Management of Hyperthyroidism

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SPECIAL ARTICLE

2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis

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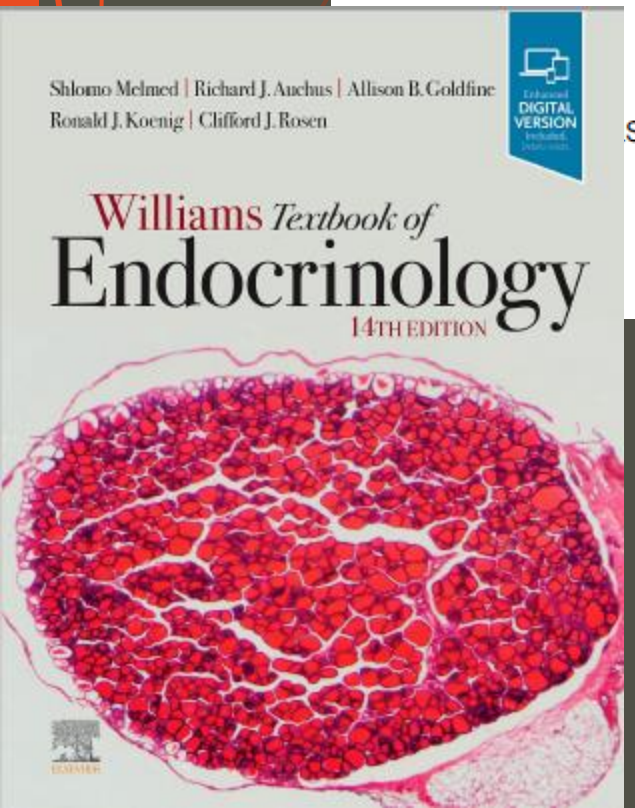

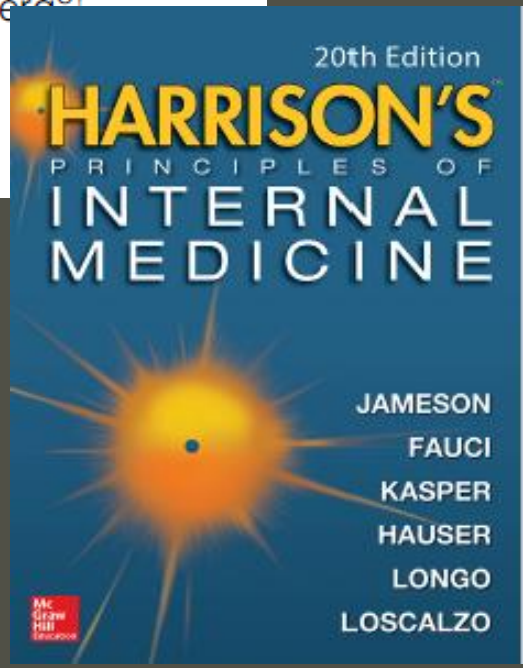

- The term “thyrotoxicosis” refers to a clinical state that results from inappropriately high thyroid hormone action in tissues.
- The term “hyperthyroidism,” as used in these guidelines, is a form of thyrotoxicosis due to inappropriately high synthesis and secretion of thyroid hormone(s) by the thyroid
- Appropriate treatment of thyrotoxicosis requires an accurate diagnosis

Primary Hyperthyroidism
Graves' disease
Toxic multinodular goiter
Toxic adenoma
Functioning thyroid carcinoma metastases
Activating mutation of the TSH receptor
Activating mutation of $G_{s\alpha}$ (McCune-Albright syndrome)
Struma ovarii
Drugs: iodine excess (Jod-Basedow phenomenon)

Thyrotoxicosis without Hyperthyroidism
Subacute thyroiditis
Silent thyroiditis
Other causes of thyroid destruction: amiodarone, radiation, infarction of adenoma
Ingestion of excess thyroid hormone (thyrotoxicosis factitia) or thyroid tissue

Secondary Hyperthyroidism
TSH-secreting pituitary adenoma
Thyroid hormone resistance syndrome: occasional patients may have features of thyrotoxicosis
Chorionic gonadotropin-secreting tumors[a]
Gestational thyrotoxicosis[a]

- Hyperthyroidism has a prevalence of 1% to 2% in women and

  0.1% to 0.2% in men

• The most common causes of an overactive thyroid are Graves disease and toxic multinodular goiter.

