Letters to the Editor

both patients and clinicians more rather than less information about their tests. However, we believe defining the ROCSD is much harder than Dr Schnadig implies. Dr Schnadig states, “A 5-cm mass with extrathyroidal extension or a macrometastasis is certainly a real malignancy, while a 1.3-cm, asymptomatic incidentaloma. . . is far more likely to be benign.” Sure, but with appropriate therapy the risk of clinical progression or death for both patients is very low and may not be very different. That is the whole point of therapy, after all. In addition, in order to report ROCSD for an indeterminate thyroid aspirate, one would need to know the risk of a lesion for a patient who does not get any surgical or medical therapy, and whose tumor type, pathologic stage, and other pathologic risk factors will not be known because their nodules will be followed rather than excised. These data may be very difficult to collect and calculate, and would require long-term follow-up of patients with indeterminate thyroid aspirates who choose not to have resection. In addition, given the overall very low pretest probability of progression for all patients with thyroid malignancies, whether the ROCSD for patients with an indeterminate aspirate could be shown to be significantly different from that of a patient with either a benign or a malignant aspirate is not at all clear. Ideally, the ROCSD should be defined by clinicians rather than pathologists, because they have access to the appropriate follow-up information and the best feel for exactly which ROCSD would be most useful to both the patients and themselves. Nevertheless, if the ROCSD (however a clinician wants to define it) could be measured for patients with indeterminate thyroid aspirates, providing it in the cytology report might lead to improved patient care.

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In Reply.—Incorporated into the neoplasia lectures that I give to first-year medical students is discussion of overdiagnosis and the need to update our definition of cancer. There is increasing evidence that many small, nonmetastatic or micrometastatic cancers are Dr H. G. Welch’s “turtles.”1 Turtles are slow-growing neoplasms that will not become clinically evident during patients’ lifetimes. Some of these could even be called lemmings because they self-destruct. I do not deny that the Bethesda System’s risk of malignancy is an accurate method for assessing the risk of finding histologically defined cancers; however, malignancy is a scary word. Malignant implies evil intent and a harbinger of death. D’Agostino et al2 found that fear generated by the word cancer affects patients’ approach to decision-making in regard to nonintervention versus surgical intervention for papillary thyroid carcinoma (PTC). A hypothetical context study by Nickel et al3 suggests that the word cancer can induce anxiety and cause patients to favor surgery over active surveillance. As Kakudo and Bychkov note, clinicians and patients may be confused by indeterminate reports, and most thyroid nodules with indeterminate cytology are benign or indolent.

Use of decision aids and implementation of shared decision-making for management of thyroid nodules are currently under investigation.4 The result could be less unnecessary surgery and fewer fine-needle aspirates in favor of limited ultrasound studies or just plain old-fashioned clinical follow-up. However, we must heed patients’ reactions to our vocabulary.

Use of the new term noninvasive follicular thyroid neoplasm with papillary-like nuclear features does not address the evidence that most occult, low-risk classical PTCs are turtles, especially those found in middle-aged to elderly patients.5,6 Deletion of the carcinoma label from thyroid neoplasms likely to be indolent is not a new concept.7 Lethal thyroid cancers of all types, including microPTC, are very rarely discovered as incidentals and generally present with obvious metastasis or extrathyroid invasion. Takano8 points out that most PTCs stop growing by early adulthood. Childhood PTCs that do progress are curable. Takano9 also discusses evidence that undifferentiated carcinomas and other lethal carcinomas may not evolve from dormant, differentiated tumor cells, but rather from fetal stem cells.

Cronan10 once asked, “Is it time to turn off the ultrasound machines?” Recommendations against screening for thyroid cancers and attempts to limit the harms of overzealous use of ultrasonography and fine-needle aspiration have followed.10,11 Is it now time to revise our neoplasia terminology and definition of cancer? Should we include patients’ values and choices when deciding follow-up of thyroid neoplasms and desist from creating unwarranted fear? Should we explain to patients that not all cancers are malignant?

