Fine-Needle Aspiration in the Work-Up of Thyroid Nodules

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Fine-needle aspiration (FNA) plays an essential role in the evaluation of patients with a thyroid nodule. It helps to minimize unnecessary thyroid surgery for patients with benign nodules and appropriately triages patients with thyroid cancer to surgery. Before the routine use of thyroid FNA, the percentage of surgically resected thyroid nodules that were malignant was 14%.1 With current thyroid FNA practice, the percentage of resected nodules that are malignant exceeds 50%.2

In October 2007, the National Cancer Institute (NCI) sponsored a multidisciplinary conference in Bethesda, Maryland, to review the state of the science of FNA in the management of thyroid nodules. After the meeting, several summary documents were published.3–6 This article draws heavily on the conclusions reached at that conference.

INDICATIONS FOR FNA

Thyroid nodules are identified by palpation or by an imaging study. Every patient with a palpable thyroid nodule is a candidate for FNA and should undergo further evaluation to determine if an FNA is warranted.7–9 Before the decision is made to perform an FNA, a serum thyrotropin level and thyroid ultrasound (US) should be obtained.7,8–12 Patients with a normal or elevated serum thyrotropin level should proceed to a thyroid US to determine if an FNA needs to be performed. Those with a depressed serum thyrotropin level should have a radionuclide thyroid scan, the results of which should be correlated with sonographic findings.7,9–11,13 In general, functioning thyroid nodules in the absence of significant clinical findings do not require an FNA because the incidence of malignancy is exceedingly low.14 A nodule that appears iso- or

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KEYWORDS

• Thyroid • Fine-needle aspiration • Cytology
• Indications • Terminology
hypofunctioning on radionuclide scan should be considered for FNA based on US findings.7–9

Incidental thyroid nodules (incidentalomas) are detected by fluorodeoxyglucose–positron emission tomography (18FDG-PET), sestamibi, US, CT, and MRI scans. Incidentalomas detected by 18FDG-PET are unusual (2%–3% of all PET scans) but have a higher risk of cancer (14%–50%) compared with the background incidence.15–23 A focally 18FDG-PET–avid thyroid nodule is more likely to be a primary thyroid cancer than metastatic disease to the thyroid, even in patients with an extrathyroidal malignancy. Therefore, a focal nodule that is 18FDG-PET avid is an indication for FNA. This applies only to focal lesions. Diffuse increased uptake on 18FDG-PET does not warrant FNA unless thyroid sonography detects a discrete nodule.

All focal hot nodules detected on sestamibi scans and confirmed by US to be a discrete nodule should undergo FNA. Thyroid incidentalomas detected on sestamibi scans have a higher risk of cancer (22%–66%).24–28

Incidentalomas detected by US (such as carotid Doppler scans or scans done for parathyroid disease) have a cancer risk of approximately 10% to 15% (range 0%–29%)29–40 and should undergo dedicated thyroid sonographic evaluation. Lesions with a maximum diameter greater than 1.0 to 1.5 cm should be considered for biopsy unless they are simple cysts or septated cysts with no solid elements. FNA may also occasionally be replaced by periodic follow-up for nodules of borderline size (between 1.0 and 1.5 cm in maximum diameter) if they have sonographic features that are strongly associated with benign cytology.

A nodule of any size with sonographically suspicious features should also be considered for FNA. Sonographically suspicious features include microcalcifications, hypoechoic solid nodules, irregular/lobulated margins, intranodular vascularity, and nodal metastases (or signs of extracapsular spread). This recommendation is controversial because it includes patients with microcarcinomas, in whom a survival benefit after an FNA diagnosis has not been documented. Nevertheless, the American Thyroid Association,7 the Academy of Clinical Thyroidologists,29 and a collaborative effort of the American Association of Clinical Endocrinologists and the Associazione Medici Endocrinologi41 have outlined this recommendation.3 There are several reasons for this. If a sonographically suspicious nodule is benign by FNA, a patient can be reassured and subsequent follow-up can be less frequent.42 On the contrary, if an FNA reveals that a nodule is malignant, surgery is generally recommended. The natural history of micropapillary carcinomas, however, is not well understood. Most remain indolent, as implied by the 13% prevalence of micropapillary cancers in the United States diagnosed at autopsy examination.43 A minority follow a more aggressive course; this subgroup might be identified by sonographic evidence of lateral cervical node metastases, tumor multifocality, extrathyroidal invasion, or cytopathologic features that suggest a high-grade malignancy.44 The development and application of even more sensitive and specific markers of aggressive potential (including molecular and genetic markers) may one day facilitate the triage of patients with a microcarcinoma.

