



# Thyroid Nodules: Investigation and Management

Practice Based Small Group Learning Program

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## INTRODUCTION

It is common to find thyroid nodules in adults incidentally during a physical examination or imaging of the neck. Frequency increases with age. Although the majority of these nodules are benign, approximately 5 to 15% may be malignant, depending on age, sex, family history and previous radiation exposure. Thyroid nodules present several challenges to primary care providers starting with the initial assessment and conducting appropriate investigations, to determining which nodules can be followed up in the primary care setting and which require referral and specialist management.

## OBJECTIVES

This module will enable clinicians to:

- Understand the initial approach to the management of thyroid nodules based on the presentation.
- Order thyroid imaging appropriately.
- Use clinical judgment based on investigations to help determine the appropriate follow-up for thyroid nodules.

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## CASES

### Case 1: Isabelle, female, age 25

Isabelle presents today to renew her oral contraceptive. To your knowledge, she is healthy. She wonders, however, about a lump or swollen gland (she isn't sure which it is) she found on her neck 2 to 3 months prior. She tells you that the lesion is not painful and doesn't seem to have gotten larger. On examination, you determine that this is likely to be a thyroid nodule measuring approximately 1 cm.

***What further information would be helpful?***

***Based on your examination, what would be your next step?***

### Part Two

Isabelle returns for the results of the ultrasound and thyroid stimulating hormone (TSH) test you ordered. The ultrasound found a 1.5 cm solid solitary nodule. Her TSH is 3.58 mU/L (normal 0.5 to 4.5 mU/L). In terms of thyroid disease or neoplasia, her personal and familial history is unremarkable. She has no known exposure to radiation.

***What would be your approach for Isabelle at this point?***

**Part Three**

Isabelle returns two weeks after fine needle aspiration (FNA) biopsy, which reported benign tissue.

**How would you counsel Isabelle?**

**What would be your management strategy if the results of the biopsy had been “atypia or follicular lesion of undetermined significance”?**

**Case 2: Marie-France, female, age 68**

Marie-France sees you today to follow up on previous investigations of a transient ischemic attack (TIA). She was treated for hypertension and has not experienced any new symptoms since the first episode. Relevant investigations are normal, but the carotid Doppler, done by an internist, mentioned a 0.8 cm solitary nodule of the right thyroid lobe. Marie-France is reassured by the other results but wonders about this nodule, since a friend of hers had thyroid cancer the previous year.

**If you decide on further investigations, what factors might influence your decision?**

**Case 3: Nick, male, age 55**

Six weeks ago, you performed a periodic health exam on Nick, a new patient. At that time, you noticed a firm nodule approximately 1.5 cm on the left lobe of his thyroid. A careful review of his past medical history was unremarkable and there were no other relevant findings on his physical examination. He returns today to discuss his blood test and ultrasound results. His TSH is 0.11 mU/L and other test results are unremarkable. The ultrasound reports a single solid nodule of 1.4 cm with no calcification and no adenopathy.

**How would you proceed?**

**Part Two**

The radionuclide scan shows a “hot” nodule in the same area as the nodule seen on ultrasound.

**Based on the results of the scan, what might be your next steps with Nick?**

**How would you proceed if the ultrasound had shown multiple nodules, with the largest being 1.4 cm, but no calcification, and Nick had normal or elevated TSH?**

**INFORMATION SECTION**

1. *Definition and description:* “A thyroid nodule is a discrete lesion within the thyroid gland that is palpably or ultrasonographically distinct from the surrounding thyroid parenchyma. A *solitary nodule* exists within a thyroid gland of normal dimensions and morphology, whereas a *dominant thyroid nodule* exists within a diffuse or multinodular goiter.”<sup>1</sup> Thyroid cysts make up 15 to 25% of thyroid nodules resulting from congenital, developmental, or neoplastic causes.<sup>2</sup>
2. *Prevalence of thyroid nodules*
  - Palpable nodules: 4 to 7% of adults;<sup>3</sup> palpation does not usually detect nodules < 1 cm.<sup>4</sup>
  - Nodules identified incidentally on ultrasound of the neck: up to 40% of patients.<sup>5</sup>
  - Nodules identified at autopsy: 36 to 50% of individuals.<sup>3</sup>
  - By age 90, virtually everyone has thyroid nodules.<sup>6</sup>
3. Thyroid cancer statistics from the Canadian Cancer Society indicated that approximately 6,000 Canadians (1,350 men and 4,600 woman) would be diagnosed with thyroid cancer in 2014 (<http://www.cancer.ca/en/cancer-information/cancer-type/thyroid/statistics/>). In 2010, 182 Canadians died from thyroid cancer.
4. *Objective of evaluation:* The primary objective of evaluating thyroid nodules is to identify or rule out the presence of malignancy. Although thyroid nodules are extremely common, the vast majority are benign.
  - The availability of advanced imaging techniques now allows identification of many previously undetectable and asymptomatic thyroid nodules.
  - Some malignant nodules can lack clinical importance, as thyroid cancer can be found incidentally at autopsy after death from an unrelated cause.<sup>6</sup>

