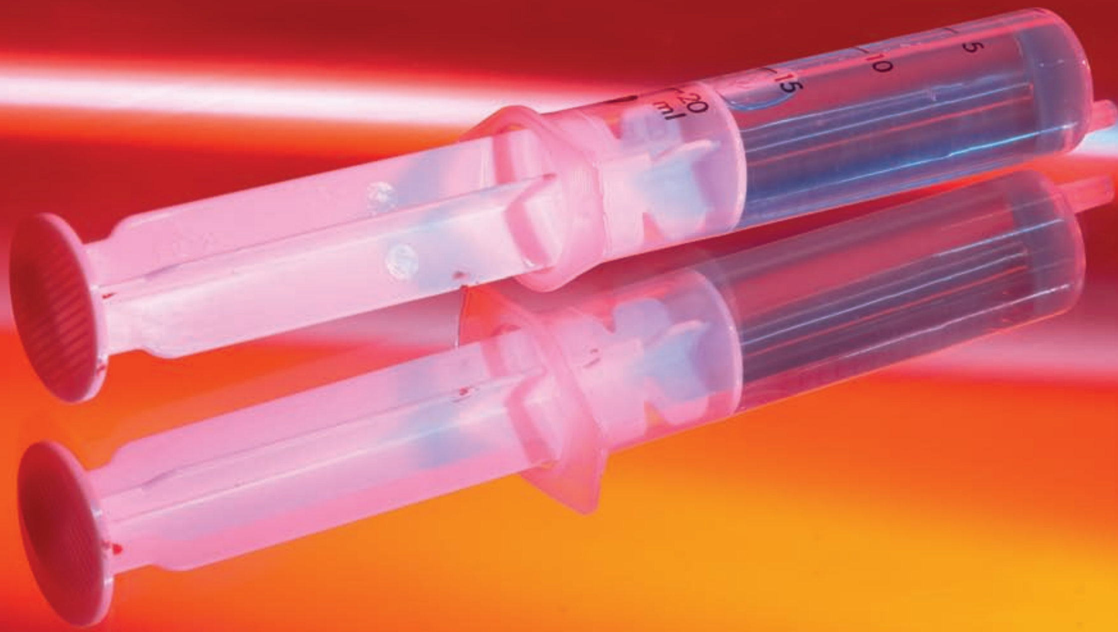


Vitamin D: *What is Optimal Level?*

UMass Memorial
Medical Center Laboratories

One Biotech Park, Suite 200
365 Plantation Street
Worcester, MA 01605-2376
800-476-4431 or 508-334-2863
FAX: 508-334-4210
Email: LabsCS@ummhc.org

L. Michael Snyder, M.D.
Chairman, Dept. of Hospital Laboratories
Professor of Medicine and Pathology
University of Massachusetts Medical School

Guy M. Vallaro, Ph.D.
Vice President, Lab Operations
Medical Center customer liaison

Betsy Harder
Sr. Director, Lab Outreach Program
Non-Medical Center customer liaison

VITAMIN D (CALCIFEROL) was recognized in the early years of the 20th Century as a fat-soluble vitamin for the prevention of “rickets”. Commonly known, as “sunshine vitamin,” it is essential for the development, growth and maintenance of a healthy skeleton. There is considerable discussion of the serum concentrations of Vitamin D associated with deficiency, adequacy of bone health and optimal overall health. Vitamin D is a steroid hormone that has long been known for its important role in regulating body levels of calcium and phosphorus and in the mineralization of bone. More recently, it has become clear that receptors for Vitamin D are present in a wide variety of cells and that this hormone has biologic effects which extend beyond control of mineral metabolism.

