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The management of Graves’ disease in New Zealand 2014
Stephanie C Cox, Jade AU Tamatea, John V Conaglen, Marianne S Elston

ABSTRACT

BACKGROUND: Treatment options for Graves’ disease (GD), namely anti-thyroid drugs (ATD), surgery or radioiodine (RAI), have not changed over the past two decades. There is no ‘gold-standard’ treatment for GD.

AIMS: To assess whether the management of GD in New Zealand has changed since the previous 1991 New Zealand survey and compare current management with that of contemporary international studies.

METHODS: We conducted an online survey of New Zealand physicians currently practising internal medicine, diabetes and/or endocrinology, using the cases and questions from the original European and 1991 New Zealand studies.

RESULTS: The first-line use of RAI was 5.5%, compared to 41% in the 1991 New Zealand survey. This corresponded to an increase in ATD use, while the rates of surgery as a first-line treatment have remained static over time. New Zealand physicians use technetium scanning for diagnosis, whereas ultrasound and radioiodine uptake were the most commonly selected investigations by European and North American physicians, respectively. The pattern of ATD use in pregnancy was similar to international practice.

CONCLUSION: Treatment of GD in New Zealand has shifted away from the use of RAI as first line treatment. There are significant differences in the investigation and treatment of Grave’s disease between New Zealand, Europe and North America.

Graves’ disease (GD) is the leading cause of thyrotoxicosis in New Zealand, accounting for approximately 64% of cases of thyrotoxicosis. Treatment is with anti-thyroid drugs (ATD), radioiodine (RAI) or thyroidectomy. Despite these treatments being in use for over 50 years, none have been proven to be superior and each has potential risks. There have been developments in our understanding of these risks over the last two decades, in particular with regard to the risks of anti-thyroid drugs in pregnancy. In addition, concerns over the long-term effects of radiation exposure have been reported, and advances in anaesthesia and surgical techniques have resulted in lower surgical morbidity.

Multiple surveys were undertaken in North America, Europe and Australasia in the late 1980s and 1990s assessing patterns of clinical practice by physicians treating patients with GD. A New Zealand survey was conducted in 1991, and an Australian study in 2000. More recently, similar surveys have been repeated in Europe and North America, and these international studies continue to show significant differences in practice throughout the world.

The aim of this study was to assess whether the management of GD by New Zealand endocrinology/internal medicine specialists has changed since the 1991 New Zealand survey, and to compare current management of GD with that of contemporary international studies.

Materials and methods

An online survey (Appendix 1) was developed using a freely available web-based service (Google forms). The index case (Box 1) and two variations were the same as those used in the recently reported surveys from North America and Europe. These in turn were based on the original 1987 European survey by Glinoer et al, as was the 1991 New Zealand survey by Ford et al.
Participants were identified from the Medical Council of New Zealand Register of Physicians. Those identified as practicing predominantly in the areas of general medicine, endocrinology/diabetes or obstetric medicine were e-mailed invitations to participate, which included an individual electronic link to the survey. Survey responses were anonymous and stored electronically in a password-protected Google Drive account. Multiple reminder emails were sent to try to improve response rates and ‘Champions’ were recruited at each main centre to promote the survey face-to-face with their colleagues (at departmental meetings, etc.) Those respondents who reported seeing less than two cases of GD per year were excluded from further analysis.

Statistical Analysis
Statistical analysis was performed using Stata (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). A p value of <0.05 was considered significant. Results are reported as number of responses/number of respondents where possible. Some questions allowed more than one option to be selected; these are presented as percentages of the respondents. Chi-square analysis was used to compare key results from the 1991 New Zealand survey to each of the recent North American and European studies, using data as available in their publications.11,13,14

Ethics
The study was conducted in accordance with the National Health Advisory Committee’s Ethical Guidelines for Observational Studies, and with approval from the Waikato District Health Board Research Committee (RD14047).

