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Contributor Disclosures

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Literature review current through: Dec 2020. | **This topic last updated:** Jan 12, 2021.

ANTITHYROID DRUGS OVERVIEW

Antithyroid drugs (also called thionamides) are most often used to treat an overactive thyroid (hyperthyroidism) caused by Graves' disease. These drugs block the formation of thyroid hormone by the thyroid gland (figure 1). (See "Patient education: Hyperthyroidism (overactive thyroid) (Beyond the Basics)".)

Antithyroid drugs have several benefits and a few risks. It is important to learn as much as possible about the treatment of Graves' disease and to discuss all of the possible effects of antithyroid drugs with your doctor or nurse. (See "Graves' hyperthyroidism in nonpregnant adults: Overview of treatment".)

FUNCTION OF ANTITHYROID DRUGS

Antithyroid drugs decrease the levels of the two hormones produced by the thyroid, thyroxine (T4) and triiodothyronine (T3). (See "Patient education: Hyperthyroidism (overactive thyroid) (Beyond the Basics)".)

Antithyroid drugs may be used:

- As a short-term treatment in people with Graves' hyperthyroidism, to prepare for thyroid surgery or radioiodine.

- As initial treatment in Graves' disease for one to two years to see if the disease resolves. Approximately 30 percent of people with Graves' disease will have a remission after treatment for one to two years with antithyroid drugs. (See "Thionamides in the treatment of Graves' disease".)

- To treat hyperthyroidism associated with toxic multinodular goiter or a toxic adenoma ("hot nodule"), usually to prepare for thyroid surgery or radioiodine. (See "Patient education: Thyroid nodules (Beyond the Basics)".)

- To treat women with hyperthyroidism during pregnancy.

- For long-term treatment of hyperthyroidism due to Graves' disease or toxic multinodular goiter or toxic adenoma when patients prefer to avoid definitive therapy with radioiodine or surgery.

You will need to take antithyroid drugs for at least three weeks (usually six to eight weeks or longer) to lower thyroid hormone levels. This is because they only block formation of new thyroid hormone; they do not remove thyroid hormones that are already in the thyroid and the blood stream. If you frequently miss taking the antithyroid drug, thyroid hormone synthesis may resume quickly and replenish thyroid gland stores, prolonging or preventing adequate control of the hyperthyroidism.

TYPES OF ANTITHYROID DRUGS

Two antithyroid drugs are currently available in the United States: propylthiouracil and methimazole (brand name: Tapazole). Carbimazole (which is converted into methimazole in the body) is available in Europe and parts of Asia but not in the United States.

Methimazole — Methimazole is usually preferred over propylthiouracil because it reverses hyperthyroidism more quickly and has fewer side effects. Methimazole requires an average of six weeks to lower T4 levels to normal and is often given before radioactive iodine treatment. Methimazole can be taken once per day.

Propylthiouracil — Propylthiouracil does not reverse hyperthyroidism as rapidly as methimazole, and it has more side effects. Because of its potential for liver damage, it is used only when methimazole or carbimazole are not appropriate. Propylthiouracil must be taken two to three times per the day.

Antithyroid drugs during pregnancy — Propylthiouracil is the drug of choice during the first trimester of pregnancy because it causes less severe birth defects than methimazole. Because there have been rare cases of liver damage in people taking propylthiouracil, some clinicians will

suggest switching to methimazole after the first trimester, while others may continue propylthiouracil.

For women who are nursing, methimazole is probably a better choice than propylthiouracil (to avoid liver side effects).

If you take antithyroid drugs, you should discuss your treatment with your doctor before becoming pregnant. Having radioiodine treatment or surgery at least six months before becoming pregnant can eliminate the need for antithyroid treatment during pregnancy. (See "Patient education: Hyperthyroidism (overactive thyroid) (Beyond the Basics)" and "Hyperthyroidism during pregnancy: Treatment".)

Antithyroid drug side effects — Most of the side effects of antithyroid drugs are minor, but major side effects can occur. Because there is no way to predict who will experience side effects, it is important to discuss all possible side effects before starting treatment. (See "Thionamides: Side effects and toxicities".)

If you cannot tolerate antithyroid treatments, you can consider radioiodine treatment or surgery. (See "Radioiodine in the treatment of hyperthyroidism" and "Surgical management of hyperthyroidism".)

Minor side effects — Up to 15 percent of people who take an antithyroid drug have minor side effects. Both methimazole and propylthiouracil can cause itching, rash, hives, joint pain and swelling, fever, changes in taste, nausea, and vomiting.