The term “Vitamin D” specifically refers to two biologically inert precursors, Vitamin D3 (Cholecalciferol) or D2 (Ergocalciferol). Both Vitamin D3 and D2 do not have significant biologic activity; rather they must be metabolized within the body to the hormonally active form. Vitamin D3 is generated in the skin when light energy is absorbed (UV radiation in the UVB spectrum 290-320 nm) by a precursor molecule 7-dehydrocholesterol (7-DHC; Provitamin D3). However, cutaneous vitamin D3 production after single prolonged UVB exposure is capped at approximately 10-20% of the original epidermal 7-DHC concentration, a limit achieved with suberythemogenic UV exposures. Vitamin D2 is plant derived, produced exogenously by irradiation of ergosterol and enters the circulation through diet. Vitamin D3 from the skin and Vitamin D3 and D2 from the diet enter the blood and are metabolized to their 25-hydroxy counterparts. Once formed 25-hydroxy vitamin D (25-OHD) is metabolized in the kidney to 1, 25 dihydroxy Vitamin D (1, 25 OHD) (Figure 1). Both Parathyroid hormone (PTH) and low serum phosphorus enhance the production of 1, 25 OHD. Once formed 1, 25 OHD regulates serum calcium, phosphorus levels by increasing the efficiency

of intestinal calcium and phosphorus absorption and by mobilizing calcium stores from the bones. The ultimate role of vitamin D is to maintain the serum calcium within the normal range in order to sustain a wide variety of metabolic and physiologic functions and optimize bone health.

The circulating concentration of 25-OHD is the barometer of the Vitamin D status. This is because conversion of 25-OHD to 1, 25 OHD is tightly controlled. The level of 1,25 OHD is maintained despite significant Vitamin D depletion since secondary hyperparathyroidism stimulates increased conversion of 25-OHD to 1,25 OHD in this situation.

Although 1, 25 OHD is the biologically active form of Vitamin D, its level in the body provides NO useful information about a patient's vitamin D status.

The kidney tightly controls serum 1, 25 OHD levels which are often normal or even elevated in Vitamin D deficiency. Therefore, a patient with a normal or high 1, 25 OHD levels is Vitamin D deficient despite high serum levels of the active hormone. At this time, there is consensus that serum 1, 25 OHD is only a measure of the endocrine function of Vitamin D, and not an indicator of the body stores or the ability of Vitamin D to perform its pleiotropic autocrine functions.