- Graves' disease accounts for 60–80% of thyrotoxicosis

  -typically occurs between 20 - 50 years of age

  -also occurs in the elderly

- In the United States, the prevalence of hyperthyroidism is approximately 1.2% (0.5% overt and 0.7% subclinical)

- Both overt and subclinical disease may lead to characteristic signs and symptoms although subclinical hyperthyroidism is usually considered milder

Clinical consequences of thyrotoxicosis

- Untreated or partially treated thyrotoxicosis is associated with
  - weight loss
  - osteoporosis
  - atrial fibrillation
  - embolic events
  - muscle weakness
  - tremor
  - neuropsychiatric symptoms
  - rarely cardiovascular collapse and death

How should clinically or incidentally discovered thyrotoxicosis be evaluated and initially managed?

- Assessment of disease severity
- Assessment of thyrotoxic manifestations

especially potential cardiovascular and neuromuscular complications, is essential in formulating an appropriate treatment plan

- the Hyperthyroid Symptom Scale did not strongly correlate with free T4 or T3

- Cardiac evaluation may be necessary, especially in the older patient

- The phenotypic appearance of Graves disease is apparently milder than in the past

this may be due to earlier diagnosis and treatment

improved iodine nutrition

a secular trend to less smoking

- All patients with known or suspected hyperthyroidism should undergo a comprehensive history and physical examination,

including measurement of pulse rate, blood pressure,respiratory rate, and body weight

Thyroid size, tenderness, symmetry, and nodularity should also be assessed along with pulmonary, cardiac, and neuromuscular function

and the presence or absence of peripheral edema, eye signs, or pretibial myxedema

Biochemical evaluation

- Serum TSH measurement has the highest sensitivity and specificity of any single blood test used in the evaluation of suspected thyrotoxicosis and should be used as an initial screening test

- when thyrotoxicosis is strongly suspected, diagnostic accuracy improves when a serum TSH, free T4, and total T3 are assessed at the initial evaluation

- In overt hyperthyroidism

serum free T4, T3, or both are elevated,

and serum TSH is subnormal (usually <0.01mU/L in a third-generation assay)

- In mild hyperthyroidism

serum T4 and free T4 can be normal,

only serum T3 may be elevated,

and serum TSH will be low or undetectable

These laboratory findings have been called “T3-toxicosis”

Determination of etiology

- RECOMMENDATION 1
- The etiology of thyrotoxicosis should be determined

- If the diagnosis is not apparent based on the clinical presentation and initial biochemical evaluation, diagnostic testing is indicated and can include, depending on available expertise and resources

(1) measurement of TRAb

(2) determination of the radioactive iodine uptake (RAIU)

(3)measurement of thyroidal blood flow on ultrasonography

- A 123 I or 99mTc pertechnetate scan should be obtained when the clinical presentation suggests a TA or TMNG

Strong recommendation, moderate-quality evidence

- In a patient with a symmetrically enlarged thyroid, recent onset of orbitopathy, and moderate to severe hyperthyroidism, the diagnosis of GD is likely and further evaluation of hyperthyroidism causation is unnecessary.

- In a thyrotoxic patient with a non nodular thyroid and no definite orbitopathy, measurement of TRAb or RAIU can be used to distinguish GD from other etiologies

- The choice of initial diagnostic testing depends on cost, availability, and local expertise.

- TRAb is cost effective because if it is positive it confirms the diagnosis of the most common cause of thyrotoxicosis.

- If negative it does not distinguish among other etiologies, however, and it can be negative in very mild GD

- Diagnostic testing may be influenced by the choice of therapy

For example, measuring TRAb in a patient with GD who plans on taking methimazole (MMI) with the hope of achieving a remission will provide a baseline measurement for disease activity

Symptomatic management

- RECOMMENDATION 2
- Beta-adrenergic blockade is recommended in all patients with symptomatic thyrotoxicosis,

especially elderly patients and thyrotoxic patients with resting heart rates in excess of 90 beats per minute or coexistent cardiovascular disease

- Strong recommendation, moderate-quality evidence

- Thyroid hormone excess increases sensitivity of the sympathetic nervous system to catecholamines.
- Drugs that block the response to catecholamines at the receptor site (e.g., propranolol) ameliorate some of the manifestations of thyrotoxicosis and are often used as adjuncts in management.

