

## Blinded Review of Papanicolaou Smears

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I am writing to expand on Dr. Frable's excellent editorial<sup>1</sup> on a report by Renshaw et al.<sup>2</sup> Pathologists became the target of malpractice litigation for misdiagnoses within the year after an article appeared in the *Wall Street Journal* in 1987.<sup>3</sup> In 1988, The Doctors Company (TDC) recorded 11 Papanicolaou smear/cervical cytology claims, a significant increase considering that only 7 had been filed in the company's entire history of insuring pathologists. Between 1988 and 1995, which to my knowledge is the last period for which TDC has published its data, 195 claims were filed.<sup>4</sup> The problem is surely worse than most of us know, because TDC is only one of many insurers.

I propose modifying Dr. Frable's version of the legal definition of "standard of practice" for cytotechnologists as follows: practice exercised with the degree of care used by a reasonably careful cytotechnologist of like qualifications in the community in which he or she practices under the same or similar circumstances *the majority of the time*. This modification supports the possibility of a Type 1 error in Dr. Holladay's multiple slide-blinded review program (MSBR).<sup>5</sup> Established in 1994, the MSBR utilizes 10 qualified cytotechnologists to screen a contested Papanicolaou test slide among a mix of 59 contemporaneous other slides from the originating laboratory to determine whether the original false-negative result was likely due to substandard screening. In this context, a Type 1 error would mean the blinded review concluded that the false-negative result of the Papanicolaou test was reached because the standard of screening practice was breached, when in fact it was not, especially for easily detected cases. Such errors can occur when a cytotechnologist experiences a lapse in vigilance, which is universal, insidious, and unpreventable.

The MSBR program addresses outcomes. It attempts to determine whether a given false-negative Papanicolaou test is a breach of a working standard of screening practice in the absence of a published consensus definition of the standard of practice. In the absence of such a definition, lay jurors cannot understand how the case before them could have been missed. After all, it appears to be so obvious now. The following proposed definition of screening encapsulates the essential elements of a standard of screening practice and highlights the complexity and probabilistic nature of the screening process—manually screening Papanicolaou tests is a process by which a slide is moved successively in small increments to promote the probability

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that at least one recognizable abnormal cell will fall within the narrow field of vision of an alert professional observer long enough to be perceived. All factors must converge in time and space if a cytotechnologist is to find an abnormal cell. Finding at least one abnormal cell is the first objective of screening a Papanicolaou test. Every false-negative Papanicolaou test is the result of failing to meet this objective. Is every false-negative result a breach of standard of practice? No. Are any? That is the question the MSBR attempts to answer objectively.

How may a competent cytotechnologist fail to find abnormal cells in a Papanicolaou test? There are many contributory limitations<sup>6</sup>: 1) psychologic (i.e., the vigilance decrement—the universal inability to pay sustained attention to a search-intensive task for more than approximately 20 minutes<sup>7</sup>); 2) physiologic (i.e., limitations in peripheral vision [abnormal cells may fall within the microscope's field of view but outside the observer's much smaller field of vision<sup>8</sup> (the conspicuity area,<sup>9</sup> which is approximately five times less in area)]); 3) screening coverage limitations<sup>10</sup>; and 4) physical (i.e., fatigue).

Cytotechnologists who are shown their false-negative Papanicolaou tests react universally: 1) I recognize those cells, 2) I do not know how I missed them, and 3) I do not know what I can do proactively to ensure I never miss them again. In fact, nothing can be done absolutely as long as humans manually screen Papanicolaou tests. Screening is more complex than most of us realize. Just because an “expert” testifies “it was a typical misread Pap test” does not make it so. I agree completely with Dr. Frable that there are two standards of practice for the interpretation of Papanicolaou smears: 1) the cytotechnologist who screens the slide to detect abnormalities and 2) the pathologist who makes the final interpretation of the case.

To my knowledge, there is no published consensus standard of the Papanicolaou test screening process—not in the Commission on Accreditation of Allied Health Education Programs (CAAHEP) 2004 cytotechnology standards and guidelines or in their accredited cytotechnology programs, not in published American Society of Cytopathology cervical cytology practice guidelines, and not in College of American Pathologists checklists. The American Society for Clinical Pathology cytotechnologist registry examinations do not ask screening-related questions, nor does the American Board of Pathology in its cytopathology subspecialty board examination. Clinical Laboratory Improvement Amendments also is silent regarding the process of screening per se. Required screening performance data collection and analyses are minimal. If, as anticipated, cellular abnormality detection rates

increase with the use of automated screening systems (e.g., the ThinPrep® Imaging System [Cytoc Corporation, Boxborough, MA] and the FocalPoint Slide Profiler [TriPath Imaging, Burlington, NC]), I believe we will begin to appreciate the extent of our errors and the limitations of our data analyses in estimating residual risk in terms of unidentified false-negative Papanicolaou tests that have been screened manually.

