

Overview**Useful For**

Determining thyroid status of sick, hospitalized patients

Determining thyroid status of patients in whom abnormal binding proteins have been identified

Possibly useful in pediatric patients

Method Name

EquilibriumDialysis/TandemMassSpectrometry(MS/MS)

NY State Available

Yes

Specimen**Specimen Type**

Serum

Advisory Information

The routine free thyroxine test (FRT4 / T4 [Thyroxine], Free, Serum) is faster and provides useful information in most patients.

Necessary Information

Include name and telephone number of contact physician.

Specimen Required**Collection Container/Tube:**

Preferred: Red top

Acceptable: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 2.6 mL

Collection Instructions:

1. Draw blood immediately before next scheduled dose.
2. Centrifuge and aliquot serum into plastic vial within 2 hours of draw.

Specimen Minimum Volume

1.2 mL

Reject Due To

Gross hemolysis	Reject
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Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Frozen	21 days	
	Ambient	7 days	

Clinical and Interpretive

Clinical Information

Thyroxine (T4) and triiodothyronine (T3) are the 2 biologically active thyroid hormones. T4 makes up more than 80% of circulating thyroid hormones.

Following secretion by the thyroid gland, approximately 70% of circulating T4 and T3 are bound to thyroid-binding globulin (TBG), while 10% to 20% each are bound to transthyretin (TTR) and albumin, respectively. Less than 0.1% circulates as free T4 (FT4) or free T3 (FT3). FT4 and FT3 enter and leave cells freely by diffusion. Only the free hormones are biologically active, but bound and free fractions are in equilibrium. Equilibrium with TTR and albumin is rapid. By contrast, TBG binds thyroid hormones very tightly and equilibrium dissociation is slow. Biologically, TBG-bound thyroid hormone serves as a hormone reservoir and T4 serves as a prohormone for T3. Within cells, T4 is either converted to T3, which is about 5 times as potent as T4, or reverse T3, which is biologically inactive. Ultimately, T3, and to a much lesser degree T4, bind to the nuclear thyroid hormone receptor, altering gene expression patterns in a tissue-specific fashion.

Under normal physiologic conditions, FT4 and FT3 exert direct and indirect negative feedback on pituitary thyrotropin (thyroid-stimulating hormone: TSH) levels, the major hormone regulating thyroid gland activity. This results in tight regulation of thyroid hormone production and constant levels of FT4 and FT3 independent of the binding protein concentration. Measurement of FT4 and FT3, in conjunction with TSH measurement, therefore represents the best method to determine thyroid function status. It also allows determination of whether hyperthyroidism (increased FT4) or hypothyroidism (low FT4) are primary (the majority of cases, TSH altered in the opposite direction as FT4) or secondary/tertiary (hypothalamic/pituitary origin, TSH altered in the same direction as FT4). By contrast, total T4 and T3 levels can vary widely as a response to changes in binding protein levels, without any change in free thyroid hormone levels and, hence, actual thyroid function status.

FT4 is usually measured by automated analog immunoassays. In most instances, this will result in accurate results. However, abnormal types or quantities of binding proteins found in some patients and most often related to other illnesses or drug treatments, may interfere in the accurate measurement of FT4 by analog immunoassays. These problems can be overcome by measuring FT4 by equilibrium dialysis, free from interfering proteins.

Reference Values

0.8-2.0 ng/dL

Reference values apply to all ages.

Interpretation

All free hormone assays should be combined with thyrotropin (thyroid-stimulating hormone) measurements.

Free thyroxine (FT4) levels below 0.8 ng/dL indicate possible hypothyroidism. FT4 levels above 2.0 ng/dL indicates possible hyperthyroidism.

Neonates can have significantly higher FT4 levels. The hypothalamic-pituitary-thyroid axis can take several days or, sometimes, weeks to mature.

Cautions

Certain drugs may cause short-term free thyroxine fluctuations.

-Heparin

-Salicylates

Â - Acetylsalicylic acid (aspirin)

Â - Salicylic acid (salsalate)

-Furosemide

-Fenclofenac

-Mefenamic acid

-Flufenamic acid

-Diclofenac

-Diflunisal

-Phenytoin

-Carbamazepine

Clinical Reference

1. De Brabandere VI, Hou P, Stockl D, et al: Isotope dilution-liquid chromatography/electrospray ionization-tandem mass spectrometry for the determination of serum thyroxine as a potential reference method. *Rapid Commun Mass Spectrom.* 1998;12:1099-1103
2. Jain R, Uy HL: Increase in serum free thyroxine levels related to intravenous heparin treatment. *Ann Intern Med.* 1996 Jan 1;124:74-75
3. Stockigt JR: Free thyroid hormone measurement. A critical appraisal. *Clin Endocrinol Metab.* 2001 Jun;30:265-289
4. Soldin SJ, Soukhova N, Janici N, Jonklaas J, Soldin OP: The measurement of free thyroxine by isotope dilution tandem mass spectrometry. *Clin Chimica Acta.* 2005;358:113-118
5. Sakai H, Nagao H, Sakurai M, et al: Correlation between serum levels of 3,3',5'-triiodothyronine and thyroid hormones measured by liquid chromatography-tandem mass spectrometry and immunoassay. *PLoS One.*

2015;10(10):e0138864 doi: 10.1371/journal.pone.0138864; Correction in: PLoS One. 2016;11(7):e0159169

6. Kahric-Janjic N, Soldin SJ, Soldin OP, West T, Gu J, Jonklaas J: Tandem mass spectrometry improves the accuracy of free thyroxine measurements during pregnancy. *Thyroid*. 2007 Apr;17(4):303-311 doi: 10.1089/thy.2006.0303

Performance

Method Description

The equilibrium dialysis method separates free thyroxine (FT4) from serum proteins and, thereby, also from protein-bound thyroxine (T4), before measuring it in the protein-free dialysate using sensitive, tandem mass spectrometry. The results are independent of the concentrations of the T4-binding proteins and unaffected by the presence of molecular variants of these proteins. (Soldin SJ, Soukhova N, Janjic N, et al: The measurement of free thyroxine by isotope dilution tandem mass spectrometry. *Clin Chim Acta* 2005 Aug;358:113-118; Masika LS, Zhao Z, Soldin SJ: Is measurement of TT3 by immunoassay reliable at low concentrations? A comparison of the Roche cobas 6000 vs. LC-MSMS. *Clin Biochem*. 2016;49[12]:846-849)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday, Wednesday, Thursday; 3 p.m.

Analytic Time

3 days

Maximum Laboratory Time

8 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

84439

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
FRT4D	T4 (Thyroxine), Free by Dialysis, S	6892-4

Result ID	Test Result Name	Result LOINC Value
8859	T4 (Thyroxine), Free by Dialysis, S	6892-4