There are few direct data on the cancer risk of thyroid incidentalomas detected by CT or MRI. Thyroid incidentalomas are seen in at least 16% of patients evaluated by neck CT or MRI.45 The risk of cancer in one study was predicted at 10%, but it included only a few patients who went on to FNA.46 CT and MRI features cannot determine the risk of malignancy, except in advanced cases that are unlikely to be incidental. Until more data are available, incidentalomas seen on CT or MRI should undergo dedicated thyroid sonographic evaluation. Any nodule with sonographically suspicious features (discussed previously) should be considered for FNA. In addition,
lesions that have a maximum diameter greater than 1.0 to 1.5 cm should also be considered for FNA (discussed previously).

PERFORMING THE FNA

FNA can be performed using palpation or US for guidance. The benefits of palpation-guided FNA of thyroid nodules are reduced cost in comparison with US-guided FNA and logistical efficiency: a practitioner can perform the procedure without a US machine or assistance from other practitioners. US evaluation and US guidance, however, can reduce the rates of nondiagnostic and false-negative aspirates and can change the management in 63% of patients with palpable thyroid nodules. In particular, US guidance should be used to aspirate nodules that are not palpable and nodules that have an appreciable (>25%) cystic component. US guidance should also be used if a prior aspiration contained insufficient cells/colloid for interpretation (nondiagnostic result).

TECHNIQUE

The principles of thyroid FNA technique are identical whether or not the needle is inserted using palpation or US for guidance. Commonly available 22- to 27-gauge needles are used for thyroid FNA, but 25- to 27-gauge needles are preferred because the specimens obtained with them tend to be less bloody and are just as cellular (if not more so). A variety of syringe holders are available (Cameco Syringe Pistol, Tao instrument, and Inrad Aspiration Biopsy Syringe Gun), but the intrinsic suction provided by surface tension with smaller diameter needles often makes devices for additional suction unnecessary.

When visualized with US imaging, different areas of large masses should be sampled. If the nodule is complex, the wall, solid elements, and suspicious calcified areas should be sampled while avoiding cystic areas. As a starting point, a dwell time of 2 to 5 seconds within the nodule, with 3 forward and back oscillations per second, usually maximizes cell yield, minimizes blood contamination, and efficiently produces 1 to 2 slides per biopsy pass. The relatively short dwell time (2–5 seconds) per pass that is recommended is not intuitive, but experience has shown that longer dwell times do not offer any significant advantage and often merely dilute the sample with excessive blood. Between 2 and 5 passes per nodule seems reasonable number to optimize the likelihood of obtaining an adequate sample.

Most thyroid FNAs are well tolerated and are not associated with significant patient discomfort or pain. The use of local anesthesia, however, assures that the procedure is not painful and offers peace of mind, resulting in an overall more comfortable experience. For this reason, some experienced FNA physicians use local anesthesia for all thyroid FNAs. Local anesthetic may cause difficulty in subsequent sample evaluation, however. For deep, nonpalpable thyroid nodules that may require more time and probing to reach the nodule, and for all biopsies using needles other than a fine needle, local anesthesia is recommended. The local anesthetic of choice is 1% lidocaine or lidocaine 2% with 1:100,000 epinephrine. Approximately 0.5 mL of anesthetic should
be injected into the subcutaneous tissue overlying the area of directed needle placement for biopsy.\textsuperscript{54}

Aspirated tissue or cyst fluid may be directly smeared on glass slides for air-dried or alcohol-fixed preparations stained by the Romanowsky or Papanicolaou technique, respectively. Liquid-based cytology (LBC) processing can be used alone or as a supplement to direct smears. For LBC, the aspiration needle should be flushed with a small amount (approximately 0.5 mL) of liquid (CytoLyt, CytoRich Red, balanced saline, or Hanks solution) and placed in a Falcon tube for transport to a laboratory. For remote transport or for specimens expected to have delayed processing, a fixative, such as PreservCyt, is necessary for optimal cell preservation. Cell-rich liquid specimens can also be used for cell block preparation when needed. Residual cyst fluid may be submitted to a laboratory fresh or fixed for further processing by LBC or cell block. Direct smears, however, are essential for immediate assessment.

