REX

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UPDATES AND INFORMATION FROM REX PATHOLOGY LABORATORY

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Thyroid Function Testing Update

Several years ago we published a semi-exhaustive look at thyroid function testing.[1] Not much has changed with regard to the tests themselves. While the subject of subclinical thyroid disease, has received more scrutiny, it remains controversial.[2-4]

Seth Haber, MD is emeritus Chief of Pathology for the Kaiser Permanente Medical Center in Santa Clara, CA. He is a regular contributor the College of American Pathologists newspaper. In some of his columns he discusses the "Kaiser approach" toward laboratory utilization for a particular set of tests – a consensual process to maximize the value of the test result, while limiting the cost to the "system". I find these helpful and have shared the contents from some of them in previous bulletins. Recently Dr. Haber reviewed the Kaiser endocrinologists' recommendations for thyroid testing and management of thyroid disease.[5] *These comments assume testing in outpatients to minimize interference from drugs or nonthyroidal illness, which is common in hospitalized patients.*[1] An edited version is presented below.

Hypothyroidism

- Routine screening for hypothyroidism not recommended, although some advocate a low threshold for testing in women or elderly (not further defined).
- Test symptomatic patients w/ nonthyroid autoimmune disease, strong family history of thyroid disease or goiter.
- TSH is the best test for detecting hypothyroidism.
- Initial FT4 generally not necessary unless hypothalamic/pituitary disease suspected.
- TSI (thyroid stimulating immunoglobulin), T4, T3, FT3, thyroglobulin or anti-thyroglobulin antibodies are almost never needed in hypothyroid patients.
- TSH interpretation
  - TSH > 10 mIU/L. Repeat TSH and FT4 before beginning lifelong thyroid replacement.
  - TSH 4.83-10 mIU/L, symptomatic.
    - L-thyroxine use in fatigued patients w/ single mildly elevated TSH is "not encouraged".
    - Repeat TSH and FT4 before beginning lifelong thyroid replacement.
    - For confirmed minimally elevated TSH w/ possible hypothyroid Sx. (usually fatigue), low-dose L-thyroxine treatment with smallest dose possible to normalize TSH **may** be prescribed (***controversial***).
  - TSH 4.83-10 mIU/L, asymptomatic.
    - Follow w/ periodic TSH testing,
    - **Consider** treatment if strong family history of thyroid disease or goiter OR thyroperoxidase (anti-thyroid) antibodies are present (***controversial***).
- Begin L-thyroxine therapy at 50-125 µg/day (1.5 µ/kg/day). If high risk for coronary artery disease, start at 25 µg/day.
- After beginning therapy, check TSH q 6 weeks (not sooner) and adjust L-thyroxine dose by 12.5-25 µg/day increments until TSH is normal. Then follow TSH yearly. FT4 or T4 levels not recommended for patients on thyroid hormone replacement therapy unless they have central hypothyroidism.
- Average full replacement dose in patients < 60 years old is 112-137 µg/day. For patients > 60 years old, the average dose is 100-125 µg/day. If TSH remains elevated on doses > 150 µg/day, consider noncompliance before increasing the dose.

Hyperthyroidism

- High clinical suspicion. Order TSH and FT4. High FT4, suppressed TSH (< 0.01 mIU/L), and symptoms confirms hyperthyroidism. Treat w/ beta-blocker if tachycardic and no contraindications. Consider anti-thyroid medication in symptomatic, clinically apparent Graves' disease. If TSH is low, but not suppressed (e.g. 0.01-0.2 mIU/L) and normal FT4 – consider nonthyroidal cause of Sx. Management options include following patient (and repeating tests), radioactive thyroid uptake scan, or endocrinology consult.
- Low clinical suspicion. Order TSH only. If TSH is normal, and there are no clinical findings, the patient is not hyperthyroid. If TSH is low, but not suppressed (e.g. 0.01-0.2 mIU/L), order FT4 and proceed as above.
- TSI, T3, FT3, thyroglobulin, or antithyroglobulin antibodies generally not helpful.

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Thyroid nodules

- CT/MRI/ultrasound not indicated for evaluation of thyroid nodules.
- Order TSH for all patients w/ thyroid nodules
  - For TSH < 0.2 mIU/L, obtain thyroid uptake scan to exclude hyperfunctioning nodule or toxic multinodular goiter.
  - For TSH >0.2 mIU/L, refer patient for thyroid FNA biopsy.
- For thyroid nodules > 1.0 cm. identified incidentally on imaging study, proceed as above.

