We are pleased to have the opportunity to respond by publishing our articles. In their letter, the authors questioned our assumption about the cost of a false negative and discussed the relevance of several important issues that were not addressed in our earlier articles. Although beyond the scope of our investigation, these very pertinent concerns include the lack of regular screening of a high percentage of women, the importance of laboratories' adherence to acceptable laboratory practices and the value of periodic cytologic smears as a longitudinal process that spans several years. We agree that the societal benefits of cervical screening are diminished significantly if a small percentage of candidate women use these services. It is also possible, however, that improved quality and the development of optimal laboratory policies will reduce the negative publicity associated with cervical screening and subsequently result in a higher percentage of use by candidate women. As more women take advantage of cervical screening, the need for optimal laboratory policies will become more important.

With respect to the cost of a false negative and the impact this assumption has on the efficiency of screening for cervical cancer, we strongly endorse the general opinion that effectiveness and total cost considerations should dictate appropriate methods of screening for cervical cancer. We hope that readers of Acta Cytologica do not have the mistaken impression that in all situations, we are advocates of double or multiple screening. We are not. Our objective, rather, was to develop flexible mathematical models that help researchers, clinicians and risk managers to understand the total cost, sensitivity and specificity of various possible screening policies. Also, these models can be used to determine the optimal screening policy for any particular situation, given, as inputs, the sensitivity and specificity of cytotechnologists, sensitivity and specificity of pathologists, incidence and cost of a false positive and false negative determination.

The development of these models was driven by our belief that quality assurance can be significantly improved by developing an analytic understanding of the process. This approach has been emphasized by W. E. Deming and is the basis for our approach to quality management. Deming repeatedly emphasized the need to develop an understanding of a system, statistically and otherwise, in order to optimize the performance and quality of that process. We suspect that this process orientation is very similar to the philosophy emphasized by Hutchinson et al, who referred to the total "process of cervical cancer prevention" beyond any single cervical screening.

In fact, our mathematical models were originally developed to examine the effectiveness of the process of using the standard 10% rescreening rate and to determine, analytically, the economics of rescreening a specified percentage of negative cervical smears. For example, as shown in one of our papers, the use of 10% rescreening of negative cervical smears only minimally reduces false negatives when compared to a policy of zero rescreening. Furthermore, additional research by Benneyan and Kaminsky has shown that the optimal policy for any combination of sensitivities, specificities, incidence and number of cytotechnologists will always employ either 0% or 100% rescreening by a pathologist. Thus, in no situation will any amount of partial rescreening ever result in the best laboratory policy. This result, which might not be reached.
without the use of an economic model, is very significant in light of the current laboratory practices and requirements imposed by federal regulations.

Alternatively, in some clinical laboratories double screening is used routinely. For these particular laboratories, the results in our papers can be used to help determine if this is an appropriate policy. These models also can be used to explore some of the other questions that were raised by Hutchinson et al. For example, if double screening is used, what is the probability of detecting the truly positive patient and the truly negative patient?

It is important to clarify that we used an example based on $5,000 for the cost of a false negative to illustrate, mathematically, that situations exist for which single screening is economically optimal and others exist for which multiple screening is economically optimal. In the questioned case, the optimum policy was to use single screening in two of the three examples. Only in the case of low specificity and high sensitivity was double screening the minimum cost policy.

As the discussion by Hutchinson et al illustrates, cytology is a complex process involving several competing costs and issues. These complexities make an objective assessment difficult without the use of analytic tools. As we stated in our article, these costs are not known with certainty, and additional research is needed to identify reasonable estimates. Nevertheless, given that some parameters, such as the exact sensitivities of cytotechnologists and pathologists and the exact cost of a false negative, may not be known with precision, an analytical expected cost model can be quite useful in an exploratory study to determine how the optimal policy might change for various values of the unknown parameters.

For example, given the uncertainty in the exact cost of a false-negative, the following question could be asked. If all parameters except the cost of a false-negative are held constant, what happens to the optimal policy for a range of values for the cost of a false-negative? Figure 1 illustrates results using our economic model software for conditions similar to those specified in Table II of a paper by Kamin-nessky et al4—namely, low sensitivity and high specificity. In this case, for a process with low sensitivities and high specificities, when the cost of a false negative is greater than $650, then the minimum cost policy is to use double screening with a 0% resampling rate. In this example, when the cost of a false negative falls below $650, then single screening with a 0% resampling rate is optimal. The exact results, of course, will differ for any particular scenario.

This example suggests that in order to avoid the use of double independent screening, the sensitivities of the personnel who do the screening would have to be improved to the point where single screening became optimal. Similarly, the model can also be used to examine, for a specific set of parameters, how the sensitivities of cytotechnologists and pathologists influence the optimal policy. For example, Figure 2 illustrates the behavior of the optimal policy for a range of possible cytotechnologist and pathologist sensitivities. Again, various uses of the models help to develop an understanding of the system performance so as to facilitate clinical decision-making with useful, quantitative information.

