Pitfalls in Salivary Gland Fine-Needle Aspiration Cytology

To the Editor.—The article “Pitfalls in Salivary Gland Fine-Needle Aspiration Cytology,” recently published in Archives of Pathology & Laboratory Medicine, is most informative and gives an overview of the diagnostic problems encountered in pathology laboratories. I note that many of the slides used in the survey were technically excellent, adequate cell-rich preparations. Therefore, in my view, the diagnostic difficulties were mainly caused by the use of the Papanicolaou stain.

To resolve this problem, I would highly recommend the use of the hematoxylin-eosin (H&E) stain in lieu of the Papanicolaou stain. I dare say that one would see a marked improvement in the interpretation of fine-needle aspirates when one switches from the Papanicolaou to the H&E stain. The latter stains the hyaline cylinders in adenoid cystic carcinoma, the fibromyxoid stroma in pleomorphic adenoma, and mucus in mucoepidermoid carcinoma far better than the Papanicolaou stain, which is notoriously deficient in the staining of stromal tissue.

There are many other advantages in using the H&E stain. Most of us who interpret fine-needle aspiration cytology are surgical pathologists. Surgical pathologists are much more accustomed to the H&E stain because it is used routinely on histologic sections and frozen sections. Furthermore, alcohol-fixed, H&E-stained slides are indispensable in interpretation of some tumors obtained from sites other than the salivary glands. A notable example is in the interpretation of hepatocellular carcinoma in liver aspirates.

KENNETH C. SUEN, MD, FRCPC
Department of Pathology
Vancouver General Hospital
University of British Columbia
Vancouver, British Columbia,
Canada V5Z 1M9


In Reply.—Currently, the College of American Pathologists (CAP) uses only Papanicolaou-type and Romanowsky-type stained material in the Nongynecologic (Non-Gyn) Program. This is largely because demographic data collected by the CAP indicates that the majority of laboratories and practitioners use these 2 stains for interpretation of fine-needle aspiration material. Therefore, it is probably not surprising that the majority of fine-needle aspiration specimens submitted to the CAP for inclusion in the Non-Gyn Program are Papanicolaou- and Romanowsky-stained cases.

It is quite possible that use of the hematoxylin-eosin (H&E) stain would lead to an improvement in performance of some of these cases, particularly among practitioners such as yourself who routinely use the H&E stain for salivary gland fine-needle aspiration specimens. Primarily because of their fellowship training experience, most cytopathologists achieve familiarity with, and come to rely on, the combination of nuclear detail and cytoplasmic/stromal detail that is afforded by the Papanicolaou and Romanowsky stains, respectively. However, we agree that there are probably many practitioners, including surgical pathologists, who are more comfortable with the H&E stain. Ultimately, a combination of a number of factors, including fine-needle aspiration technique, education, and experience, will determine the best approach to salivary gland lesions for each individual practitioner. We encourage all cytologists to use the techniques and stains with which they are most comfortable. Individuals who find the combination of Papanicolaou and Romanowsky stains to be suboptimal may wish to include the H&E stain in their staining armamentarium.

We thank you for your thoughtful comments and helpful suggestions. The CAP Non-Gyn Program is designed to be a continuing education experience, and dialogues such as this facilitate this activity through sharing of ideas and expertise.

JONATHAN H. HUGHES, MD, PhD
Laboratory Medicine Consultants, Ltd
Las Vegas, NV 89109

DAVID C. WILBUR, MD
Department of Pathology
Massachusetts General Hospital
Boston, MA 02114

Immunohistochemical Expression of Cyclooxygenase 2 in Follicular Carcinomas of the Thyroid

