# **Comprehensive Interrogatory Compendium on Thyroidology: Patient and Professional Perspectives**

## **Introduction**

This document contains a comprehensive list of questions related to thyroid health, categorized for ease of reference. The questions are designed to cover a wide array of topics from both patient and professional perspectives. No answers or explanations are provided, as per the request. The aim is to provide an exhaustive resource for inquiry into all facets of thyroid anatomy, physiology, pathology, diagnosis, treatment, and research.

## **Table of Question Categories**

| **Part** | **Section** | **Approximate Question Focus** |
| --- | --- | --- |
| **Part A: Patient's Perspective** | 1. Understanding My Thyroid & General Concerns | Basic anatomy, function, normal variations, prevention, wellness, genetic concerns. |
|  | 2. Symptoms and Seeking Diagnosis | Recognizing symptoms, diagnostic process (tests, exams), interpreting initial results, emotional aspects. |
|  | 3. Specific Thyroid Conditions | Hypothyroidism (Hashimoto's), Hyperthyroidism (Graves'), Nodules/Goiter, Thyroiditis, Thyroid Cancer – causes, symptoms, specifics of each. |
|  | 4. Treatment Options and Decisions | Medications, Radioactive Iodine (RAI), Surgery – how they work, risks, benefits, decision-making, second opinions. |
|  | 5. Living with Thyroid Disease | Diet, lifestyle, mental health, long-term monitoring, special considerations (pregnancy, menopause). |
|  | 6. Questions for My Doctor | Preparing for appointments with GP, endocrinologist, surgeon; advocating for oneself. |
| **Part B: Professional Perspective (Endocrinologists, Surgeons, Researchers)** | 7. Foundational Science & Pathophysiology | Hormone synthesis/regulation/action, autoimmunity, molecular basis of neoplasia, deiodinases, HPT axis intricacies. |
|  | 8. Diagnostics and Imaging Challenges | TFT assay limitations, antibody interpretation, ultrasound/FNA challenges, molecular markers, advanced imaging. |
|  | 9. Clinical Management of Hypothyroidism | Treatment targets, subclinical hypothyroidism, persistent symptoms, T3/T4 debate, specific etiologies, complications. |
|  | 10. Clinical Management of Hyperthyroidism | Choice of therapy (ATD/RAI/surgery), Graves' orbitopathy, thyroid storm, AIT, subclinical hyperthyroidism. |
|  | 11. Evaluation and Management of Thyroid Nodules and Goiter | Risk stratification, indeterminate cytology, management of benign vs. malignant nodules, ablation techniques, AFTN. |
|  | 12. Surgical Considerations in Thyroid Disease | Indications, extent of surgery, innovative techniques (MIVAT, TOETVA), IONM, parathyroid preservation, complications, surgeon volume. |
|  | 13. Management of Thyroid Cancer | Pathology/staging updates, DTC (RAI, TSH suppression, TKIs), MTC, ATC, PDTC, surveillance, QoL. |
|  | 14. Thyroid Disease in Special Populations | Pregnancy, pediatrics, geriatrics, critical illness, drug interactions. |
|  | 15. Pharmacotherapy and Novel Treatments | Levothyroxine formulations, ATD optimization, targeted cancer therapies, immunomodulation, ICI-induced thyroiditis, future targets. |
|  | 16. Research Questions and Unmet Needs in Thyroidology | Etiopathogenesis (microbiome, EDCs), novel diagnostics/therapeutics, personalized medicine, PROs/QoL, health services research, disparities. |

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## **Part A: Questions from the Patient's Perspective**

### **Section 1: Understanding My Thyroid & General Concerns**

#### **1.1 Anatomy and Function**

1. Where exactly is my thyroid gland located in my neck?
2. What does the thyroid gland look like? How big is it normally?
3. What is the main job of my thyroid gland?
4. What are thyroid hormones? What are their names?
5. How do thyroid hormones (T4​ and T3​) work in my body?
6. What parts of my body are affected by thyroid hormones?
7. What is metabolism, and how is it related to my thyroid?
8. Does my thyroid control my body temperature?
9. Does my thyroid affect my heart rate?
10. Does my thyroid play a role in my energy levels?
11. How does my brain tell my thyroid to work?
12. What is TSH, and what does it do?
13. What is iodine, and why is it important for my thyroid?
14. How much iodine do I need for my thyroid to be healthy?
15. Can my thyroid work too much or too little?
16. What happens if my thyroid makes too many hormones?
17. What happens if my thyroid doesn't make enough hormones?
18. Is the thyroid an endocrine gland? What does that mean?
19. Are there other glands that work with the thyroid?
20. Does stress affect how my thyroid gland functions?

#### **1.2 Normal Variations vs. Problems**

1. How do I know if my thyroid is working normally?
2. Are there any symptoms that are always a sign of a thyroid problem?
3. Can thyroid problems run in families?
4. If my parent has a thyroid condition, am I likely to get one too?
5. Are thyroid problems more common in men or women?
6. At what age do thyroid problems usually start?
7. Can children have thyroid problems?
8. Can my weight affect my thyroid, or does my thyroid affect my weight?
9. Is it normal for the thyroid gland to change during pregnancy?
10. Can I feel my own thyroid gland? Should it be noticeable?
11. If I feel tired all the time, could it be my thyroid?
12. How can I tell if my symptoms are due to my thyroid or something else, like stress or aging?
13. Are there specific types of fatigue associated with thyroid problems versus general tiredness?
14. If my blood tests for thyroid are "normal," does that mean my thyroid is definitely healthy?
15. Can "normal" thyroid levels be different for different people?
16. What does "subclinical" mean in relation to thyroid problems?
17. Can I have a thyroid problem without any symptoms?
18. If I have a lump in my neck, is it always a thyroid problem?
19. Are all thyroid problems serious?
20. Can lifestyle factors make me more prone to thyroid issues?

#### **1.3 Prevention and Wellness**

1. What can I do to keep my thyroid healthy?
2. Is there a special diet for thyroid health?
3. Are there any foods I should eat more of for my thyroid?
4. Are there any foods I should avoid for my thyroid?
5. Does exercise help my thyroid?
6. How does stress management impact thyroid wellness?
7. Are there any vitamins or supplements that support thyroid health?
8. Should I take iodine supplements?
9. Who should be screened for thyroid problems?
10. How often should I get my thyroid checked if I don't have symptoms?
11. Is there a simple screening test for thyroid issues?
12. Can I prevent thyroid disease if it runs in my family?
13. Are there environmental factors that can harm my thyroid?
14. What is a goiter, and can it be prevented?
15. Can regular check-ups with my doctor catch thyroid problems early?
16. If I am trying to conceive, should I have my thyroid checked?
17. Are there any common medications that can affect thyroid function?
18. How does smoking affect thyroid health?
19. Is there a link between gut health and thyroid health?
20. What are the most important things I can do for general thyroid wellness?

#### **1.4 Addressing Misconceptions and Genetic Concerns**

1. I read online that many common symptoms are due to thyroid issues; how much of this is true?
2. If my mother had Hashimoto's disease, what is my specific risk of developing it?
3. What is the pattern of inheritance for common thyroid diseases like Graves' or Hashimoto's?
4. Should my children be regularly tested for thyroid problems if I have a thyroid condition?
5. Are there genetic tests that can tell me if I will get a thyroid disease?
6. If I have one autoimmune disease, am I more likely to get an autoimmune thyroid disease?
7. Is it true that thyroid problems are often misdiagnosed as depression or anxiety?
8. Can "adrenal fatigue" be related to thyroid problems?
9. Are "natural" thyroid supplements safer or better than prescription medication?
10. If I lose weight, will my thyroid problem go away?
11. Is it true that everyone with a thyroid problem feels cold all the time?
12. Can I "boost" my thyroid naturally?
13. If I have a family history of thyroid cancer, what is my risk?
14. Are there specific genetic mutations I should be concerned about if thyroid cancer runs in my family?
15. How do I discuss my family history concerns with my doctor effectively?

### **Section 2: Symptoms and Seeking Diagnosis**

#### **2.1 Recognizing Symptoms**

1. What are the most common symptoms of an underactive thyroid (hypothyroidism)?
2. What are the most common symptoms of an overactive thyroid (hyperthyroidism)?
3. Can thyroid problems cause changes in my weight (gain or loss)?
4. Is there a particular pattern to thyroid-related weight gain or loss that makes it distinct?
5. Can thyroid issues cause hair loss or changes in hair texture?
6. Can thyroid problems affect my skin (e.g., dryness, oiliness)?
7. Can thyroid conditions cause changes in my mood, like depression or anxiety?
8. Are palpitations or a racing heart a sign of a thyroid problem?
9. Can thyroid issues cause me to feel unusually hot or cold?
10. Is "brain fog" or difficulty concentrating a symptom of thyroid dysfunction?
11. How does thyroid fatigue differ from just feeling tired?
12. Can thyroid problems affect my menstrual cycle?
13. Can thyroid issues cause muscle weakness or aches?
14. Are changes in bowel habits (constipation, diarrhea) linked to thyroid conditions?
15. Can a thyroid problem cause swelling in my neck?
16. What does a goiter feel or look like?
17. Can thyroid nodules cause symptoms?
18. Could difficulty swallowing or a hoarse voice be related to my thyroid?
19. How quickly do thyroid symptoms usually develop?
20. Can symptoms come and go, or are they usually constant?
21. What constellation of symptoms is most strongly suggestive of a thyroid problem?
22. Are there any eye-related symptoms associated with thyroid disease (e.g., bulging, dryness, double vision)?
23. Can thyroid problems cause carpal tunnel syndrome?
24. Is infertility sometimes linked to undiagnosed thyroid issues?
25. If I have several of these symptoms, does it definitely mean I have a thyroid problem?
26. At what point should I see a doctor if I suspect my symptoms are thyroid-related?
27. Can thyroid symptoms be different in older adults?
28. Are there any "silent" thyroid problems that don't cause obvious symptoms?
29. Can a thyroid problem cause changes in my cholesterol levels?
30. Is swelling in the legs or face a sign of a thyroid issue?

#### **2.2 The Diagnostic Process**

1. Which type of doctor should I see if I think I have a thyroid problem (GP, endocrinologist)?
2. What should I expect during a physical examination for a suspected thyroid issue?
3. Will the doctor feel my neck? What are they checking for?
4. What questions will the doctor likely ask me about my symptoms and medical history?
5. What are the common blood tests used to diagnose thyroid problems?
6. What does a TSH (Thyroid Stimulating Hormone) test measure?
7. What do T4​ (thyroxine) tests measure? What is "free T4​"?
8. What do T3​ (triiodothyronine) tests measure? What is "free T3​"?
9. Why are thyroid antibody tests (e.g., TPOAb, TgAb, TRAb) done? What do they indicate?
10. Do I need to fast before having my thyroid blood tests?
11. Are there certain times of day that are better for thyroid blood tests?
12. What is a "normal" range for TSH, T4​, and T3​? Can these ranges vary by lab?
13. Can my "normal" thyroid levels be different from someone else's?
14. What is a thyroid ultrasound? Why is it done?
15. What can a thyroid ultrasound show about my thyroid gland and any nodules?
16. Is a thyroid ultrasound painful or risky?
17. What is a thyroid scan (radioactive iodine uptake scan)? How does it work?
18. What information does a thyroid scan provide that an ultrasound doesn't?
19. Are there any risks or preparations needed for a thyroid scan?
20. What is a Fine Needle Aspiration (FNA) biopsy of a thyroid nodule?
21. Why would my doctor recommend an FNA biopsy?
22. What happens during an FNA procedure? Is it painful?
23. What are the risks associated with an FNA biopsy?
24. What kind of information can an FNA biopsy provide about a thyroid nodule?
25. How long does it take to get results from these tests?
26. Can other medications I'm taking affect my thyroid test results?
27. Can supplements, like biotin, interfere with thyroid lab tests?
28. If my initial blood tests are normal, but I still have symptoms, what are the next steps?
29. What is a thyroglobulin (Tg) test used for?
30. What does it mean if my doctor wants to do "molecular testing" on a nodule biopsy?

#### **2.3 Interpreting Preliminary Results and Managing Uncertainty**

1. My TSH is slightly high, but my T4​ is normal. What does this mean?
2. What does "subclinical hypothyroidism" mean for my health in the long run?
3. If my TSH is a little high but I feel fine, do I still need treatment?
4. My doctor said I have thyroid antibodies, but my thyroid hormone levels are normal. What does this signify?
5. If I have thyroid antibodies, does it mean I will definitely develop a thyroid disease?
6. The ultrasound found a small thyroid nodule. Should I be worried?
7. What are the chances that a thyroid nodule is cancerous?
8. My FNA biopsy result was "indeterminate" or "AUS/FLUS." What does that mean, and what happens next?
9. How can I manage my anxiety while waiting for test results or a definitive diagnosis?
10. What are reliable sources of information I can consult while I'm waiting for a diagnosis?
11. Is it okay to seek a second opinion on my test results or diagnosis?
12. How can I best prepare for my follow-up appointment to discuss my results?
13. What questions should I ask my doctor about my preliminary findings?
14. If a problem is found, what is the general process for determining the best course of action?
15. How does my doctor differentiate between different types of thyroid problems based on test results?