In discussing the high cost of litigation and settlements related to a false negative, Hutchinson et al argued that high settlements were made in those cases in which “laboratories simply were practicing at standards below the norm,” such as those established by federal regulation under CLIA ‘88. This certainly appears to have been true in some cases. Due to results discussed above, however, mere conformity with CLIA ‘88 and other approaches that attempt to “inspect quality in” would be difficult to defend against an expert witness who argues that better quality control methods, which go beyond the minimal questionable standards mandated by federal regulations, should have been used.

Alternatively, as demonstrated in a companion paper by Kaminsky et al5 and one by Levy et al,6 modern methods of statistical quality control can be effectively applied to order to control and improve laboratory process quality. For example, Hutchin-
son et al suggest the use of seeded positive slides as an alternative to massive rescreening as a means of improving quality. This approach also has been discussed by Lundberg,7 Melamed8 and Paris9 and should be explored further with the use of analytic models. Quality control charts, ranging from simple p charts to more advanced methods, could be very effective in such a scenario as a means of monitoring and improving quality.

In summary, we hope that use of mathematical models to improve quality in the clinical laboratory is a topic that will receive more attention in the literature. We would appreciate any comments that others may have.

References


Keywords: quality control, mass screening, cervical smears. (Acta Cytol 1996;40:837-841)

Unusual Plant Cell Contamination in a Vaginal Smear

To the Editors:

Fungi, parasites and bacteria are frequently observed during the routine examination of vaginal and cervical smears.2,4,6,8 Although plant cells have been observed by Avrin et al1 and Koss5 in vaginal smears and sputum samples, this occurrence is rare.

During study of a vaginal smear from a 40-year-old woman, we encountered an unusual formation suggestive of plant cells. The elongated cells had wavy cell walls and abundant stomata (Figure 1). These unusual plant cells were classified as belonging to the genus Cyperus. The characteristic features of Cyperus are undulating cell walls and abundant stomata.3,4

To confirm our finding, we examined microscopically thin sections from the fresh leaves of Cyperus obtained with a razorblade. As shown in Figures 1 and 2, the patterns in the vaginal smear and in fresh Cyperus were similar.

The gynecologist indicated that there was a Cyperus plant in the room in front of the window when she took the smear sample. The sample remained under the Cyperus plant after fixation by hair spray. In order to resolve the issue of the origin of the plant

![Figure 1](image-url) Surface view of the epidermis of Cyperus in a vaginal smear. Wavy cell wall (arrow), stoma (double arrow) (Papanicolaou stain, ×500).
cell, we placed one fixed and one unfixed smear under the Cyperus plant for two days. The slides were stained with Papanicolaou stain and examined under a light microscope. Neither of them contained plant cells. We are therefore at a loss to explain the presence of the Cyperus cell in the vaginal smear.

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References

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Pitfalls in the Diagnosis of Germ Cell Tumors on Fine Needle Aspiration Biopsy

To the Editors:
A 5-month-old, male infant was referred to our hospital with complaints of cough, breathlessness and poor feeding for 10 days. On examination, the infant was afebrile, with a heart rate of 140 beats per minute and respiratory rate of 84 per minute, with subcostal and intercostal retraction. The anterior fontanelle was open and measured 3 cm. The systolic blood pressure was 100 mm Hg. There was no
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Subsequently the mass was excised. Gross examination revealed an encapsulated mass measuring 8×7×4 cm, with a smooth, bosselated external surface except for a 1.5×1-cm raw area where it was attached to the pericardium. The cut surface of the mass was white, myxoid, lobulated, gritty, cartilaginous and partly cystic. Histology showed a teratoma consisting mainly of mature elements—skeletal and smooth muscle, cartilage, and gastrointestinal and respiratory epithelia. Small foci of glial tissue with neuroepithelial rosettes were also seen.

This case is described to bring attention to the pitfalls in the diagnosis of germ cell tumors on FNAB material.

Pleuropulmonary blastoma is a highly aggressive and rare tumor occurring in children at various anatomic locations in the thoracic cavity. On gross examination, large, cystic areas are seen near the tumor mass. Microscopically the tumor is composed of small, primitive blastemal cells with a malignant uncommitted or differentiated stromal component.

Teratomas are germ cell neoplasms originating with pleuripotential cells capable of differentiating into a variety of tissues. The presence of different tissue elements in the aspirated material suggests a germ cell tumor, especially teratoma, and the presence of mitotic activity suggests that the teratoma is immature. Squamous and columnar epithelial cells are often found in the aspirates of mature teratomas from sites other than testis. They were absent from the aspirate in our case. Round cells of the neuroepithelium were misinterpreted as primitive blastemal cells of the pleuropulmonary blastoma. Due attention does not appear to have been given to the presence of skeletal muscle fibers in the aspirate.