Results
Responses and demographics
A total of 117 physicians were initially identified. Six were not able to be located, two had retired, and one had permanently emigrated. The remaining 108 were sent the survey and 47 responses were received. Of these, 11 were from physicians who reported seeing <2 patients with GD in the past year, and so were excluded from further analysis. Respondent demographics are shown in Table 1.

Diagnostic evaluation of the index case
Serum free T4 and thyroid-stimulating hormone (TSH) were the most frequently selected tests (requested by 35/36, [97%]), followed by free T3 (30/36 [83%]). The use of thyroid antibody testing and thyroid imaging studies is shown in Figure 2.

Management of the index case
First-line treatment
ATD use, aiming for remission, was the treatment of choice for the index case by 33/36 (92%) respondents. RAI was selected as first-line treatment by 2/36 (5%) and one respondent selected thyroidectomy as first-line treatment. One third (12/36) would definitely use beta-blockers as adjuvant treatment, 19/36 (52%) would consider beta-blockade, whereas 5/36 (14%) would definitely not use beta blockers in the index case. Metoprolol was the most commonly selected beta-blocker (16/31, 52%), followed closely by propranolol (13/31, 42%).

Table 1: Medical practice of respondents.

<table>
<thead>
<tr>
<th>Subspecialty</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>Endocrinology</td>
<td>27</td>
<td>57</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>General Physician</td>
<td>11</td>
<td>23</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>New Graves’ pts/yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–5</td>
<td>3</td>
<td>7</td>
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<td>6–10</td>
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<td>9</td>
</tr>
<tr>
<td>11–50</td>
<td>20</td>
<td>45</td>
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<tr>
<td>&gt;50</td>
<td>9</td>
<td>20</td>
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</tbody>
</table>

Box 1: Index case.
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 years 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, with an undetectable thyrotrphin level (TSH<0.01mIU/L).
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ATD treatment

All respondents reported that they would use carbimazole (CBZ) as the ATD of choice (methimazole is not available in New Zealand). Most respondents would use a starting dose of 20–30mg administered daily (29/36, 81%). None of the respondents would use a ‘block and replace’ regimen, with 36/36 opting for dose titration aiming for euthyroidism. To assist dose titration, most respondents would repeat thyroid hormone levels 4–6 weeks after commencing treatment. There was a large spread of opinion on the best interval for monitoring thyroid hormone levels once the patient was euthyroid, with a fairly even spread across 4 weeks, 6 weeks, and 2 months, although a 3-month interval was most commonly selected (22%, 17%, 19%, and 39% respectively). Three quarters of respondents would not request any routine monitoring apart from thyroid hormone levels, whereas routine monitoring of liver enzymes and complete blood count would be requested by 22% and 25% of respondents, respectively. TSH-receptor antibody (TRAb) titers were routinely measured by 11% of respondents in addition to thyroid function. The majority would recommend 12–18 months of ATD treatment aiming for remission, before recommending an alternative form of therapy. Criteria for cessation of ATD treatment were a clinically and biochemically euthyroid patient (89%), duration of treatment (58%), and undetectable TRAb (25%). In the presence of a pruritic macular rash unresponsive to antihistamine treatment, 30/36 respondents would switch to an alternate ATD, while 6/36 would select an alternate mode of therapy.

ATD treatment as an adjunct to radiiodine (RAI) and thyroid surgery

The majority of physicians surveyed would pretreat with ATDs in preparation for RAI (28/35, 80%). A further 14% would pretreat with ATDs prior to the use of RAI only in the presence of additional clinical factors such as severe thyrotoxicosis, underlying heart disease, patients with multiple comorbidities or over the age of 65. ATDs are withdrawn 5–7 days prior to RAI by 70% of respondents. Only 15% would routinely use ATDs after RAI therapy with the majority reserving them for selective use only (73%). When thyroid surgery was proposed, 90% (27/30) of physicians would aim to restore normal thyroid function preoperatively with ATDs.