- It is also important to identify or rule out hyperfunctioning nodules and toxic multinodular goitre.<sup>1</sup>
  - The challenge for primary care clinicians is to determine which nodules need investigation and intervention.<sup>6</sup>
5. *Malignancy in thyroid nodules:*
- For most adults, the risk of malignancy in a thyroid nodule is approximately 5 to 15%.<sup>7,8</sup>
  - Although the risk of malignancy in thyroid nodules is estimated to be as high as 27% in children < 18 years of age, these nodules are rare, with an incidence of 1 to 2%.<sup>9,10</sup>
  - The risk of malignancy is similar in patients both with and without Hashimoto's thyroiditis.<sup>1</sup>
  - Single and multiple nodules of similar sizes have the same risk of malignancy.
  - Although thyroid nodules develop faster in pregnant women, the thyroid cancer rate is no higher than the average population and the evaluation is no different than with other patients.<sup>11</sup>
  - 90% of all thyroid malignancies are differentiated papillary or follicular thyroid carcinomas and about 15% of differentiated thyroid carcinomas may metastasize.
  - Following surgery, patients < 40 years with localized papillary thyroid carcinoma have a 98% 25-year survival rate.
  - The prognosis for follicular thyroid cancer (about 9% of thyroid nodule cancers) is similar. The mortality rate of 0.5/100,000 is very low and compares to that of tuberculosis.<sup>6</sup>
6. *Malignancy in multinodular goitre versus solitary nodules:* A systematic review and meta-analysis compared the prevalence of thyroid cancer in multinodular goitre and in solitary nodules. From the identified 14 studies involving 23,565 patients with multinodular goitre and 20,723 patients with solitary nodules, multinodular goitre was associated with a lower risk of thyroid cancer than solitary nodules: pooled odds ratio (OR) 0.8 (95% confidence interval 0.67–0.96). Subgroup analysis indicated this difference may be skewed by studies conducted outside the United States, particularly in iodine-deficient areas. American studies found no difference in the risk of thyroid cancer between multinodular goitre and solitary nodules.<sup>12</sup>
7. The U.S. Preventive Services Task Force currently does not recommend screening for thyroid nodules in the average risk population using either physical exam or ultrasound (there is currently no Canadian guideline on thyroid screening).<sup>13</sup> These recommendations, however, are presently being reviewed as of the writing of this module.