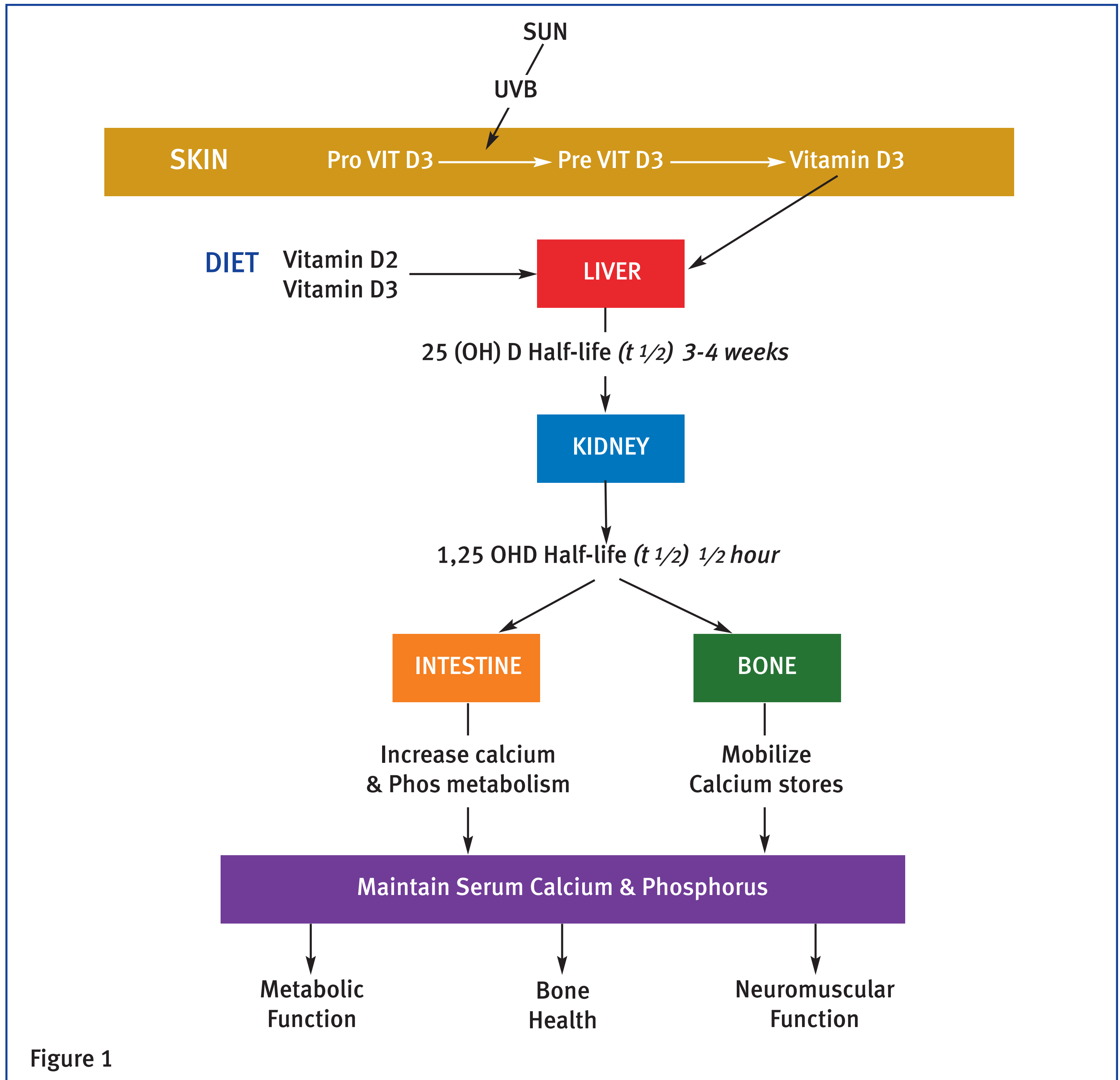
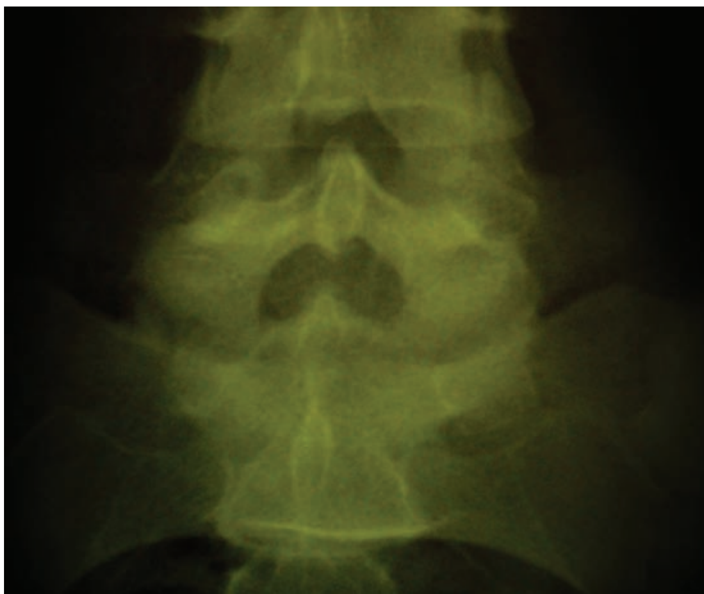


Figure 1



What is ideal 25-OHD level?

Undiagnosed Vitamin D deficiency is not uncommon. Vitamin D produced cutaneously and that obtained from food supplements and has a fairly long circulating half-life of 15 hours. Serum 25-OHD is not only a predictor of bone health, but also an independent predictor of risk for cancer, cardiovascular disease, hypertension, stroke, diabetes, multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, periodontal disease, macular degeneration, mental illness, propensity to fall and chronic pain. A recent meta-analyses of 18 randomized control trials indicating that 25-OHD, even in relatively low doses, reduces the total mortality, adds to the growing evidence that this is a unique vitamin.