### **Section 3: Questions About Specific Thyroid Conditions**

#### **3.1 Hypothyroidism (including Hashimoto's Thyroiditis)**

1. What is hypothyroidism? What causes it?
2. What are the most common causes of an underactive thyroid?
3. What is Hashimoto's thyroiditis? Is it different from regular hypothyroidism?
4. Why is Hashimoto's called an autoimmune disease? What does that mean for my body?
5. If I have Hashimoto's, what is happening to my thyroid gland?
6. Will my thyroid eventually "burn out" completely if I have Hashimoto's?
7. What are the specific symptoms of Hashimoto's, beyond general hypothyroid symptoms?
8. Can Hashimoto's cause a goiter (enlarged thyroid)?
9. What are the long-term effects if hypothyroidism or Hashimoto's is not treated?
10. What is myxedema? Is it related to hypothyroidism?
11. What is a myxedema coma? How serious is it, and what are the warning signs?
12. How common is myxedema coma?
13. Are there different types or severities of hypothyroidism?
14. How is Hashimoto's diagnosed specifically (e.g., antibody tests)?
15. If I have Hashimoto's, am I at higher risk for other autoimmune diseases? Which ones?
16. Is there a cure for Hashimoto's, or is it a lifelong condition?
17. Can lifestyle changes, like diet, help manage Hashimoto's?
18. What is the typical progression of Hashimoto's disease over time?
19. Can hypothyroidism be temporary?
20. What is congenital hypothyroidism?
21. How does hypothyroidism affect children differently than adults?
22. Can iodine deficiency cause hypothyroidism?
23. Can certain medications cause hypothyroidism?
24. What is central hypothyroidism? How is it different?
25. If I had my thyroid removed, is that considered hypothyroidism?

#### **3.2 Hyperthyroidism (including Graves' Disease)**

1. What is hyperthyroidism? What causes the thyroid to be overactive?
2. What is Graves' disease? How is it related to hyperthyroidism?
3. Why is Graves' disease an autoimmune condition? What antibodies are involved?
4. What are the specific symptoms of Graves' disease, apart from general hyperthyroid symptoms?
5. Can Graves' disease cause a goiter?
6. What is Thyroid Eye Disease (TED) or Graves' ophthalmopathy/orbitopathy?
7. What are the symptoms of Thyroid Eye Disease (e.g., bulging eyes, double vision, pain)?
8. What are my chances of developing eye problems if I have Graves' disease?
9. Can my eye problems get worse or better over time? Can they be treated?
10. What is pretibial myxedema (thyroid dermopathy)? Is it common in Graves' disease?
11. What are the long-term effects if hyperthyroidism or Graves' disease is not treated?
12. What is a thyroid storm (thyrotoxic crisis)? How dangerous is it?
13. What are the early warning signs of a thyroid storm I should watch for?
14. How is Graves' disease diagnosed (e.g., antibody tests, uptake scan)?
15. If I have Graves' disease, am I at risk for other autoimmune conditions?
16. Can Graves' disease go into remission? Can it come back?
17. Are there other causes of hyperthyroidism besides Graves' disease?
18. What is a toxic nodule or toxic multinodular goiter?
19. Can hyperthyroidism be temporary?
20. How does hyperthyroidism affect pregnancy?
21. Can taking too much thyroid hormone medication cause hyperthyroidism?
22. Does smoking make Graves' disease or Thyroid Eye Disease worse?
23. What is the typical course of Graves' disease if treated?
24. Are there lifestyle factors that can affect the severity of Graves' disease?
25. How does hyperthyroidism affect my heart?

#### **3.3 Thyroid Nodules and Goiter**

1. What is a thyroid nodule? Is it common to have them?
2. How are thyroid nodules usually found?
3. Are most thyroid nodules cancerous or benign? What is the approximate percentage?
4. If a nodule is benign, can it become cancerous later? How often does this happen?
5. What makes a nodule "suspicious" for cancer on an ultrasound?
6. What are "hot" nodules versus "cold" nodules on a thyroid scan? What do they mean?
7. Can thyroid nodules cause symptoms like pain, difficulty swallowing, or voice changes?
8. What is a goiter? Is it just an enlarged thyroid gland?
9. What can cause a goiter (e.g., iodine deficiency, Hashimoto's, Graves', nodules)?
10. Can a goiter cause symptoms by pressing on structures in the neck?
11. If I have a goiter, does it mean I have a serious thyroid problem?
12. How are goiters and nodules evaluated (ultrasound, FNA, blood tests)?
13. What is a multinodular goiter?
14. If I have benign thyroid nodules, how often do they need to be monitored?
15. What kind of follow-up is typically needed for benign nodules (e.g., repeat ultrasound)?
16. Can benign nodules grow over time? At what point would treatment be considered?
17. Are there treatments to shrink benign thyroid nodules or goiters if they are causing problems?
18. What is a "thyroid cyst"? Is it different from a solid nodule?
19. Can I have multiple thyroid nodules? Is that more concerning?
20. If an FNA biopsy of a nodule is benign, how certain is that result?
21. What are the chances of a false negative or false positive with an FNA?
22. What does it mean if a nodule is "autonomously functioning" or "toxic"?
23. Can a goiter affect my breathing?
24. Is it possible for a goiter to go away on its own?
25. Are there different types of goiters?

#### **3.4 Thyroiditis (e.g., De Quervain's, Postpartum, Silent)**

1. What is thyroiditis? Does it mean my thyroid is infected?
2. What are the different types of thyroiditis (e.g., subacute, postpartum, silent, drug-induced)?
3. What is subacute thyroiditis (De Quervain's thyroiditis)? What causes it?
4. What are the typical symptoms of subacute thyroiditis (e.g., neck pain, fever)?
5. Does subacute thyroiditis usually resolve on its own? How long does it take?
6. Can subacute thyroiditis cause temporary hyperthyroidism followed by temporary hypothyroidism?
7. What is postpartum thyroiditis? Who gets it?
8. When does postpartum thyroiditis typically occur after childbirth?
9. What are the symptoms of postpartum thyroiditis? Can it be mistaken for postpartum depression?
10. Does postpartum thyroiditis lead to permanent thyroid problems?
11. What is silent thyroiditis (painless thyroiditis)? How is it different from subacute thyroiditis?
12. What is the typical course of silent thyroiditis?
13. Can medications (e.g., amiodarone, lithium, interferon, checkpoint inhibitors) cause thyroiditis?
14. How is thyroiditis diagnosed?
15. How is thyroiditis treated? Does it always need treatment?
16. Is it possible to have recurring episodes of thyroiditis?
17. Can radiation exposure cause thyroiditis?
18. What is Riedel's thyroiditis? Is it common?
19. If I have one type of thyroiditis, am I more likely to get another type?
20. How can I differentiate symptoms of thyroiditis from other neck problems?

#### **3.5 Thyroid Cancer**

1. What is thyroid cancer? How does it start?
2. How common is thyroid cancer compared to other cancers?
3. Are there different types of thyroid cancer? What are they?
4. What is papillary thyroid cancer? Is it the most common type?
5. What is follicular thyroid cancer? How is it different from papillary?
6. What is medullary thyroid cancer? Is it often genetic?
7. What is anaplastic thyroid cancer? Is it very aggressive?
8. What are the main risk factors for developing thyroid cancer (e.g., radiation exposure, family history)?
9. What are the typical symptoms of thyroid cancer? Can it be asymptomatic?
10. How is thyroid cancer usually diagnosed (e.g., ultrasound, FNA, biopsy after surgery)?
11. What does "staging" of thyroid cancer mean? How is it determined?
12. What is the general prognosis for most types of thyroid cancer? Is it usually curable?
13. How does the prognosis differ between the types of thyroid cancer?
14. What is a "low-risk" thyroid cancer?
15. What is thyroid microcarcinoma?
16. What is the emotional impact of receiving a thyroid cancer diagnosis?
17. What support resources are available for people diagnosed with thyroid cancer?
18. If I have thyroid nodules, what is the chance one of them is or will become cancerous?
19. Can Hashimoto's disease increase the risk of thyroid cancer?
20. What does it mean if cancer cells are found in lymph nodes near the thyroid?
21. Will I need further tests to see if thyroid cancer has spread?
22. How quickly does thyroid cancer typically grow or spread?
23. Are there specific genetic mutations associated with different types of thyroid cancer?
24. If I have a family history of medullary thyroid cancer, should I be screened for RET gene mutations?
25. What are the first steps my doctor will take after a diagnosis of thyroid cancer?

### **Section 4: Treatment Options and Decisions**

#### **4.1 Medications**

1. What is levothyroxine? How does it work for hypothyroidism?
2. Is levothyroxine a lifelong medication for most people with hypothyroidism?
3. How is the correct dosage of levothyroxine determined for me?
4. How often will my levothyroxine dose need to be checked and possibly adjusted?
5. When is the best time to take levothyroxine? Does it matter if I take it with food?
6. Are there foods, supplements, or other medications I should avoid taking at the same time as levothyroxine?
7. What are the differences between brand-name levothyroxine (e.g., Synthroid, Levoxyl) and generic levothyroxine? Is one better?
8. What are the potential side effects of levothyroxine? What if my dose is too high or too low?
9. What happens if I frequently miss doses of my thyroid medication?
10. Are there other types of thyroid hormone medication besides levothyroxine (e.g., liothyronine/T3​, desiccated thyroid extract/DTE)?
11. Why might my doctor prescribe T3​ (liothyronine) in addition to or instead of T4​ (levothyroxine)?
12. What is desiccated thyroid extract (DTE) (e.g., Armour Thyroid, NP Thyroid)? Is it safe and effective?
13. What are anti-thyroid drugs (ATDs) like methimazole (Tapazole) or propylthiouracil (PTU)? How do they work for hyperthyroidism?
14. How long do I need to take anti-thyroid drugs? Can I stop them eventually?
15. What are the common side effects of methimazole or PTU? Are there any serious ones I should watch for (e.g., agranulocytosis, liver problems)?
16. How will my doctor monitor me while I'm taking anti-thyroid drugs?
17. Can I take anti-thyroid drugs if I am pregnant or breastfeeding?
18. What are beta-blockers (e.g., propranolol)? Why are they sometimes used for hyperthyroidism? Do they treat the thyroid itself?
19. Are there medications to treat Thyroid Eye Disease?
20. If I have thyroiditis, what medications might be used to manage symptoms like pain or inflammation?
21. What medications are used after thyroid cancer treatment?
22. How important is it to take my thyroid medication exactly as prescribed?
23. Can I switch brands of levothyroxine without consulting my doctor?
24. What should I do if I think I'm experiencing side effects from my thyroid medication?
25. How will my doctor know if my levothyroxine dose is correct? What tests are used?

#### **4.2 Radioactive Iodine (RAI) Therapy**

1. What is radioactive iodine (RAI) therapy? How does it work?
2. Why is RAI therapy used for hyperthyroidism (like Graves' disease)?
3. How effective is RAI therapy in treating hyperthyroidism? Will I need more than one dose?
4. What preparation is needed before RAI therapy for hyperthyroidism (e.g., diet, stopping medications)?
5. What are the safety precautions I need to follow after receiving RAI therapy for hyperthyroidism (e.g., around family, children, pets)? For how long?
6. What are the potential side effects of RAI therapy for hyperthyroidism?
7. Will RAI therapy for hyperthyroidism make me hypothyroid? If so, when?
8. Can RAI therapy worsen Thyroid Eye Disease?
9. Is RAI therapy safe in the long term? Does it increase cancer risk?
10. Why is RAI therapy used after surgery for some types of thyroid cancer? What is its purpose (remnant ablation, treatment of spread)?
11. How is the dose of RAI for thyroid cancer determined? Is it different from the dose for hyperthyroidism?
12. What does an RAI isolation period involve if I'm treated for thyroid cancer? What can I expect?
13. What are the potential short-term and long-term side effects of RAI therapy for thyroid cancer (e.g., nausea, dry mouth, salivary gland issues, fertility concerns)?
14. How will my doctor know if the RAI therapy for thyroid cancer was successful?
15. Are there alternatives to RAI therapy for hyperthyroidism or thyroid cancer?
16. Who is not a good candidate for RAI therapy?
17. How does RAI get into the thyroid cells specifically?
18. Will I be radioactive after the treatment? For how long?
19. What is a "low iodine diet" and why is it important before RAI therapy?
20. Can RAI therapy affect my taste or smell?