## INITIAL ASSESSMENT OF THE PATIENT AND NODULE

8. At discovery, all thyroid nodules should be assessed in the same way, regardless of how they were discovered (carotid Doppler, physical examination, patient complaint, computed tomography), as all discovered nodules carry a similar risk of neoplasia.<sup>4</sup>
9. Initial investigation of a patient with a thyroid nodule consists of a history and physical examination focused on the thyroid gland and the cervical lymph nodes; an assessment of TSH levels; and an ultrasound evaluation of the thyroid and neck. Generally, only nodules > 1 cm require further investigation. For nodules < 1 cm, the exception occurs in the presence of suspicious ultrasound results, lymphadenopathy, history of irradiation, or family history.<sup>11</sup>
10. *History:* It is important to identify potential risk factors for malignancy as they relate to patient history. These include the following:<sup>6,7,11</sup>
- Age < 30 years (especially children) or > 60 years.
  - Symptoms of tracheal or esophageal compression, such as persistent hoarseness, dysphagia, or dysphonia.
  - Painless mass enlarging rapidly.
  - Pain lasting several weeks.
  - Radiation therapy at < 20 years of age.
  - Family history of thyroid cancer, multiple endocrine neoplasia type 2.
  - Familial syndromes (Gardner [familial adenomatous polyposis], Cowden [a PTEN hamartoma syndrome], Pendred, Werner, Carney) in a first-degree relative.
11. *Physical examination:* Potential indicators of malignancy include the following:<sup>6,11</sup>
- Fixed and/or hard mass.
  - Palpable cervical lymphadenopathy.
  - Obvious respiratory abnormality.
  - Stridor associated with a goitre.
  - Visible vocal cord abnormality.
12. *Thyroid stimulating hormone (TSH):* Although most patients with thyroid nodules are euthyroid, serum TSH is strongly recommended as a standard part of evaluation of thyroid nodules. An increased risk of malignancy is linked to high-normal and high TSH.<sup>11</sup>
13. *Imaging Ultrasound:* Ultrasound is the imaging modality of choice,<sup>4</sup> and is strongly recommended for all known or suspected thyroid nodules.<sup>11</sup> Ultrasound is more sensitive in detecting thyroid nodules than physical examination and scintigraphy.<sup>1</sup> A well-performed case-control study found the

following ultrasound characteristics associated with malignancy: completely solid nodules, nodules > 2 cm, and nodules with microcalcifications.<sup>6</sup> Pure cystic nodules are generally benign.<sup>1</sup>

14. *Imaging Scintigraphy:* In patients with below-normal TSH, Technetium 99 is the radiopharmaceutical of choice and is strongly recommended for thyroid evaluation.<sup>1</sup> In patients with suppressed TSH levels, radionuclide scintigraphy can differentiate between hyperfunctioning (“hot”) nodules, an overactive thyroid gland, normally functioning nodules (“warm”) and non-functioning (“cold”) nodules. Approximately 5% of nodules are thought to have escaped normal regulation and autonomously produce thyroid hormone.<sup>8</sup> American and European Thyroid Association recommendations indicate that thyroid scintigraphy may also be considered for:
- Patients with low-normal TSH (< 0.6 mU/L) who also live in an iodine-deficient region and present with a multinodular goitre.
  - Patients who refuse FNA.<sup>14</sup>

#### FINE NEEDLE ASPIRATION (FNA)

15. *Nodules requiring FNA:*<sup>4,6</sup>
- Nodules > 1 cm in size or > 0.5 cm in the presence of risk factors.
  - Nodules in a multinodular goitre — assess nodules independently. If meeting criteria, in general biopsy two or three; more assessment may be unnecessary.
  - Nodules with extracapsular invasion or other high-risk features on ultrasound.
  - Nodules associated with cervical lymphadenopathy.
  - Nodules in patients with a history of head and neck cancer, thyroid cancer, or familial history of multiple endocrine neoplasia type 2 in a first-degree relative.
  - Benign nodules that demonstrate growth on serial ultrasound during follow-up.
  - FNA results that are repeatedly non-diagnostic or unsatisfactory (see Info point 15). The nodule should be surgically removed for diagnosis.

**Note:** The role of FNA in children is controversial because of uncertainty regarding accuracy. However, some studies indicate accuracy may be as high as 90%, compared with 97% in adults.

16. *Ultrasound-guided FNA:* Overall, ultrasound guidance may increase diagnostic accuracy of FNA and for repeated FNA. It may provide additional helpful information, thereby reducing the rate of inconclusive results.<sup>7</sup> This technique is strongly recommended

to reassess nodules with previous nondiagnostic or unsatisfactory cytopathologic results.<sup>11,15</sup> Ultrasound-guided FNA is useful for nonpalpable nodules and nodules deep within the thyroid.<sup>1</sup> Cystic nodules should also be assessed with ultrasound-guided FNA, as it is important to sample the solid portion of the nodule.<sup>4</sup>

17. *Bethesda system for reporting thyroid cytopathology:* Most large centres in Canada use the Bethesda reporting system, which allocates each FNA sample to a specific diagnostic category as follows:<sup>15</sup>
- Nondiagnostic or unsatisfactory (2 to 20% of cases)\*
  - Benign
  - Atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS)
  - Follicular neoplasm or suspicious for a follicular neoplasm
  - Suspicious for malignancy
  - Malignant
- \*Note:** A repeat FNA with ultrasound guidance is recommended for all nondiagnostic or unsatisfactory samples.<sup>15</sup>