RAI treatment

All of the physicians surveyed treat patients with RAI, either by directly prescribing and administering it, or by referral to another specialist. The aim of treatment was to restore euthyroidism off medication for 14/36 (39%), whereas an attempt to achieve hypothyroidism followed by thyroid hormone replacement was the goal for 22/36 (61%). A fixed dose was used by 50%, with 7/36 reporting the use of a variable dose. Thirty percent of respondents did not know how the dose was calculated as treatment was administered by another specialist. All of those surveyed would administer a second dose of RAI if the patient was not cured by the initial treatment. The majority (20/32), would wait 6 months prior to the second dose, with 5/32 re-treating at 12 months.

Surgical management

The majority of physicians had previously referred patients with GD for thyroid surgery, although six respondents reported they did not ever refer patients for surgery. Referral to an endocrine surgeon was made by 49% of respondents, 20% to a general surgeon and the remainder to either head and neck, or ear nose and throat surgeons. Thirty-seven percent of the physicians surveyed were unaware of the number of thyroidectomies performed per year by the surgeon to whom they refer. The remainder were fairly evenly distributed between low-volume and high-volume surgeons. The operation of choice was total thyroidectomy (87%). The majority of centres did not discharge patients routinely on prophylactic doses of calcium and vitamin D (19/30, 63%).

Variation 1: moderate active Graves’ ophthalmopathy

The majority of physicians surveyed (94%) would recommend evaluation by an ophthalmologist for patients presenting with ophthalmopathy, and if the patient required corticosteroid therapy this was most likely to be administered and super-
vised by an ophthalmologist (19/36, 53%). The presence of ophthalmopathy would alter the choice of first-line treatment, with only 23/36 (64%) now opting for ATDs, and no respondents selecting RAI, with or without adjuvant corticosteroid treatment. Twenty-five percent would recommend thyroidectomy as first line treatment for the patient with ophthalmopathy, compared with 2.8% for the index case.

Variation 2: planning pregnancy in the next 6–12 months

ATDs remained the first line treatment of choice, but decreased from 91% to 67%. Correspondingly, RAI treatment and thyroid surgery were each selected by 4/36 (11%) of respondents, compared with 2/36 (5.5%) and 1/36 (2.8%), respectively, for the index case. The choice of ATD was now split between CBZ (20/36 56%) and propylthiouracil (PTU) (16/36, 44%). Eighty-six percent of respondents reported they would change from CBZ to PTU in a euthyroid patient with a positive pregnancy test. If the patient was on PTU in the first trimester, 23/36 (63.9%) reported they would switch to CBZ from the second trimester, assuming the patient still required ATDs. The majority would monitor thyroid function tests 4-weekly during pregnancy (28/36, 78%), and 75% (27/36) routinely measure TRAb during pregnancy. Of those, 31/36 (86%) would monitor TRAb every 12 weeks, or once per trimester. Of those who measure TRAb levels during pregnancy, only 25% would alter treatment based on these results.

Comparison with 1991 New Zealand study

Practice in New Zealand has changed over the last 20 years, with a move away from radioiodine treatment as first line treatment (Figure 1). In comparison to the 1991 New Zealand survey, the first-line use of radioiodine is now only 5.5%, compared with 41%, using the same clinical scenario (p<0.0005). This corresponded with an increase in the use of ATDs (92% vs 55%, p<0.0005), while the rates of surgery as a first-line treatment do not appear to have changed over time (3% vs 4%, p=0.709). An exception was in active ophthalmopathy, where thyroidectomy was a more frequent choice, selected by 25% in our survey.

Comparison with American and European surveys

The responses to this survey were compared with those from the 2011 American survey by Burch et al, and the 2013 European survey reported by Bartalena et al. There were significant differences between the laboratory and radiological investigations selected by New Zealand physicians and those from Europe and North America (Figure 2a & b). New Zealand physicians requested TPOAb and
Figure 2a: Comparison of thyroid-associated antibody testing rates.

TgAb titres more frequently than either of the other two groups (TPOAb 69% vs 42% US [p<0.0005] vs 65% EU [p=0.585]), whereas TRAb titres were requested at similar rates to North American physicians (61% vs 52%, p=0.289), but significantly less than European physicians (61% vs 86%, p=0.001). Technetium scanning was the modality of choice for New Zealand physicians (31%), whereas ultrasound was the most commonly selected investigation by European physicians (71%) and radioiodine uptake scanning (RAIU) by those from North America (47%) (Figure 3).