#### **4.3 Surgery (Thyroidectomy)**

1. When is surgery (thyroidectomy) recommended for thyroid problems?
2. What are the main reasons for having a thyroidectomy (e.g., thyroid cancer, very large goiter, suspicious nodules, Graves' disease not responding to other treatments)?
3. What is a total thyroidectomy? What does it involve?
4. What is a partial thyroidectomy or thyroid lobectomy? When might this be done?
5. What are the potential risks and complications of thyroid surgery?
6. How common is damage to the recurrent laryngeal nerve, and what effect does it have on voice? Is it usually temporary or permanent?
7. What are parathyroid glands? Why are they at risk during thyroid surgery?
8. What is hypoparathyroidism? What are the symptoms of low calcium (e.g., tingling, muscle cramps)?
9. How common is temporary or permanent hypoparathyroidism after thyroidectomy? How is it managed?
10. What are other risks like bleeding or infection after thyroid surgery?
11. How long will I be in the hospital after thyroid surgery?
12. What is the typical recovery process and timeline after a thyroidectomy?
13. Will I have a scar? What can be done to minimize scarring?
14. Will I need to take thyroid hormone medication for life after a total thyroidectomy? What about after a lobectomy?
15. What is a "neck dissection"? Why might it be done along with a thyroidectomy, especially for thyroid cancer?
16. Are there different ways to perform thyroid surgery (e.g., traditional incision, minimally invasive, robotic, transoral)?
17. What are the pros and cons of these different surgical approaches?
18. How do I choose a surgeon for my thyroid operation? What questions should I ask them about their experience?
19. What kind of anesthesia is used for thyroid surgery?
20. What post-surgical care will I need (e.g., pain management, drain care, follow-up appointments)?

#### **4.4 Making Treatment Choices and Understanding Long-Term Implications**

1. How do I decide which treatment option is best for my specific thyroid condition (e.g., medication vs. RAI vs. surgery for Graves')?
2. What are the pros and cons of each treatment option for my condition?
3. What are my doctor's recommendations, and why?
4. How does my age, overall health, and lifestyle preferences factor into treatment decisions?
5. Is it okay to get a second opinion before deciding on a treatment, especially for surgery or cancer? How do I go about that?
6. What are the success rates for the different treatments proposed for me?
7. What are the chances of my thyroid problem recurring after treatment?
8. If I choose medication for hyperthyroidism, what happens if it doesn't work or I can't tolerate it?
9. If I choose RAI, what are the implications if I become hypothyroid?
10. If I choose surgery, what are the long-term adjustments I'll need to make (e.g., lifelong medication, calcium monitoring)?
11. Will I be on medication for the rest of my life if I have my thyroid removed or treated with RAI?
12. How will having a chronic thyroid condition affect my daily life in the long term?
13. How will my thyroid condition or its treatment affect my ability to get life insurance or my future job prospects?
14. What are the psychological or emotional aspects of choosing a treatment, especially an irreversible one like surgery or RAI?
15. How can I participate in shared decision-making with my doctor to ensure my preferences are considered?
16. What are the most common long-term side effects or consequences I should be aware of for each treatment option?
17. If my condition requires lifelong medication, what are the practicalities of managing this (e.g., refills, travel, cost)?
18. What are the potential financial costs associated with each treatment option, including long-term care?
19. Are there any clinical trials for new treatments for my condition that I could consider?
20. What happens if I choose not to have any treatment for my condition right now (e.g., for a small benign nodule or very mild subclinical hypothyroidism)?

### **Section 5: Living with Thyroid Disease**

#### **5.1 Diet and Nutrition**

1. Is there a specific "thyroid diet" I should follow if I have a thyroid condition? What is the scientific evidence for it?
2. How does iodine intake affect my thyroid condition (e.g., hypothyroidism, hyperthyroidism, Hashimoto's)? Should I limit or increase it?
3. What are goitrogenic foods (e.g., cruciferous vegetables like broccoli, cabbage, kale)? Do I need to avoid them if I have a thyroid problem?
4. Does cooking goitrogenic foods reduce their impact on the thyroid?
5. How does soy consumption affect thyroid function or the absorption of thyroid medication? Do I need to avoid soy products?
6. Is there a link between gluten intolerance (celiac disease) and autoimmune thyroid diseases like Hashimoto's or Graves'?
7. Should I follow a gluten-free diet if I have an autoimmune thyroid condition? What does the evidence say?
8. Are there specific supplements (e.g., selenium, zinc, vitamin D, iron, B vitamins) that can help my thyroid condition? What is the evidence?
9. Can certain supplements interfere with my thyroid medication or thyroid function? Which ones?
10. How can I manage my weight if I have hypothyroidism and struggle with weight gain?
11. Are there specific dietary strategies for weight loss that are more effective with hypothyroidism?
12. If I have hyperthyroidism and have lost weight, how can I regain it healthily?
13. Should I avoid caffeine or other stimulants if I have hyperthyroidism?
14. Are there any foods or drinks that can interfere with the absorption of levothyroxine?
15. How long should I wait between taking levothyroxine and eating or drinking certain things (e.g., coffee, calcium-rich foods)?
16. Can "natural" or herbal remedies help my thyroid condition? Are they safe to take with my prescribed medications?
17. Should I discuss all supplements and dietary changes with my doctor?
18. Is it important to stay well-hydrated for thyroid health?
19. Can probiotics help with thyroid health, especially autoimmune conditions?
20. What are some common dietary myths about thyroid disease that I should be aware of?

#### **5.2 Lifestyle Adjustments**

1. How does exercise affect my thyroid condition? Is it safe to exercise?
2. What types and intensity of exercise are best if I have hypothyroidism and fatigue?
3. What types and intensity of exercise are advisable if I have hyperthyroidism and a fast heart rate?
4. How can I manage fatigue that persists despite my thyroid levels being "normal" with treatment?
5. How important is stress management when living with a thyroid condition?
6. What are some effective stress-reduction techniques I can try (e.g., yoga, meditation, mindfulness)?
7. Can stress trigger flare-ups of autoimmune thyroid disease (Hashimoto's, Graves')?
8. How can thyroid disease affect my sleep? Can it cause insomnia or excessive sleepiness?
9. What can I do to improve my sleep quality if I have a thyroid condition?
10. Does smoking affect my thyroid condition or its treatment? Should I quit?
11. How does alcohol consumption impact thyroid health or interact with thyroid medications?
12. Are there any environmental toxins or chemicals I should try to avoid to protect my thyroid?
13. How can I explain my energy limitations or other invisible symptoms to family, friends, or employers?
14. What adjustments might I need to make at work or in my daily routine to accommodate my thyroid condition?
15. How can I maintain a good quality of life while managing a chronic thyroid condition?
16. Are there any hobbies or activities that are particularly beneficial for people with thyroid disease?
17. How do I manage traveling with thyroid medication, especially with time zone changes or needing refrigeration?
18. What should I do if I run out of my thyroid medication while traveling?
19. Is it important to maintain a consistent daily routine for taking medication and managing symptoms?
20. How can I advocate for my needs if I feel my symptoms are not being fully addressed or understood?

#### **5.3 Mental and Emotional Health**

1. Is there a direct link between thyroid dysfunction and mental health issues like depression or anxiety?
2. Can hypothyroidism cause or worsen symptoms of depression?
3. Can hyperthyroidism cause or worsen symptoms of anxiety, irritability, or panic attacks?
4. What is "brain fog" associated with thyroid conditions? What does it feel like?
5. How can I cope with cognitive symptoms like poor memory, difficulty concentrating, or brain fog?
6. Will treatment for my thyroid condition improve my mood and cognitive symptoms? How long might it take?
7. What if my mood or cognitive symptoms persist even after my thyroid hormone levels are normalized?
8. Are there specific coping strategies for dealing with the emotional ups and downs of thyroid disease?
9. Should I consider psychological counseling or therapy to help manage the emotional impact of my thyroid condition?
10. Are there support groups (online or in-person) for people with thyroid disease? How can they help?
11. How can I talk to my family and friends about how my thyroid condition affects me emotionally?
12. Can the stress of having a chronic illness itself impact my mental well-being?
13. How do I differentiate between symptoms caused by my thyroid and primary psychiatric conditions?
14. Can thyroid medication itself have side effects that affect mood?
15. What is the emotional impact of dealing with changes in appearance due to thyroid disease (e.g., weight changes, hair loss, eye changes in Graves')?
16. How can I build resilience while living with a chronic thyroid condition?
17. Are there resources to help me cope with brain fog at work or school?
18. How can I manage feelings of frustration or hopelessness if my symptoms are difficult to control?
19. Is it common to feel misunderstood by others because my symptoms are often "invisible"?
20. What role can mindfulness or meditation play in managing anxiety or stress related to my thyroid condition?

#### **5.4 Long-Term Monitoring and Care**

1. How often will I need to see my doctor for follow-up appointments for my thyroid condition?
2. What blood tests will be done regularly to monitor my thyroid condition and medication? How often?
3. What is the target range for my TSH (and other thyroid hormones) once I am on treatment?
4. Do I need to monitor for any long-term complications of my thyroid disease or its treatment?
5. If I had thyroid cancer, what kind of long-term surveillance will I need (e.g., blood tests like Tg, ultrasounds, scans)? How often?
6. What are the signs that my thyroid medication dose might need adjustment?
7. If I have benign thyroid nodules, how often should they be re-checked with an ultrasound?
8. If I have Hashimoto's, will my thyroid function be monitored indefinitely?
9. If I had Graves' disease treated with RAI or surgery, what long-term monitoring is needed?
10. Can my thyroid condition change over time, requiring adjustments to my management plan?
11. Is it important to see an endocrinologist for long-term care, or can my GP manage it?
12. What information should I keep track of regarding my thyroid health (e.g., test results, medication changes, symptoms)?
13. Are there any warning signs of recurrence or worsening of my thyroid condition that I should look out for?
14. How does aging affect my thyroid condition or medication needs?
15. If I develop other medical conditions, how might they interact with my thyroid disease or treatment?

#### **5.5 Special Considerations (Pregnancy, Menopause, etc.)**

1. If I have a thyroid condition, can I still have a healthy pregnancy?
2. How does pregnancy affect thyroid function and thyroid medication needs (especially levothyroxine)?
3. How will my levothyroxine dose need to change during pregnancy if I am hypothyroid? How quickly?
4. How often will my thyroid levels need to be monitored during pregnancy?
5. What are the risks to me or my baby if my thyroid condition is not well-controlled during pregnancy?
6. Is it safe to take levothyroxine during pregnancy?
7. How is hyperthyroidism (e.g., Graves' disease) managed during pregnancy? Are anti-thyroid drugs safe?
8. Which anti-thyroid drug (methimazole or PTU) is preferred during different trimesters of pregnancy and why?
9. What are the risks of untreated or poorly controlled hyperthyroidism during pregnancy for mother and baby?
10. Can I breastfeed if I am taking thyroid medication (levothyroxine or anti-thyroid drugs)?
11. What is postpartum thyroiditis? How common is it, and what are the symptoms?
12. If I have a history of thyroid disease, am I more likely to develop postpartum thyroiditis?
13. Should I have my thyroid checked before trying to conceive?
14. How can thyroid problems affect fertility in women and men?
15. How does menopause interact with thyroid function or symptoms? Can they be confused?
16. If I am going through menopause, will my thyroid medication need adjustment?
17. Are older adults more susceptible to thyroid problems or side effects of treatment?
18. How should thyroid conditions be managed in children or adolescents? Are there unique considerations?
19. If my child is diagnosed with a thyroid condition, what support and resources are available?
20. Can other chronic illnesses (like diabetes or autoimmune conditions) affect my thyroid management?

### **Section 6: Questions for My Doctor (Endocrinologist, Surgeon, GP)**

#### **6.1 Before Diagnosis**

1. Based on my symptoms [list them], could a thyroid problem be a possible cause?
2. What specific thyroid tests do you recommend for me, and why?
3. Are there any other conditions that could be causing my symptoms that we should also consider?
4. How should I prepare for the recommended thyroid tests (e.g., fasting, medication adjustments)?
5. When can I expect to get the results of these tests?
6. If the initial tests are inconclusive, what would be the next steps?
7. Given my family history of [specific thyroid condition], what is my likelihood of developing it?
8. Are there any lifestyle factors I should be aware of that might be impacting my symptoms or potential thyroid health?
9. What is your general approach to diagnosing thyroid disorders?
10. If a thyroid issue is suspected, at what point would you refer me to an endocrinologist?

