# Test Definition: FRT4D

T4 (Thyroxine), Free, Dialysis, Serum

## 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

Equilibrium Dialysis/Tandem Mass Spectrometry (MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Ordering Guidance

The routine free T4 is faster and provides useful information for most patients; order FRT4 / T4 (Thyroxine), Free, Serum.

### Necessary Information

Include name and telephone number of ordering healthcare professional

### Specimen Required

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
**Collection Container/Tube:**
**Preferred:** Red top
**Acceptable:** Serum gel
**Submission Container/Tube:** Plastic vial
**Specimen Volume:** 2.6 mL Serum
**Collection Instructions:**
1. Collect specimen immediately before next scheduled dose.
2. Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.

### Forms

If not ordering electronically, complete, print, and send a Renal Diagnostics Test Request (T830) with the specimen.

### Specimen Minimum Volume

Serum: 1.2 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |
| Gross icterus | Reject |

### Specimen Stability Information

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

## Clinical & Interpretive

### Clinical Information

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

After secretion by the thyroid gland, approximately 70% of circulating T4 and T3 bind to thyroid-binding globulin (TBG), and 10% to 20% bind 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 free hormones are biologically active; however, the bound and free fractions remain in equilibrium. Equilibrium with TTR and albumin occurs rapidly, whereas, TBG binds thyroid hormones very tightly and equilibrium dissociation is slow. 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 nuclear thyroid hormone receptors, altering gene expression in a tissue-specific manner.

Under normal physiologic conditions, FT4 and FT3 exert direct and indirect negative feedback on pituitary thyrotropin (TSH), the major hormone regulating thyroid gland activity. This feedback tightly regulates thyroid hormone production and maintains stable FT4 and FT3 concentrations independent of binding protein concentrations. Therefore. measurement of FT4 and FT3 in conjunction with TSH provides the best assessment of thyroid function. It also allows determination of whether hyperthyroidism (increased FT4) or hypothyroidism (low FT4) are primary (most cases; TSH altered in the opposite direction as FT4) or secondary/tertiary (hypothalamic/pituitary origin; TSH altered in the same direction as FT4). In contrast, total T4 and T3 levels may 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.

Free T4 is usually measured using automated analog immunoassays, which provide accurate results in most cases. 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 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
-Acetylsalicylic acid (aspirin)
-Salicylic acid (salsalate)
-Furosemide
-Fenclofenac
-Mefenamic acid
-Flufenamic acid
-Diclofenac
-Diflunisal
-Phenytoin
-Carbamazepine

## Clinical Reference

1. De Brabandere VI, Hou P, Stockl D, Thienpont LM, De Leenheer AP. 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(16):1099-1103
2. Jain R, Uy HL. Increase in serum free thyroxine levels related to intravenous heparin treatment. Ann Intern Med. 1996;124(1 Pt 1):74-75
3. Stockigt JR. Free thyroid hormone measurement. A critical appraisal. Endocrinol Metab Clin North Am. 2001;30(2):265-289
4. 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 [published correction appears in PLoS One. 2016;11(7):e0159169]. PLoS One. 2015;10(10):e0138864.doi:10.1371/journal.pone.0138864
5. Kahric-Janicic 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;17(4):303-311.doi:10.1089/thy.2006.0303

## Performance

### Method Description

The tandem mass spectrometry method utilizes an equilibrium dialysis technique to separate free thyroxine (FT4) from serum proteins, including protein-bound T4. An isotope of thyroxine (L-thyroxine-[thyrosine-ring-(13)C6]) is added to the dialysate and serves as an internal standard. A liquid-liquid extraction with ethyl acetate further purifies the dialysate. After being dried down and reconstituted, the remaining extract is injected onto the tandem mass spectrometer where it undergoes high-throughput liquid chromatography combined with an electrospray ion source.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Monday, Wednesday, Thursday

### Report Available

3 to 8 days

### Specimen Retention Time

2 weeks

### Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

## Fees & 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 account representative. 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. It has not been cleared or approved by the US 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 |