TABLE 4. BETA-ADRENERGIC RECEPTOR BLOCKADE IN THE TREATMENT OF THYROTOXICOSIS

Drug[a]	*Dosage*	*Frequency*	*Considerations*
Propanolol[b]	10–40 mg	3–4 times per day	Nonselective β-adrenergic receptor blockade Longest experience May block T_4 to T_3 conversion at high doses Preferred agent for nursing and pregnant mothers
Atenolol	25–100 mg	1–2 times per day	Relative β-1 selectivity Increased compliance Avoid during pregnancy
Metoprolol[b]	25–50 mg	2–3 times per day	Relative β-1 selectivity
Nadolol	40–160 mg	1 time per day	Nonselective β-adrenergic receptor blockade Once daily Least experience to date May block T_4 to T_3 conversion at high doses
Esmolol	IV pump 50–100 μg/kg/min		In intensive care unit setting of severe thyrotoxicosis or storm

[a]Each of these drugs has been approved for treatment of cardiovascular diseases, but to date none has been approved for the treatment of thyrotoxicosis.
[b]Also available in once daily preparations.
T_4, thyroxine.

How should overt hyperthyroidism due to GD be managed?

Natural History and Prognosis

- Case histories from the older literature

-patients with Graves hyperthyroidism can be divided into three groups, each with a different natural history:

(1) patients who have a prolonged continuous episode of hyperthyroidism that never goes into remission (~10%)

(2) patients who follow a relapsing and remitting course over many years (~50%)

(3) patients who have a single episode of hyperthyroidism followed by permanent remission (~40%).

- RECOMMENDATION 3

- Patients with overt Graves’ hyperthyroidism should be treated with any of the following modalities:

ATDs

RAI therapy

thyroidectomy

Strong recommendation, moderate-quality evidence

- In the United States, RAI has been the therapy most preferred by physicians, but a trend has been present in recent years to increase use of ATDs and reduce the use of RAI

- In Europe, Latin America, and Japan, there has been a greater physician preference for ATDs

- Once the diagnosis has been made, the treating physician and patient should discuss each of the treatment options

including the logistics, benefits, expected speed of recovery, drawbacks, potential side effects, and Costs.

- Allow the final decision to incorporate the personal values and preferences of the patient.

- The treatment selection should also take into account the local availability and the associated costs.
- Whenever surgery is selected as treatment one should consider the use of expert high-volume thyroid surgeons with on average lower risk of complications

TABLE 5. CLINICAL SITUATIONS THAT FAVOR A PARTICULAR MODALITY AS TREATMENT FOR GRAVES' HYPERTHYROIDISM

Clinical situations	*RAI*	*ATD*	*Surgery*
Pregnancy[a]	x	√√ / !	√ / !
Comorbidities with increased surgical risk and/or limited life expectancy	√√	√	x
Inactive GO	√	√	√
Active GO	√[b]	√√	√√
Liver disease	√√	!	√
Major adverse reactions to ATDs	√√	x	√
Patients with previously operated or externally irradiated necks	√√	√	!
Lack of access to a high-volume thyroid surgeon	√√	√	!
Patients with high likelihood of remission (especially women, with mild disease, small goiters, and negative or low-titer TRAb)	√	√√	√
Patients with periodic paralysis	√√	√	√√
Patients with right pulmonary hypertension, or congestive heart failure	√√	√	!
Elderly with comorbidities	√	√	!
Thyroid malignancy confirmed or suspected	x	-	√√
One of more large thyroid nodules	-	√	√√
Coexisting primary hyperparathyroidism requiring surgery	-	-	√√

√√ = preferred therapy; √ = acceptable therapy; ! = cautious use; - = not first-line therapy but may be acceptable depending on the clinical circumstances; X = contraindication.

[a] For women considering a pregnancy within 6 months, see discussion in Section [T2].

- ATDs:

- Patients with high likelihood of remission (patients, especially women, with mild disease, small goiters, and negative or low-titer TRAb)

-pregnancy

- the elderly or others with comorbidities increasing surgical risk or with limited life expectancy

-individuals in nursing homes or other care facilities who may have limited longevity and are unable to follow radiation safety regulations

- patients with previously operated or irradiated necks

- patients with lack of access to a high-volume thyroid surgeon

- patients with moderate to severe active GO

- patients who need more rapid biochemical disease control

Contraindications

to a particular modality as treatment for Graves' hyperthyroidism:

- RAI therapy:

  -Definite contraindications include pregnancy, lactation, coexisting thyroid cancer, or suspicion of thyroid cancer, individuals unable to comply with radiation safety guidelines

  -used with informed caution in women planning a pregnancy within 4–6 months.