**INFORMATION REQUIRED ON THE REQUISITION FORM THAT ACCOMPANIES A THYROID FNA**

Federal regulations in the United States require that certain identifying information be provided to laboratories with all specimens submitted for laboratory testing,\textsuperscript{55} including

- Name and address of person requesting the test
- Patient’s name or unique identifier
- Patient’s gender
- Patient’s age or date of birth
- Name of the test to be performed
- Specimen source
- Date of specimen collection
- Any additional relevant information.

The additional relevant information that a laboratory needs to properly evaluate a thyroid FNA specimen was considered at the 2007 NCI conference.\textsuperscript{3} To facilitate cytologic interpretation or histologic correlation (in the case of a subsequent surgical specimen), it was concluded that, at a minimum, the following data should appear on the requisition form that accompanies a thyroid FNA to a laboratory:

1. Usual required data for laboratory test submission (discussed previously)
2. Location of the nodule
3. Size of the nodule
4. History of hypothyroidism, autoimmune thyroiditis, or a positive test for antithyroid antibodies
5. History of Graves disease
6. History of $^{131}$I or external radiation therapy
7. Personal history of cancer
8. Family history of thyroid cancer.

**REPORTING TERMINOLOGY—THE BETHESDA SYSTEM**

It is critical that pathologists communicate thyroid FNA interpretations to referring physicians in terms that are succinct, unambiguous, and clinically helpful. Historically, terminology for thyroid FNA has varied significantly from one laboratory to another, creating confusion and hindering the sharing of clinically meaningful data among multiple institutions.
The 2007 NCI Thyroid Fine Needle Aspiration State of the Science Conference participants acknowledged the importance of developing a uniform terminology for reporting thyroid FNA results. The discussions and conclusions regarding terminology and morphologic criteria from the NCI meeting, summarized in the publications by Baloch and colleagues, form the framework of the terminology presented in this article and in atlas form, called The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). It is intended as a flexible framework that can be modified to suit the needs of the particular laboratory and the patients it serves.

**Format of TBSRTC**

For clarity of communication, TBSRTC recommends that each report begin with 1 of 6 general diagnostic categories (Table 1). Some categories have 2 options as names; a consensus was not reached at the NCI conference on a single name for these categories. Each of the categories has an implied cancer risk (ranging from 0% to 3% for the benign category to virtually 100% for the malignant category) that links it to a rational clinical management guideline (Table 2).

For some of the general categories, some degree of subcategorization can be informative and is often appropriate; recommended terminology is shown in Table 1.

### Table 1

**The Bethesda System for Reporting Thyroid Cytopathology: recommended diagnostic categories**

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Nondiagnostic or unsatisfactory</td>
<td>CFO</td>
</tr>
<tr>
<td></td>
<td>Virtually acellular specimen</td>
</tr>
<tr>
<td></td>
<td>Other (obsuring blood, clotting artifact, etc)</td>
</tr>
<tr>
<td>II. Benign</td>
<td>Consistent with a BFN (includes adenomatoid nodule, colloid nodule, etc)</td>
</tr>
<tr>
<td></td>
<td>Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context</td>
</tr>
<tr>
<td></td>
<td>Consistent with granulomatous (subacute) thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
<tr>
<td>III. Atypia of undetermined significance or follicular lesion of undetermined significance</td>
<td></td>
</tr>
<tr>
<td>IV. Follicular neoplasm or suspicious for a follicular neoplasm</td>
<td>Specify if Hürthle cell (oncocytic) type</td>
</tr>
<tr>
<td>V. Suspicious for malignancy</td>
<td>Suspicious for papillary carcinoma</td>
</tr>
<tr>
<td></td>
<td>Suspicious for medullary carcinoma</td>
</tr>
<tr>
<td></td>
<td>Suspicious for metastatic carcinoma</td>
</tr>
<tr>
<td></td>
<td>Suspicious for lymphoma</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
<tr>
<td>VI. Malignant</td>
<td>PTC</td>
</tr>
<tr>
<td></td>
<td>Poorly differentiated carcinoma</td>
</tr>
<tr>
<td></td>
<td>Medullary thyroid carcinoma</td>
</tr>
<tr>
<td></td>
<td>Undifferentiated (anaplastic) carcinoma</td>
</tr>
<tr>
<td></td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>Carcinoma with mixed features (specify)</td>
</tr>
<tr>
<td></td>
<td>Metastatic carcinoma</td>
</tr>
<tr>
<td></td>
<td>Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
</tbody>
</table>

From Ali SZ, Cibas ES, editors. The Bethesda System for Reporting Thyroid Cytopathology: definitions, criteria and explanatory notes. New York: Springer; 2009; with permission.
Additional descriptive comments (beyond such subcategorization) are optional and left to the discretion of the cytopathologist.

