

Graves' Disease Survey

1. Graves' Disease Management Survey Instructions

This survey contains 32 questions and takes approximately 10 minutes to complete. Your answers will remain strictly confidential. As you answer the questions please consider the last several Graves' disease patients you have treated, as the survey would like to assess actual current practices rather than idealized approaches. To decrease ambiguity, assume that the patient wants to defer to your judgment as to the preferred approach.

A 42-year-old woman presents with moderate hyperthyroid symptoms of 2 months duration. She is otherwise healthy, takes no medications, and does not smoke cigarettes. She has two children, the youngest of whom is 10 yr old, and does not plan on being pregnant again. This is her first episode of hyperthyroidism. She has a diffuse goiter, approximately two to three times normal size, pulse rate of 105 beats per minute, and has a normal eye examination. Thyroid hormone levels are found to be twice the upper limit of normal (free T4 = 3.6 ng/dl, normal range = 1.01-1.79 ng/dl (46.33 pmol/L; normal range = 12.99 - 23.03 pmol/L), with an undetectable thyrotropin level (TSH < 0.01 mIU/liter).

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2. Diagnostics

1. Which of the following tests do you obtain in the majority of patients such as the index case? Check all that apply.

- Complete blood count (CBC)
- Liver associated laboratory tests
- TSH-receptor antibody (TRAb)
- Thyroid-stimulating immunoglobulin (TSI)
- TSH-binding inhibitory immunoglobulin (TBII)
- Repeat TSH
- Repeat FT4
- Total T3
- Free T3
- Anti thyroid peroxidase Ab
- Anti thyroglobulin Ab
- Calcium
- Other (please specify)

2. Which of the following tests do you obtain in the majority of patients such as the index case? Check all that apply.

- RAIU 131-I
- RAIU 123-I
- Radioiodine scan
- Technetium-99m scan
- Thyroid ultrasound
- No additional studies are needed
- Other (please specify)

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3. Treatment

3. Assuming the evaluation of the above patient reveals uncomplicated Graves' disease, which principal (long term) mode of therapy would you recommend?

- Antithyroid drug therapy
- Radioiodine therapy
- Thyroidectomy

4. If you selected antithyroid drugs as the primary treatment modality rather than radioiodine, what are the main factors contributing to this preference? Check all that apply.

- Patient and /or your preference to avoid permanent hypothyroidism
- Patient and /or your preference to avoid potential consequences of exposure to radioactivity
- Patient and/or your preference to avoid new or worsening thyroid eye disease
- Patient and/ or your hope of achieving a remission from Graves' disease after a course of antithyroid drugs

5. What would be the preferred drug and doses for initial antithyroid drug therapy?

- Methimazole 10 mg once daily
- Methimazole 15 mg once daily
- Methimazole 20 mg once daily
- Methimazole 30mg once daily
- Methimazole 40 mg once daily
- Methimazole 10 mg bid
- Methimazole 10mg tid
- Propylthiouracil 50 mg tid
- Propylthiouracil 100 mg bid
- Propylthiouracil 100 mg tid
- Carbimazole 5 mg once daily
- Carbimazole 10 mg once daily
- Carbimazole 20 mg once daily
- Carbimazole 30 mg once daily
- Carbimazole 40 mg once daily
- Carbimazole 5 mg bid
- Carbimazole 10 mg bid
- Carbimazole 15 mg bid
- Carbimazole 20 mg bid
- Other (please specify)

6. When starting antithyroid drugs, when would you first check thyroid labs? Please choose one of the following.

- 1 week
- 2 weeks
- 3 weeks
- 4 weeks
- 6 weeks
- 8 weeks
- 12 weeks
- 18 weeks
- 24 weeks

7. How often would you monitor antithyroid drug therapy after attaining biochemical euthyroidism?

- Every month for the next year
- Every 2 months for the next year
- Every 3 months for the next year
- Every 4 months for the next year
- Other (please specify)

8. Would you monitor liver associated laboratory tests during antithyroid drug treatment?

- Yes
- No

9. Would you monitor serial complete blood cell counts during antithyroid drug treatment?

- Yes
- No

10. After two weeks of antithyroid drug therapy, your patient develops a pruritic macular rash, which fails to improve with antihistamine. There are no systemic signs or symptoms. Which one of the following most closely describes your usual approach to this circumstance?