#### **6.2 After Diagnosis**

1. Can you explain my specific thyroid diagnosis to me in simple terms?
2. What do my specific test results (TSH, T4​, T3​, antibodies, ultrasound findings, biopsy results) mean?
3. What is the likely cause of my thyroid condition?
4. What is the typical course or progression of this condition?
5. What are the treatment options available for my condition?
6. What treatment do you recommend for me, and why is it the best option in my case?
7. What are the potential benefits, risks, and side effects of this recommended treatment?
8. Are there any alternative treatments I should consider?
9. How will this condition and its treatment affect my daily life and long-term health?
10. What is the goal of the proposed treatment (e.g., cure, symptom management, preventing complications)?
11. How will we monitor my condition and the effectiveness of the treatment? How often?
12. Are there any lifestyle changes (diet, exercise, stress management) you recommend for me?
13. What are the three most important things I should know or do regarding my condition right now?
14. Are there any warning signs or symptoms I should watch for that would require urgent attention?
15. Where can I find reliable information and support resources for my condition?
16. If medication is prescribed, how should I take it? What are potential interactions?
17. How long will it take for the treatment to start working and for me to feel better?
18. If my condition is autoimmune (Hashimoto's, Graves'), does this have implications for my overall health?
19. What is the prognosis for my specific condition?
20. Should my family members be screened for thyroid problems?

#### **6.3 Considering Surgery**

1. Why is surgery being recommended for my thyroid condition over other treatments?
2. What specific type of thyroid surgery are you recommending (e.g., total thyroidectomy, lobectomy), and why?
3. What is your experience with this type of thyroid surgery? How many have you performed?
4. What are your personal complication rates for this procedure (e.g., nerve injury, hypoparathyroidism)? How do they compare to national averages?
5. What are the specific risks and potential complications I should be aware of for this surgery?
6. What are the chances of voice changes, and are they usually temporary or permanent?
7. What are the chances of needing calcium and vitamin D supplements long-term due to parathyroid issues?
8. What will the surgery involve? How long will it take? What kind of anesthesia will be used?
9. How long will my hospital stay be? What can I expect during recovery in the hospital and at home?
10. What kind of scar will I have? Are there techniques to minimize it?
11. Will I need lifelong thyroid hormone replacement after this surgery?
12. What are the alternatives to surgery for my condition, and what are their pros and cons?
13. What is the plan if cancer is found unexpectedly during surgery for a presumed benign condition?
14. Will a neck dissection be necessary? Why or why not?
15. Do you use intraoperative nerve monitoring during thyroid surgery?
16. What measures do you take to preserve parathyroid gland function?
17. What is the follow-up care plan after surgery?
18. When can I return to normal activities, work, and exercise?
19. What specific symptoms should I report to you immediately after surgery?
20. Can you walk me through the day of surgery and what to expect?

#### **6.4 Ongoing Management**

1. How often do I need follow-up appointments and blood tests now that my condition is being managed?
2. What specific blood tests will you be monitoring, and what are the target levels for me?
3. What are the signs that my medication dose might be too high or too low?
4. If my symptoms persist despite my lab tests being in the "normal" range, what can we do?
5. Are there any long-term side effects of my medication or treatment that I should be aware of?
6. How can we work together to optimize my quality of life with this condition?
7. Are there any new treatments or research findings relevant to my condition that I should know about?
8. When should I consider seeing you sooner than my scheduled appointment?
9. How do changes in my weight, starting new medications, or developing other health issues affect my thyroid management?
10. If I plan to become pregnant, what adjustments need to be made to my thyroid care?
11. Are there any dietary or lifestyle recommendations that are particularly important for my ongoing health?
12. If I have benign nodules, what is the plan for monitoring them? How often will I need ultrasounds?
13. If I have had thyroid cancer, what is the surveillance plan to check for recurrence?
14. How do we manage any long-term side effects from my previous treatments (e.g., dry mouth from RAI, calcium issues from surgery)?
15. Is it necessary for me to continue seeing an endocrinologist, or can my primary care physician manage my condition now?

#### **6.5 Advocating for Oneself and Broader Concerns**

1. I'm concerned about [specific symptom or side effect]; can we discuss this further?
2. I've read about [alternative treatment or dietary approach]; what are your thoughts on this for my situation?
3. Can you explain why you are recommending this specific test or treatment over other available options?
4. What are the goals of this particular test or medication adjustment?
5. I would like to understand my condition better. Can you recommend any reliable patient education materials?
6. If I'm not feeling well despite "normal" lab results, what other factors could be contributing?
7. How will this condition or its treatment impact my ability to work, travel, or engage in my hobbies?
8. Are there any patient support programs, financial assistance, or counseling services you can recommend?
9. I'm feeling overwhelmed by this diagnosis/treatment; what support can you offer?
10. If I wanted to get a second opinion, how would I go about that, and would you support it?
11. How can I best communicate my needs and concerns to you and other members of my healthcare team?
12. What is the best way to contact you or your office if I have urgent questions or concerns between appointments?
13. Are there any clinical trials or research studies I might be eligible for?
14. How can I ensure all my doctors are coordinated in my care, especially if I have other health conditions?
15. What are the most important questions I *haven't* asked that I should be asking?

## **Part B: Questions from the Professional Perspective (Endocrinologists, Surgeons, Researchers)**

### **Section 7: Foundational Science & Pathophysiology**

#### **7.1 Thyroid Hormone Synthesis and Regulation**

1. What are the precise molecular mechanisms governing iodide uptake by the sodium-iodide symporter (NIS), including its regulation by TSH and iodide itself?
2. How is thyroperoxidase (TPO) activity regulated at the post-translational level during thyroid hormone synthesis?
3. What are the specific roles of DUOX1/DUOX2 and DUOXA1/DUOXA2 in H2​O2​ generation for thyroid hormonogenesis, and how are they coordinated?
4. What determines the ratio of T4​ to T3​ synthesized and secreted by the thyroid gland under various physiological and pathological conditions?
5. Beyond TSH, what are the non-TSH regulators of thyroid gland function and growth (e.g., IGF-1, EGF, cytokines)?
6. What are the detailed mechanisms of thyroglobulin (Tg) processing, lysosomal degradation, and hormone release?
7. How do intrathyroidal iodine levels modulate gene expression and thyroid cell function independent of TSH (the Wolff-Chaikoff effect and escape mechanisms)?
8. What are the finer points of pulsatile TSH secretion and its physiological significance?
9. How do somatostatin, dopamine, and glucocorticoids modulate TSH secretion at the pituitary level?
10. What is the full spectrum of non-thyroidal illness syndrome (NTIS) effects on the HPT axis, including central components and peripheral hormone metabolism?
11. What are the molecular mechanisms by which leptin and other adipokines influence the HPT axis?
12. How is thyrotropin-releasing hormone (TRH) synthesis and release regulated by neuronal inputs and feedback signals?
13. Are there undiscovered components or modulators of the HPT axis feedback loop?
14. What is the role of thyrostimulin (GPA2/GPB5) in thyroid physiology or pathophysiology?
15. How does selenium status specifically impact thyroid hormone synthesis, beyond its role in selenoprotein deiodinases?

#### **7.2 Thyroid Hormone Action**

1. What are the structural and functional differences between thyroid hormone receptor isoforms (TRα1,TRα2,TRβ1,TRβ2,TRβ3) and their tissue-specific expression patterns?
2. How do TR isoforms achieve specificity in gene regulation despite binding to similar thyroid hormone response elements (TREs)?
3. What is the role of corepressors (e.g., NCoR, SMRT) and coactivators (e.g., SRC family) in modulating TR-mediated transcription?
4. How does ligand binding induce conformational changes in TRs leading to coregulator exchange?
5. What are the mechanisms of non-genomic thyroid hormone actions, and what are their physiological significances (e.g., via integrin αvβ3)?
6. How do different thyroid hormone transporters (e.g., MCT8, MCT10, OATPs) contribute to tissue-specific uptake of T4​ and T3​?
7. What are the clinical consequences of mutations in SLC16A2 (MCT8) beyond the Allan-Herndon-Dudley syndrome?
8. How is the expression and activity of deiodinases (D1, D2, D3) regulated in different tissues and under different physiological states (e.g., fasting, illness, development)?
9. To what extent do polymorphisms in deiodinase genes (DIO1,DIO2,DIO3) explain inter-individual variations in response to levothyroxine or predisposition to thyroid disease?
10. What is the relative contribution of local T3​ generation by D2 versus circulating T3​ for thyroid hormone action in specific target tissues like the brain or pituitary?
11. How does D3 protect tissues from thyroid hormone excess, particularly during development?
12. Are there endogenous inhibitors or activators of deiodinase activity beyond known substrates and cofactors?
13. What are the epigenetic mechanisms (e.g., DNA methylation, histone modification) that regulate TR expression or thyroid hormone sensitivity?
14. How does thyroid hormone interact with other nuclear receptor signaling pathways (e.g., steroid receptors, RXR)?
15. What are the downstream target genes responsible for the diverse metabolic effects of thyroid hormones in tissues like liver, muscle, and adipose tissue?

#### **7.3 Autoimmunity in Thyroid Disease**

1. What are the key HLA class II alleles (e.g., DR3,DR4,DQAI∗0501,DQBI∗0201) most strongly associated with Graves' disease and Hashimoto's thyroiditis, and how do they contribute to pathogenesis?
2. Beyond HLA, what are the most significant non-HLA susceptibility genes for AITD (e.g., PTPN22,CTLA4,CD40,TG,TSHR,FOXP3,IL2RA) and their functional implications?
3. What are the critical gene-environment interactions that precipitate the loss of self-tolerance in Hashimoto's thyroiditis or Graves' disease?
4. What is the role of molecular mimicry (e.g., with Yersinia enterocolitica or other pathogens) in initiating autoimmune responses against thyroid antigens?
5. How do environmental factors like iodine excess, selenium deficiency, smoking, stress, or infections modulate immune responses and AITD risk?
6. What are the mechanisms of TSH receptor antibody (TRAb) generation in Graves' disease? Are there different subclasses of TRAb (stimulating, blocking, neutral) with distinct pathogenic roles?
7. How do stimulating TRAbs activate the TSH receptor, leading to thyroid hormone overproduction and goiter?
8. What is the role of T cell subsets (Th1, Th2, Th17, Treg) and their signature cytokines in the immunopathology of Graves' disease versus Hashimoto's thyroiditis?
9. How does intrathyroidal dendritic cell and B cell activation contribute to the perpetuation of autoimmune responses in AITD?
10. What are the mechanisms of thyrocyte apoptosis or destruction in Hashimoto's thyroiditis (e.g., Fas/FasL, perforin/granzyme, antibody-dependent cell-mediated cytotoxicity)?
11. What is the role of the TSHR A-subunit shedding and its potential as an immunogen?
12. Can we identify predictive biomarkers for individuals at high genetic risk of developing AITD, prior to clinical onset?
13. What is the contribution of fetal microchimerism to the increased prevalence of AITD in women?
14. How do sex hormones influence susceptibility to and severity of AITD?
15. What are the shared pathogenic pathways between AITD and other autoimmune diseases that commonly co-occur (e.g., type 1 diabetes, celiac disease, pernicious anemia)?

#### **7.4 Molecular Basis of Thyroid Neoplasia**

1. What are the initiating and progression-driving genetic events in papillary thyroid carcinoma (PTC) (e.g., BRAFV600E, RAS mutations, RET/PTC rearrangements)?
2. How do BRAFV600E and RAS mutations activate the MAPK pathway, and what are their distinct downstream effects contributing to PTC pathogenesis?
3. What is the role of PAX8/PPARγ rearrangements in the development of follicular thyroid carcinoma (FTC) and follicular-variant PTC?
4. What are the key genetic alterations in Hürthle cell carcinoma, and how do they differ from FTC?
5. What is the spectrum of RET proto-oncogene mutations (germline and somatic) in medullary thyroid carcinoma (MTC), and how do they correlate with phenotype and aggressiveness?
6. What are the critical molecular events driving dedifferentiation from DTC to poorly differentiated thyroid carcinoma (PDTC) and anaplastic thyroid carcinoma (ATC) (e.g., TP53,TERT promoter, PIK3CA,CTNNB1 mutations)?
7. How do TERT promoter mutations synergize with BRAF or RAS mutations to promote aggressive tumor behavior and mortality in thyroid cancer?
8. What are the key epigenetic alterations (DNA methylation, histone modifications, miRNA dysregulation) involved in thyroid carcinogenesis and progression?
9. Can specific epigenetic signatures predict tumor behavior or response to therapy in thyroid cancer?
10. What signaling pathways (e.g., PI3K/AKT/mTOR, Wnt/β-catenin) are commonly dysregulated in advanced thyroid cancers, and are they druggable targets?
11. What is the role of tumor microenvironment (e.g., cancer-associated fibroblasts, immune cells, angiogenesis) in thyroid cancer growth and metastasis?
12. How does loss of NIS expression and function occur in dedifferentiated thyroid cancers, leading to RAI-refractory disease?
13. Are there molecular mechanisms that can be targeted to re-induce NIS expression or function in RAI-refractory cancers?
14. What are the molecular drivers of metastatic spread in thyroid cancer, including mechanisms of invasion, intravasation, and colonization of distant sites?
15. Can circulating tumor DNA (ctDNA) or other liquid biopsy markers be used for early detection, prognostication, or monitoring of thyroid cancer?