There were significant differences in the choice of first-line treatment across the continents (Figure 3). New Zealand physicians reported higher rates of ATD use than those in North America (92% vs 54%, p=<0.0005), similar to those reported in the European study (92% vs 84%, p=0.226). US physicians were much more likely to use RAI as first-line treatment, with New Zealand physicians reporting the lowest rate of RAI use as first-line (5.5% vs 45%, p<0.0005). Surgery was infrequently selected as first-line treatment across all groups studied, and no significant differences identified.

Preferred treatment in preparation for and during pregnancy

As preparation for pregnancy, New Zealand physicians appear to use PTU much
the same as North American physicians (56% vs 46%, p=0.156) and the majority would switch to PTU in early pregnancy (31/36, 86%) (Figure 4).

Most New Zealand physicians (63%) and 60% (p=0.391) of European physicians switch back to CBZ from the second trimester, when compared with 46% of US physicians (p=0.035) (Figure 4).

Discussion

There are three effective treatments for Graves’ disease: ATD, RAI and thyroidectomy. Despite all of these being used regularly in clinical practice since the 1940s, there have been few head-to-head studies comparing treatment options, and those that have been done have failed to show any significant difference in overall efficacy or safety.\(^1\) With no ‘gold standard’ of treatment, physicians need to guide patients to select a treatment based on individual clinical circumstances and patient preferences. Therefore, trends in practice can vary depending on the population involved, the ease of access to treatments and patients perceptions and understanding of treatment options.

The impetus behind the shift away from RAI towards ATDs in New Zealand is unknown, but proposed factors include New Zealand’s ‘nuclear-free’ policies and their effects on the practicalities of treatment, as well as public perception of nuclear medicine treatments. The passage of the New Zealand Nuclear Free Zone, Disarmament, and Arms Control Act in 1987 not only prohibited the use of nuclear weapons, but also nuclear-powered ships and nuclear-generated electricity. The status of New Zealand as a nuclear-free nation has become increasingly popular over time, and a source of nationalist feeling.\(^1\) This stance, and widespread media coverage of international nuclear disasters such as Chernobyl and, more recently, Fukushima, have likely increased the level of distrust felt by the public towards ionising radiation and its long-term effects. Studies of public perception of the risks of radiation from medical diagnostic tests and treatments, including RAI, show that their estimation of risk is often greater than reality, and differs significantly from that of health professionals.\(^1\) Two recent papers on thyroidectomy for GD both found that the majority of patients were referred for surgery over RAI due to patient preference and/or patient refusal of RAI.\(^1,2\) Non-radiologic physicians have also been shown to have major deficiencies in their ability to accurately assess the risk of radiation exposures.\(^1\) This issue has been highlighted in recent times by the concerns over the long-term cancer risk of patients...
Figure 4: Preferred treatment in preparation for and during pregnancy.

A. Choice of ATD in a patient planning pregnancy

B. Switch to PTU on confirmation of pregnancy

C. Switch to Carbimazole in second trimester
exposed to multiple CT scans. This over-estimation of the risks of radiation by doctors and patients alike may be combined with an underestimation of the risks of treatment with ATDs. While these agents are remarkably well tolerated and serious adverse events are rare, when they do occur they can be severe, and even fatal.

On a practical level, the lack of nuclear facilities in New Zealand means that radioisotopes have to be imported from Australia, creating restrictions on supply. This is particularly relevant with regard to I\textsuperscript{123}, used primarily in diagnostic imaging. This isotope has a short half-life, and is therefore not readily available in New Zealand. This is likely to be the reason technetium scanning is used in New Zealand in comparison to RAIU scanning in the US.

Although the majority of physicians surveyed did not report impediments to accessing surgical services, over half of those surveyed did not have access to a high-volume thyroid surgeon. This may contribute to the low rates of surgery as first line treatment. It is worth noting that these numbers reflect only the physician's knowledge of the practice of their surgical colleagues and may not represent the true picture of surgical practice in New Zealand for thyroid patients.