18. Usually, FNA accurately classifies nodules. False-negative (benign cytology and malignant histology) rates range from 1 to 11%<sup>11,16,17</sup> and false-positive (indeterminate or malignant cytology and benign histology) about 2%. It is important to note that many trials exclude indeterminate results from calculations of sensitivity, specificity, and positive and negative predictive values, contributing to the low levels listed above.<sup>6</sup> “Suspicious for follicular neoplasm” samples have a risk of malignancy of 15 to 30%.<sup>16</sup> “Suspicious for malignancy” samples have a 60 to 75% chance of malignancy.<sup>16,18</sup> Up to 7% of nodules with repeatedly indeterminate results may be malignant.<sup>11</sup>

19. In order to avoid unnecessary surgery, indeterminate category results (AUS or FLUS) may be further categorized by molecular testing. Such tests include somatic mutation testing, mRNA gene expression platforms, protein immunocytochemistry and mRNA panels — mRNA and protein immunocytochemistry are not currently routinely available in Canada. Although none are perfectly accurate and availability and cost may limit their use, molecular testing in the future may become an important part of diagnosis.<sup>19</sup>

20. Differential diagnosis of thyroid nodules:<sup>1,6</sup>

<p><b>Benign thyroidal neoplastic lesions</b></p> <ul style="list-style-type: none"> <li>• Dominant portion of multinodular goitre</li> <li>• Adenomas (various)</li> </ul>	<p><b>Thyroidal non-neoplastic lesions</b></p> <ul style="list-style-type: none"> <li>• Cysts</li> <li>• Agenesis of thyroid lobe</li> <li>• Thyroiditis</li> <li>• Remnant hyperplasia (postoperative or post-radioiodine)</li> </ul>
<p><b>Malignant thyroidal neoplastic lesions</b></p> <ul style="list-style-type: none"> <li>• Papillary carcinoma (88%)</li> <li>• Follicular carcinoma (9%)</li> <li>• Hürthle cell carcinoma</li> <li>• Medullary carcinoma (&lt; 2%)</li> <li>• Anaplastic carcinoma (&lt; 2%)</li> <li>• Metastasis (rare)</li> </ul>	<p><b>Nonthyroidal lesions</b></p> <ul style="list-style-type: none"> <li>• Parathyroid cyst or adenoma</li> <li>• Inflammatory or neoplastic lymph node</li> <li>• Aneurysm</li> <li>• Cele of bronchus</li> <li>• Laryngocele</li> </ul>

21. *Nodules requiring surgery for diagnosis:* Nodules > 4 cm should be assessed through diagnostic lobectomy, rather than FNA, in order that malignancy is not missed.<sup>4</sup>

**REFERRAL OF PATIENTS WITH THYROID NODULES**

22. *Referral guidelines* (British Thyroid Association, Royal College of Physicians [UK])

- a) *Manage in primary care:*<sup>20</sup>
  - Nodules that have not changed in years.
  - Asymptomatic non-palpable nodules < 1 cm in diameter with no suspicious features.
- b) *Refer non-urgently:*<sup>20</sup>
  - Nodules in patients with abnormal thyroid function tests.
  - Sudden onset of pain in a nodule (likely bleeding into benign cyst).
  - New nodule.
  - Nodule that has increased in size over months.

- c) *Refer urgently (< 2 weeks):*<sup>20</sup>
  - Nodules with any of the following features suggesting malignancy: large size (> 4 cm), rapid growth, pain, hard texture, lymphadenopathy, hoarseness, and stridor (same-day referral).
  - Nodules in children.
  - Family history of thyroid cancer or history of irradiation of neck.