The definition of vitamin D deficiency is changing almost every year, as research shows low end of ideal 25-OHD ranges are much higher than we thought only a few years ago. The critical question is—What is an ideal 25-OHD level? Levels needed to prevent rickets and osteomalacia (15 ng/mL) is lower than those that dramatically suppress parathyroid hormone levels (20-30 ng/mL). In turn, those levels are lower than levels needed to optimize intestinal calcium absorption (34 ng/mL). Neuromuscular peak performance is associated with levels ~38 ng/mL. A recent study states that increasing mean baseline levels from 29 to 38 ng/mL was associated with a 50% lower risk for colon cancer and levels of 52 ng/mL with a 50% reduction in the incidence of breast cancer.

Although some experts believe the lower limit of adequate 25-OHD levels are low 30's, others recommend up to 40 ng/mL, there is certainly no consensus. Ideal levels are unknown and natural levels that are found in individuals who live or work in the sun, are 50-70 ng/mL.

Methodological Concerns:

Vitamin D deficiency is an important concern, but the assays for serum 25-OHD, are not standardized. Various methods are available for measuring circulating concentrations 25-OHD. Current methods include Radioimmunoassays, Chemiluminiscence immunoassays, HPLC and LCMS/MS Tandem mass spectrometry. Immunoassays measure **total 25-OHD, which includes levels of both 25-OHD2 and 25-OHD3.** The antibodies cross react 100% with both D2 and D3 to give the total 25-OHD. Some commercial labs use LCMS/MS technology and report 25-OHD2 and 25-OHD3 separately and add both values to get the total 25-OHD. Correlations and agreement studies between immunoassays and LCMS methods have been reported by several investigators. These studies report reasonable correlations but with significant differences, the reasons for which are not well understood. There could be many reasons for these variations, including drifts in the reagents being manufactured and there is an urgent need for harmonization and standardization.

Currently there are no specific guidelines or agreement among clinical labs on the optimum reference intervals of vitamin D to classify patients with moderate to severe deficiency. There is no consensus on a specific level of 25O-HD that is indicative of Vitamin D deficiency. **The reference ranges discussed above are related to total 25-OHD and as long as the combined total is 30 ng/mL or more, the patient has sufficient Vitamin D.** Given the absence of assay standardization and lack of consensus regarding clinical cut off values, Vitamin D levels must be interpreted with in the clinical context of each patient and one should not rely solely on cut off values based on so-called normal values.

Based on above, the following ranges are recommended for evaluating Vitamin D status.

Vitamin D Status	25-OH Vitamin D
Deficiency	<10 ng/mL
Insufficiency	10-30 ng/mL
Sufficiency	30-100 ng/mL
Toxicity	>100 ng/mL

Effective August 25, 2008, the above canned comment will be attached to every patient report.

If you have questions, comments or suggestions, please contact:

Dr. L.V. Rao, Director at 508-334-7593 or
via email at RaoL@ummhc.org

Varicella IgG (Mnemonic: VARG) Test Reference Range *Changes*

Varicella vaccine is generally administered to all children as a part of childhood immunizations. The majority (94%) of the time they are "Positive" for the IgG serology testing. Traditionally, we used the reference range for Varicella IgG serology as "Negative". Based on several physicians' recommendations, **effective August 25, 2008,** the reference range will be changed to "Positive". All negative results will be flagged as "High" to alert physicians that the patient may be susceptible to primary infection.

If you have questions, comments or suggestions, please contact:

Dr. L.V. Rao, Director at 508-334-7593 or
via email at RaoL@ummhc.org

Ms. R. Ambacher, Manager at 508-334-7316 or
via email at Ambacher@ummhc.org

Hemoglobin Evaluation (Mnemonic: HGBSCR) Test *Changes*

Effective August 25, 2008, HGBSCR testing will be performed by the Bio-Rad D-10 Hemoglobin testing system, using Ion-exchange High Performance Liquid Chromatography. There are no changes in reference ranges and specimen collection requirements. One EDTA plasma (Lavender Top) is required.

This test quantitatively measures Hemoglobin A, A2 and F as a percentage of total hemoglobin in the sample. In addition it yields qualitative information regarding the detection of abnormal hemoglobins. As follow up to this initial screen, all suspected hemoglobin variants will be confirmed by further electrophoretic evaluation.