Contrary to oft-repeated statements by experts, cytotechnologists do not examine each and every cell among the multiple tens of thousands of cells on a Papanicolaou test slide. That is a physical impossibility. At least one expert pathologist has testified that cytotechnologists are taught to do so—the implication being that the cytotechnologist who screened the false-negative Papanicolaou test must have been negligent. Having reviewed several depositions by cytotechnologist and pathologist expert witnesses for the plaintiff, I am struck by the relevant scientific ignorance of all parties—cytologists and lawyers alike.

Cytotechnology programs teach the same things about screening—differently. For example, when asked in a 1996 informal poll the number of abnormal cells that must be present on a Pap slide to find at least 1, 28 education coordinator respondents answers ranged from as few as 1 to as many as 500. Indeed, one expert cytotechnologist has testified that even one abnormal cell present on a slide must be found. Contrast this statement with the findings of Mitchell and Medley that when there were < 50 abnormal cells present, the odds of a false-negative result was 23.7 times greater (with a 95% confidence interval of 3.7–150) than when  $\geq 200$  abnormal cells were present.<sup>11</sup> Obviously, not all cytotechnologists are qualified to legitimately determine whether any given false-negative Papanicolaou test resulted from a breach of the standard of practice. Indeed, I would argue that few are. They have not been taught the relevant information.

Graduating cytotechnology students enter the work world, therefore, with a knowledge deficit relative to limitations of screening practices and unrealistically high expectations of their screening performance. These expectations exist among their pathologist employers and the public, and are nearly insurmountable before a lay jury sympathetic to the plaintiff or her survivors.

Consider the following medicolegally relevant observations. First, the standard of screening practice is not defined, not taught, not measured, not reported, and the limitations of screening are not publicized. Expectations exceed performance, which allows plaintiff attorneys to use their blame-finding “culposcopes” with great success. Second, the standard of screening practice cannot be determined based on a single case.

The legal process of determining medical liability for a false-negative Papanicolaou test is unsuited for the task.<sup>12</sup> Third, all common screening performance metrics (e.g., the ratio of atypical squamous cells of undetermined significance to squamous intraepithelial lesion,<sup>13</sup> false-negative proportions<sup>14,15</sup>) overestimate screening sensitivity and underestimate residual risk in terms of unidentified false-negative Papanicolaou test results. Fourth, 100% rapid review is ineffective in identifying false-negative Papanicolaou tests and should not be considered.<sup>16</sup> If as effective as claimed, it would identify 10 times as many false-negative Papanicolaou tests results as does 10% random review, but it does not. It is neither quality control nor quality assurance. Fifth, pathologists who do not admit to the possibility of an “acceptable” false-negative Papanicolaou test result based on an understanding of the limitations of the process<sup>17</sup> are suspect as expert witnesses.<sup>18</sup> Because none of these expert witnesses screen Papanicolaou tests for a living, how in good conscience can one testify that a false-negative Papanicolaou test in litigation is the result of screening outside the standard of practice? Pathologists should restrict their testimony to opinions regarding cytomorphologic findings, as suggested by Dr. Frable. Sixth, many unidentified false-negative Papanicolaou test slides similar to those being litigated reside in the filing cabinets of expert pathologist witnesses for the plaintiff—whether they know it or not—yet the experts believe their laboratories are the exception and not the rule. Seventh, errors are part of the standard of practice. There is nothing morphologically distinctive about a false-negative Papanicolaou test slide that ultimately harms a patient and one that does not. A higher level of accountability, therefore, should not apply. An unfortunate health outcome does not automatically entitle a plaintiff or her survivors to financial compensation. Finally, I believe that the MSBR program remains the best way to establish whether a false-negative Papanicolaou test represents a breach of the standard of practice.

I believe cytotechnologists and pathologists should not be held accountable for the local outcome consequences of global process shortcomings. Even if all identifiable process control factors were addressed and implemented, errors still would occur. False-negative Papanicolaou tests arise from the nature of the process, not the negligence of the practitioner. Re-

spected cancer advocacy organizations (e.g., the American Cancer Society) should educate the public regarding the limitations of Papanicolaou test performance.<sup>19</sup>

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