- Switch to the other antithyroid drug
- Select an alternative mode of therapy (radioiodine or surgery)
- Refer to an allergist to perform desensitization to methimazole

11. After 12-18 months of antithyroid drug therapy, what is your usual practice in patients with persistent TSH-receptor antibodies and no adverse drug effects?

- Continue antithyroid drugs as long as required to achieve remission or maintain euthyroidism
- Increase the dose of antithyroid drug and add levothyroxine therapy
- Refer for radioactive iodine therapy
- Refer for thyroidectomy

12. Would you routinely use an antithyroid drug to prepare patients for RAI therapy?

- Only in selected patients
- Routinely for most patients
- No pretreatment

13. Would you restart antithyroid drug therapy after RAI therapy has been administered?

- Only in selected patients
- Routinely for most patients
- Would not restart the antithyroid drug

14. Would you use antithyroid drug to achieve euthyroidism prior to surgery?

- Yes
- No

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Variation 1 - Thyroid Eye Disease

The next questions refer to modifications in your approach to Graves' disease based on the presence of Thyroid Eye Disease.

Rather than a normal eye exam, your patient, who is an active tobacco smoker, has pain with eye movement, moderate scleral injection, eyelid edema (clinical activity score 3), proptosis to 23 mm bilaterally, 2 mm upper lid retraction, and normal visual acuity.

15. In addition to your previous responses, which of the following (if any) would you obtain in this patient with active, moderate-to-severe thyroid eye disease? Check all that apply.

- Consultation with an ophthalmologist with expertise in thyroid eye disease
- Visual field testing
- Orbital CT scan (non-contrast)
- Orbital MRI
- No additional testing or consultation
- Other (please specify)

16. Would you recommend any type of treatment specifically for her thyroid eye disease (TED)? Check all that apply.

- Quit smoking
- Lubricating eye drops
- Sodium selenite (100 µg twice daily) for 6 months
- Glucocorticoids
- Teprotumumab
- Other (please specify)

17. What would be the preferred primary treatment modality for hyperthyroidism due to Graves' disease in the presence of active TED?

- Prolonged therapy with antithyroid drugs
- Radioiodine therapy (alone)
- Radioiodine therapy with prophylactic corticosteroid therapy
- Thyroidectomy

18. Who would be responsible for prescribing medical therapy (glucocorticoids, teprotumumab, other agents) to a patient with active thyroid eye disease?

- Endocrinologist
- Ophthalmologist
- Primary care physician
- Other (please specify)

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Variation 2 - Pregnancy

The following questions relate to the management of Graves' disease in the soon to be pregnant or currently pregnant patient.

32-year-old woman presents with moderate hyperthyroid symptoms of 2 months duration. She is otherwise healthy, takes no medications, and does not smoke cigarettes. She has no children and is planning pregnancy within the next 6 -12 months. This is her first episode of hyperthyroidism. She has a diffuse goiter, approximately two to three times normal size, pulse rate of 105 beats per minute, and a normal eye examination. Thyroid hormone levels are found to be twice the upper limit of normal (free T4 = 3.6 ng/dl, normal range = 1.01-1.79 ng/dl (46.33 pmol/L; normal range = 12.99 - 23.03 pmol/L), with an undetectable thyrotropin level (TSH < 0.01 mIU/liter).

19. What would you recommend to this patient in terms of the preferred primary mode of therapy?

- Antithyroid drug therapy
- Radioiodine therapy
- Thyroidectomy

20. If an antithyroid drug is chosen for primary treatment, which drug would you recommend?

- Methimazole
- Propylthiouracil
- Carbimazole

21. The patient becomes euthyroid, and now has a positive pregnancy test. If you had started methimazole prior to pregnancy, would you now switch to propylthiouracil?

- Yes
- No

22. If you gave the patient propylthiouracil during the first trimester, would you switch to methimazole as the patient enters the second trimester, assuming she still requires antithyroid drugs?

- Yes
- No

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Variation 3 - Elderly

A 72-year-old woman presents with moderate hyperthyroid symptoms of 2 months duration. She has no history of cardiovascular disease, and does not smoke cigarettes. This is her first episode of hyperthyroidism. She has a pulse rate of 105 beats per minute, no goiter, and has a normal eye exam. Thyroid hormone levels are found to be twice the upper limit of normal (free T4 = 3.6 ng/dl, normal range = 1.01-1.79 ng/dl (46.33 pmol/L; normal range = 12.99 - 23.03 pmol/L), with an undetectable thyrotropin level (TSH < 0.01 mIU/liter).