If you have questions, comments or suggestions, please contact:

Dr. L.V. Rao, Director at 508-334-7593 or
via email at RaoL@ummhc.org

Ms. R. Ambacher, Manager at 508-334-7316 or
via email at Ambacher@ummhc.org

Lupus Screen *Changes*

Effective July 1, 2008, please note the change in reference range.

LA Screen	
Old Reference Range	21.3 – 24.9 seconds
New Reference Range	22.0 – 26.0 seconds

If you have questions, comments or suggestions, please contact:

Dr. Liberto Pechet, Directory of Hematology at 508-334-0265 or
via email at pechetl@ummhc.org

UMass Memorial Laboratories
Patient Service Centers in Central Massachusetts

Belmont Street PSC
67 Belmont Street
Worcester, MA 01605
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-334-5396

City Hospital Campus PSC
26 Queen Street, 1st Floor
Worcester, MA 01610
Mon–Fri 8am - 5pm
Closed 12pm - 1pm
508-334-7881

Grove Medical PSC
26 Queen Street, 6th Floor
Worcester, MA 01610
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-334-0275

Hahnemann Professional PSC
291 Lincoln Street
Worcester, MA 01605
Mon–Fri 8:30am - 5pm
Closed 12:30pm - 1pm
508-792-8208

Medical Office Building
25 Oak Avenue
Worcester, MA 01605
Mon–Fri 8am - 5pm
508-792-3656

Medical Office Building PSC
116 Belmont Street
Worcester, MA 01605
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-753-6854

Park Avenue PSC
255 Park Avenue, Suite 210
Worcester, MA 01609
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-798-5127

UMass Memorial Hahnemann Campus
281 Lincoln Street
Worcester, MA 01605
Mon–Fri 7am - 5:30pm
508-334-8100

UMass Memorial Memorial Campus
119 Belmont Street
Worcester, MA 01605
Mon–Fri 7am - 6pm
Sat & Sun 8am - 1pm
508-334-6486

UMass Memorial University Campus
55 Lake Avenue North
Worcester, MA 01655
Mon–Fri 7:30am - 5:30pm
508-856-7797

Vernon Medical Center PSC
10 Winthrop Street
Building #2, 1st Floor
Worcester, MA 01604
Mon–Fri 8am - 5pm
508-831-0624

Clinton PSC
Clinton Hospital
201 Highland Street
2nd Floor, Suite 1
Clinton, MA 01510
Mon & Wed 8am - 5:30pm
Tues, Thurs & Fri 8am - 5pm
Closed 1pm - 1:30pm
978-368-3704

Douglas PSC
15 West Street
Douglas, MA 01516
Mon–Fri 8am - 12pm
508-476-2365

Fitchburg PSC
HealthAlliance/Burbank Hospital Campus
275 Nichols Street, 4th Floor
Fitchburg, MA 01420
Tues, Wed, & Thurs 8:30am - 9pm
Mon & Fri 8:30am - 5:30pm
978-665-5914

Holden PSC
52 Boyden Street
Holden, MA 01520
Mon–Fri 7am - 3:30pm
Closed 12:30pm - 1pm
508-829-8262

Lancaster PSC
136 High Street Ext
Lancaster, MA 01523
Mon–Fri 8am - 5pm
Closed 12pm - 1pm
978-368-1683

Marlborough Bolton Street PSC
320 Bolton Street, Suite G1
Marlborough, MA 01752
Mon–Fri 8am - 5pm
Closed 11:15am - 12:15pm
508-229-0574

Marlborough Lakeview PSC
640 Bolton Street
Marlborough, MA 01752
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-303-1990

Marlborough Maple Street PSC
340 Maple Street
Marlborough, MA 01752
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
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Northborough PSC
112 Main Street
Northborough, MA 01532
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-393-3704

Shrewsbury Julio Drive PSC
26 Julio Drive
Shrewsbury, MA 01545
Mon–Fri 8am - 5pm
Closed 12pm - 1pm
508-845-3615

Shrewsbury Main Street PSC
604 Main Street
Shrewsbury, MA 01545
Mon–Fri 8am - 5pm
Closed 12:15pm - 1:15pm
508-845-6521

Sterling PSC
104 Leominster Road
Sterling, MA 01564
Mon–Fri 8am - 5pm
978-422-5109

Westborough PSC
154 Main Street
Westborough, MA 01581
Mon 7:30am - 4:30pm
Tues–Thurs 8:30am - 5:30pm
Fri 7am - 4pm
Closed 12:30pm - 1:30pm
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Other locations available throughout New England

Subject to change.