The use and selection of anti-thyroid drugs in pregnancy is an area where there has been significant debate in response to new research and recent changes in international guidelines. CBZ and methimazole have been associated with an increased risk of congenital abnormalities, in particular choanal atresia and aplasia cutis. Therefore, the recommendations for many years were to use PTU as first-line during pregnancy. However, over the last 20 years there has been increased awareness of the risk of fulminant hepatitis from PTU, leading to the FDA issuing a black box warning in 2010. A recent, large, Danish registry study showed similar rates of malformation after foetal exposure to PTU and CBZ (8.0 and 9.1% respectively) although the types of abnormalities differ. The most recent published guidelines continue to recommend PTU in the first trimester, and CBZ in subsequent trimesters. In this study, New Zealand physicians' use of ATDs in pregnancy is similar to that of their international colleagues. The only significant finding was that fewer North American physicians would switch to CBZ from the second trimester. This may reflect the fact that this is the oldest of the three studies, and was undertaken prior to the release of the most recent North American guidelines.

This study was limited by the small number of responses received. This is due to both the small number of physicians in New Zealand and a relatively low response rate (41%). Response rates of physicians to surveys are low compared to the general population, and have been shown to be declining over time. Possible explanations include increased time pressure, 'survey fatigue', and an increasing number of physicians who have a policy of not replying to surveys. Endocrinologists were more likely to reply than general physicians, with 32/70 responses (44%) compared with 13/38 (34%). Regardless of speciality, 83% of those who responded see >10 new cases per year. This suggests that responses received do represent a sample from the group of physicians for whom the management of GD is part of their core practice.

**Conclusion**

The results of this survey provide an up to date overview of the management of GD by physicians in New Zealand. Treatment of GD in New Zealand over the past 25 years has moved towards ATDs, and away from the use of RAI as a first-line treatment. Outside the setting of pregnancy there are significant differences in the investigations and treatment of GD between New Zealand, Europe and the US. Currently, there is no evidence to say which approach is superior, but if future research alters this perspective this study would provide a useful baseline from which to assess the impact of such information on the practice of New Zealand physicians.
Thyroid Survey 2014
This survey aims to investigate the current patterns of diagnosis and management of Graves’ disease in New Zealand. It takes approximately 15 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 judgement as to the preferred approach.

1. How many new cases of Graves’ disease do you see, on average, per year? * Mark only one oval.
   - <2
   - 2-5
   - 6-10
   - 11-50
   - >50

Demographics
2. What is your main area of practice? * Mark only one oval.
   - Endocrinology
   - Diabetes
   - General Medicine
   - Other:

3. Which of the following best describe your practice location? * Check all that apply.
   - Tertiary Public Hospital
   - Secondary Public Hospital
   - Rural Hospital
   - Private Practice
   - Primary Care
   - University/Academic
   - Other:

4. What year did you attain your FRACP or equivalent qualification? *

5. Which of the following professional associations do you belong to? * Check all that apply.
   - Royal Australasian College of Physicians
   - NZ Society of Endocrinology
   - Endocrinology Society of Australia
   - The Endocrine Society
   - American Thyroid Association

Appendix

Index Case
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 years old, and does not plan on being pregnant again. This is her first episode of hyperthyroidism. She has a diffuse goitre, 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, with an undetectable thyrotropin level (TSH <0.01 mIU/L).