- ATDs:

  - Definite contraindications to ATD therapy include previous known major adverse reactions to ATDs

Contraindications

to a particular modality as treatment for Graves' hyperthyroidism:

- Surgery:

- comorbidity such as cardiopulmonary disease, end-stage cancer, or other debilitating disorders, or lack of access to a high-volume thyroid surgeon

Pregnancy is a relative contraindication

and surgery should only be used in the circumstance when rapid control of hyperthyroidism is required and antithyroid medications cannot be used

- Thyroidectomy is best avoided in the first and third trimesters of pregnancy because of teratogenic effects associated with anesthetic agents and

  increased risk of fetal loss in the first trimester and increased risk of preterm labor in the third

- Optimally, thyroidectomy is performed in the second trimester;
- however, although it is the safest time, it is not without risk (4.5%–5.5% risk of preterm labor)

Preparation of patients with GD for RAI therapy

- RECOMMENDATION 4
- Because RAI treatment of GD can cause a transient exacerbation of hyperthyroidism, b-adrenergic blockade should be considered

even in asymptomatic patients who are at increased risk for complications due to worsening of hyperthyroidism (i.e., elderly patients and patients with comorbidities).

- Weak recommendation, low-quality evidence

Preparation of patients with GD for RAI therapy

- RECOMMENDATION 5
- In addition to b-adrenergic blockade ,pretreatment with MMI prior to RAI therapy for GD should be considered in patients who are at increased risk for complications due to worsening of hyperthyroidism.
- MMI should be discontinued 2–3 days prior to RAI.
- Weak recommendation, moderate-quality evidence

- RECOMMENDATION 6
- In patients who are at increased risk for complications due to worsening of hyperthyroidism, resuming MMI 3–7 days after RAI administration should be considered

- Weak recommendation, low-quality evidence

- patients with severe hyperthyroidism, the elderly, and individuals with substantial comorbidity that puts them at greater risk for complications of worsening thyrotoxicosis .
- patients with cardiovascular complications such as atrial fibrillation, heart failure, or pulmonary hypertension and those with renal failure, infection, trauma, poorly controlled diabetes mellitus, and cerebrovascular or pulmonary disease

Administration of RAI in the treatment of GD

- RECOMMENDATION 8
- Sufficient activity of RAI should be administered in a single application, typically a mean dose of 10–15 mCi to render the patient with GD hypothyroid.
- Strong recommendation, moderate-quality evidence.

- RECOMMENDATION 9
- A pregnancy test should be obtained within 48 hours prior to treatment in any woman with childbearing potential who is to be treated with RAI.

The treating physician should obtain this test and verify a negative result prior to administering RAI

- Strong recommendation, low-quality evidence

RECOMMENDATION 11

- Follow-up within the first 1–2 months after RAI therapy for GD should include

an assessment of free T4, total T3, and TSH

Biochemical monitoring should be continued at 4- to 6-week intervals for 6 months, or until the patient becomes hypothyroid and is stable on thyroid hormone replacement

- Strong recommendation, low-quality evidence.

- Since TSH levels may remain suppressed for a month or longer after hyperthyroidism resolves, the levels should be interpreted cautiously and only in concert with free T4 and total T3.

If ATDs are chosen as initial management of GD, how should the therapy be managed?

Table 1. Mechanism of action of antithyroid drugs

Intrathyroidal inhibition of:
Iodine oxidation/organification
Iodotyrosine coupling
Thyroglobulin biosynthesis
Follicular cell growth
Extrathyroidal inhibition of T4/T3 conversion (PTU)

- when given in adequate doses, they are very effective in controlling the hyperthyroidism.
- When they fail to achieve euthyroidism, the usual cause is nonadherence
- The treatment itself might have a beneficial immunosuppressive role

- In fact, the rate of remission with ATD therapy is much higher than the historical rates of spontaneous remission

- MMI should be used in virtually every patient who chooses ATD therapy for GD,

except during the first trimester of pregnancy when PTU is preferred,

in the treatment of thyroid storm,

in patients with minor reactions to MMI who refuse RAI therapy or surgery

- Strong recommendation, moderate-quality evidence

- At the start of MMI therapy,
  - initial doses of 10–30 mg daily are used to restore euthyroidism
  - and the dose can then be titrated down to a maintenance level (generally 5–10 mg daily)

- The dose of MMI should be targeted to the degree of thyroid dysfunction because too low a dose will not restore a euthyroid state in patients with severe disease and an excessive dose can cause iatrogenic hypothyroidism in patients with mild disease
- adverse drug reactions are more frequent with higher MMI doses.