Thyroid cancer

- Most patients should be followed by endocrinologist and placed on sufficient L-thyroxine to produce low TSH.
- Do not change dose of L-thyroxine w/o consulting patient's endocrinologist.

Final note

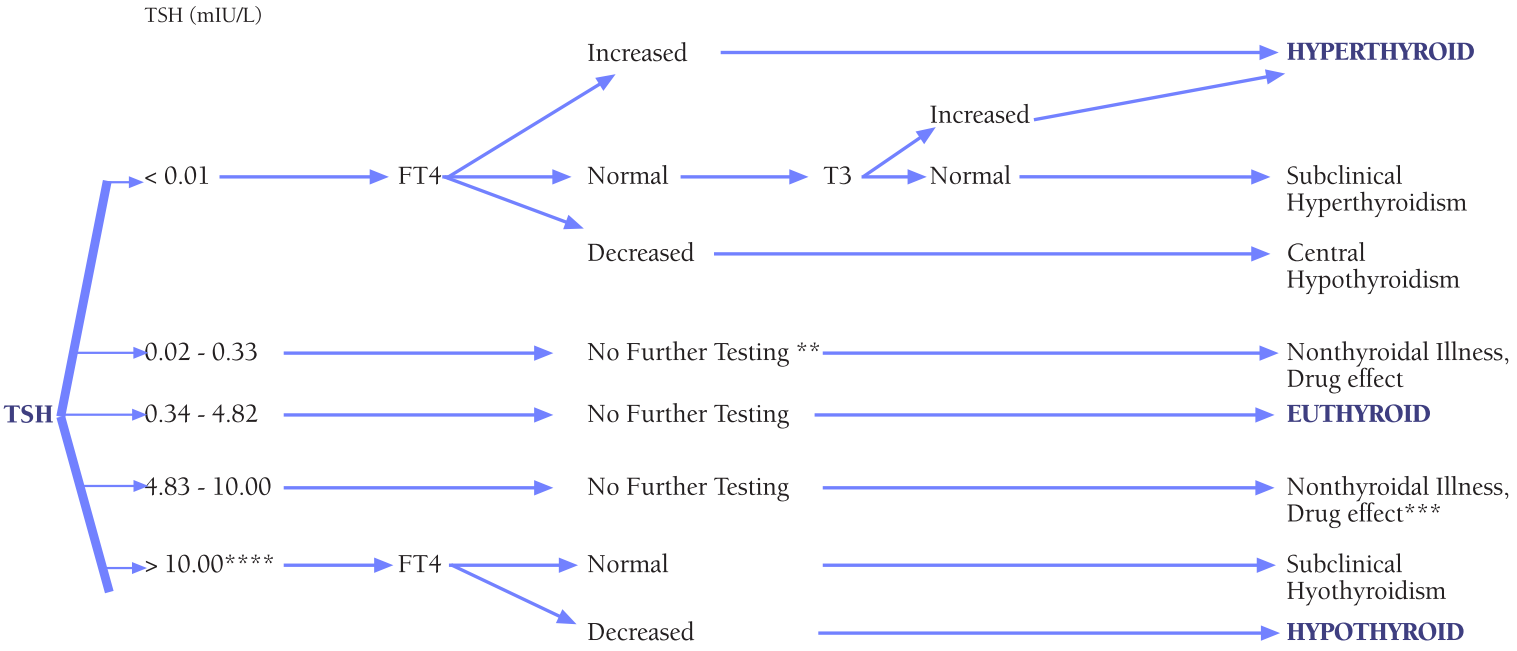
We continue to see patients referred to the laboratory with orders for "thyroid panel". There is no longer a Medicare approved thyroid panel and we do not offer such a test package. As indicated earlier, and implied above, TSH is the preferred screening test for thyroid test.[1,2] Orders for "thyroid panel" will be treated as an order for TSH. An updated version of an earlier TSH algorithm is enclosed.[1]