23. What would be the preferred primary treatment modality in this case?

- Antithyroid drug therapy
- Radioiodine therapy now
- Radioiodine therapy after normalization of thyroid function with an antithyroid drug
- Thyroidectomy

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Variation 4 - Relapse

A 42-year-old woman has the diagnosis of Graves' disease. She underwent treatment with antithyroid drug for 18 months (titration regimen), without adverse side effects and this treatment was tapered and stopped when TRAb levels became undetectable.

However 8 months later, the patient returns with symptoms of thyrotoxicosis, and laboratory testing shows elevated serum free T4 and T3 levels and a suppressed serum TSH.

24. What would be the preferred treatment modality in this situation?

- Restart antithyroid drug therapy
- Radioiodine therapy
- Thyroidectomy

25. If antithyroid drugs are restarted, how long would you continue them before considering alternative therapies such as radioiodine or surgery, assuming persistent TSH-receptor antibodies and no adverse drug effects?

- 6 months
- 12 months
- 18 months
- 24 months
- 36 months
- More than 36 months
- Indefinitely

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Demographic questions

26. Which of the following professional associations do you belong to? (Select all that apply).

- American Thyroid Association
- American Association of Clinical Endocrinologists
- Asia and Oceania Thyroid Association
- European Thyroid Association
- Latin America Thyroid Association
- The Endocrine Society
- Other:

27. How many newly diagnosed Graves' disease patients do you personally see each month?

- None
- 1- 5
- 6-10
- 11-15

28. In what state/country do you practice? These data are used to assess regional and international differences.

State / Province:

Country:

29. Which of the following geographical regions corresponds to the location of your practice?

- North America (United States and Canada)
- Latin America (South America, Central America, Mexico, Caribbean)
- Asia (China, Indonesia, Japan, North Korea, Philippines, South Korea, Thailand)
- Europe (Balkans, Central Europe, Eastern Europe, Russia, Western Europe, Turkey)
- Oceania (Australia, New Zealand)
- Africa
- the Middle East

30. What is your specialty?

- | | |
|---|---|
| <input type="radio"/> Adult Endocrinology | <input type="radio"/> Nuclear Medicine |
| <input type="radio"/> Head and Neck Surgery | <input type="radio"/> Pediatric Endocrinology |
| <input type="radio"/> Endocrine Surgery | <input type="radio"/> General Internal Medicine |

31. What is your age?

- | | |
|-----------------------------|---|
| <input type="radio"/> 26-30 | <input type="radio"/> 56-60 |
| <input type="radio"/> 31-35 | <input type="radio"/> 61-65 |
| <input type="radio"/> 36-40 | <input type="radio"/> 66-70 |
| <input type="radio"/> 41-45 | <input type="radio"/> 71-75 |
| <input type="radio"/> 46-50 | <input type="radio"/> 76-80 |
| <input type="radio"/> 51-55 | <input type="radio"/> Prefer not to state |