- The task force suggests the following as a rough guide to
- initial MMI daily dosing:
- 5–10 mg if free T4 is 1–1.5 times the upper limit of normal;
- 10–20 mg for free T4 1.5–2 times the upper limit of normal;
- 30–40 mg for free T4 2–3 times the upper limit of normal

- These rough guidelines should be tailored to the individual patient, incorporating additional information on symptoms, gland size, and total T3 levels where relevant.

- Serum T3 levels are important to monitor initially because some patients normalize their free T4 levels with MMI but have persistently elevated serum T3, indicating continuing thyrotoxicosis

- MMI has the benefit of once-a-day administration and a reduced risk of major side effects compared to PTU.

- PTU has a shorter duration of action and is usually administered two or three times daily, starting with 50–150 mg three times daily, depending on the severity of the hyperthyroidism.
- As the clinical findings and thyroid function tests return to normal, reduction to a maintenance PTU dose of 50 mg two or three times daily is usually possible.

- When more rapid biochemical control is needed in patients with severe thyrotoxicosis, an initial split dose of MMI (e.g., 15 or 20 mg twice a day) may be more effective than a single daily dose because the duration of action of MMI may be less than 24 hours

- Higher doses of antithyroid medication are sometimes administered continuously and combined with L-thyroxine in doses to maintain euthyroid levels (so-called block and replace therapy).

this approach is not generally recommended

because it has been shown to result in a higher rate of ATD side effects

Adverse Effects

- Patients should be informed of side effects of ATDs and the necessity of informing the physician promptly if they should develop pruritic rash, jaundice, acolic stools or dark urine, arthralgias, abdominal pain, nausea, fatigue, fever, or pharyngitis.
- Preferably, this information should be in writing.
- Before starting ATDs and at each subsequent visit, the patient should be alerted to stop the medication immediately and call their physician if there are symptoms suggestive of agranulocytosis or hepatic injury.

- Strong recommendation, low-quality evidence

- Prior to initiating ATD therapy for GD,

  we suggest that patients have a baseline CBC , including white blood cell (WBC) count with differential, and a liver profile including bilirubin and transaminases

- Weak recommendation, low-quality evidence.

Adverse Effects

- Minor cutaneous reactions such as skin rash and urticaria usually can be managed by antihistamine therapy without stopping the drug.

The lesions may resolve spontaneously or after switching to another ATD.

- Persistent symptomatic minor side effects of antithyroid medication should be managed by cessation of the medication

- Prescribing the alternative drug is not recommended in the case of serious allergic reactions

Adverse Effects

- Agranulocytosis (<500 neutrophils/mm3) is a serious side effect, with an incidence of 0.28% in the first 3 months of therapy
- Risk factors are older age, higher doses of ATD, and the presence of particular HLA-B and HLA-DRB1 alleles or rare NOX3 genetic variants.

- The onset of agranulocytosis is rather abrupt, accompanied by fever and sore throat.
- When therapy with ATD is begun, the patient should be instructed to discontinue the drug and to notify the physician immediately should these symptoms develop.

This precaution is more important than the frequent measurement of white blood cell counts because agranulocytosis may develop within 1 to 2 days.

- Neither the ATA nor the ETA recommend routine monitoring of white blood cells during ATD therapy.
- If agranulocytosis occurs, the drug should be discontinued immediately and the patient treated with antibiotics as appropriate.
- GCSF may speed the recovery that invariably takes place.
- thionamides should not be given again.

Adverse Effects

- Although rare, PTU has been associated with fulminant hepatic necrosis, and it is the third most common cause of drug related liver failure, accounting for 10% of all drug-related liver transplants.