Although this is difficult in today’s medical care system, I believe that it should be the responsibility of clinicians and pathologists to attempt to communicate with one another prior to reporting thyroid needle aspiration or biopsy results. This enables the generation of more patient-oriented reports. Perhaps the attitude of “send out report and let the clinician decide what to do with it” is not in the best interest of patients.

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1. Schnadig VJ. Overdiagnosis of thyroid cancer: is this not an ethical issue for pathologists as well as radiologists and clinicians? Arch Pathol Lab Med. 2018;142(9):1018–1020.

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Cytologically Borderline Thyroid Nodules as a Key Target to Reduce Overdiagnosis and Overtreatment of Thyroid Cancer

To the Editor.—We read with great interest an editorial by Dr Schnadig\(^1\) on the medical and ethical issues of thyroid cancer overdiagnosis. The medical community is currently making a move to address these challenges, best illustrated by the “less is more” approach advocated by the recent clinical guidelines of the American Thyroid Association.\(^2\) On the other hand, as the author pointed out, an increasing number of patients are physically and financially harmed by the growing number of tests promoted by commercially motivated clinicians and pathologists. Apart from the ethical concerns, Dr Schnadig emphasized that stating risk of malignancy (ROM) in cytologically indeterminate aspirates from incidentally found nodules (incidentalomas) could create potential harm by scaring patients and clinicians because almost all incidentalomas exhibit indolent behavior.\(^1\) The ROMs in the Bethesda system were once suggested as one of the most useful features and were considered the most objective evidence to decide clinical management for a patient.\(^2\) However, ROMs of indeterminate thyroid nodules are quite heterogeneous—from 6% for atypia of undetermined significance (AUS) to 40% for follicular neoplasm (FN) categories—being higher in clinically suspected in indeterminate thyroid nodules.\(^2\) Some authors have proposed that AUS and FN categories in thyroid cytology should be accepted as borderline/precursor tumors (equivalent to dysplasia/carcinoma in situ).

The changing concept of cytologic-histologic correlation for thyroid nodules (modified from Valderratano and McVerr). The traditional view (upper) is based on the third edition World Health Organization (WHO) classification, with only 2 diagnostic choices, benign and malignant tumors; the current view (lower) is based on the fourth edition WHO classification, with 3 diagnostic choices, benign, borderline, and malignant tumors. The atypia of undetermined significance (AUS) and follicular neoplasm (FN) categories are not indeterminate but clear-cut categories aimed to accommodate thyroid borderline/precursor tumors (equivalent to dysplasia/carcinoma in situ).

Here, we are bringing attention to an alternative solution to avoid overdiagnosis and overtreatment of thyroid carcinoma diagnosed or suspected in indeterminate thyroid nodules, which is not well acknowledged in the United States. Close follow-up instead of immediate surgery for patients with clinically low-suspicion indeterminate (AUS or FN) thyroid nodules is a common practice in Asia as recommended by the Japanese Thyroid Association since 2013.\(^4\) In this conservative approach to AUS and FN nodules, more than half of the patients are spared from diagnostic surgery.\(^4\) Furthermore, because the vast majority of AUS/FN thyroid nodules are not advanced cancer, a lethal malignancy is rarely missed.\(^4\) This has also been confirmed in the Western experience by Rago et al,\(^5\) who reported that the risk of true malignancy developing into persistent disease among 1520 operated indeterminate (Thy3) nodules was 1.9%, which dropped to 0.26% when high-clinical-risk patients were excluded.

From the pathologist’s perspective, we believe that AUS and FN categories should no longer be called “indeterminate,” “uncertain,” or “gray zone,” because all of these classifiers convey a confusing message to clinicians and patients. Instead, these 2 categories in thyroid cytology should be accepted as borderline/precursor lesions equivalent to dysplasia and carcinoma in situ in other organs (Figure), which require no radical cancer treatment. This proposal is

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