**TREATMENT AND FOLLOW-UP**

23. *Small, incidental nodules:* Both the American Thyroid Association and the British Thyroid Association recommend that no further investigations are required for small nodules (< 1 cm) that are discovered incidentally through imaging but without worrisome features.<sup>11,20</sup>

24. *Nodules in children:* The American Thyroid Association strongly recommends that nodules in children be managed the same way as nodules in adults.<sup>11</sup> A meta-analysis concluded that there is good evidence in favour of FNA biopsy (especially with ultrasound guidance)<sup>10</sup> as a useful tool for excluding malignancy in a pediatric population.<sup>22</sup> Excision of nodules/lobectomy,<sup>9,10</sup> however, may be considered for direct, initial assessment in younger children who cannot tolerate an FNA. If the nodule turns out to be positive for cancer, total thyroidectomy should follow.<sup>10</sup>

25. *Nodules in pregnant women:* Initial evaluation is the same as for nonpregnant individuals.

- The American Thyroid Association strongly recommends FNA, if required, for euthyroid and hypothyroid women.
- A retrospective study suggests that delaying treatment for < 1 year after a thyroid cancer diagnosis does not affect outcome.
- Thyroid surgery is associated with more complications in pregnant than in nonpregnant women.
- It is strongly recommended that a radionuclide scan be performed after pregnancy and cessation of lactation in women with suppressed TSH.<sup>11</sup>
- Pregnant patients with abnormal TSH or FNA would be referred to an endocrinologist for further evaluation.<sup>20</sup>

26. *Benign nodules:*

- Because of the false negative rate (up to 5%)<sup>11</sup>, within 6 to 12 months, it is important to follow up on nodules that are benign on FNA with ultrasound.
- If there is no change in size, repeat ultrasound should be performed 12 to 24 months later; The American Thyroid Association and international bodies recommend that the follow-up interval be increased to 3 to 5 years.<sup>4</sup>
- There is fair evidence to recommend ultrasound-guided FNA for nodules with growth exceeding 20% in at least two dimensions, or 2 mm.  
**Note:** Growth of mixed cystic-solid nodules refers to the solid component only.
- Symptomatic benign solid nodules may be surgically removed.<sup>21</sup>

27. *Cystic nodules:* Cystic nodules are generally drained. There is moderate evidence for surgical removal (generally hemithyroidectomy) or ethanol injection in the case of symptomatic cystic nodules that recur or pose a cosmetic concern.<sup>11</sup>

28. *Hyperfunctioning nodules:* Patients with suppressed TSH are referred to an endocrinologist for evaluation.<sup>20</sup> The first-line treatment for hyperfunctioning nodules is iodine 131 ablation, which does not damage the gland outside the nodule.<sup>4</sup> Thyroid storm may occur with multinodular goitre. It is less common with a solitary toxic nodule and is usually less severe, but caution is required given the severity of this condition.<sup>23</sup>

29. *Cytology suggesting malignancy:* If cytology suggests malignancy, surgery is strongly recommended.<sup>11</sup> These patients would be referred to a surgeon.<sup>20</sup> Differentiated thyroid malignancies require thyroid surgery. Additional diagnostic workup is strongly recommended for anaplastic malignancies, metastatic lesions, and lymphoma.<sup>21</sup>

**THE BOTTOM LINE**

- Perform a history and physical examination and order TSH and ultrasound for initial investigation of thyroid nodules.
- Order FNA on nodules in patients with elevated or normal TSH levels.
- Order scintigraphy in patients with suppressed TSH levels.
- Manage benign nodules in primary care.

**CASE COMMENTARIES****Case 1: Isabelle, female, age 25*****What further information would be helpful?***

With thyroid nodules, several risk factors for malignancy can be identified with a good history, including associated persistent pain, a family history of thyroid cancer, problems swallowing, rapid growth of the nodule, and childhood radiation (Info points 9, 10). Relevant findings on physical examination include attachment of the nodule to surrounding tissues and palpable cervical lymphadenopathy (Info point 11).

***Based on your examination, what would be your next step?***

Guidelines suggest that nodules  $\geq 1$  cm should be investigated (Info point 9). Appropriate investigations at this stage are TSH and ultrasound (Info points 12, 13; Appendix 1).

**Part Two*****What would be your approach for Isabelle at this point?***

The size of the nodule is a concern (Info point 15). In addition, solid nodules are more likely to harbour malignancy than cystic nodules (Info point 13). FNA is both accurate and cost effective and is the procedure of choice to evaluate thyroid nodules (Info points 15–19; Appendix 1). Isabelle should be referred for FNA of this nodule to a surgeon or interventional radiologist.