**Nondiagnostic or Unsatisfactory**

Every thyroid FNA must be evaluated for adequacy. Inadequate samples are reported as nondiagnostic (ND) or unsatisfactory (UNS). This category applies to specimens that are UNS due to obscuring blood, overly thick smears, air-drying of alcohol-fixed smears, or an inadequate number of follicular cells. For a thyroid FNA specimen to be satisfactory for evaluation (and benign), at least 6 groups of benign follicular cells are required, each group composed of at least 10 cells.\(^{57,58}\)

There are several exceptions to the numerical requirement of benign follicular cells. Any specimen that contains abundant colloid is considered adequate (and benign), even if 6 groups of follicular cells are not identified: a sparsely cellular specimen with abundant colloid is, by implication, a predominantly macrofollicular nodule and, therefore, almost certainly benign. Whenever a specific diagnosis (eg, lymphocytic thyroiditis) can be rendered and whenever there is any atypia, the specimen is, by definition, adequate for evaluation. ND/UNS results occur in 2% to 20% of cases but ideally should be limited to no more than 10% of thyroid FNAs, excluding samples exclusively composed of macrophages.\(^{8,59,60}\)

Specimens that consist only of cyst contents (macrophages) are problematic. Many laboratories have traditionally considered a macrophages-only sample UNS and included them in the ND/UNS category, with the understanding that, because the parenchyma of the nodule has not been sampled, a cystic papillary carcinoma cannot be excluded. In such laboratories, macrophages-only samples often constituted the

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### Table 2

**The Bethesda System for Reporting Thyroid Cytopathology: implied risk of malignancy and recommended clinical management**

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>Risk of Malignancy (%)</th>
<th>Usual Management(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Nondiagnostic or unsatisfactory</td>
<td>—(^b)</td>
<td>Repeat FNA with US guidance</td>
</tr>
<tr>
<td>II. Benign</td>
<td>0%–3%</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>III. Atypia of undetermined significance or follicular lesion of undetermined significance</td>
<td>~5%–15%(^c)</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>IV. Follicular neoplasm or suspicious for a follicular neoplasm</td>
<td>15%–30%</td>
<td>Surgical lobectomy</td>
</tr>
<tr>
<td>V. Suspicious for malignancy</td>
<td>60%–75%</td>
<td>Near-total thyroidectomy or surgical lobectomy(^d)</td>
</tr>
<tr>
<td>VI. Malignant</td>
<td>97%–99%</td>
<td>Near-total thyroidectomy(^d)</td>
</tr>
</tbody>
</table>

\(^a\) Actual management may depend on other factors (eg, clinical or sonographic) besides the FNA interpretation.

\(^b\) See text for discussion.


\(^d\) In the case of suspicious for metastatic tumor or a malignant interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be indicated.

*Modified from* Ali SZ, Cibas ES, editors. The Bethesda System for Reporting Thyroid Cytopathology: definitions, criteria and explanatory notes. New York: Springer; 2009; with permission.
great majority of ND/UNS cases, with rates that ranged from 15% to 30%. Other laboratories considered the risk of a false-negative result negligible and reported macrophages-only samples as benign. At the 2007 NCI conference, it was decided that cyst fluid–only (CFO) cases should be considered a clearly identified subset of ND/UNS. The significance (and clinical value) of a CFO result depends in large part on sonographic correlation. If the nodule is almost entirely cystic with no worrisome sonographic features, an endocrinologist might proceed as if the CFO were a benign result. On the other hand, it might be clinically equivalent to a ND result if the sonographic features are worrisome and an endocrinologist is not convinced that the sample is representative. In a study that segregated CFO cases and analyzed them separately, the risk of malignancy for a CFO sample was 4%. The risk of malignancy for ND/UNS (not including CFO) is 1% to 4%.