A. Diagnosis
7. Which of the following tests do you obtain in the majority of patients such as the index case? * Check all that apply.
   - Thyroid Stimulating Hormone (TSH)
   - Free T4
   - Total T4
   - Free T3
   - Total T3
   - Thyroglobulin
   - Anti-Thyroglobulin Antibodies (Anti-Tg)
   - Anti-Thyroid Peroxidase Antibodies (Anti-TPO)
   - Anti-TSH Receptor antibodies (Thyroid Stimulating Immunoglobulins)
   - TRH test
   - Full Blood Count
   - Serum Electrolytes and Creatinine
   - Liver function panel
   - Serum Corrected Calcium
   - Thyroid Ultrasound Scan
   - Thyroid Scintiscan (Technetium)
   - Radioactive Iodine Uptake (I-131)
   - Radioactive Iodine Uptake (I-123)
   - Urinary Iodide excretion
   - Other:

B. Management - General
8. Would you start this patient on Beta Blockers? * Mark only one oval.
   - Yes
   - No  Skip to question 11.
   - Maybe

9. Which beta blocker would you use? Mark only one oval.
   - Metoprolol
   - Atenolol
   - Propranolol
   - Carvedilol
   - Other:
ARTICLE

10. If using beta blockers in this patient, what target heart rate would you aim for? Mark only one oval.
   - <110bpm
   - <100bpm
   - <90bpm
   - <80bpm
   - <70bpm
   - <60bpm
   - Don’t titrate to heart rate
   - Other:

11. Assuming the evaluation of the above patient reveals uncomplicated Graves’ disease, which first-line (long term) mode of therapy would you recommend? * Mark only one oval.
   - Beta blockers alone
   - Anti-thyroid drugs aiming for remission
   - Antithyroid drugs as a long term treatment
   - Radioactive iodine
   - Thyroid Surgery
   - No therapy

C. Management - Radioactive Iodine

12. Do you use radioiodine to treat patients with Graves’ disease? (Either by prescribing and administering it yourself, or by referral to another specialist) * Mark only one oval.
   - Yes
   - No Skip to question 23.

13. What is your primary aim of therapy with radioiodine? Mark only one oval.
   - To restore euthyroidism off medication
   - Ablation of the thyroid followed by thyroid hormone replacement

14. How do you calculate the dose of radioiodine used? Mark only one oval.
   - Use a fixed dose
   - Thyroid uptake function
   - Size of thyroid gland
   - Unknown (treatment administered by other specialists)
   - Other:

15. If you use a fixed dose of radioiodine, what dose do you use?

16. Do you use a “split dose” for initial treatment? Mark only one oval.
   - Yes
   - No
   - Don’t know what this is

17. If the patient is not cured by the initial dose(s), would you administer a second dose? Mark only one oval.
   - No
   - Yes

18. If you answered “Yes” to the questions above, how long (in months) would you wait before giving the second dose?

19. Do you pretreat patients with antithyroid drugs as a means of preparation for radioiodine therapy? Mark only one oval.
   - Yes
   - No
   - Only in selected cases

20. If you answered “Only in selected cases”, which clinical circumstances would lead you to use pretreatment with anti-thyroid drugs before radioiodine?
   Check all that apply
   - Age >65
   - Underlying Heart Disease
   - Multiple co-morbidities
   - Severe thyrotoxicosis
   - Other:

21. If you use pretreatment with antithyroid drugs before radioiodine, how many days before giving radioiodine do you recommend stopping the antithyroid drug? Mark only one oval.
   - Don’t stop anti-thyroid drugs
   - 1 day
   - 2 days
   - 3 days
   - 4 days
   - 5 days
   - 7 days
   - 14 days
   - Unsure
   - Other:

22. Do you administer antithyroid drugs to most patients after radioiodine therapy? Mark only one oval.
   - Yes
   - No
   - Selective use only

D. Management - Anti-thyroid drugs

The next questions apply to patients receiving prolonged courses of anti-thyroid drugs in an attempt at achieving a remission.