- Children are at a higher risk than adults.
- Fortunately, stopping PTU results in recovery in most cases.
- This PTU-associated liver failure may occur at any time during therapy,

so routine monitoring of liver function may not be helpful

- in June 2009 the FDA issued an advisory that PTU should not be used as a first-line agent in hyperthyroidism

- The use of PTU should be restricted to the first trimester of pregnancy ,to thyroid storm, and to patients who experience minor side effects of MMI and are unable or unwilling to undergo 131I therapy or thyroidectomy.

- MMI is associated in a dose-dependent manner with an increased risk for hepatitis and cholestasis.
- There are no reported cases of liver transplantation attributed to MMI toxicity

TABLE 12.4 Adverse Events of Antithyroid Drugs

Common (1–5%)	Skin rash Urticaria Arthralgia, polyarthritis Transient mild leukopenia
Rare (0.2–1%)	Gastrointestinal Abnormal smell and taste Agranulocytosis
Very rare (<0.1%)	Aplastic anemia (PTU, CBZ) Thrombocytopenia (PTU, CBZ) Vasculitis, lupus-like, ANCA+ve (PTU) Hepatitis (PTU) Hypoglycemia (anti-insulin antibodies) (PTU) Cholestatic jaundice (CBZ, MMI)

ANCA+ve, Antineutrophil cytoplasmic antibody positive; *CBZ*, carbimazole; *PTU*, propylthiouracil; *MMI*, methimazole.

Adapted from Strieder TG, Prummel MF, Tijssen JG, et al. Risk factors for and prevalence of thyroid disorders in a cross-sectional study among healthy female relatives of patients with autoimmune thyroid disease. *Clin Endocrinol.* 2003;59:396–401.

Monitoring of patients taking ATDs

- Periodic clinical and biochemical evaluation of thyroid status in patients taking ATDs is necessary, and it is essential that patients understand its importance.
- An assessment of serum free T4 and total T3

should be obtained about 2–6 weeks after initiation of therapy,

depending on the severity of the thyrotoxicosis, and the dose of medication should be adjusted accordingly.

Serum T3 should be monitored because the serum free T4 levels may normalize despite persistent elevation of serum total T3.

- Serum TSH may remain suppressed for several months after starting therapy, and it is therefore not a good parameter for monitoring therapy early in the course.

- Once the patient is euthyroid, the dose of MMI can usually be decreased by 30%–50%, and biochemical testing repeated in 4–6 weeks.

- Once euthyroid levels are achieved with the minimal dose of medication, clinical and laboratory evaluation can be undertaken at intervals of 2–3 months.

- If a patient is receiving long-term MMI (>18 months), this interval can be increased to 6 months

- A differential WBC count

should be obtained during febrile illness and at the onset of pharyngitis in all patients taking antithyroid medication.

- Strong recommendation, low-quality evidence.

- There is insufficient evidence to recommend for or against routine monitoring of WBC counts in patients taking ATDs.
- No recommendation; insufficient evidence to assess benefits and risks

- Liver function and hepatocellular integrity should be assessed in patients taking MMI or PTU who experience pruritic rash, jaundice, light-colored stool or dark urine, joint pain, abdominal pain or bloating, anorexia, nausea, or fatigue.
- Strong recommendation, low-quality evidence

- Hyperthyroidism can itself cause mildly abnormal liver function tests in up to 30% of patients

- Routine monitoring of liver function in all patients taking ATDs has not been found to prevent severe hepatotoxicity.
- If monitoring is employed, the maximum benefit would be for the first 120 days of therapy, when the vast majority of instances of hepatotoxicity occur.

- PTU should be discontinued if transaminase levels (found incidentally or measured as clinically indicated) reach >3 times the upper limit of normal or if levels elevated at the onset of therapy increase further.

- After discontinuing the drug, liver function tests should be monitored weekly until there is evidence of resolution.
- If resolution is not evident, prompt referral to a gastroenterologist or hepatologist for specialty care is warranted

- Except in cases of severe PTU-induced hepatotoxicity, MMI can be used to control the thyrotoxicosis without ill effect

Duration of ATD therapy for GD

- If MMI is chosen as the primary therapy for GD, the medication should be continued for approximately 12–18 months, then discontinued if the TSH and TRAb levels are normal at that time.
- Strong recommendation, high-quality evidence

- Measurement of TRAb levels prior to stopping ATD therapy is suggested

because it aids in predicting which patients can be weaned from the medication, with normal levels indicating greater chance for remission.