A repeat aspiration with US guidance is recommended for ND/UNS, including the clinically/sonographically worrisome CFO cases, and is diagnostic in 50% to 88% of cases, but some nodules remain persistently ND/UNS. Surgical excision is considered for persistently ND/UNS nodules because approximately 10% prove malignant.

Benign

The benefit of a thyroid FNA derives in large part from the ability to make a reliably benign interpretation that avoids unnecessary surgery. A benign result is obtained in 60% to 70% of thyroid FNAs. Descriptive comments that follow are used to subclassify the benign interpretation. The term, benign follicular nodule (BFN), applies to the most common benign pattern: an adequately cellular specimen comprised of varying proportions of colloid and benign follicular cells arranged as macrofollicles and macrofollicle fragments (Fig. 1). If resected, virtually all BFNs turn out to be nodules of a multinodular goiter (MNG) or follicular adenomas (FAs). This distinction cannot be made by FNA and is of no consequence to patients. The false-negative rate of a benign interpretation is low (0%–3%), but patients are nevertheless followed with repeat assessment by palpation or US at 6- to 18-month intervals. If a nodule shows significant growth or suspicious sonographic changes, a repeat FNA is considered.

Other benign subcategories include consistent with lymphocytic (hashimoto) thyroiditis in the proper clinical context and consistent with granulomatous (subacute) thyroiditis. This is a partial list and does not include a variety of other benign conditions, such as infections and amyloid goiter. Additional benign findings (eg, black thyroid, reactive changes, radiation changes, or cyst-lining cells) can be mentioned as descriptive diagnoses at the discretion of pathologists.

Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance

Some thyroid FNAs are not easily classified into the benign, suspicious, or malignant categories. Such cases represent a minority of thyroid FNAs and in TBSRTC are reported as atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS). The necessity for this category was debated at the NCI conference, after which a vote (limited to the clinicians in attendance) was taken, and the majority voted in favor of this category.

The heterogeneity of this category precludes outlining all scenarios for which an AUS interpretation is appropriate. The most common scenarios are described in the TBSRTC atlas.
An AUS result is obtained in 3% to 6% of thyroid FNAs.\textsuperscript{2,60} Higher rates likely represent an overuse of this category when other interpretations are more appropriate. The recommended management is clinical correlation and a repeat FNA at an appropriate interval.\textsuperscript{2,42} In most cases, a repeat FNA results in a more definitive interpretation; only about 20% of nodules are repeatedly AUS.\textsuperscript{2} In some cases, however, a physician may choose not to repeat the FNA but follow the nodule clinically or, alternatively, refer a patient for surgery because of concerning clinical or sonographic features.

The risk of malignancy for an AUS nodule is difficult to ascertain because only a minority of cases in this category have surgical follow-up. Those that are resected represent a selected population of patients with repeatedly AUS results or patients with worrisome clinical or sonographic findings. In this selected population, 20% to 25% of patients with AUS prove to have cancer after surgery, but this is undoubtedly an overestimate of the risk for all AUS interpretations.\textsuperscript{2,60} The risk of malignancy is certainly lower and probably closer to 5% to 15%. An effort should be made to use this category as a last resort and limit its use to approximately 7% or fewer of all thyroid FNAs.

**Follicular Neoplasm or Suspicious for Follicular Neoplasm**

The purpose of this diagnostic category is to identify a nodule that might be a follicular carcinoma (FC) and triage it for surgical lobectomy. FNA is diagnostic of many thyroid conditions (eg, papillary carcinoma or lymphocytic thyroiditis), but, with regard to FC, it is better considered a screening test. FCs have cytomorphologic features that distinguish them from BFNs. Although these cytomorphologic features do not permit distinction from a FA, they are reportable as follicular neoplasm (FN) or suspicious for a follicular neoplasm (SFN), leading to a definitive diagnostic procedure, usually lobectomy.\textsuperscript{42,62,65} SFN is preferred by some laboratories over FN for this category because a significant proportion of cases (up to 35%) prove not to be neoplasms but rather hyperplastic proliferations of follicular cells, most commonly those of MNG.\textsuperscript{60,66–69} About 15% to 30% of cases called FN/SFN prove to be malignant.\textsuperscript{2,60,67,70} The majority of SFN cases turn out to be FAs or adenomatoid nodules of MNG, both of which are more common than FC. Of those that prove malignant, many are FCs, but a significant proportion are follicular variants of papillary carcinoma.\textsuperscript{2,8,61,67}
Cytologic preparations typically have high cellularity, and colloid is scant or absent. The hallmark of this diagnostic category is an altered cytoarchitecture: follicular cells are arranged predominantly in microfollicular or trabecular arrangements (Fig. 2). Cases that demonstrate the nuclear features of papillary carcinoma are excluded from this category. Cellular crowding and overlapping are conspicuous, and the follicular cells are usually larger than normal. Nuclear atypia/pleomorphism and mitoses are uncommon. A minor population of macrofollicles (intact spheres and fragments) can be present. Conspicuous cellularity alone does not qualify the nodule for a suspicious interpretation.71 If a sample is cellular but mostly macrofollicular (intact spheres and flat fragments of evenly spaced follicular cells), a benign interpretation is appropriate. BFNs often have a small population of macrofollicles and crowded groups. If these compose the minority of the follicular cells, they have little significance and the FNA can be interpreted as benign. A suspicious interpretation is rendered only when the majority of the follicular cells are arranged in abnormal architectural groupings (such as microfollicles or crowded trabeculae).