Index Case

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 years old, and does not plan on being pregnant again. This is her first episode of hyperthyroidism. She has a diffuse goitre, 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, with an undetectable thyrotropin level (TSH < 0.01 mIU/L).
23. Which anti-thyroid drug would you generally use first? * Mark only one oval.
   - Carbimazole
   - Propylthiouracil
   - Other:

24. When using carbimazole, what starting dose would you use in the index case? *
Mark only one oval.
   - 40mg daily
   - 30mg daily
   - 20mg daily
   - 10mg daily
   - 20mg BD
   - 30mg BD
   - Other:

25. When using propylthiouracil, what starting dose would you use in the index case? *
Mark only one oval.
   - 200mg three times daily
   - 200mg twice daily
   - 200mg daily
   - 150mg three times daily
   - 150mg twice daily
   - 150mg daily
   - 100mg three times daily
   - 100mg twice daily
   - 100mg daily
   - 50mg three times daily
   - 50mg twice daily
   - 50mg daily
   - Other:

26. After starting anti-thyroid drugs, when would you first check thyroid hormone levels? *
Mark only one oval.
   - 1 week
   - 2 weeks
   - 3 weeks
   - 4 weeks
   - 6 weeks
   - 8 weeks
   - 12 weeks
   - 18 weeks
   - 24 weeks
   - Other:

27. Do you most often titrate the dose of anti-thyroid drug to euthyroidism, or use antithyroid drugs to fully suppress thyroid hormone production and then administer thyroxine replacement (“block and replace”)? * Mark only one oval.
   - Dose titration
   - Block and Replace

28. How often do you adjust the dose of anti-thyroid drug? * Mark only one oval.
   - Never
   - Weekly
   - 4 weeks
   - 6 weeks
   - 8 weeks
   - 12 weeks
   - Other:

29. Which do you use most when deciding on dose adjustments? * Mark only one oval.
   - Clinical findings
   - Thyroid function tests
   - Both of the above equally
   - Other:

30. After achieving euthyroidism on anti-thyroid drugs, how often do you monitor thyroid hormone levels? * Mark only one oval.
   - Monthly
   - Every 2 months
   - Every 3 months
   - Every 6 months
   - Other:

31. When using anti-thyroid drugs, in addition to thyroid hormone levels, which of the following do you routinely monitor? * Check all that apply.
   - Liver Enzymes
   - Full blood count
   - No routine monitoring
   - TSH receptor antibodies / Thyroid stimulating immunoglobulin

32. After two weeks of anti-thyroid 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? * Mark only one oval.
   - Continue same antithyroid drug plus an antihistamine
   - Switch to a different anti-thyroid drug
   - Select an alternative mode of therapy (radioactive iodine or surgery)

33. When using anti-thyroid drugs in an attempt to achieve a remission, how long of a course do you recommend before attempting an alternate form of therapy? * Mark only one oval.
   - 3 months
   - 6 months
   - 9 months
   - 12 months
   - 18 months
   - 24 months
   - Other:
34. What criteria do you use to stop treatment? * Check all that apply.  
- Clinical and biochemical euthyroidism  
- Negativisation of TSH receptor antibodies / TSI  
- Negativisation of Anti-Tg and Anti-TPO antibodies  
- Thyroglobulin level  
- TRH test  
- Normalisation of suppression test  
- Duration of treatment  
- Other:  

35. Do you ever refer patients with Graves' disease for surgery? * Mark only one oval.  
- Yes  
- No  
- Not sure  
Skip to question 43.  

36. Are Graves' disease patients at your center routinely given SSRI or Lugol's solution prior to thyroidectomy, even if euthyroid on anti-thyroid drugs? Mark only one oval.  
- No  
- Yes  
- Not sure  

37. Do you generally render patients euthyroid with anti-thyroid drugs prior to thyroidectomy? Mark only one oval.  
- Yes  
- No  
- Not sure  

38. Are Graves' disease patients undergoing thyroidectomy at your center routinely discharged on prophylactic doses of calcium and/or vitamin D therapy, even if the serum calcium is within the normal range? Mark only one oval.  
- No  
- Yes  
- Not sure  
- Other:  

39. Which form of thyroid surgery is most often recommended/preferred by the surgeon(s) you refer to? Mark only one oval.  
- Near-total or total thyroidectomy  
- Subtotal thyroidectomy  
- Not sure  

40. Who is responsible for the long-term follow-up of patients after thyroid surgery? Mark only one oval.  
- Surgeon  
- Referring Physician  
- General Practitioner  

