

Cytopathology - from an Immunohistochemist's Perspective

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Cytopathologists have made tremendous strides in their ability to render clinically useful diagnoses based on ever shrinking amounts of diagnostic material. Because of the technical ease and low morbidity associated with fine needle aspiration (FNA) cytology procedures, they have become increasingly popular as an initial diagnostic procedure for expanding numbers of patients. Particularly when combined with ancillary diagnostic methods such as immunohistochemistry, flow cytometry, FISH, or other molecular techniques, FNA can be the definitive diagnostic procedure. In this situation, FNA can save the patient a great deal of potential expense and discomfort that might be suffered during the course of obtaining additional diagnostic material that might otherwise have been required to render a useful diagnosis.

However, we must also be realistic about the limitations of FNA. By its very nature the amount of diagnostic material can be minimal, and assessment of tissue architecture with FNA is far more challenging than with a standard H&E paraffin section. There are probably some cytopathologists in the world who can render specific accurate diagnoses on nearly any FNA specimen based on standard morphologic examination alone. However, people like me (and indeed essentially all of the board-certified cytopathologists that I have known) receive cases that we can study by standard morphology until we are blue in the face, and have about as much of a chance of getting the case right as throwing darts at a list of diagnostic possibilities tacked onto the dartboard. In these cases, additional diagnostic modalities are essential, and immunohistochemistry is very

Miller's Cardinal Rules of Cytopathology:

1. GET A CELL BLOCK
2. USE NON-ADHESIVE SLIDES
FOR CYTOLOGIC SMEARS

frequently the method that we first turn to for help. After struggling with many such FNA cases over the years, we have adopted a very successful approach at ProPath, and this month we share this approach with our readers. We hope this will make our readers think a bit more clearly about planning for a potential difficult diagnosis up front, which will be to the benefit of both the pathologists interpreting the material and the clinicians and patients that they serve.

In my (non-subspecialty-boarded cytopathologist) mind, the **first cardinal rule of cytopathology** can be summed up very succinctly: **GET A CELL BLOCK**. Unfortunately, this rule is frequently ignored, as we see far too many cases that consist of one or more trays of cytologic smears containing great diagnostic material, without an accompanying cell block. To me, it makes no sense to make more than a few smears, since having a few smears plus a cell block is far more useful than having numerous smears which frequently all show the same thing, (i.e., some type of tumor that we can't figure out on

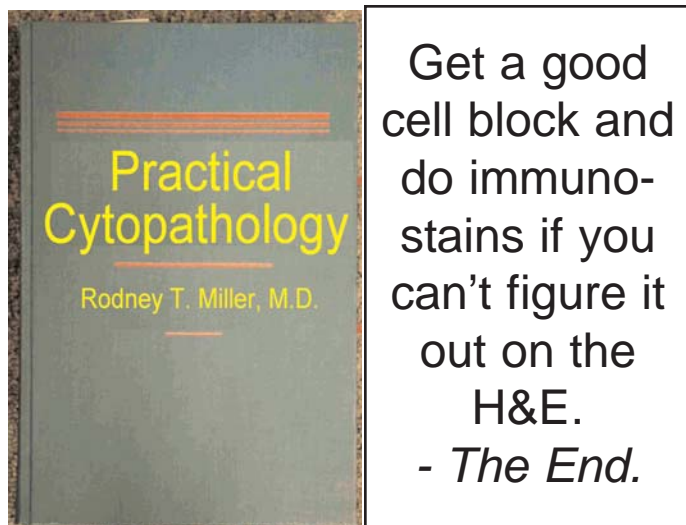


Figure 1: Photograph and complete contents of my textbook on "Practical Cytopathology".

morphology). In order to emphasize this point to readers, I have included a photograph and complete text of a book that I wrote called "Practical Cytopathology" (Figure 1, above). I think everyone would agree that workup of difficult cytology cases is far easier if an adequate cell block is available for use, since this allows numerous immunostains or other studies to be performed, often allowing the pathologist to render a specific diagnoses.

Unfortunately, as we all know, not all cases come with cell blocks, and these are the ones that give us the most trouble. Although undoubtedly some would argue with my **second cardinal rule of cytopathology**, here it is: **USE NON-ADHESIVE SLIDES FOR YOUR CYTOLOGY SMEARS.** Although this might seem counterintuitive because of a potential risk of diagnostic material not sticking to the slide, in practical terms this fear is unfounded, since provided the smears are not horrendously thick, the cells will stick adequately to the slides to survive routine H&E, pap, Diff-Quik, or Wright-Giemsa staining. **The main advantage of using non-adhesive slides for cytology smears is that it renders the use of tissue transfer immunohistochemistry far easier to perform.**

Tissue transfer immunohistochemistry involves removal of the coverslip, placing tissue transfer media on the slide, and subsequently peeling off the tissue transfer media along with the diagnostic mate-

rial. Once the diagnostic material (embedded in the transfer media) has been removed from the slide, it can be subdivided into as many smaller portions as needed, transferred onto adhesive slides (along with immunostain positive control material), and then immunostained as usual. A huge advantage of this approach is that it allows the performance of numerous immunostains on material obtained from a single cytologic smear. Indeed, in several cases we have performed 20-30 immunostains on cytologic material derived from a single slide. This technique also allows the use of antigen retrieval procedures for cytology material (since when transferred the material is placed on adhesive slides), and antigen retrieval procedures are critical for obtaining optimal results on cytologic material. If the original FNA material was placed on an adhesive slide, it is substantially more difficult for the diagnostic material to be removed and transferred using tissue transfer techniques, and in some cases it does not work at all.

At ProPath, we have extensive experience doing immunohistochemistry on cytologic material, and our approach (which entails the use of tissue transfer techniques on nearly every case) has worked extremely well for our clients and us. We are ideally suited to offer our expertise to assist other pathologists with difficult cytologic cases when only slide material is available for study.

REFERENCE:

Miller RT, Kubier P: Immunohistochemistry on Cytologic Specimens and Previously Stained Slides (When No Paraffin Block Is Available). *Journal of Histotechnology*, 25(4):251-257, 2002.

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