John D. Benson, MD

References

1. *Benson JD. TFTs for Y2K. Rex Healthcare Laboratory Bulletin Issue 40, August 1999.*
2. *Surks ML et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA 291:228-38, 2004.*
3. *Col NF et al. Subclinical thyroid disease: clinical applications. JAMA 291:239-43, 2004.*
4. *Am Assoc Clin Chem. New subclinical thyroid dysfunction guidelines highlight screening. Controversies: evidence-based vs. clinical-based perspectives. Clin Lab Strategies Feb 10,2005.*
5. *Haber SL. As LUCK would have it. Innovations in Pathology. CAP Today July 2004, p. 135-6.*

TSH Algorithm*



* *Not applicable for patients suspected of having pituitary disease*
** *Perform FT4 only if concerned about central (pituitary, hypothalamic) hypothyroidism*
*** *Repeat TSH periodically. Controversial. Some endocrinologists favor treatment in some clinical scenarios.*
**** *For inpatients, substitute 20.00*
***** *Controversial. Some endocrinologists favor treatment in some clinical scenarios*

J Benson 8/99 (rev. 8/05)

Web-based Resources for Rex Lab Clients

There are several internet and Rex intranet sites that may be useful for patrons of the Laboratory. A listing and brief review is given below. Many of these links can be found using an internet search engine, but current specific internet addresses are provided for those who wish to use them.

- ***RexWeb MD intranet*** (http://rexwebmd/) Use of this site requires linkage to the Rex intranet. There is a laboratory link (http://rexwebmd/lab.htm) which permits access to an electronic index of previous lab bulletins, an on-line laboratory handbook, and toxicology interferences.
  - The lab bulletin index focuses on a key word in the title or subject. A link is provided to the specific bulletin. The user may have to scroll through the bulletin to find the specific article. Early lab bulletins are saved in Word format, while later bulletins require Adobe Acrobat Reader®. http://docserv/df/LAB/PUBLICAT/labbulletinindex.xls
  - The laboratory handbook can be used to look up information about specific tests (including specimen requirements, reference ranges, patient preparation, and aids for test interpretation). http://www.crlonline.com/crlsql/servlet/crlonline
  - The toxicology interferences information consists of scanned reagent method specification sheets associated with the rapid/emergency drug screen we offer at Rex for use in evaluation of patients suspected of acute illicit drug intoxication. It is not particularly user-friendly and requires some patience in navigation on the part of the user. Nevertheless, it provides information regarding the sensitivity of the assays used, drugs which will be detected, and drugs which may or may not cross-react with the test. Again Adobe Acrobat Reader® is required.
- ***Rex Healthcare Internet Portal*** (http://www.rexhealth.com/) can be used to access the laboratory handbook. While there is no direct link on the home page, you can search the site (enter "Pathology Laboratory" in the search box) or type in the following: http://www.rexhealth.com/centers/laboratory/index_laboratory.htm. At the bottom of the webpage is a link to *Laboratory and Ancillary Services Handbook*.Clicking on the link takes you to *Lexi-Comp Online* – the publisher of our ancillary services handbook (http://www.crlonline.com/login). Type in "Rex" for both the Username and Password. You will be directed to the laboratory handbook as described above.
- ***Mayo Medical Laboratory*:** Mayo is the primary reference lab for Rex Laboratory. An on-line catalog can be accessed from the following portal: (http://www.mayoreferenceservices.org/mrs/mml/mml-test.asp). Scroll down the page until you reach the following link: "Test Catalog – On-line; Click here to access". After linking to "Mayo Medical Laboratories Test Catalog" page (http://216.245.161.151/malite.aspx), I would recommend modifying the search as follows:
  - Search In: select "Everywhere"
  - Search Method: select "Contains", de-select "Include obsolete"