#### **7.5 Addressing Gaps in Understanding Gene-Environment Interactions and Tissue-Specific Effects**

1. What specific methodologies are best suited to unravel complex gene-environment interactions in large-scale epidemiological studies of AITD?
2. Are there critical windows of susceptibility to environmental triggers for AITD development during an individual's lifespan?
3. How do endocrine-disrupting chemicals (EDCs) specifically interfere with thyroid hormone synthesis, transport, metabolism, or action, and at what exposure levels do these effects become clinically relevant?
4. Can we develop robust biomarkers of EDC exposure that correlate with thyroid dysfunction?
5. To what extent do polymorphisms in genes encoding thyroid hormone transporters or deiodinases explain persistent symptoms in levothyroxine-treated hypothyroid patients with normal serum TSH?
6. Are there non-invasive methods to assess intracellular thyroid hormone status or deiodinase activity in key target tissues (e.g., brain, liver, muscle) in humans?
7. What is the clinical utility of measuring serum reverse T3​ (rT3​) or T3​/rT3​ ratios in assessing tissue-specific thyroid hormone status, particularly in NTIS?
8. How does local thyroid hormone regulation within the hypothalamus and pituitary contribute to the fine-tuning of the HPT axis setpoint?
9. What are the molecular mechanisms by which thyroid hormones regulate brain development and function beyond critical perinatal periods?
10. Can we develop tissue-specific thyroid hormone analogs or modulators that target specific TR isoforms or deiodinase activities for therapeutic benefit with fewer side effects?
11. What are the key epigenetic events that drive the transition from differentiated to anaplastic thyroid carcinoma, and are these reversible?
12. How does the tumor microbiome, if present, influence thyroid cancer initiation or progression?
13. What is the precise contribution of iodine status (deficiency vs. excess) to the changing epidemiology of thyroid cancer subtypes?
14. Can we identify specific dietary components, beyond iodine and selenium, that significantly modulate thyroid autoimmunity or cancer risk?
15. What are the long-term consequences of subclinical thyroid dysfunction (both hypo- and hyperthyroidism) on organs that are highly dependent on thyroid hormone, such as the brain and cardiovascular system, even if serum TSH normalizes spontaneously or with treatment?

### **Section 8: Diagnostics and Imaging Challenges**

#### **8.1 Thyroid Function Tests (TFTs)**

1. What are the most common pre-analytical, analytical, and post-analytical interferences affecting TSH, FT4, and FT3 immunoassays (e.g., heterophile antibodies, biotin, anti-streptavidin antibodies, specific drug interferences)?
2. How can clinicians best detect and manage suspected TFT assay interference? What reflex testing algorithms are most effective?
3. What is the optimal approach to interpreting discordant TFT results (e.g., elevated TSH with normal/high FT4; low TSH with normal/low FT4)?
4. What is the true prevalence and clinical significance of thyroid hormone resistance syndromes (RTH-β, RTH-α) versus other causes of discordant TFTs?
5. How should age- and sex-specific reference intervals for TSH be established and implemented in clinical practice, particularly for pediatric and geriatric populations?
6. Is there a universal TSH reference range applicable during pregnancy, or are trimester-specific and method-specific ranges essential? What are the challenges in establishing these?
7. What is the clinical utility of routine reverse T3 (rT3) measurement in diagnosing or managing non-thyroidal illness syndrome (NTIS) or other thyroid disorders?
8. Does the FT4/FT3 ratio or T3/rT3 ratio offer superior diagnostic or prognostic information compared to individual hormone measurements in specific clinical scenarios?
9. What is the role of thyroglobulin (Tg) measurement in the evaluation of benign thyroid disorders (e.g., thyroiditis, goiter) or as a marker of thyroid tissue mass?
10. How should Tg and anti-Tg antibody (TgAb) levels be interpreted in the context of DTC surveillance, particularly in TgAb-positive patients? What are the limitations of current Tg assays in this setting?
11. Are there novel biomarkers of thyroid function or thyroid hormone action at the tissue level that could supplement or replace current serum TFTs?
12. What is the impact of diurnal variation, seasonality, or acute illness on TSH and thyroid hormone levels, and how should this be considered in clinical interpretation?
13. How do we define an individual's "setpoint" for the HPT axis, and can deviations from this setpoint be identified even within population-based reference ranges?
14. What is the current status and potential future role of liquid chromatography-tandem mass spectrometry (LC-MS/MS) for routine measurement of FT4 and FT3?
15. How does the choice of FT4/FT3 assay methodology (e.g., analog-based immunoassays vs. equilibrium dialysis followed by immunoassay) impact clinical decision-making?

#### **8.2 Thyroid Autoantibodies**

1. What is the optimal cut-off level for TPOAb and TgAb positivity to define autoimmune thyroiditis, and do quantitative levels correlate with disease severity or progression risk?
2. What is the predictive value of TPOAb positivity in euthyroid individuals for the future development of overt hypothyroidism or postpartum thyroiditis?
3. How does the presence and titer of TgAb interfere with Tg measurement in DTC surveillance, and what are the best strategies to mitigate this (e.g., reflex to LC-MS/MS Tg, serial TgAb monitoring)?
4. What is the clinical utility of measuring different subclasses of TSH receptor antibodies (TRAb) – stimulating (TSI), blocking (TBAb), and neutral – in Graves' disease diagnosis, prognosis, and management?
5. How do TRAb levels (particularly TSI) predict the likelihood of remission after ATD therapy or relapse after withdrawal in Graves' disease?
6. Is there a role for routine TRAb measurement in patients with Graves' orbitopathy to guide treatment or predict outcomes?
7. What are the challenges in the standardization and harmonization of thyroid autoantibody assays across different platforms and laboratories?
8. Are there novel thyroid autoantigens or autoantibodies with diagnostic or prognostic significance yet to be fully characterized?
9. What is the significance of isolated TgAb positivity in the absence of TPOAb or overt thyroid dysfunction?
10. Can changes in thyroid autoantibody titers be used to monitor response to immunomodulatory therapies in AITD?

#### **8.3 Thyroid Ultrasound**

1. How can inter-observer variability in the application of ultrasound risk stratification systems (e.g., ACR TI-RADS, EU-TIRADS, K-TIRADS) be minimized through training, standardization, and quality assurance programs?
2. What is the comparative diagnostic performance (sensitivity, specificity, PPV, NPV) of different TI-RADS systems in various populations and nodule subtypes?
3. What is the incremental value of ultrasound elastography (strain or shear wave) when added to conventional B-mode ultrasound and TI-RADS for nodule risk stratification? Which elastography technique is superior?
4. Are there specific sonographic features (e.g., microcalcifications, irregular margins, taller-than-wide shape, rim calcifications with extrusion) that have higher predictive value for malignancy, and how should they be weighted in risk models?
5. What is the role of contrast-enhanced ultrasound (CEUS) in differentiating benign from malignant thyroid nodules or assessing nodule vascularity?
6. How can ultrasound be optimized for the detection of subtle signs of extrathyroidal extension (ETE) or lymph node metastasis in patients with known or suspected thyroid cancer?
7. What is the optimal ultrasound follow-up strategy (frequency, duration) for nodules classified as benign after FNA or low-suspicion by TI-RADS?
8. Can quantitative texture analysis or radiomics based on thyroid ultrasound images improve diagnostic accuracy or predict molecular subtypes of thyroid cancer?
9. What is the role of AI and machine learning algorithms in assisting with thyroid nodule detection, characterization, and risk stratification on ultrasound? Can AI outperform human readers?
10. How should incidental thyroid nodules (thyroid incidentalomas) detected on other imaging modalities (CT, MRI, PET) be evaluated, and what is the role of dedicated thyroid ultrasound in this context?

#### **8.4 Fine Needle Aspiration (FNA) Cytology and Molecular Markers**

1. What are the current challenges in reducing the rate of indeterminate thyroid FNA cytology (Bethesda categories III - AUS/FLUS, and IV - FN/SFN)?
2. What is the inter-observer variability among cytopathologists in classifying thyroid FNAs, particularly for indeterminate categories, and how can it be improved?
3. What is the optimal management strategy for nodules with repeat AUS/FLUS cytology?
4. What is the comparative diagnostic performance and cost-effectiveness of different commercial molecular marker panels (e.g., ThyroSeq, Afirma GSC/Xpression Atlas, ThyGeNEXT/ThyraMIR) for risk stratifying indeterminate thyroid nodules?
5. How should molecular test results (e.g., "benign," "suspicious," specific mutations identified) be integrated with cytological and sonographic features to guide clinical management (observation vs. surgery)?
6. What is the long-term risk of malignancy in nodules deemed "benign" by molecular testing if managed non-surgically? What is the optimal follow-up?
7. Can molecular markers reliably distinguish between benign Hürthle cell neoplasms and Hürthle cell carcinomas preoperatively?
8. What is the role of next-generation sequencing (NGS)-based molecular testing in identifying specific driver mutations (e.g., BRAF,RAS,TERT) that may have prognostic or therapeutic implications beyond just cancer detection?
9. Is there a role for immunohistochemical markers (e.g., galectin-3, HBME-1, CK19) on cell blocks from FNA samples to improve diagnostic accuracy for indeterminate nodules?
10. How does the pre-test probability of malignancy (based on ultrasound and clinical features) influence the interpretation and utility of molecular test results?
11. What is the optimal reflex testing strategy for a Bethesda III nodule to minimize diagnostic thyroidectomies for benign disease while ensuring timely cancer diagnosis?
12. Can miRNA profiling from FNA samples add value to existing molecular marker panels for indeterminate nodules?
13. What are the ethical and counseling considerations when discussing complex molecular test results with patients?
14. How do different molecular classifier results correlate with long-term risk of malignancy in nodules managed non-surgically?
15. Are there specific nodule characteristics (e.g., size, growth rate) that should prompt consideration of repeat FNA or molecular testing even after an initial benign cytology?

#### **8.5 Advanced Imaging and Nuclear Medicine**

1. What is the precise role and diagnostic accuracy of 18F-FDG PET/CT in the evaluation of aggressive or dedifferentiated thyroid cancers, particularly RAI-refractory disease?
2. Can 18F-FDG PET/CT predict treatment response to TKIs or other systemic therapies in advanced thyroid cancer?
3. Is there a role for 18F-FDG PET/CT in the initial evaluation of large, suspicious thyroid nodules or rapidly growing goiters, especially if FNA is inconclusive?
4. What are the emerging novel radiotracers for thyroid imaging (e.g., targeting SSTR, PSMA, NIS expression, or specific cancer mutations), and what is their potential clinical utility?
5. How can 123I versus 131I scintigraphy be optimally utilized for the diagnosis of hyperthyroidism, assessment of nodule function, or pre-RAI therapy planning? What are the pros and cons of each?
6. What is the role of SPECT/CT in conjunction with planar scintigraphy for better anatomical localization of functioning nodules or metastatic thyroid cancer deposits?
7. Can quantitative parameters from thyroid scans (e.g., uptake percentage, washout rates) provide prognostic information or guide treatment decisions?
8. What is the utility of sestamibi scans for parathyroid localization in primary hyperparathyroidism, and how does it compare/complement neck ultrasound or 4D-CT? (Relevant due to proximity and surgical considerations).
9. Are there advanced MRI techniques (e.g., DWI, DCE-MRI) that can improve characterization of thyroid nodules or assess tumor aggressiveness non-invasively?
10. How can imaging be used to monitor response to non-surgical ablative therapies for thyroid nodules (e.g., RFA, MWA)?