Germ cell tumors should be considered in the differential diagnosis of midline tumors in infants and children. The anterior mediastinum is the most frequent site of extragonadal germ cell tumors after the sacrococcygeal region. Diagnosis of FNAB is given on the assumption that the material aspirated is representative of the rest of the tumor. In order to obtain a representative aspirate, multiple passes are usually done. However, while performing guided FNAB in a vital anatomic site like the pericardial space, the number of passes is severely restricted, and the sample obtained may not be representative of the entire lesion. The cytopathologist should be aware of these problems while interpreting guided FNABs from vital anatomic sites.
Pneumothorax: A Complication of Fine Needle Aspiration of Breast Tumors

To the Editors:

We read with interest the recent article by Kaufman and colleagues entitled “Pneumothorax: A Complication of Fine Needle Aspiration of Breast Tumors.” The article reported four instances of pneumothorax that developed in 417 fine needle aspirations (FNAs) of breast. The authors did not describe the cytologic findings, nor did authors of other articles on this subject that we were able to review.

We recently examined the smears from breast FNA complicated by pneumothorax. The case involved a 17-year-old girl who presented with a 1.5-cm, circumscribed mass at the 6 o’clock, peripheral portion of the left breast. She was thin, and her breasts were relatively small. FNA using an 18-gauge needle was performed. No syringe holder was used, and the lesion was approached with the needle perpendicular to the chest wall. At one point, air was aspirated, and the patient complained of chest pain. The procedure was terminated and smears prepared. A chest roentgenogram revealed a small (5%) pneumothorax, which resolved spontaneously.

The aspiration smears showed scattered cells oc-
curring singly or in small clusters (Figure 1). Cells arranged in clusters were exclusively bland and columnar, and many were ciliated. The single cells were either columnar cells, some of which were ciliated, or histiocytes, some of which possessed yellow-brown pigment.

When we first examined the smears, without knowledge of the complication, we were puzzled by the predominant cell type, ciliated columnar, which is not known to occur in the breast or breast lesions except for cysts of cutaneous origin. When the complication of pneumothorax was revealed to us, it became clear that the cytologic findings were those of normal lung.

Since the onset of symptoms from pneumothorax complicating needle aspiration may be delayed, the FNA smears may provide the first clue to the occurrence of this complication after aspiration of breast or other chest wall lesions.

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Keywords: pneumothorax, breast neoplasms, aspiration biopsy. (Acta CytoI 1996;40:844-845)

Rhinospordiodoma of Bone: Diagnosis by Fine Needle Aspiration

Letter to the Editors:
We recently saw a case of isolated bone involvement by rhinosporidiosis that was diagnosed on fine needle aspiration cytology.

A 36-year-old male presented with a swelling on the ring finger of the right hand of three months’ duration. A nasal polypectomy for epistaxis had been performed five years earlier. However, details...
of the histologic evaluation were not available. On examination, the ring finger showed a 5-cm, oblong swelling involving the proximal phalanx of the ring finger. Erosion of the lateral end of the fifth metacarpal was also noted (Figure 1). In view of the expansile, lytic nature of the lesion, a metastatic tumor was suspected, and fine needle aspiration was performed with a 22-gauge needle.

Papanicolaou and May-Grünwald-Giemsa smears showed multiple spores within sporangia as well as outside them. The sporangia measured 300–400 µm, and each contained 20–100 spores (Figure 2). Each spore measured about 15 µm in diameter; had a thick, refractile wall; and contained an area of clearing (Figure 3). Empty sporangia, granulation tissue, fibroblasts and endothelial cells were also seen.

The patient was advised to undergo surgical excision but refused and was lost to follow-up.

A bone tumor was diagnosed on clinical and radiologic grounds because of the presentation. Even if the previously removed polyp had proved to be rhinosporidiosis, it is unlikely that it would have been considered as a possible diagnosis. Although involvement of bone in rhinosporidiosis is known, most cases represent local bone invasion in the skull. "Metastatic" lesions are extremely uncommon in bone.

On purely morphologic grounds, a diagnosis of myospherulosis was a possibility. However, the spores of Rhinosporidium seeberi are twice the size of red blood cells. Further, in the given clinical context, myospherulosis was unlikely. Cytologic material has been used before for the diagnosis of rhinosporidiosis in bronchoalveolar lavage specimens and sputum. To our knowledge, this is the first documented case of rhinosporidiosis of bone diagnosed on fine needle aspiration cytology. This case is similar to one reported by Aravindan et al., and like them, we think that the "metastasis" probably took place at the time of the previous surgery on the nose.

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References


Keywords: rhinosporidiosis, aspiration biopsy.

(Cytology of Tumors of the Central Nervous System

To the Editors:

Two recently published articles in Acta Cytologica have attracted my attention. The first dealt with the diagnosis of meningiomas that displayed malignant features and illustrated six cases in which the cytologic diagnosis was made from specimens obtained with biopsy forceps or by surgical resection. Crush preparations were fixed in 95% ethanol and stained with hematoxylin and eosin or were air-dried and stained by the Diff-Quik technique. The second article described the cytologic features of some brain tumors, including meningiomas, neurilemmomas and astrocytomas. Crush preparations were obtained from intraoperative fresh tissue and were fixed in 95% ethanol prior to Papanicolaou staining.