**Part Three*****How would you counsel Isabelle?***

It is important to reassure Isabelle that benign nodules are common and not a clinical concern (Info point 5). Appropriate follow up in this case is to monitor clinically and repeat the ultrasound in 6 to 12 months, as there is a slight chance of a false negative biopsy (Info point 26).

***What would be your management strategy if the results of the biopsy had been “atypia or follicular lesion of undetermined significance”?***

With indeterminate nodules, it is important to repeat the FNA, preferably with ultrasound guidance, within a reasonable time frame (such as several weeks) (Info points 16, 18, 19; Appendix 1). A second indeterminate biopsy result may warrant referral to a surgeon for core biopsy, further molecular testing, or excision for larger nodules or close follow up with ultrasound for smaller nodules (Info points 19, 21; Appendix 1).

**Case 2: Marie-France, female, age 68**

***If you decide on further investigations, what factors might influence your decision?***

Non-palpable lesions have the same risk of malignancy as palpable ones and should be investigated the same way (Info points 5, 8). Based on the size of the nodule, it can be followed in the primary care setting (Info points 22, 23). Clinical findings would be the primary influence on your decision as to appropriate follow up of this nodule. Relevant factors from the history include any associated pain or other symptoms, such as problems swallowing; a family history of thyroid cancer; and childhood radiation (Info point 10; Appendix 1). Physical findings that are of concern are attachment of the nodule to surrounding tissues and palpable cervical lymphadenopathy (Info point 11). Her age (> 60 years) is also a risk factor for malignancy (Info point 10).

The patient's concern about the nodule may also be a factor in determining your follow-up strategy. Although guidelines suggest 1 cm as a cut-off size for investigation, in this situation it may be appropriate to perform a TSH and dedicated ultrasound of the thyroid (Info points 12, 13). Assuming that the TSH is normal and the ultrasound shows no change from the original carotid Doppler, ultrasound could be repeated in six months looking for stability in the size of the nodule (Info point 26). Stable ultrasound results can reassure the patient that there is no need to be concerned about the nodule.

**Case 3: Nick, male, age 55**

***How would you proceed?***

It is appropriate to order a radionuclide scan (Info point 14; Appendix 1) and refer Nick to an endocrinologist or internist on an urgent (within two weeks) basis, due to the rare risk of thyroid storm (dangerously high heart rate, blood pressure, and body temperature) (Info points 22, 28). It is important to warn Nick about symptoms of hyperthyroidism and thyroid storm.

**Part Two**

***Based on the results of the scan, what might be your next steps with Nick?***

Although hyperfunctioning nodules do not require FNA, Nick still needs to be seen by endocrinology or internal medicine on an urgent basis (Info point 22). Treatment may consist of surgery or radioactive iodine (Info point 28; Appendix 1).

***How would you proceed if the ultrasound had shown multiple nodules, with the largest being 1.4 cm, but no calcification, and Nick had normal or elevated TSH?***

The frequency of malignancy is similar in single and multiple nodules of a similar size (Info point 6). With normal or elevated TSH, nodules > 1 cm need to be assessed with FNA (Info point 15; Appendix 1). It would therefore be appropriate to refer Nick to an interventional radiologist or a surgeon, and determine follow-up based on biopsy results (Info points 22, 26, 27, 29).

*We always welcome your input. If you would like to provide feedback on this module, the following link will take you to an electronic survey: <http://members.fmpe.org/modulefeedback>*

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*While every care has been taken in compiling the information contained in this module, the Program cannot guarantee its applicability in specific clinical situations or with individual patients. Physicians and others should exercise their own independent judgment concerning patient care and treatment, based on the special circumstances of each case.*

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*Web-based resources cited within the module were active as of July 2015.*