#### **8.6 Optimizing Indeterminate Nodule Management and Refining Testing Paradigms**

1. What are the most effective training and calibration methods to reduce inter-observer variability in TI-RADS application among radiologists and endocrinologists performing ultrasounds?
2. Can AI-assisted ultrasound interpretation improve the accuracy and consistency of thyroid nodule risk assessment compared to human readers alone, and how can such systems be validated and integrated into clinical workflows?
3. Are there validated biomarkers beyond TSH (e.g., metabolomic, proteomic signatures) that better reflect symptomatic relief or tissue euthyroidism in levothyroxine-treated patients?
4. Under what specific circumstances, if any, does T3​/T4​ combination therapy offer superior objective and patient-reported outcomes to T4​ monotherapy, and how can these patients be identified prospectively?
5. What is the long-term clinical impact (e.g., on cardiovascular health, bone density, quality of life) of managing indeterminate thyroid nodules conservatively based on molecular marker results versus proceeding with diagnostic surgery?
6. How can the cost-effectiveness of various diagnostic algorithms for indeterminate nodules (involving different molecular tests, repeat FNA, or direct surgery) be modeled and compared in different healthcare systems?
7. What are the psychological impacts on patients living with an indeterminate thyroid nodule, and how can shared decision-making be optimized in this context of uncertainty?
8. Is there a role for serial molecular testing or imaging beyond ultrasound (e.g., advanced MRI) in the surveillance of molecularly "low-risk" indeterminate nodules that are growing or developing new suspicious features?
9. How do we address the challenge of "normal" TSH ranges that may not reflect an individual's optimal thyroid status, particularly in patients with persistent symptoms?
10. What quality assurance measures and ongoing education are necessary for cytopathology laboratories to maintain high accuracy in thyroid FNA interpretation, especially for challenging cases?

### **Section 9: Clinical Management of Hypothyroidism**

#### **9.1 Treatment Initiation and Titration**

1. What is the optimal TSH target range for levothyroxine replacement therapy in different patient populations: young adults, pregnant women (trimester-specific), elderly individuals, and those with specific comorbidities (e.g., heart disease)?
2. How should the initial dose of levothyroxine be determined (e.g., weight-based, age-based, degree of TSH elevation)?
3. What is the appropriate frequency for TSH monitoring after initiating or adjusting levothyroxine therapy until a stable dose is achieved?
4. What factors are known to affect levothyroxine absorption (e.g., food, coffee, calcium, iron, PPIs, malabsorptive syndromes), and how should patient counseling and dosing instructions be tailored?
5. Are there clinically significant differences in bioavailability or consistency between various generic and brand-name levothyroxine preparations? How should switches be managed?
6. What is the evidence for treating subclinical hypothyroidism (SCH)? At what TSH levels and in which patient groups (e.g., symptomatic, pregnant, TPOAb positive, dyslipidemia) is treatment most beneficial?
7. What are the potential risks versus benefits of treating mild SCH (TSH < 10 mU/L) in older adults (>70-80 years)?
8. If SCH is treated, what TSH target should be aimed for?
9. How should levothyroxine therapy be adjusted in patients undergoing significant weight changes or starting medications known to interact with thyroid hormone metabolism (e.g., estrogens, androgens, anticonvulsants)?
10. What is the best approach to managing a patient who reports symptom recurrence after a switch between bioequivalent levothyroxine preparations?

#### **9.2 Persistent Symptoms Despite "Normal" TSH and T3/T4 Combination Therapy Debate**

1. What is the comprehensive differential diagnosis for persistent hypothyroid-like symptoms (fatigue, weight gain, cognitive dysfunction) in a levothyroxine-treated patient with a TSH within the reference range?
2. How can one objectively assess and differentiate between symptoms truly related to inadequate thyroid hormone action at the tissue level versus other coexisting conditions or psychosocial factors?
3. Are there specific genetic polymorphisms (e.g., in DIO2 - Thr92Ala) that reliably predict a better symptomatic response to T3​/T4​ combination therapy?
4. What is the current evidence from randomized controlled trials regarding the efficacy and safety of T3​/T4​ combination therapy compared to T4​ monotherapy for improving quality of life, mood, cognitive function, or weight?
5. If combination therapy is considered, what is the optimal patient selection criteria, T3​/T4​ ratio, dosing regimen (e.g., immediate-release vs. sustained-release T3​), and monitoring strategy?
6. What are the potential long-term risks of combination therapy, particularly concerning cardiovascular health (arrhythmias) and bone mineral density, especially if supraphysiological T3​ levels occur?
7. What is the evidence base for the use of desiccated thyroid extract (DTE) in hypothyroidism? How does its efficacy and safety compare to synthetic hormone preparations?
8. What are the challenges in monitoring patients on DTE due to its variable T3​/T4​ ratio and impact on TFTs?
9. How should patient preference and subjective well-being be weighed against biochemical targets and trial evidence when considering alternative thyroid hormone preparations?
10. Are there validated questionnaires or patient-reported outcome measures (PROMs) specifically for assessing treatment satisfaction and residual symptoms in hypothyroidism?

#### **9.3 Specific Etiologies and Management Challenges**

1. How is central hypothyroidism (secondary or tertiary) diagnosed, and how does its management (levothyroxine dosing and monitoring with FT4) differ from primary hypothyroidism?
2. What are the common causes of central hypothyroidism, and what associated pituitary hormone deficiencies need to be screened for?
3. How should hypothyroidism developing after thyroidectomy (total or partial) or radioactive iodine therapy be managed in terms of levothyroxine initiation and long-term targets?
4. What is the management of hypothyroidism induced by medications such as amiodarone, lithium, tyrosine kinase inhibitors, or immune checkpoint inhibitors? Does it always require lifelong L-T4?
5. How should transient hypothyroidism (e.g., during the hypothyroid phase of thyroiditis) be managed? Is levothyroxine always indicated?
6. What are the specific considerations for managing congenital hypothyroidism, including screening, prompt treatment initiation, dosing, and long-term neurodevelopmental follow-up?
7. How should one approach a patient with consistently elevated TSH despite high doses of levothyroxine (poor compliance, malabsorption, drug interactions, assay interference)?
8. Are there specific excipients in levothyroxine formulations that are more commonly associated with patient-reported intolerance or allergic reactions?
9. What is the role of liquid or softgel levothyroxine formulations, and in which patient populations might they offer an advantage?
10. How should levothyroxine be managed perioperatively in patients undergoing non-thyroid surgery?

#### **9.4 Complications and Comorbidities**

1. What are the cardiovascular consequences of overt and subclinical hypothyroidism (e.g., dyslipidemia, hypertension, diastolic dysfunction, atherosclerosis, heart failure)? Does treatment reverse these?
2. What is the association between hypothyroidism and neurocognitive or psychiatric manifestations (e.g., depression, anxiety, cognitive impairment, psychosis)? How responsive are these to levothyroxine?
3. How does hypothyroidism impact fertility, menstrual cycles, and pregnancy outcomes? What are the implications for preconception counseling?
4. What is myxedema coma: pathophysiology, clinical presentation, diagnostic criteria, and optimal multidisciplinary management in an ICU setting? What is the role of IV levothyroxine +/- liothyronine?
5. How does hypothyroidism affect other endocrine systems (e.g., adrenal function, growth hormone)?
6. What is the relationship between hypothyroidism and obstructive sleep apnea?
7. How should hypothyroidism be managed in patients with coexisting conditions like diabetes mellitus, chronic kidney disease, or liver disease, considering potential impacts on hormone metabolism and medication dosing?
8. Are patients with autoimmune hypothyroidism (Hashimoto's) at increased risk for other autoimmune diseases? What screening is appropriate?
9. What are the risks of overtreatment with levothyroxine (iatrogenic hyperthyroidism), particularly in older adults (e.g., atrial fibrillation, osteoporosis)?
10. How can clinicians balance the goals of alleviating hypothyroid symptoms with avoiding overtreatment, especially in sensitive populations?

#### **9.5 Subclinical Hypothyroidism and Levothyroxine Management Nuances**

1. What are the most reliable predictors of progression from subclinical to overt hypothyroidism in an untreated individual?
2. Does treatment of mild subclinical hypothyroidism (TSH 4.5-10 mU/L) in individuals over 70-80 years improve quality of life, cognitive function, or reduce cardiovascular events, or does it primarily increase risks?
3. What is the optimal TSH threshold for initiating levothyroxine treatment in asymptomatic younger adults with SCH, considering potential long-term benefits versus the burden of lifelong therapy?
4. Are there specific subgroups of patients with SCH (e.g., those with goiter, rapidly rising TSH, or planning pregnancy) who unequivocally benefit from treatment regardless of TSH level?
5. What is the evidence for de-prescribing levothyroxine in patients, particularly older adults, who were started on treatment for unclear indications or very mild SCH, and how should this be approached?
6. How should clinicians address patient concerns about brand-to-brand variability in levothyroxine efficacy or side effects, even if preparations are deemed bioequivalent?
7. What investigations are warranted for a patient on a stable levothyroxine dose who develops new or worsening symptoms, or whose TSH becomes unexpectedly abnormal?
8. Is there a role for routine FT3 measurement in monitoring levothyroxine monotherapy, or is TSH (and possibly FT4) sufficient?
9. How can adherence to levothyroxine therapy be assessed and improved in patients with persistently poor biochemical control?
10. What are the best practices for patient education regarding levothyroxine therapy to ensure optimal understanding, adherence, and self-management?

### **Section 10: Clinical Management of Hyperthyroidism**

#### **10.1 Choice of Primary Therapy and Remission Prediction**

1. What are the key patient-specific factors (age, comorbidities, pregnancy plans, goiter size, severity of thyrotoxicosis, TRAb levels, patient preference) that should guide the choice between anti-thyroid drugs (ATDs), radioactive iodine (RAI), and thyroidectomy as first-line treatment for Graves' disease?
2. What is the comparative long-term efficacy (remission rates, relapse rates) and safety profiles of ATDs, RAI, and surgery for Graves' disease based on current evidence?
3. What is the optimal duration of ATD therapy (e.g., methimazole) for Graves' disease to maximize the chance of durable remission (typically 12-18 months, but is longer better)?
4. Can a combination of clinical, biochemical (TRAb, TSH, FT4/FT3), genetic, or imaging markers improve the prediction of long-term remission in Graves' disease after ATD withdrawal?
5. What are the current "block-and-replace" versus "titration" regimens for ATD therapy, and is one superior in terms of remission rates or side effects?
6. What is the role of long-term low-dose methimazole therapy as an alternative to definitive treatment (RAI/surgery) in patients who relapse after a standard course of ATDs or prefer to avoid definitive therapy?
7. How should common ATD side effects (rash, arthralgia, GI upset) be managed? When is it necessary to switch ATDs or discontinue therapy?
8. What are the risk factors, incidence, and management of severe ATD-induced adverse events like agranulocytosis and hepatotoxicity? What patient counseling is critical?
9. In patients with toxic adenoma or toxic multinodular goiter, are ATDs primarily for pre-treatment before definitive therapy (RAI/surgery), or is long-term ATD therapy a viable option for some?
10. How does patient preference and shared decision-making influence the selection of primary therapy for hyperthyroidism, and how can clinicians best facilitate this process?

#### **10.2 Management of Graves' Disease Specifics (Orbitopathy, Pregnancy)**

1. What are the most significant risk factors for the development or worsening of Graves' orbitopathy (GO/TED) (e.g., smoking, high TRAb, RAI therapy, female sex)?
2. What are the most effective screening protocols for early detection of GO in patients newly diagnosed with Graves' disease? When should ophthalmology referral occur?
3. How is GO severity and activity assessed (e.g., NOSPECS, CAS, EUGOGO guidelines), and how does this guide management?
4. What is the role of selenium supplementation in preventing progression or improving outcomes in mild GO?
5. What are the indications for and efficacy of glucocorticoids (oral or IV pulse) in managing moderate-to-severe, active GO? What are the optimal regimens and side effect mitigation strategies?
6. What is the current place of orbital radiotherapy or surgical decompression in the management of GO?
7. What is the mechanism of action, efficacy, and safety profile of teprotumumab for moderate-to-severe active GO? Who are the ideal candidates, and what are the long-term outcomes?
8. Are there other emerging biologic therapies or targeted treatments for GO?
9. How should hyperthyroidism due to Graves' disease be managed preconception and during pregnancy? What are the maternal and fetal risks of uncontrolled disease?
10. What is the preferred ATD during the first trimester of pregnancy (PTU) versus later trimesters and breastfeeding (methimazole), and what are the rationales and risks (e.g., PTU hepatotoxicity, MMI embryopathy)?
11. What are the target FT4/TSH levels during pregnancy for a woman on ATDs? How frequently should TFTs be monitored?
12. What is the management of gestational transient thyrotoxicosis (GTT) versus true Graves' hyperthyroidism in early pregnancy?
13. How should Graves' disease be managed in the postpartum period, considering the risk of relapse or flare?
14. What is the approach to treating neonatal Graves' disease due to transplacental passage of maternal TRAbs?
15. How does smoking cessation impact GO risk and progression?

