

# Thyroid Nodules

## *When Is a Lump Cancer?*

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**T**hyroid nodules are among the most common thyroid disorders encountered in routine family practice. Data from the Framingham database show the prevalence rate to be 4.2% (6.4% in women, 1.5% in men). An autopsy study from the Mayo Clinic found a prevalence rate for thyroid nodules of 50.5% in 821 consecutive autopsies.

The above data must be examined in the context of thyroid cancer frequency. For 2001, the American Cancer Society reported 19,500 new cases of thyroid cancer. This represents 1.5% of all new cancers. In the same year, there were 1,300 thyroid cancer-related deaths.

### *How is thyroid cancer diagnosed?*

#### *Clues from the clinical exam*

There are important elements in a patient's history that may suggest a malignant nodule (Table 1).

The physical exam is of little help in distinguishing benign from malignant nodules. Generally, palpable nodules are at least 15 mm in diameter. Although most malignant nodules are firm, the texture of the nodule is a poor

### Rose's case

Rose, 29, comes in for her annual physical exam. She is completely free of complaints. In the course of her exam, a firm, 2-cm nodule is palpated in the left lobe of the thyroid gland. No cervical adenopathy is detected. The remainder of the exam is unremarkable.



**How would you approach this case?**

Table 1

**Elements of patient history that suggest a malignant nodule**

- Male gender (although nodules are less common in women than men, nodules in men are more likely to be malignant)
- Age (age less than 20 or over 60 increases the risk of malignancy)
- Rapid nodule growth (anaplastic carcinoma and lymphoma of the thyroid are among the most rapidly growing thyroid neoplasms)
- Irradiation to the neck, especially before the age of 15

discriminator in determining whether a nodule is malignant. Evidence of local invasion (*e.g.*, a nodule that does not move with swallowing) is an ominous sign consistent with malignancy, but this is seldom found. Any nodule in the company of cervical lymphadenopathy should also raise suspicion for cancer (although benign thyroid conditions, such as Graves' disease and Hashimoto's thyroiditis, may be associated with cervical lymphadenopathy).

On the whole, the clinical exam seldom gives clear clues as to whether a thyroid nodule is benign or malignant, therefore, laboratory investigations are required.

**Laboratory studies**

Thyroid scans are popular with many physicians, but are of little practical help. Although thyroid cancers show up as "cold nodules" on technetium scanning, the overwhelming majority of cold nodules are benign. Because of this, routine use of thyroid scanning in the assessment of thyroid nodules should not be done.

My approach is to first measure the thyroid-stimulating hormone (TSH) level.

- If the TSH is normal, go right to a fine needle aspiration biopsy (FNAB) of the nodule.
- If the TSH is low, do a thyroid scan to see if the nodule is hot. If the nodule is indeed hot, treat with radioactive iodine or surgery; if the nodule is cold or "warm" (a warm nodule is one that takes of the radionucleotide equivalent to the rest of the thyroid gland), biopsy the nodule and treat the concomitant hyperthyroidism.
- If the TSH is high, do a FNAB of the nodule and treat the concomitant hypothyroidism.

With a multinodular goiter, the approach is the same. The first step is to measure TSH.

- If the TSH is normal, go right to a FNAB and sample all nodules > 1 cm in diameter (although the size criteria has been questioned).
- If the TSH is high or low, proceed as you would with a single nodule (as described).

Although we do not traditionally sample small nodules (< 1 cm), a recent study by Papini et al. has questioned this strategy. These authors performed 494 ultrasound-directed FNABs on 402 patients with nodules between 8 mm and 15 mm in diameter. All patients with suspicious

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cytology or a malignant nodule were referred for surgery. Post-operatively, the authors compared the ultrasound findings to the final pathology and noted that 87% of all cancers had similar ultrasound characteristics (Table 2).

The authors extrapolated that if these ultrasound characteristics were to have been applied to their patient population, 125 of 402 patients (31%) would have been sampled and 87% of cancers would have been detected. If only nodules > 1 cm were sampled, 271 of the 402 patients (64%) would have had a biopsy and only 61% of the cancers would have been detected. Using Papini's ultrasound criteria would reduce the number of FNABs by half and yield more cancers than only sampling nodules > 1 cm.