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#### REFERENCE LIST

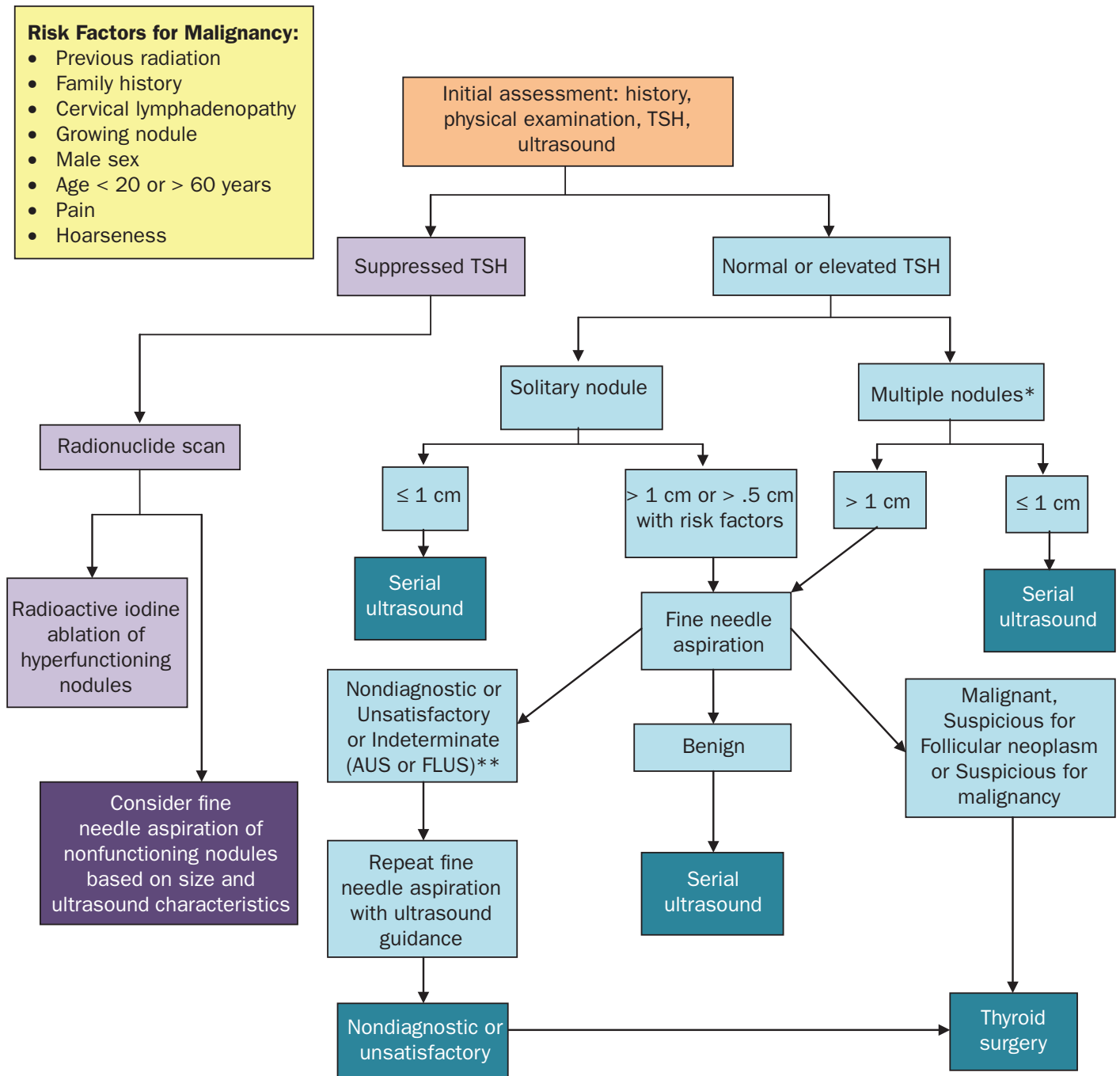
1. Polyzos SA, Kita M, Avramidis A. Thyroid nodules - stepwise diagnosis and management. *Hormones (Athens)*. 2007;6:101-19. PM:17704042.
2. Hodak SP, Mahmud H. Assessment of thyroid mass. *BMJ Best Practice (available by subscription)*. 2013
3. Stang MT, Carty SE. Recent developments in predicting thyroid malignancy. *Curr Opin Oncol*. 2009;21:11-7. PM:19125013.
4. Knox MA. Thyroid nodules. *Am Fam Physician*. 2013;88:193-6. PM:23939698.
5. Yoon DY, Chang SK, Choi CS, et al. The prevalence and significance of incidental thyroid nodules identified on computed tomography. *J Comput Assist Tomogr*. 2008;32:810-5. PM:18830117.
6. Davies L, Randolph G. Evidence-Based Evaluation of the Thyroid Nodule. *Otolaryngol Clin North Am*. 2014;47:461-74. PM:25041951.
7. Mehanna HM, Jain A, Morton RP, Watkinson J, Saha A. Investigating the thyroid nodule. *BMJ*. 2009;338:b733. PM:19286747.
8. Hegedus L, Bonnema SJ, Bendedbaek FN. Management of simple nodular goiter: current status and future perspectives. *Endocr Rev*. 2003;24:102-32. PM:12588812.
9. Iqbal CW, Wahoff DC. Diagnosis and management of pediatric endocrine neoplasms. *Curr Opin Pediatr*. 2009;21:379-85. PM:19421059.
10. Guille JT, Opoku-Boateng A, Thibeault SL, Chen H. Evaluation and management of the pediatric thyroid nodule. *Oncologist*. 2015;20:19-27. PM:25480825.
11. American Thyroid Association Guidelines Taskforce on Thyroid N, Differentiated Thyroid C, Cooper DS, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19:1167-214. PM:19860577.
12. Brito JP, Yarur AJ, Prokop LJ, McIver B, Murad MH, Montori VM. Prevalence of thyroid cancer in multinodular goiter versus single nodule: a systematic review and meta-analysis. *Thyroid*. 2013;23:449-55. PM:23067375.
13. *Draft Research Plan: Thyroid Cancer: Screening*. U.S. Preventive Services Task Force; January, 2015.
14. Burger AG. Should 99mTcO4 Thyroid Scintigraphy Still Be Used In Investigating Thyroid Nodules In Multinodular Goiter. *Clin Thyroidol*. 2013;25:13-5.