#### **10.3 Thyroid Storm and Amiodarone-Induced Thyrotoxicosis (AIT)**

1. What are the diagnostic criteria (e.g., Burch-Wartofsky Point Scale) for thyroid storm, and how can it be rapidly recognized and differentiated from severe thyrotoxicosis?
2. What is the optimal multimodal treatment protocol for thyroid storm, including ATDs (PTU preferred initially?), iodine solutions (Lugol's or SSKI), beta-blockers, glucocorticoids, and supportive care in an ICU setting?
3. What is the role of plasmapheresis or emergency thyroidectomy in refractory thyroid storm?
4. What are the common precipitating factors for thyroid storm?
5. How can amiodarone-induced thyrotoxicosis (AIT) Type 1 (iodine-induced, underlying thyroid disease) be differentiated from AIT Type 2 (destructive thyroiditis)? What is the role of color flow Doppler ultrasound and RAIU?
6. Can mixed/indefinite forms of AIT occur?
7. What is the optimal management for AIT Type 1 (ATDs, potassium perchlorate?) versus AIT Type 2 (glucocorticoids)? How should mixed forms be treated?
8. How long should treatment continue for AIT, and what is the risk of recurrence if amiodarone is continued or restarted?
9. When is thyroidectomy indicated for severe or refractory AIT?
10. What thyroid monitoring strategy is recommended for patients initiating or on long-term amiodarone therapy?

#### **10.4 Subclinical Hyperthyroidism**

1. How is subclinical hyperthyroidism (SH) defined (consistently suppressed TSH with normal FT4/FT3)? Are there grades of severity based on TSH level?
2. What are the common etiologies of endogenous SH (e.g., Graves', autonomous nodules) versus exogenous SH (overtreatment with levothyroxine)?
3. What are the potential long-term adverse consequences of untreated SH, particularly in older adults (e.g., atrial fibrillation, cardiovascular mortality, osteoporosis, dementia)?
4. In which patients with SH is treatment generally recommended (e.g., TSH <0.1 mU/L, elderly, presence of risk factors like heart disease or osteoporosis, symptomatic)?
5. What are the treatment options for endogenous SH (low-dose ATDs, RAI, surgery, or observation for mild cases)? How should the approach be individualized?
6. If SH is due to levothyroxine overtreatment, how should the dose be adjusted and monitored?
7. What is the natural history of untreated mild SH (TSH 0.1-0.4 mU/L)? Does it often progress or resolve?
8. How frequently should patients with untreated SH be monitored (TFTs and clinically)?
9. Does treatment of SH improve patient-reported outcomes or quality of life?
10. Are there specific considerations for managing SH in younger, asymptomatic individuals?

### **Section 11: Evaluation and Management of Thyroid Nodules and Goiter**

#### **11.1 Risk Stratification of Nodules and Indeterminate Cytology**

1. Beyond established TI-RADS criteria, are there novel sonographic features or patterns that can improve the discrimination between benign and malignant thyroid nodules?
2. What is the current consensus on the management of nodules classified as Bethesda I (Non-diagnostic/Unsatisfactory) after FNA? When is repeat FNA versus core needle biopsy or surgery warranted?
3. For nodules with Bethesda III (AUS/FLUS) cytology, what factors (ultrasound pattern, nodule size/growth, patient preference, molecular testing results) guide the decision between observation, repeat FNA, or diagnostic surgery?
4. What is the positive predictive value (PPV) and negative predictive value (NPV) of currently available molecular marker panels for malignancy in Bethesda III and IV nodules, and how do these vary based on the underlying prevalence of cancer?
5. How should conflicting information between cytology, ultrasound, and molecular testing be reconciled in clinical decision-making for indeterminate nodules?
6. Is there a role for routine use of molecular markers in nodules with Bethesda V (Suspicious for Malignancy) or VI (Malignant) cytology to refine risk or guide surgical extent?
7. What is the optimal follow-up for nodules that are cytologically benign (Bethesda II) but have suspicious ultrasound features or are growing?
8. Can quantitative analysis of nodule growth kinetics on serial ultrasounds help predict malignancy risk?
9. What is the role of core needle biopsy (CNB) in the evaluation of thyroid nodules, particularly when FNA is repeatedly non-diagnostic or indeterminate? What are its advantages and limitations compared to FNA?
10. How can the integration of AI-driven image analysis with molecular data potentially create more accurate and personalized risk stratification models for thyroid nodules?

#### **11.2 Management of Benign Nodules/Goiter and Minimally Invasive Techniques**

1. What are the indications for intervention (surgery, RAI, thermal ablation) in patients with cytologically benign thyroid nodules or multinodular goiter (e.g., compressive symptoms, cosmetic concerns, substernal extension, documented growth)?
2. What is the efficacy and safety of TSH suppression therapy with levothyroxine for reducing the volume of benign nodules or diffuse goiters? In which patients, if any, is it still considered appropriate given potential side effects?
3. What are the key patient and nodule characteristics (size, location, vascularity, composition) that predict optimal outcomes with radiofrequency ablation (RFA) for benign thyroid nodules?
4. What is the comparative efficacy, safety, and durability of different thermal ablation techniques (RFA, microwave ablation (MWA), laser ablation (LA), high-intensity focused ultrasound (HIFU)) for benign thyroid nodules?
5. What are the common complications of thyroid thermal ablation procedures, and how can they be minimized or managed?
6. What is the definition of treatment success after thermal ablation (e.g., percentage volume reduction, symptom improvement), and what is the long-term recurrence rate?
7. Is there a risk of missing malignancy with thermal ablation, and what pre-procedural workup (e.g., two benign FNAs) is necessary to minimize this?
8. How should patients be monitored after thermal ablation (ultrasound, symptoms), and what is the management for partial response or regrowth?
9. What are the training standards and credentialing requirements for performing thyroid thermal ablation procedures?
10. Is ethanol ablation still a viable option for predominantly cystic benign thyroid nodules, and how does it compare to thermal ablation?

#### **11.3 Autonomously Functioning Thyroid Nodules (AFTN)**

1. At what TSH level (e.g., subclinical vs. overt hyperthyroidism) and/or nodule size should treatment be considered for an autonomously functioning thyroid nodule (AFTN) or toxic multinodular goiter (TMNG)?
2. What is the preferred definitive treatment for AFTN/TMNG causing hyperthyroidism: radioactive iodine or surgery? What are the pros and cons of each?
3. Can thermal ablation techniques (e.g., RFA) be effective for treating AFTNs and inducing remission of hyperthyroidism? What is the current evidence?
4. How should AFTNs that are not yet causing overt hyperthyroidism (i.e., causing only subclinical hyperthyroidism or euthyroid with suppressed TSH) be managed?
5. What is the natural history of untreated AFTNs? What percentage progress to overt hyperthyroidism?
6. Is there a role for long-term ATD therapy in patients with AFTN/TMNG who are poor candidates for or refuse definitive treatment?
7. How is the diagnosis of AFTN/TMNG confirmed (thyroid scintigraphy in the context of suppressed TSH)?
8. What is Marine-Lenhart syndrome (Graves' disease with coexisting functioning nodules), and how does its management differ?
9. After successful treatment of an AFTN with RAI or ablation, what is the risk of subsequent hypothyroidism?
10. Are there specific genetic mutations (e.g., in TSHR or GNAS) commonly found in AFTNs, and do they have clinical implications?

#### **11.4 Active Surveillance for Low-Risk PTMC**

1. What are the generally accepted inclusion criteria (tumor size, location, cytology, patient factors) for offering active surveillance (AS) as a management option for papillary thyroid microcarcinoma (PTMC, $\leq$1 cm)?
2. What is the optimal follow-up protocol for PTMC on AS (frequency of neck ultrasound, TSH monitoring)?
3. What are the defined triggers for recommending delayed surgery in patients on AS for PTMC (e.g., significant tumor growth, new lymph node metastases, patient preference)?
4. What is the long-term risk of tumor growth, nodal metastasis, or extrathyroidal extension in PTMCs managed with AS, based on large cohort studies? Are there reliable predictors for such progression?
5. How does the risk of progression on AS differ for PTMCs with BRAFV600E mutation compared to wild-type? Should molecular status influence AS eligibility?
6. What are the patient-reported outcomes, including anxiety levels and quality of life, for patients undergoing AS for PTMC compared to immediate surgery?
7. How can shared decision-making be effectively implemented when discussing AS versus surgery for PTMC, ensuring patients understand the risks, benefits, and uncertainties?
8. Are there specific subgroups of PTMC (e.g., subcapsular location, multifocality) for whom AS might be less appropriate?
9. What is the role of TSH suppression in patients on AS for PTMC?
10. If delayed surgery is performed for PTMC progression on AS, are oncologic outcomes comparable to those of immediate surgery?

### **Section 12: Surgical Considerations in Thyroid Disease**

#### **12.1 Indications for Thyroidectomy and Extent of Surgery**

1. What are the current evidence-based indications for thyroidectomy in benign thyroid disease (e.g., goiter size thresholds, degree of compressive symptoms, rate of growth)?
2. In patients with indeterminate thyroid nodules (Bethesda III/IV), when is diagnostic lobectomy preferred over total thyroidectomy, considering molecular marker results, ultrasound findings, and patient factors?
3. For differentiated thyroid cancer (DTC), what are the current ATA (or equivalent) guideline criteria for recommending total thyroidectomy versus thyroid lobectomy based on tumor size, risk factors, and patient age?
4. For a 1-4 cm intrathyroidal papillary thyroid cancer with no adverse features, what are the comparative 10-year disease-free survival rates and overall survival rates for lobectomy versus total thyroidectomy in appropriately selected patients?
5. What is the role of prophylactic central neck dissection (pCND) in patients with clinically node-negative (cN0) DTC? Which patients benefit most, and what are the associated risks (hypoparathyroidism, RLN injury)?
6. How does the finding of occult micrometastases in pCND specimens impact adjuvant therapy decisions (RAI) or long-term prognosis?
7. When is completion thyroidectomy indicated after an initial lobectomy reveals more extensive or aggressive cancer than anticipated?
8. What are the indications for therapeutic lateral neck dissection in patients with DTC and clinically or radiologically evident lateral neck metastases (cN1b)?
9. What is the surgical management strategy for Graves' disease refractory to or unsuitable for ATDs/RAI? Is total or near-total thyroidectomy preferred?
10. What are the specific surgical considerations for prophylactic thyroidectomy in asymptomatic RET mutation carriers (e.g., timing based on codon risk level, extent of CND)?

#### **12.2 Surgical Techniques, Innovations, and Nerve Monitoring**

1. What are the established benefits and limitations of minimally invasive video-assisted thyroidectomy (MIVAT) and other minimally invasive approaches compared to conventional open thyroidectomy?
2. What is the current status and learning curve associated with transoral endoscopic thyroidectomy vestibular approach (TOETVA) and other remote-access/scarless techniques (e.g., transaxillary, retroauricular)? Who are ideal candidates?
3. What is the evidence for routine versus selective use of intraoperative nerve monitoring (IONM) for the recurrent laryngeal nerve (RLN) and external branch of the superior laryngeal nerve (EBSLN)? Does it definitively reduce rates of nerve injury?
4. How should IONM findings (e.g., loss of signal) guide intraoperative decision-making, particularly regarding the contralateral lobe in a planned total thyroidectomy?
5. What are the best surgical techniques for meticulous dissection and preservation of the RLN and its branches?
6. How can the EBSLN be reliably identified and preserved during superior pole dissection, and what is the functional impact of its injury?
7. What is the role of energy-based devices (e.g., Harmonic Scalpel, LigaSure) in thyroid surgery for hemostasis and dissection? Do they offer advantages over traditional techniques?
8. Are there emerging technologies or surgical adjuncts (e.g., AI-assisted surgical navigation, augmented reality) that could enhance precision or safety in thyroid surgery?
9. What are the principles of oncologic thyroid surgery, including en bloc resection for invasive cancers and appropriate lymph node compartment dissection?
10. How does reoperative thyroid or parathyroid surgery differ in complexity and risk compared to primary surgery?