32. What is your gender?

- Female
- Male
- Prefer not to state

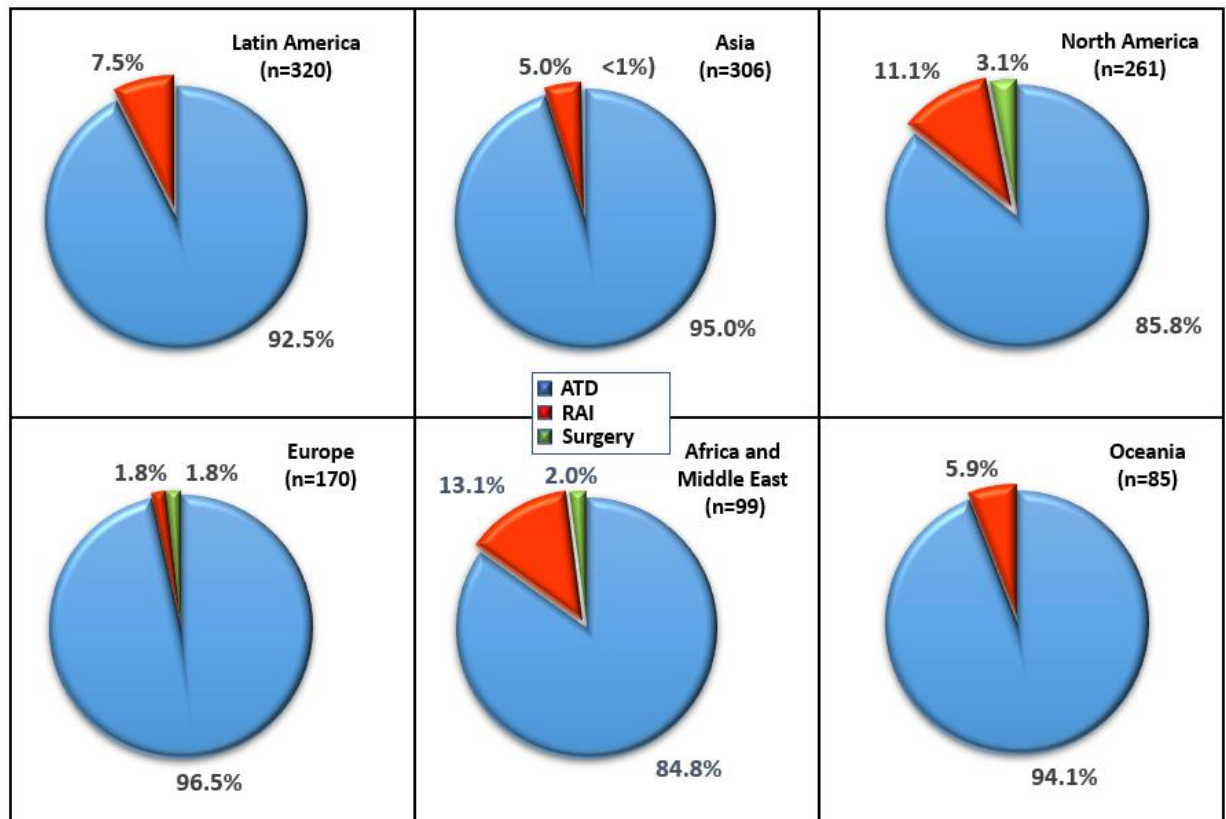
1 **Supplemental Figure S1 (Color figure)**

2 **Figure S1:** Geographical differences in preferred primary therapy for Graves'

3 disease according to United Nations grouping of world regions. Abbreviations:

4 ATD, antithyroid drugs; RAI, radioactive iodine therapy.

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14 **Supplemental Table S1**

15 **Table S1:** Number of members of each society and total responses

	Number of Members	Total Responses
Endocrine Society	18,000	695 (3.6%)
American Association of Clinical Endocrinology	5,700	300 (5.2%)
American Thyroid Association	1,700	292 (17.2%)
European Thyroid Association	900	174 (19.3%)
Brazilian Society of Endocrinology and Metabolism	3,500	150 (4.2%)
Latin America Thyroid Association	517	130 (25.4%)

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18 **Supplement Table S2A: ATD Drug and Dose Selection**

Drug and Dose	Number Respondents	Percent of 1325 Respondents
MMI 20 mg once daily	383	28.9%
MMI 10 mg once daily	189	14.3%
MMI 30 mg once daily	177	13.4%
MMI 10 mg twice daily	162	12.2%
MMI 15 mg once daily	131	9.9%
MMI 10 mg three times daily	50	3.8%
CBM 10 mg twice daily	49	3.7%
CBM 20 mg once daily	41	3.1%
MMI 40 mg once daily	30	2.3%
CBM 15 mg twice daily	28	2.1%
CBM 30 mg once daily	23	1.7%
CBM 20 mg twice daily	22	1.7%
CBM 15 mg once daily	15	1.1%
CBM 40 mg once daily	9	0.7%
PTU 50 mg three times daily	5	0.4%
PTU 100 mg three times daily	4	0.3%
CBM 5 mg twice daily	3	0.2%
PTU 100 mg twice daily	3	0.2%
CBM 5 mg once daily	1	0.1%

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20 **Supplement Table S2B: Total Daily ATD and Dose Selection**

Drug and Dose	Number Respondents	Percent of 1340 Respondents
MMI 20 mg	545	40.7%
MMI 30 mg	231	17.2%
MMI 10 mg	190	14.2%
MMI 15 mg	131	9.8%
CARB 20 mg	90	6.7%
CARB 30 mg	55	4.1%
CARB 40 mg	31	2.3%
MMI 40 mg	31	2.3%
CARB 10 mg	18	1.3%
PTU 150 mg	5	0.4%
PTU 300 mg	4	0.3%
CARB 45 mg	3	0.2%
PTU 200 mg	3	0.2%
CARB 5 mg	1	0.1%
CARB 15 mg	1	0.1%
MMI 60 mg	1	0.1%

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