

Thyroxine, Total (T4)

MDL Test Number: 613

Methodology: Immunoassay

CPT Codes: 84436 x 1



Specimen Collection Platform:

Serum in Serum Separator Tube (SST)

Turnaround Time:

24 - 72 hours

Stability:

Room temperature

Test Additions*:

30 days to add tests

Specimen Collection:



1. Immediately after blood collection, invert the tube(s) gently 5 times to ensure mixing of clot activator.



2. Allow the tube to rest upright for at least 30 minutes after collection to ensure proper clotting.



3. Centrifuge for at least 15 minutes at 2200-2500 RPM within one hour of collection.



4. Do not remove the stopper or pour off serum.



What is Total T4?

Thyroxine, almost always shortened to T4, is the main hormone made by the thyroid gland, a butterfly-shaped gland at the base of the front of the neck. The thyroid builds it out of iodine taken in from food, and it then travels in the blood to nearly every tissue in the body, where it sets the pace at which

cells use energy. That reach is why thyroid problems produce such scattered symptoms: heart rate, body temperature, digestion, mood, menstrual cycles, and the ability to conceive and carry a pregnancy are all influenced by it. Most thyroxine is not active on its own — tissues convert it into a stronger hormone called triiodothyronine (T3) when they need it.

More than 99 percent of the thyroxine in blood is not moving freely but is carried by transport proteins, chiefly one called thyroxine-binding globulin. This test measures the total: the carried portion and the free portion added together. Total T4 does not rise and fall through the day the way some hormones do, and it does not change across the menstrual cycle. That steadiness is why one adult range covers women and men at every age. What does move it is how much transport protein is available. A total T4, therefore, has to be read alongside anything that changes that supply.

Why test for Total T4?

A healthcare provider may order a total T4 test to measure the amount of thyroxine circulating in the blood. Common reasons include:

- **Confirming a thyroid problem and judging its severity** after a thyroid-stimulating hormone (TSH) result comes back outside the expected range
- **Sorting out symptoms that overlap heavily with gynecological ones.** Irregular, absent, or heavy periods, difficulty conceiving, recurrent pregnancy loss, fatigue, and weight change come from thyroid disease as readily as from a problem of the ovaries or uterus
- **Investigating an underactive thyroid**, most commonly Hashimoto thyroiditis, in which the immune system gradually damages the gland; it is several times more common in women than in men
- **Investigating an overactive thyroid**, most commonly Graves' disease, which is likewise far more common in women and often first appears during the reproductive years
- **Assessing thyroid status before or during pregnancy, and in women being evaluated for infertility**, because the demand placed on the thyroid rises sharply in the first months of pregnancy
- **Monitoring a patient already being treated for a thyroid condition**, to judge whether the current dose is holding hormone levels where they should be
- **Explaining a thyroid result that does not fit the clinical picture**, where a change in transport proteins is a more likely cause than disease of the thyroid itself



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Special Instructions:

- **Estrogen, pregnancy, and hormonal contraceptives:** Estrogen raises the amount of thyroxine-binding globulin in the blood. A total T4 measured during pregnancy, on estrogen therapy, or while taking a combined contraceptive pill, patch, or ring is therefore often above the usual range even when the thyroid is entirely healthy. Patients should tell the ordering provider whether any of these apply, and roughly for how long, so the result is read against the right expectation.
- **Medicines that can change the result:** Phenytoin, large doses of aspirin or other salicylates, and liothyronine all compete with thyroxine for room on its transport proteins and can lower a total T4 in someone whose thyroid is working normally. Androgens and anabolic steroids reduce the amount of transport protein itself. Patients should give the ordering provider a complete list of what they take, including over-the-counter products.
- **Biotin supplements:** Biotin, sold on its own as vitamin B7 and included in many hair, skin, and nail products, interferes with this test above the manufacturer's stated threshold of 1500 nanograms per milliliter. No stop-taking interval has been established, so patients should tell the ordering provider about any biotin they take and follow that provider's advice on timing.
- **Comparing results over time:** Thyroxine methods differ from one another, and the same sample can give different numbers on different systems. When results are being tracked over time, use the same test at the same laboratory each time so the comparison is meaningful.

Limitations:

Every laboratory test has limits. For total T4, the main ones are:

- Because this test measures the carried and free portions together, anything that changes the amount of transport protein in the blood moves the result without the thyroid having changed at all. Pregnancy, estrogen therapy, and combined contraceptives raise it; kidney disease that loses protein into the urine, chronic liver disease, serious undernutrition, androgen therapy, and an uncommon inherited shortage of the transport protein lower it. A measurement of only the free, unbound portion is not affected in the same way.
- More than 20 percent of patients who are critically ill from a condition having nothing to do with the thyroid have a low total T4. In that setting, the low value usually reflects the body's response to serious illness rather than thyroid disease, and thyroid results drawn during an acute illness are difficult to interpret.
- Triiodothyronine (T3), the more active hormone that tissues make from thyroxine, is close enough in structure that a small amount of it is measured by this test. Reverse T3, an inactive form that the body also produces, is not detected.
- A sample containing broken-down red blood cells (hemolysis) may have been mishandled somewhere between the draw and the laboratory. Results from such a sample are interpreted with caution. A heavily fatty sample needs additional processing before it can be measured reliably.
- A small number of patients carry natural antibodies in their blood — often people who work closely with animals or who have received certain antibody-based treatments — that can interfere with the test and produce an unexpected result.
- A total T4 result is one piece of a larger picture. It is meant to be read together with the patient's symptoms, medical history, and other test results — never on its own.

Reference Range(s):

Total T4 is measured in micrograms per deciliter ($\mu\text{g}/\text{dL}$). It carries a single adult interval. The same range applies to women and to men, and it does not shift with age, because the thyroid is not governed by sex hormones or by the reproductive cycle. The interval below is specific to serum, which is the sample type this laboratory reports:

- **Adults (serum): 4.5–12.5 $\mu\text{g}/\text{dL}$ (58–161 nmol/L)**

A result outside these ranges is not automatically a problem, and a result inside them does not rule one out. Only the ordering provider can interpret what a given number means for a given patient. Patients should always go by the reference range printed on their own laboratory report.

Analyte	Disorder	Expected Value*
Total T4	Hyperthyroidism (Graves' disease)	↑↑
Total T4	Normal early pregnancy	↑
Total T4	Underactive thyroid (Hashimoto)	↓
Total T4	Chronic liver disease	↓

*↓ – Decreased, ↑ – Increased, ↑↑ – Markedly Increased.

What are some references that discuss the medical necessity of testing Total T4?

1. Ross DS, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*, **26**, 1343–1421 (2016).
2. Chaker L, et al. Hypothyroidism. *Nat Rev Dis Primers*, **8**, 30 (2022).
3. Korevaar T, et al. American Thyroid Association 2026 guidelines for thyroid disease in preconception, pregnancy, and postpartum. *Thyroid*, **36**, 481–544 (2026).
4. Jonklaas J, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. *Thyroid*, **24**, 1670–1751 (2014).
5. Piantanida E, et al. The interplay between thyroid and liver: implications for clinical practice. *J Endocrinol Invest*, **43**, 885–899 (2020).
6. Krassas GE, et al. Thyroid function and human reproductive health. *Endocr Rev*, **31**, 702–755 (2010).



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