A FNAB can be done as an office procedure or under ultrasound guidance. By doing the biopsy under ultrasound guidance, inadequate samples are less likely, as the tip of the needle can be targeted to the portion of the nodule that would yield the best sample. On the whole, about 10% to 15% of FNABs yield insufficient cytology for an accurate exam. If this is the case, the nodule should be re-biopsied.

About 75% of biopsies yield cytology consistent with a benign nodule and 5% yield cytology consistent with a malignant nodule. Benign nodules are followed conservatively and malignant nodules are, of course, sent to surgery. It is important to note that about 20% of nodules are reported as a "follicular neoplasm". Since 20% of follicular neoplasms are malignant, surgery is indicated in most cases.

Table 2

### Post-operative ultrasound characteristics seen in clinical study

- Nodules were hypoechoic (showing less echoes than the surrounding normal thyroid tissue)
- Nodules had irregular margins
- Nodules either showed evidence of intranodal vascularity or there were microcalcifications

#### Reference

Papini E, Guglielmi R, Bianchini, et al: Risk of malignancy in non-palpable thyroid nodules. J Clin Endocrinol Metab 2002; 87(5):1941-6.

### How is a thyroid nodule managed?

If any malignant or suspicious nodule is found, the patient should undergo surgery. If a well-differentiated thyroid cancer is found at surgery,

*Using Papini's ultrasound criteria would reduce the number of FNABs by half and yield more cancers than only sampling nodules > 1 cm.*

a total thyroidectomy is performed for all tumours > 1 cm.

The management of nodules that demonstrate benign cytology on FNAB is somewhat more controversial. The classic approach to dealing with these nodules is to give suppressive doses of levothyroxine, such that the TSH is suppressed below the lower limit of normal. The rationale for this approach is that TSH is a growth factor for the normal thyroid and, by

extension, it should also be a growth factor for benign thyroid nodules. By suppressing TSH, we effectively remove any stimulus for nodule growth. Unfortunately, there are very few well-conducted studies that have evaluated the effect of suppressive therapy with levothyroxine.

One recent review evaluated only randomized trials where the end point was a 50% reduction in nodule volume. After combining the results of five trials, the response rate for the placebo groups was 15.7%, whereas the response rate for the levothyroxine-treated patients was 26.6%. This finding suggests that only about 10% more benign thyroid nodules shrink with thyroxine as opposed to no treatment.

My approach to any nodule that initially demonstrated benign cytology on FNAB and, subsequently, shows evidence of growth, is to re-biopsy the nodule. If the repeat cytology confirms the nodule is benign, only then would I consider the use of suppressive doses of thyroxine. **Dx**

## Resources

1. Burch HB: Evaluation of and management of the solid thyroid nodule. *Endocrinol Metab Clin North Am* 1995; 24(4):663-710.
2. Papini E, Guglielmi R, Bianchini A, et al: Risk of malignancy in non-palpable thyroid nodules: Predictive value of ultrasound and color-Doppler features. *J Clin Endocrinol Metab* 2002; 87(5):1941-6.
3. Cersosimo E, Gharib H, Suman VJ, et al: "Suspicious" thyroid cytologic findings: Outcome in patients without immediate surgical treatment. *Mayo Clin Proc* 1993; 68(4):343-8.
4. Kuo SW, Hu CA, Pei D, et al: Efficacy of thyroxine-suppressive therapy and its relation to serum thyroglobulin levels in solitary nontoxic thyroid nodules. *J Formos Med Assoc* 1993; 92(1):55-60.

## Frequently Asked Questions

1. **How common are thyroid nodules?**  
They are present in 67% of adults.
2. **Are there any clues on history and physical exam that a thyroid nodule may be malignant?**  
Age, sex, rapid growth, history of irradiation to the neck, evidence of local invasion, and cervical lymphadenopathy are some clues.
3. **How useful is a thyroid scan?**  
A thyroid scan is seldom useful and should not be done as a matter of routine.
4. **How do you interpret the results of a FNAB?**  
About 10% to 15% of FNABs yield insufficient cytology. About 75% of biopsies yield cytology consistent with a benign nodule and 5% yield cytology consistent with a malignant nodule. Twenty per cent of nodules are reported as a "follicular neoplasm".
5. **What is the best way to manage benign thyroid nodules?**  
Generally, no treatment is required; suppressive therapy with thyroxine is seldom helpful.

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