#### **12.3 Parathyroid Preservation and Management of Complications**

1. What are the most effective intraoperative techniques for identifying and preserving parathyroid glands and their vascular supply during thyroidectomy (e.g., capsular dissection, meticulous ligation)?
2. Does routine use of parathyroid autofluorescence (e.g., near-infrared imaging) during thyroidectomy significantly reduce rates of inadvertent parathyroid excision or postoperative hypoparathyroidism compared to meticulous visual inspection alone?
3. What are the indications for and optimal techniques of parathyroid autotransplantation (e.g., site of implantation, number of glands, tissue preparation)? What is the expected success rate?
4. How should transient postoperative hypocalcemia be managed (oral calcium +/- calcitriol, IV calcium)? What are the criteria for discharge and outpatient monitoring?
5. What is the definition of permanent hypoparathyroidism after thyroidectomy, and what is its incidence in high-volume centers?
6. What are the long-term management strategies for chronic hypoparathyroidism, including optimization of calcium, vitamin D analogs, and the role of recombinant PTH (rhPTH(1-84))?
7. What are the risk factors for postoperative RLN injury (transient and permanent)? How is it diagnosed and managed (e.g., voice therapy, vocal cord medialization procedures)?
8. What are the best practices for prevention, recognition, and management of postoperative hematoma, seroma, or surgical site infection after thyroidectomy?
9. What is the management of chyle leak, a rare complication of extensive neck dissection?
10. How can patient-reported outcomes regarding voice, swallowing, and calcium-related symptoms be systematically collected and used to improve quality of surgical care?

#### **12.4 Surgeon Volume and Outcomes**

1. What is the relationship between surgeon volume (annual number of thyroidectomies performed) and patient outcomes, including complication rates (RLN injury, hypoparathyroidism), length of stay, and cost?
2. Is there a minimum surgeon volume threshold below which thyroidectomy outcomes are significantly worse? How should this inform referral patterns or centralization of care?
3. Does hospital volume also correlate with thyroidectomy outcomes, independent of surgeon volume?
4. How does specialized training (e.g., endocrine surgery fellowship) impact thyroidectomy outcomes?
5. What are the key components of a high-quality thyroid surgery program (e.g., multidisciplinary team, standardized protocols, outcomes tracking)?
6. How can simulation and advanced training models be used to improve surgical skills and decision-making in thyroid surgery, particularly for less common or complex procedures?
7. What are the challenges in implementing and enforcing volume standards for thyroid surgery?
8. How do surgeon experience and technique impact the completeness of cancer resection and risk of recurrence in DTC?
9. Are there differences in outcomes for thyroid surgery performed by general surgeons versus specialist endocrine surgeons?
10. What metrics should be used for ongoing quality assessment and continuous quality improvement in thyroid surgery?

### **Section 13: Management of Thyroid Cancer**

#### **13.1 Pathology, Staging, and Molecular Markers**

1. What are the key changes and clinical implications of the most recent WHO classification of thyroid tumors (e.g., NIFTP, high-grade DTC)?
2. How does the AJCC/TNM staging system (currently 8th edition) for DTC risk-stratify patients, and what are its limitations?
3. How should molecular marker status (e.g., BRAFV600E,RAS,TERT promoter mutations, RET/PTC,PAX8/PPARγ) be integrated with clinicopathological features to refine initial risk stratification (e.g., ATA risk categories) for DTC?
4. Does the presence of a TERT promoter mutation, particularly in conjunction with BRAF or RAS mutations, warrant upstaging or more aggressive initial therapy in DTC?
5. What is the prognostic significance of specific BRAF non-V600E mutations or other less common driver mutations in PTC?
6. How can gene expression classifiers or multi-gene panels further enhance prognostication in DTC beyond individual mutations?
7. What is the clinical utility of assessing tumor mutational burden (TMB) or microsatellite instability (MSI) status in advanced or aggressive thyroid cancers?
8. Are there specific pathological features (e.g., tumor subtype, extent of vascular invasion, mitotic count, Ki-67 index) that strongly predict recurrence or mortality in DTC, independent of stage?
9. How is poorly differentiated thyroid carcinoma (PDTC) defined pathologically (e.g., Turin criteria), and what is its typical clinical behavior and prognosis?
10. What is the role of preoperative molecular testing on FNA samples in guiding the extent of initial surgery for DTC (e.g., lobectomy vs. total thyroidectomy +/- CND)?

#### **13.2 Differentiated Thyroid Cancer (DTC - Papillary, Follicular)**

1. What are the current indications for radioactive iodine (RAI) remnant ablation (RRA) after total thyroidectomy for DTC, based on ATA risk stratification? Who can safely avoid RRA?
2. If RRA is indicated, what is the optimal administered activity of 131I (e.g., 30 mCi vs. 100+ mCi)? Does a "one-size-fits-all" approach apply, or should it be risk-adapted?
3. What is the role of recombinant human TSH (rhTSH) versus thyroid hormone withdrawal for preparation for RRA or diagnostic 131I scanning? What are the pros and cons?
4. What are the goals of TSH suppression therapy with levothyroxine after initial treatment for DTC? What are the risk-adapted TSH targets (e.g., <0.1, 0.1-0.5, 0.5-2.0 mU/L)?
5. What is the optimal duration of intensive TSH suppression, and when can targets be relaxed in low-risk patients with excellent response to therapy?
6. What are the potential long-term adverse effects of TSH suppression (atrial fibrillation, osteoporosis), and how can they be monitored and mitigated?
7. How should recurrent or persistent locoregional DTC (neck lymph nodes, thyroid bed) be managed (e.g., surgery, RAI, external beam radiotherapy (EBRT), observation)?
8. What is the management of distant metastases from DTC (e.g., pulmonary, bone)? When is systemic therapy indicated versus localized treatments (surgery, EBRT, ablation)?
9. For RAI-refractory advanced/metastatic DTC, what are the indications for initiating systemic therapy with multi-kinase inhibitors (MKIs) like lenvatinib or sorafenib?
10. How should MKIs be selected and sequenced? What are their comparative efficacy and toxicity profiles? How are MKI-related adverse events best managed to maintain quality of life and dose intensity?
11. What are the primary mechanisms of acquired resistance to lenvatinib or sorafenib in RAI-refractory DTC, and can these be targeted to restore sensitivity or improve outcomes with subsequent therapies?
12. Is there a role for "drug holidays" or intermittent dosing with TKIs?
13. What is the role of EBRT in the management of DTC (e.g., for unresectable gross residual disease, painful bone metastases, prevention of airway compromise)?
14. Are there emerging targeted therapies (e.g., selective RET inhibitors like selpercatinib/pralsetinib for RET-fusion PTC, selective BRAF/MEK inhibitors) or immunotherapies for specific molecular subtypes of advanced DTC?
15. How does dynamic risk stratification (DRS) throughout follow-up guide ongoing management and surveillance intensity in DTC patients?

#### **13.3 Medullary Thyroid Cancer (MTC)**

1. What is the importance of routine preoperative serum calcitonin measurement in patients with thyroid nodules, particularly if suspicious for MTC or with a family history?
2. What is the optimal extent of initial surgery for MTC (total thyroidectomy with prophylactic bilateral CND and often level VI/VII dissection)? When is lateral neck dissection indicated?
3. What is the role of germline RET mutation testing in all patients diagnosed with MTC to identify hereditary syndromes (MEN2A, MEN2B, FMTC) and guide family screening?
4. How do specific RET codons (e.g., M918T in MEN2B) correlate with MTC aggressiveness and age of onset, influencing timing of prophylactic thyroidectomy in carriers?
5. What is the role of adjuvant therapy (e.g., RAI, EBRT) after surgery for MTC? (Generally not effective for MTC).
6. How are postoperative calcitonin and CEA levels used for surveillance and detection of persistent/recurrent MTC? What do doubling times signify?
7. What imaging modalities (ultrasound, CT, MRI, 18F-DOPA PET, 68Ga-DOTATATE PET) are most sensitive for localizing recurrent or metastatic MTC?
8. What are the indications for systemic therapy in advanced/metastatic MTC?
9. What is the efficacy and safety of MKIs approved for MTC (vandetanib, cabozantinib)? How are they selected and managed?
10. What is the role of selective RET inhibitors (selpercatinib, pralsetinib) in RET-mutated advanced MTC, and how do they compare to older MKIs?
11. Is there a role for peptide receptor radionuclide therapy (PRRT) (e.g., 177Lu-DOTATATE) in somatostatin receptor-positive metastatic MTC?
12. How should patients with MEN2A/2B be managed for associated conditions (pheochromocytoma, hyperparathyroidism)?
13. What is the management of MTC during pregnancy?
14. What are the challenges in treating MTC that is not RET-mutated?
15. What is the prognosis for sporadic versus hereditary MTC?

#### **13.4 Anaplastic (ATC) and Poorly Differentiated (PDTC) Thyroid Cancer**

1. How can a rapid and accurate diagnosis of anaplastic thyroid cancer (ATC) be achieved, often requiring integration of clinical presentation, imaging, cytology/biopsy, and immunohistochemistry?
2. What is the role of immediate molecular testing (e.g., for BRAFV600E, NTRK fusions, TMB, PD-L1) in guiding systemic therapy for ATC?
3. What is the optimal multidisciplinary management approach for ATC, considering its aggressive nature and poor prognosis?
4. Is there a role for neoadjuvant therapy (chemotherapy, targeted therapy +/- radiation) to downstage initially unresectable ATC and potentially enable surgery?
5. In which highly selected patients with ATC is surgical resection (R0 or R1) feasible and potentially beneficial for locoregional control or survival?
6. What are the current systemic therapy options for ATC, including conventional chemotherapy (e.g., taxanes, anthracyclines, platinums), targeted therapy (e.g., dabrafenib/trametinib for BRAF-mutated ATC, larotrectinib/entrectinib for NTRK-fusion ATC), and immunotherapy (e.g., pembrolizumab)?
7. What is the role of palliative radiation therapy for symptom control in ATC?
8. How can supportive care and early integration of palliative care improve quality of life for patients with ATC?
9. What are the diagnostic criteria for poorly differentiated thyroid carcinoma (PDTC), and how does its clinical behavior bridge DTC and ATC?
10. What is the optimal treatment strategy for PDTC, which may involve aggressive surgery, RAI (if avid), EBRT, and potentially systemic therapies similar to ATC or aggressive DTC? Is there a standard of care?

#### **13.5 Long-Term Surveillance, Quality of Life, and Advanced Disease Management**

1. What constitutes an "excellent response," "biochemical incomplete response," "structural incomplete response," or "indeterminate response" in DTC surveillance, and how does this guide follow-up intensity?
2. What is the optimal frequency and combination of surveillance tools (serum Tg/TgAb, neck ultrasound, diagnostic WBS, cross-sectional imaging) based on initial risk and dynamic risk assessment?
3. How should Tg elevation with negative imaging (TENIS) or TgAb-positive patients with rising TgAb levels be managed and investigated?
4. What are the common long-term physical and psychosocial sequelae of thyroid cancer and its treatments (e.g., hypothyroidism, hypoparathyroidism, voice changes, dry mouth, fatigue, anxiety, fear of recurrence)?
5. How can patient-reported outcome measures (PROMs) be integrated into routine thyroid cancer survivorship care to identify and address unmet needs?
6. What are effective interventions (pharmacologic, rehabilitative, psychological) to improve quality of life and manage long-term symptoms in thyroid cancer survivors?
7. What is the approach to managing RAI-refractory bone metastases to prevent skeletal-related events (SREs), including bisphosphonates, denosumab, EBRT, and orthopedic intervention?
8. How should symptomatic brain metastases from thyroid cancer be managed?
9. What are the criteria for transitioning from curative-intent therapy to palliative care in patients with widely metastatic, progressive thyroid cancer?
10. Are there specific nutritional or lifestyle recommendations for thyroid cancer survivors to optimize health and potentially reduce recurrence risk?

### **Section 14: Thyroid Disease in Special Populations**

#### **14.1 Pregnancy and Postpartum Period**

1. What are the current recommendations for universal versus targeted case-finding for thyroid dysfunction in early pregnancy? What are the arguments for each approach?
2. What are the optimal trimester-specific reference ranges for TSH and FT4, and how should they be established (laboratory-specific vs. general guidelines)?
3. What is the evidence linking maternal subclinical hypothyroidism or isolated hypothyroxinemia during pregnancy to adverse neurodevelopmental outcomes in offspring? Does treatment improve these outcomes?
4. What is the optimal TSH and/or FT4 target range during each trimester of pregnancy for women with pre-existing hypothyroidism on levothyroxine, and how aggressively should doses be adjusted? Does this vary by maternal TPOAb status?
5. How should newly diagnosed overt or subclinical hypothyroidism during pregnancy be managed?
6. What are the risks of using methimazole versus PTU for Graves' hyperthyroidism during the first trimester versus later pregnancy and lactation? What is the current best practice?
7. What is the target FT4/TSH for pregnant women on ATDs? How can fetal/neonatal thyroid dysfunction due to ATD passage be monitored and managed?
8. What is the role of TRAb measurement during pregnancy in women with Graves' disease to predict fetal/neonatal hyperthyroidism?
9. How should thyroid nodules or thyroid cancer discovered during pregnancy be evaluated and managed? When is surgery indicated versus deferred