  For example, if you don't modify the default settings as instructed above, a search for "cat scratch" yields no "hits". If you run the same search with the above modifications, you get links to Bartonella serology, Bartonella PCR (two tests), and Steiner (modified Dieterle) stain. Click on the test of interest for more information regarding specimen type, reference range, test code, and CPT code. Unfortunately, Mayo does not give much interpretive information when the site is accessed in this fashion, nor is the test charge listed. They restrict access to such information to clients who have been assigned specific user identification and passwords (e.g. your friendly neighborhood pathologist). Nevertheless, the site may be helpful in identifying the test one wishes to order, but cannot recall from your personal memory bank (e.g. what is the test that I want to look for concerning celiac disease?) The site **DOES** include many tests which are not performed on site at Mayo, but are referred to tertiary reference labs through Mayo.
- ***Focus Diagnostics Laboratory*:** To help keep references manageable and to provide the most efficient service for our patients and medical staff, we send the overwhelming majority of reference tests to *or through* Mayo Medical Laboratories. Occasionally physicians request tests that may not be listed in the Mayo catalog. Focus Laboratories (formerly known as Microbiology Reference Laboratory) has an online catalog (http://www.focusdx.com/focus/1-reference_laboratory/index.asp) that may offer additional tests not found at the Mayo site. As you might guess from its heritage, this lab specializes in infectious disease and immunology tests. Mayo **WILL** forward tests to Focus if it does not offer comparable testing itself. Mayo **WILL NO LONGER** forward tests to Specialty Laboratories due to regulatory problems encountered by the latter several years ago. The test offerings at Focus and Specialty are quite similar.
- ***North Carolina State Laboratory of Public Health*:** Used for occasional specimens (e.g. neonatal screening, Bordetella pertussis, pediatric lead screening, West Nile virus serology). The website gives useful information about testing geared for patients as well as physicians (http://204.211.171.13/). For example, the rabies section allows one to determine the incidence of rabies detection in various animal species on a county - by - county basis.
- ***Genomic Health Oncotype DX™***: There is currently considerable interest in the oncology community about commercial tests designed to predict the likelihood of breast cancer recurrence based upon multiple genetic probes. One of the more popular assays is performed by this commercial laboratory and is designed for women with newly diagnosed stage I or II, node negative ERA (+) breast cancer who are candidates for tamoxifen

therapy. The test is performed on a representative paraffin-embedded tumor block. The website provides information regarding the test itself, insurance coverage, and has requisitions and "pathology pre-order" forms which can be downloaded/printed and completed. It is very helpful to us if the oncologist requesting such studies completes the forms and forwards them to us at the time the test is requested. (http://www.genomichealth.com/oncotype/lab/treating_physicians.aspx)

***Lab Tests Online*:** This is a NICE peer-reviewed, non-commercial website that provides excellent information about the role of laboratory tests for diagnosis and management of disease. While designed for patients, clinicians may find it helpful as well. The site was originally conceived and organized by the American Association of Clinical Chemists, but has ongoing support by a variety of clinical laboratory organizations including the College of American Pathologists, American Society of Clinical Pathologists, Clinical Laboratory Standards Institute (formerly NCCLS), American Society of Hematology, American Society for Microbiology, and the Joint Commission on Accreditation for Healthcare Organizations. Information is categorized by specific test, conditions or diseases, and recommendations for screening tests. Discussions about genetic tests, home testing, test reliability, and test safety are provided. Patients who are interested in knowing more about the reasons for a particular test or the significance of a particular result will find this site helpful. (http://www.labtestsonline.org/index.html)

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New *hs*CRP Assay (Redux)

Effective immediately, Rex Hospital Laboratory will have a more sensitive assay for high sensitivity C-Reactive Protein (hsCRP) for use in assessing cardiac risk in selected patients. The new assay has a functional sensitivity < 0.2 mg/L (compared to the current CRP assay which has a functional sensitivity of 1.1 mg/L). The newer assay is superior in discriminating between "low risk" and "moderate risk" individuals using the American Heart Association/Centers for Disease Control 2003 guidelines. This test is available as a ***routine test only*** and ***should be ordered as "high sensitivity C-reactive protein" or "hsCRP"***. C-reactive protein testing for inflammatory disease ("C-reactive protein" or "CRP") is available stat or routine. CRP is capable of distinguishing "high risk" from "low or moderate risk" patients, but lacks the sensitivity of the newer test.

AHA/CDC hsCRP Risk Stratification - 2003

Risk	hsCRP Concentration mg/L (*mg/dL*)
Low	< 1.0 (< *0.1*)
Average	1.0 –3.0 (*0.1 –0.3*)
High	> 3.0 (> *0.3*)

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References

1. *Benson JD, Johnson J, Patterson, E. CRP and cardiac risk. Rex Laboratory Bulletin Issue 78, March 2003.*
2. *Benson JD, Johnson J, Patterson, E. High Sensitivity C-Reactive Protein Rex Laboratory Bulletin Issue 60, September 2001.*
3. *Benson JD. C-reactive protein: the lab test that medicine forgot. Rex Laboratory Bulletin Issue 20, May 1997.*

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