Quality Improvement in Cytology
Where Do We Go From Here?

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Context.—Cytology is a success because of the many quality controls used to ensure the accuracy of its results. Nevertheless, additional information is becoming available to the cytologist, often from untraditional sources, and the best way to use that information to improve the quality of cytology is not yet known.

Objective.—To review ways to use new information to improve the quality of cytology.

Data Sources.—Review of relevant literature.

Results.—Information contained in many sources can be used in new ways to improve the quality of cytology. These include the timing of cytologic and histologic correlation, electronic medical records, workload information, prior aspirations, and molecular tests.

Conclusions.—To maintain their high standard of excellence, cytologists should seek to define the most appropriate way to incorporate this new information into their interpretation of individual cases.


Cytology is an undeniable success in screening patients and obtaining accurate diagnoses with the least intervention. A significant part of this success is due to the high level of quality found in how the test is performed. Cytology is conducted successfully in every type of practice setting, from the solo pathologist in the community hospital doing it all to the fully specialized practitioner in a tertiary care setting. Even though cytology is composed of complex tests that can be extremely challenging to interpret, success is seen with all types of personnel, including cytotechnologists, private practice pathologists, and academic experts. A cornerstone of this success is the highly effective quality-assessment programs that are used in all these different settings and by all these different personnel.

Given this success, one may ask, how can cytology improve on its current level of quality, or where should we go from here? An area in which cytology can improve is in how it uses and integrates prior information into the diagnostic process. Today, there is more information, more types of information, and more different sources of information available to the cytologist than ever before. This information can be specific to the patient (eg, a history of breast cancer that can only be found in the electronic medical record), may be results from large clinical trials, or may be results from new types of testing technologies. Indeed, a recent addition to the College of American Pathologists checklist is the requirement to ensure that the results of all other studies (not just anatomic tests) are correlated with the final diagnosis.1

This review focuses on selected areas of cytology in which there is new information available to the cytologists that may be important in either ensuring or improving the quality of cytology. This review is not meant to be all inclusive. Topics reviewed here include cytologic and histologic correlation, the electronic medical record, workload reporting and monitoring in gynecologic cytology, the importance of prior aspiration results on the significance of current thyroid aspiration results, and correlation of molecular and cytologic studies in urine. In most cases, the best way to use this additional information is not yet known. Nevertheless, by recognizing areas in which changes are coming, cytologists can better direct their efforts to finding answers to these questions.

CYTOLOGIC AND HISTOLOGIC CORRELATION: WHEN?

Although there are many aspects to quality assessment in cytology, one of the fundamental tools used in cytology is cytologic and histologic correlation. It has always been incumbent on the practicing pathologist to correlate the results found through cytology with those seen in histology, to evaluate any discrepancies to determine why they occurred, and to ensure appropriate patient care. Cytologic and histologic correlation is not going away, but the way in which it is performed has changed over time. Although, years ago, simply collecting all cases every 6 months and going through them was deemed an acceptable method of correlation, for practical purposes, that is no longer the case. Patients are not sympathetic to being notified about a mistake months after it could have been corrected, nor should they be. Indeed, with the advent of improved information systems, most cytologic and histologic correlations are, and should be, performed
THE ELECTRONIC MEDICAL RECORD: HOW MUCH?

As more of a patient’s medical record is placed in interconnected information systems, the amount of information available to a pathologist doing cytology continues to increase. Because cytologists have always worked with minimal material, they are quite familiar with using other sources of information to improve the accuracy of their diagnoses (for example, the triple test in breast fine-needle aspiration cytology). At some point, the entire medical record for a patient may be available for review by a cytologist. Given this, what is the obligation of the cytologist to review that record? How hard and how long should a cytologist look for this information?

Many pathologists would agree that knowledge of prior pathologic material within the same department is likely already a standard of care. For example, in gynecologic cytology, it is incumbent on a pathologist to review the department’s own records to see whether there is a history of a high-grade lesion. Often, that history is provided by the clinician. However, I know, in my own practice, I have resorted to looking up the entire cytology/pathology history on the computer in every case, simply because, in too many cases, the clinician did not provide information about prior pathologies, and I was tired of looking foolish for not knowing the results in my own laboratory.

However, even looking up every case, I still miss important information because sometimes it is hard to recognize the information is there (e.g., I missed a prior diagnosis of lymphoma because the case was labeled “toe amputation,” and I did not think I needed to examine the case closely). On the other hand, not everyone reviews the pathologic record on every case. Sometimes, it is hard to imagine how prior history could be important for diagnosing some types of cases. For example, I cannot recall a case in which I found relevant history for a cholecystectomy. Such cases are less likely in cytology.

Nevertheless, the questions remain, in how many different places, and how hard should a cytologist look? What about the clinical notes? Sometimes the relevant history (say, a history of breast cancer when performing a pleural fluid test) is only present in the clinical notes of a case, not in the pathology records and not in the clinical information on the cytology requisition, and with more and more material online, I suspect that clinicians will be less likely to put the relevant information down on the requisition. After all, it is all there in the record, anyway.