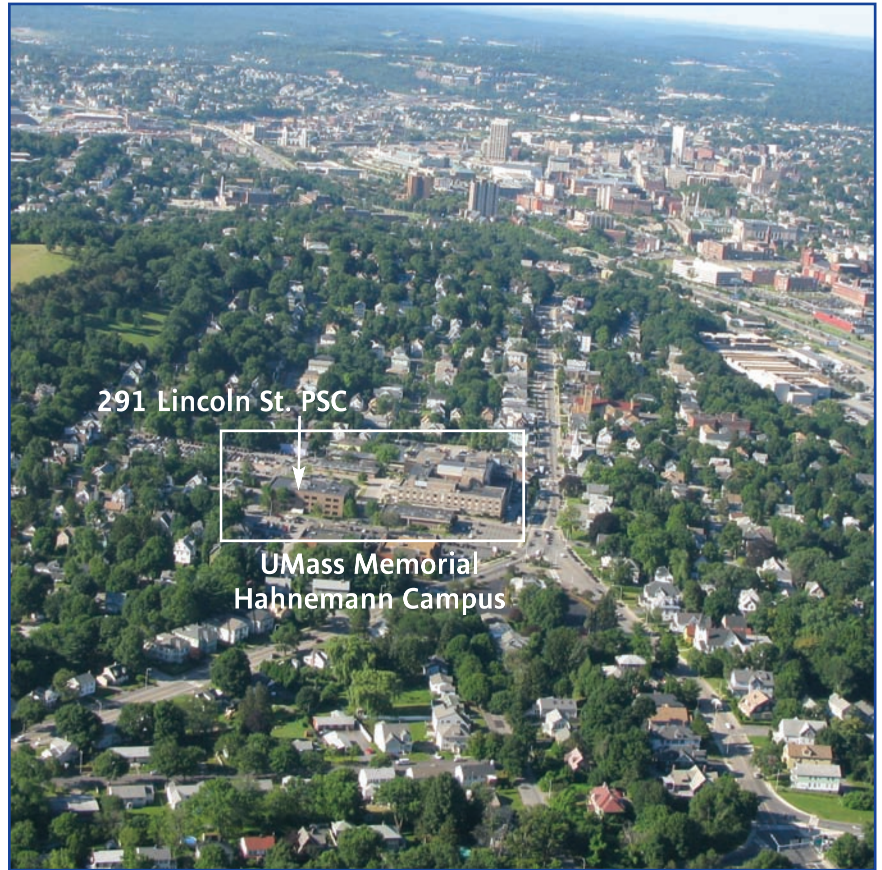
New Patient Service Center

We are one of the largest laboratory providers in New England

UMass Memorial Laboratories has opened a Patient Service Center (phlebotomy draw station) at 291 Lincoln St., Worcester, MA

The vision of UMass Memorial Laboratories is:

- To be a leading provider of laboratory services throughout New England, meeting the needs of patients and providers in the region, and
- To be one of the top ten academic medical center-based laboratories in the United States



Hahnemann Professional PSC

291 Lincoln St., Worcester, MA

Hahnemann Professional PSC is located at 291 Lincoln St., Worcester, MA. The hours are Monday through Friday 8:30am-5:00pm, closed 12:30-1:00pm. The phone number at Hahnemann Professional PSC is 508-792-8208.

Providing a higher level of service. If you don't believe it, put us to the test!™

UMass Memorial
Medical Center Laboratories
One Biotech Park, Suite 200
365 Plantation Street
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