The general category FN/SFN is a self-sufficient interpretation; narrative comments that follow are optional.

In the World Health Organization classification, Hürthle cell adenoma (HA) and Hürthle cell carcinoma are considered oncocytic variants of FA and FC, respectively.72 Studies suggest, however, that follicular and Hürthle cell tumors have different underlying genetics.6,73 For this reason, and because they have such distinctive morphologic features, it is helpful to specify that a sample raises the possibility of a Hürthle cell rather than a follicular neoplasm. This interpretation applies to cellular samples that are composed exclusively (or almost exclusively) of Hürthle cells. Oncocytic cells with nuclear features of papillary carcinoma are excluded from this interpretation. A significant proportion of these cases (16%–25%) prove not to be neoplasms but rather hyperplastic proliferations of Hürthle cells in nodular goiter or lymphocytic thyroiditis.74,75 Fifteen percent to 45% nodules are malignant, and the remainder of the neoplasms prove to be HAs.70,74,75

Suspicious for Malignancy

Many thyroid cancers, especially papillary thyroid carcinoma (PTC), can be diagnosed with certainty by FNA. The nuclear and architectural changes of some

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Fig. 2. FN/SFN. This aspirate shows significant architectural atypia of the follicular cells. Rather than arranged in a flat sheet (ie, a fragmented macrofollicule), the follicular cells are crowded into ring-like structures called microfollicles.
PTCs, however, are subtle and focal. This is particularly true of the follicular variant of PTC, which can be difficult to distinguish from a BFN. Other PTCs may be incompletely sampled and yield only a few abnormal cells. If only 1 or 2 characteristic features of PTC are present, if they are only focal and not widespread throughout the follicular cell population, or if the sample is sparsely cellular, a malignant diagnosis cannot be made with certainty. Such cases occur with some regularity and they are best classified as suspicious for malignancy, qualified as suspicious for papillary carcinoma. Nodules called suspicious for papillary carcinoma are resected by lobectomy or thyroidectomy. Most (60%–75%) prove to be papillary carcinomas and the rest are usually FAs.

The same principle applies to other thyroid malignancies, such as medullary carcinoma and lymphoma, but these are encountered less frequently than PTC.

**Malignant**

The general category, malignant, is used whenever cytomorphologic features are conclusive for malignancy (Fig. 3). Descriptive comments that follow are used to subclassify the malignancy and summarize the results of special studies, if any. Approximately 3% to 7% of thyroid FNAs have conclusive features of malignancy, and most are papillary carcinomas. Malignant nodules are usually removed by thyroidectomy, with some exceptions (eg, metastatic tumors, non-Hodgkin lymphomas, and anaplastic carcinomas). The positive predictive value of a malignant FNA interpretation is 97% to 99%.

**SUMMARY**

Given the considerable clinical value of thyroid FNA, it is important to understand its indications, some principles of optimal technique, the need for communicating relevant clinical information to pathologists on the requisition form, and the advantages of a reporting framework linked to management guidelines. The value of thyroid FNA is maximized when it is used for the appropriate indications, performed with good technique, and reported with terminology that is unambiguous and clinically useful.
REFERENCES


64. van Hoeven KH, Gupta PK, LiVolsi VA. Value of repeat fine needle aspiration (FNA) of the thyroid [abstract]. Mod Pathol 1994;7:43A.