To our knowledge, at present there are no agreed upon standards. Is it the duty of the pathologist to review admission notes in all cases? Is it the duty of the pathologist to seek out prior material from other laboratories that might be mentioned in those notes but were not sent for review by the clinician? Is it the duty of the pathologist to review imaging reports? Many pathologists believe it is incumbent on pathologists who are reviewing breast core biopsies to review the mammograms to ensure that the radiographic and pathologic lesions correlate. Should cytologists also be obligated in that way whenever they do an image-guided fine-needle aspiration? The bottom line is that there will be increasing access to increasing amounts of information, and sorting through that information is time consuming and progressively less rewarding. What is the obligation of a cytologist to use this additional information when attempting to make a significant diagnosis with limited material to review? The answer is not clear at this time. Although it is possible that future versions of the electronic medical record will contain search engines that can automatically identify and bring relevant information to the cytologist, those search engines are not yet available. Indeed, identifying what cytologists think is important and where that information might be is an important first step in building such a search engine. Further evaluation of this topic appears worthwhile, and a successful definition of the appropriate degree of investigation needed is likely to improve the quality of cytology.

GYNECOLOGIC CYTOLOGY: HOW FAST?

Most quality assessment performed in gynecologic cytology is mandated by the Clinical Laboratory Improvement Amendment Amendments of 1988 (CLIA). Although those quality assessment activities do provide a good starting place to ensure that the process of receiving, processing, and reporting gynecologic cytology is done reliably, they are less effective at ensuring the quality of the interpretation. Although cytologic and histologic correlation and other methods are good at measuring the specificity of interpretation, studies have shown that most standard methods used to evaluate and interpret gynecologic cytology are themselves not very sensitive and not strongly correlated with screening sensitivity.

Nevertheless, recent studies have shown that workload may be an effective surrogate for sensitivity in manual screening, whereas the epithelial cell abnormality (ECA)–adjusted workload (ECA rate × workload) may be a more-effective surrogate for automated screening. Using these surrogates, the maximum workload for cytotechnologists can be estimated so they have the best chance of achieving near-100% sensitivity. That workload is 30 slides/d for manual screening of conventional and SurePath (BD Biosciences, Franklin Lakes, New Jersey) cases, and an ECA-adjusted workload of 7 cases/d (or 70 cases/d for a laboratory with an ECA rate of 10% where 1 slide is counted as 1 slide) for screening with the ThinPrep Imaging System (Cytyc Corporation, Boxborough, Massachusetts). Unfortunately, those workloads are less than the workloads currently being employed in some, if not many, cytology laboratories. Whether the cytology community would be willing to change their practices to comply with these recommendations is not clear. In addition, these results have implications for the effectiveness of automated screening methodologies in primary human papilloma virus screening and a subsequent increase in the ECA rate that will be seen in a laboratory. How important this will be in determining the best way to combine human papilloma virus testing and cytology is not clear.

Given the difficulty in measuring screening sensitivity in gynecologic cytology, one proposed shortcut is to simply have laboratories report the workload of individual cytotechnologists in their report. Some think this is a way in which laboratories that spend additional effort and time screening individual cases can distinguish themselves from those that spend less time at this activity. Figuring out the best way to use this new information concerning workload and screening sensi-
tivity will be important in ensuring the quality of cytologic screening.

**THYROID FINE-NEEDLE ASPIRATION: ACCOUNTING FOR PRIOR FINE-NEEDLE ASPIRATIONS**

The Bethesda Classification System,\(^\text{12}\) based on the National Institutes of Health State-of-the-Science conference, represents a significant step forward in standardizing and improving the quality of thyroid fine-needle aspirations. Already, major progress has been made toward its main goal—standardizing reporting of these specimens across a wide variety of practice settings to allow better comparison of performance and more-uniform treatment of patients.

A major advance incorporated in this system is the recognition of the “risk of malignancy”\(^\text{13}\) as an appropriate standard upon which to measure the quality of a specimen. This standard is particularly important for this type of specimen because so many of the most difficult and controversial interpretations are not diagnostic, but result in only an increase or decrease in the pretest probability of the patient having a malignancy. Interestingly, this approach has already led to recognition of some inconsistent uses of terminology in the system. For example, although different terminology is used for different types of specimens (atypical follicular cells versus suspicious for a follicular neoplasm), the actual risk of malignancy for these 2 patterns is very similar.\(^\text{14}\) Whether these 2 patterns should be merged into a single diagnostic entity is currently controversial.

More-recent work emphasizes that the risk of malignancy associated with a particular diagnosis is not independent of the results of prior aspirations. For example, a common recommendation in the Bethesda system is to perform a repeat aspiration for patients who receive a diagnosis of atypical follicular cells.\(^\text{12}\) Although repeat aspirations that result in more-worrisome findings are clearly useful, the value of a subsequent benign diagnosis is less well characterized in the literature because only a handful of such cases have come to resection. More-extensive analysis on a large series of cases suggests that the risk of malignancy for a patient with an atypical and subsequent benign diagnosis is intermediate between the risks of patients with either a single, benign diagnosis and an atypical diagnosis.\(^\text{15}\) In other words, the risk associated with an atypical diagnosis does not disappear and is not overruled by any subsequent benign diagnosis. How clinicians will choose to manage their patients in such a setting is not known. In addition, the best way to communicate the risk, which is different than that for a single benign aspirate on its own, is also not clear. Determining the best way to use these prior results and to accurately present the risk to the patient from the subsequent aspirate will be important for cytologists to determine.