To the Editor.—With respect to the article by Haynik and Frayson, “Immunohistochemical Expression of Cyclooxygenase 2 in Follicular Carcinomas of the Thyroid,”1 in the June 2005 issue of the ARCHIVES, I question whether the cover picture (Figure 2 in the article) represents follicular carcinoma of the thyroid, unless that term is being used generically. The figure demonstrates elongated and irregular nuclei; some good examples of nuclear grooves; overlapping nuclei; some nuclei that are relatively empty of chromatin; and rare, although small, intranuclear inclusions. In addition, the colloid pictured seems to be quite dense. These are all features defining the follicular variant of papillary carcinoma.
In Reply.—Dr Frable’s letter in response to the cover picture associated with the article on follicular carcinomas of the thyroid brings up the issue of minimal criteria for the diagnosis of the follicular variant of papillary carcinoma. The figure in question certainly is marked by cleaved nuclei, a few overlapping nuclei, and some nuclear irregularities. The other features (nuclear clearing and intranuclear inclusions) are perhaps more subjectively observed, and we think are not clearly illustrated in this figure. It is well recognized that many of the morphologic features that are typically looked for in making a diagnosis of papillary carcinoma are not individually (or sometimes in combination) diagnostic of the lesion. The bottom line is that there is a lack of accepted and reproducible minimal criteria for the pathologic diagnosis of the follicular variant of papillary thyroid carcinoma. Given this premise, we tend to look for a constellation of findings and evaluate them in the context of the whole lesion.1,2 Particularly regarding cleaved nuclei, which are the most salient of the features depicted in the figure, Scopa et al3 meticulously examined 80 nonpapillary thyroid lesions, including 35 follicular adenomas and 8 follicular carcinomas, evaluating the frequency of grooved nuclei per microscopic field. Grooved nuclei were found in all of the follicular adenomas and follicular carcinomas examined. In 5 of the carcinomas, nuclear grooves were designated as “numerous.” Additionally, nuclear grooves were also observed in a variety of other nonpapillary carcinoma lesions, including medullary carcinomas, Hashimoto thyroiditis, and diffuse hyperplasia. The same paper illustrates follicular carcinoma showing a rare intranuclear inclusion, some nuclear elongation, and nuclear crowding; all of these features that we classically associate with papillary carcinoma can be encountered in follicular carcinoma.

DENISE M. HAYNIK, DO
RICHARD A. PRAYSON, MD
Department of Pathology
Cleveland Clinic Foundation
Cleveland, OH 44195


Hepatocellular Carcinoma In Situ: Does the Entity Exist?

To the Editor.—In the May 2005 issue, Dr Quaglia et al1 described some interesting observations in 5 cases of intravascular free-floating hepatocellular carcinoma (HCC) tumor clusters coated with intact endothelium. The authors proposed that the endothelial coating may protect the tumor projections from thrombus formation and may also act as a barrier to tumor extravasation.

The authors’ observations prompt another question: does hepatocellular carcinoma in situ exist? Clinically, despite its rich blood circulation, HCCs uncommonly metastasize outside the liver.2 Histologically, well-differentiated HCCs demonstrate distinct trabecular architecture coated by a layer of endothelial cells, which resemble thickened liver cell plates. Poorly differentiated HCCs lose their trabecular architecture and become solid sheets of tumor cells with a haphazard arrangement lacking a distinct endothelial coating. Considering the predominantly arterial supply of HCC and the complex network of capillarized sinusoids that communicate with the adjacent large vascular structures,3 all of the HCC that have trabecular architecture and intact endothelial coating could be considered protrusions of tumor cells into the vascular space.

Dispersion from the cohesive tumor trabeculae and invasion through the basement membrane are the 2 key events for HCC tumor cells to enter the blood circulation and subsequently metastasize. Tumor cell dispersion relies on the loss of homotypic cell-cell adhesion, which is largely mediated by an E-cadherin/catenin complex.4 Invasion through the basement membrane and interstitial matrix requires the action of a series of proteolytic enzymes named matrix metalloproteinases,5 the activity of which is regulated by their tissue inhibitors.6 Information on the balance between certain matrix metalloproteinases and certain tissue inhibitors of matrix metalloproteinases and on the tissue expression of E-cadherin have proved to have predictive value for the invasion and metastasis of HCC.7,8

Therefore, well-differentiated HCCs with trabecular architecture, undisrupted endothelial coating, a high level of E-cadherin expression, and a low ratio of matrix metalloproteinases to tissue inhibitors of matrix metalloproteinases could probably be considered in situ HCCs. Surgical resection may be sufficient treatment for these types of tumor. The diagnosis of in situ HCC does not necessarily indicate a favorable prognosis, because large in situ HCCs can still kill the patient by compromising liver function or by massive hemorrhage from rupture. Because heterogeneity of tumor differentiation is very common in large-sized HCCs,8 extensive sampling would be critical to confidently diagnose in situ HCC.

ZU-HUA GAO, MD, PhD
Department of Pathology
University of Calgary
Calgary, Alberta, Canada T2N 2T9

Letters to the Editor