15. Cibas ES, Ali SZ. The Bethesda System For Reporting Thyroid Cytopathology. *Am J Clin Pathol*. 2009;132:658-65. PM:19846805.
16. Wang CC, Friedman L, Kennedy GC, et al. A large multicenter correlation study of thyroid nodule cytopathology and histopathology. *Thyroid*. 2011;21:243-51. PM:21190442.
17. Lewis CM, Chang KP, Pitman M, Faquin WC, Randolph GW. Thyroid fine-needle aspiration biopsy: variability in reporting. *Thyroid*. 2009;19:717-23. PM:19485775.
18. Hoang JK, Raduazo P, Yousem DM, Eastwood JD. What to do with incidental thyroid nodules on imaging? An approach for the radiologist. *Semin Ultrasound CT MR*. 2012;33:150-7. PM:22410363.
19. Keutgen XM, Filicori F, Fahey TJ, 3rd. Molecular diagnosis for indeterminate thyroid nodules on fine needle aspiration: advances and limitations. *Expert Rev Mol Diagn*. 2013;13:613-23. PM:23895130.
20. Perros P, Colley S, Boelaert K, et al. Guidelines for the management of thyroid cancer (3rd edition). *Clinical Endocrinology*. 2014;81-supplement 136 pgs.
21. Gharib H, Papini E, Paschke R, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. *J Endocrinol Invest*. 2010;33:51-6. PM:20543551.
22. Stevens C, Lee JK, Sadatsafavi M, Blair GK. Pediatric thyroid fine-needle aspiration cytology: a meta-analysis. *J Pediatr Surg*. 2009;44:2184-91. PM:19944231.
23. Ross DS. Treatment of toxic adenoma and toxic multinodular goiter. In: Cooper DS, ed. *UpToDate*. Waltham, MA: UpToDate; 2015.

Web-based resources cited within the module were active as of July 2015.

## MANAGEMENT OF THYROID NODULES



\*Multiple nodules: the size cut-off for multiple nodules has not been clearly established.

\*\*AUS: atypia of undetermined significance FLUS: follicular lesion of undetermined significance

**Sources**

- 1) Weiss RE, Lado-Abeal J. Thyroid nodules: diagnosis and therapy. *Curr Opin Oncol.* 2002;14(1):46-52.
- 2) Davies L, Randolph G. Evidence-based evaluation of the thyroid nodule. *Otolaryngol Clin North Am.* 2014;47(4):461-74.
- 3) Single thyroid nodule management. *Thyroid manager.* <http://www.thyroidmanager.org/algorithm/single-thyroid-nodule-management> June 25, 2014.