- Strong recommendation, moderate-quality evidence

- If a patient with GD becomes hyperthyroid after completing a course of MMI, consideration should be given to treatment with RAI or thyroidectomy.
- Continued low-dose MMI treatment for longer than 12–18 months may be considered in patients not in remission who prefer this approach.
- Weak recommendation, low-quality evidence

Other Drugs Used in Hyperthyroidism

- **Beta-Adrenoceptor Blocking Agents**
- ameliorate some of the manifestations of thyrotoxicosis and are often used as adjuncts in management.

- are recommended in all patients with symptomatic thyrotoxicosis, especially in elderly patients and patients with resting heart rates in excess of 90 beats per minute or coexistent cardiovascular disease.

- **Iodine**
- the major action of iodine is to inhibit hormone release
- aside from its use in preparation for thyroid surgery, iodine is useful mainly in patients with actual or impending thyrotoxic crisis, severe thyrocardiac disease, or acute surgical emergencies.
- If iodine is used in these circumstances, it should be administered with large doses of a thionamide

- KI can be given as

  5–7 drops (0.25 – 0.35 mL) of Lugol’s solution (8 mg iodide/drop)

  or

  1–2 drops (0.05–0.1 mL) of SSKI (50 mg iodide/drop)

  three times daily mixed in water or juice for 10 days before surgery.

Lithium

- Lithium carbonate inhibits thyroid hormone secretion,
- Lithium, 300 to 450 mg every 8 hours, is used only to provide temporary control of thyrotoxicosis in patients who are allergic to both thionamides and iodide

Selenium.

- Selenium levels were higher in patients in remission and correlated inversely to TSHRAb
- Therefore it was hypothesized that selenium supplementation might increase remission rate
- Addition of 300 µg sodium selenite daily to methimazole did not, however, increase remission rate in a placebo-controlled trial

If thyroidectomy is chosen for treatment of GD, how should it be accomplished?

- Preparation of patients with GD for thyroidectomy
- patients should be rendered euthyroid prior to the procedure with ATD pretreatment, with or without b-adrenergic blockade.

A KI containing preparation should be given in the immediate preoperative period.

- Strong recommendation, low-quality evidence

- Calcium and 25-hydroxy vitamin D should be assessed preoperatively and repleted if necessary, or given prophylactically.
- Calcitriol supplementation should be considered preoperatively in patients at increased risk for transient or permanent hypoparathyroidism.
- Strong recommendation, low-quality evidence.

- If surgery is chosen as the primary therapy for GD, near total or total thyroidectomy is the procedure of choice.
  - Strong recommendation, moderate-quality evidence

- If surgery is chosen as the primary therapy for GD, the patient should be referred to a high-volume thyroid surgeon.
  - Strong recommendation, moderate-quality evidence

Postoperative care

- Following thyroidectomy for GD, alternative strategies may be undertaken

<u>for management of calcium levels</u>:

- serum calcium with or without iPTH levels can be measured, and oral calcium and calcitriol supplementation administered based on these results

or

- prophylactic calcium with or without calcitriol prescribed empirically

- Weak recommendation, low-quality evidence

- ATD should be stopped at the time of thyroidectomy for GD,
- and b-adrenergic blockers should be weaned following surgery

- Strong recommendation, low-quality evidence.

- RECOMMENDATION 31
- Following thyroidectomy for GD, L-thyroxine should be started at a daily dose appropriate for the patient's weight (0.8 micg/lb or 1.6 micg/kg), with elderly patients needing somewhat less, and serum TSH measured 6–8 weeks postoperatively.

2018 European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism

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- Patients with newly diagnosed Graves' hyperthyroidism should be treated with ATD.

RAI therapy or thyroidectomy may be considered in patients who prefer this approach. 1, ØØØØ

- MMI (CBZ) should be used in every non-pregnant patient who chooses ATD therapy for Graves' hyperthyroidism. 1, ØØØØ
- MMI is administered for 12–18 months then discontinued if the TSH and TSH-R-Ab levels are normal. 1, ØØØØ

- Measurement of TSH-R-Ab levels prior to stopping ATD therapy is recommended, as it aids in predicting which patients can be weaned from the medication, with normal levels indicating a greater chance of remission. 1, ØØØØ
- Patients with persistently high TSH-R-Ab at 12–18 months can continue MMI therapy, repeating the TSH-R-Ab measurement after an additional 12 months, or opt for RAI or thyroidectomy. 1, ØØØ○