If one antithyroid drug causes side effects, switching to the other drug may be helpful. However, approximately one-half of people who have side effects with one drug will have similar side effects with the other. Nausea and vomiting may depend on the dose; spreading large doses out through the day can reduce side effects.

Major side effects — Fortunately, the major side effects of antithyroid drugs are very rare.

- **Agranulocytosis** – Agranulocytosis is a term used to describe a severe decrease in the production of white blood cells. This condition is extremely serious but affects only 1 out of every 200 to 500 people who take an antithyroid drug. Older people taking propylthiouracil and those who take high doses of methimazole may be at higher risk of this side effect.

  Agranulocytosis more commonly occurs within the first three months of starting treatment with an antithyroid drug but rarely can occur later. If you develop a sore throat, fever, or other signs or symptoms of infection, you should stop your medicine and immediately call your doctor or nurse to have a complete blood count (CBC). Serious and potentially life-threatening infections,

or even death, can occur before agranulocytosis resolves. However, once the antithyroid drug is stopped, agranulocytosis usually resolves within a week.

- **Other** – There are other very rare complications of antithyroid drugs: liver damage (more common with propylthiouracil), pancreatitis with methimazole, aplastic anemia (failure of the bone marrow to produce blood cells), and vasculitis (inflammation of blood vessels associated with propylthiouracil).

  Propylthiouracil-related liver damage typically occurs within three months of starting the drug. If you develop jaundice, dark urine, light stools, abdominal pain, loss of appetite, nausea, or other evidence of liver dysfunction, you should discontinue the drug immediately and contact your clinician for assessment of liver function. Propylthiouracil-related liver failure can be serious and potentially life threatening.

  The risk of liver damage from propylthiouracil is an important concern, particularly in children. For this reason, methimazole is the first choice for treating hyperthyroidism.

MONITORING THYROID HORMONES DURING TREATMENT

During treatment, your blood thyroid hormone levels will be monitored periodically. Antithyroid drugs typically reduce levels of both triiodothyronine (T3) and thyroxine (T4), but levels of T3 may take longer to return to normal. Thyroid-stimulating hormone (TSH) levels usually take the longest to return to normal.

Approximately 30 percent of people who take an antithyroid drug for one to two years will have prolonged remission of Graves' disease. It is not known if the antithyroid drug plays an active role in this remission or if it simply controls thyroid hormone levels until Graves' disease resolves on its own.

Checking for remission and recurrence — No test can reliably predict remission of Graves' disease. While imperfect, the measurement of TSH-receptor antibodies (TRAb) is widely used in the United States and Europe to determine if a person is in remission.

Usually, after one to two years of treatment, TRAb is measured, and if low, your clinician will recommend stopping the antithyroid drug, and the chance of a remission is 80 percent. However, if TRAb remains high, the chance of a remission is under 20 percent, and it is appropriate to reconsider definitive therapy with radioiodine or surgery or continue antithyroid drugs.

If antithyroid drugs are stopped, thyroid blood tests are usually performed four to eight weeks later. The blood tests are periodically repeated over 12 months to determine if hormone levels remain

normal or increase over time (this is called a recurrence).

If your levels of T3, T4, and TSH remain normal for 12 months, the long-term prognosis is good. Recurrence after this time occurs in only 8 to 10 percent of people.

WHERE TO GET MORE INFORMATION

Your health care provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our website (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for health care professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient education: Thyroid nodules (The Basics)
Patient education: Multinodular goiter (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient education: Hyperthyroidism (overactive thyroid) (Beyond the Basics)
Patient education: Thyroid nodules (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Beta blockers in the treatment of hyperthyroidism
Cardiovascular effects of hyperthyroidism
Clinical manifestations and diagnosis of Graves disease in children and adolescents
Hyperthyroidism during pregnancy: Treatment
Diagnosis of hyperthyroidism

Disorders that cause hyperthyroidism
Neurologic manifestations of hyperthyroidism and Graves' disease
Overview of the clinical manifestations of hyperthyroidism in adults
Radioiodine in the treatment of hyperthyroidism
Subclinical hyperthyroidism in nonpregnant adults
Surgical management of hyperthyroidism
Thionamides in the treatment of Graves' disease
Graves' hyperthyroidism in nonpregnant adults: Overview of treatment
Thionamides: Side effects and toxicities

The following organizations also provide reliable health information.

- National Library of Medicine

  (www.nlm.nih.gov/medlineplus/healthtopics.html)

- The American Thyroid Association

  (www.thyroid.org)

- Thyroid Foundation of Canada

  (www.thyroid.ca)

- Hormone Health Network

  (www.hormone.org, available in English and Spanish)

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Topic 2168 Version 17.0