Similarly, a major source of frustration in thyroid fine-needle aspiration is the nondiagnostic specimen. Patients who receive such a diagnosis are obligated to return and have the aspirate repeated. Although often this repeated test is of diagnostic value, in some cases, patients subsequently receive yet another nondiagnostic interpretation. The significance of this finding has not been well studied, but some clinicians will elect to ressect lesions from which they are unable to obtain a diagnostic aspirate.\(^\text{12}\) However, several studies\(^\text{16,17}\) suggest that, in fact, the risk of malignancy for patients with 2 sequential nondiagnostic aspirates is actually quite low, approaching the same risk as patients with a benign diagnosis.\(^\text{18}\) In such a setting, it may be advisable to follow such patients, unless radiologic or clinical findings raise further reason for the need for resection. Obviously, because nondiagnostic aspirates are dependent on the quality of the aspiration service as well as the nature of the thyroid nodule, these results may not be true in the setting where the aspiration service routinely fails to obtain adequate material on malignant cases, and application of these findings may not be suitable in all circumstances. Defining the best way to incorporate this additional information will be important for cytology to determine.

In addition, in the same study,\(^\text{19}\) the significance of cyst fluid was compared with all other nondiagnostic aspirates. The best way to classify cases in which only cyst fluid can be obtained is not entirely clear. Although the Bethesda System clearly states that such aspirates should be classified as nondiagnostic,\(^\text{12}\) some pathologists prefer to classify such cases as negative under the assumption that the risk of malignancy in such a setting is lower than in other cases of nondiagnostic aspirates and the belief that reaspiration is unlikely to provide additional diagnostic information. However, the results of this study suggest that, in fact, the risk of malignancy for cases with cyst fluid alone is quite similar to the risk of other nondiagnostic cases, and reaspiration with a second nondiagnostic interpretation does provide additional information and dramatically reduces the patient’s risk of malignancy. As a result, the proposal to classify cases with cyst fluid only as benign cannot be supported. These results strongly suggest that the current practice of placing cyst fluid into a separate category from other nondiagnostic results is not beneficial.

**URINE CYTOLOGY: CYTOLOGY OR MOLECULAR TESTS?**

Urine cytology remains a source of frustration for many cytologists.\(^\text{19}\) Because urine is a toxic environment that is constantly working to degrade cells, it is usually possible to identify atypical but degenerated cells in a urine specimen. Usually these poorly preserved cells will be of no significance, but not always. Some urothelial carcinomas have markedly degenerative features, and sometimes, the cells of such tumors will appear similar to healthy urothelial cells that are also degenerating. To many cytologists, urine cytology represents an example of where morphology meets its diagnostic limits.

At the same time, other diagnostic methodologies are becoming more prevalent,\(^\text{20}\) in particular, UroVysion bladder cancer kit (Vysis, Inc., Downers Grove, Illinois).\(^\text{21,22}\) This test represents an alternative way to obtain a diagnosis in urine specimens, and studies suggest that it may be more sensitive than cytology alone.\(^\text{23}\) Nevertheless, this test is significantly more expensive than cytology, and there are significant issues regarding the standardization of how these tests are performed,\(^\text{24}\) as well as issues regarding specificity in certain patients,\(^\text{25}\) which limits the ability to accurately define the advantage this test (both in accuracy and cost effectiveness) has over cytology.

Going forward, the most important question for cytologists is defining the best way for these 2 tests to interact. Because both tests have advantages, it is likely that the combination of the 2 tests will be superior to either one alone. The lack of standardization of UroVysion\(^\text{24}\) and in defining atypia in urine cytology\(^\text{26}\) will make this quite challenging. Some authors have suggested increasing use
of interlaboratory surveys to better define the precision of UroVysion testing.\textsuperscript{24} Whether a consensus conference like those seen for the Bethesda System for gynecologic cytology and thyroid cytology would be of value with the currently available performance data is not clear. Nevertheless, although molecular testing does, in some respects, represent a competitor to traditional cytology, molecular tests can also be useful allies in improving patient care. Indeed, molecular testing and personalized medicine may improve the utility of cytology. The goal for cytologists will be to define the most appropriate way for these 2 tests to work together, rather than at odds with each other, to improve patient care.

\textbf{CONCLUSION}

Although there is no question that the quality of cytologic interpretation in the United States remains high, the field continues to evolve. In particular, new types and sources of information are becoming available to cytologists, and the best way to incorporate those data into improved diagnoses and patient care is not yet clear. It is likely that the field will benefit from having a flexible attitude as it adapts to new technologies and new sources of information. Cytology continues to have the potential to significantly improve the care of people in the United States, today and into the future.

\textbf{References}