41. Does the location of long term follow-up influence the surgical strategy chosen? e.g. Patients followed by surgeon more likely to have total thyroidectomies vs patients who are followed by physician, or preference for subtotal thyroidectomy for patients with limited access to health care etc.  
- Mark only one oval.  
  - Yes  
  - No  
  - Don’t know  

42. If so, how?  

43. In addition to your previous responses, which of the following (if any) would you obtain in this patient with moderate active Graves' ophthalmopathy? * Check all that apply.  
- Visual field testing  
- CT Orbits (non-contrast)  
- Orbital ultrasound  
- MRI Orbits  
- Ophthalmologist evaluation  
- Other:  

44. What is your usual therapeutic approach to hyperthyroidism for a patient with moderate active ophthalmopathy? * Mark only one oval.  
- Anti-thyroid drugs to achieve remission  
- Radioactive iodine alone  
- Radioactive iodine plus corticosteroids  
- Thyroidectomy once euthyroid on anti-thyroid drugs  
- Thyroidectomy plus radioactive iodine ablation  
- Other:  

45. If your patient's ophthalmopathy requires corticosteroid therapy, who is most likely to administer this? * Mark only one oval.  
- Endocrinologist  
- General Physician  
- Ophthalmologist  
- General Practitioner  
- Other:  

46. G. Pregnancy  
The following questions relate to the management of Graves' disease in the soon to be pregnant or currently pregnant patient.
Case 2
The patient is a 22 year old woman with newly diagnosed thyrotoxicosis who wishes to become pregnant within the next 6-12 months. She has a diffuse goitre, 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, with an undetectable thyrotropin level (TSH < 0.01 mIU/L). Assume that the diagnosis of Graves’ disease is already confirmed.

46. Which principal mode of therapy would you recommend to this patient who plans to become pregnant in the next 6-12 months? * Mark only one oval.
   - Anti-thyroid drugs
   - Radioactive Iodine
   - Thyroid surgery
   - No treatment
   - Other:

47. If the patient elects to use anti-thyroid drugs as the principal mode of therapy, which anti-thyroid drug would you use in this patient before pregnancy? * Mark only one oval.
   - Carbimazole
   - Propylthiouracil

48. The patient becomes euthyroid, and now has a positive pregnancy test. If you had started carbimazole prior to pregnancy, would you now switch to propylthiouracil? * Mark only one oval.
   - Yes
   - No

49. If you gave the patient propylthiouracil during the first trimester, would you switch to carbimazole as the patient enters the second trimester, assuming she still requires anti-thyroid drugs? * Mark only one oval.
   - Yes
   - No

50. How often do you routinely monitor thyroid function tests in pregnancy in a patient with Graves’ disease? * Mark only one oval.
   - 4 weekly
   - 6 weekly
   - 8 weekly
   - 12 weekly
   - Other:

51. Do you measure TSH receptor antibodies (TSI) during pregnancy? * Mark only one oval.
   - Yes
   - No

52. If you do measure TSH receptor antibodies during pregnancy, how often do you do so? * Mark only one oval.
   - 4 weekly
   - 6 weekly
   - 8 weekly
   - 12 weekly
   - Other:

53. If you measure TSH receptor antibodies during pregnancy, do you alter treatment based on antibody levels? * Mark only one oval.
   - Yes
   - No
   - Not sure

H. Access to services
45. Do you have difficulties in accessing any of the following for your patients? Check all that apply.
   - Specialist Endocrinology Services
   - Nuclear Medicine Imaging
   - Radioactive Iodine
   - Surgical Services
   - Appropriate laboratory investigations
   - Other:

55. With respect to the Surgeon(s) you refer to, is their main area of practice: Mark only one oval.
   - Endocrine surgery
   - General surgery
   - Head and Neck surgery
   - ENT surgery
   - Other:

56. Approximately how many thyroidectomies are performed per year by the surgeon(s) you refer to? Mark only one oval.
   - 1-5
   - 6-10
   - 11-20
   - 21-50
   - 51-100
   - >100
   - Don’t know
   - Other:

Survey Complete
Thank you for taking the time to complete this survey

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REFERENCES:


