Interpretation of Fine-Needle Aspirates Processed by the ThinPrep® Technique:
Cytologic Artifacts and Diagnostic Pitfalls.

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The improvement in quality of cytologic preparations with the use of the ThinPrep® methodology has been well-documented, but the cytologic artifacts resulting from this technique have not been adequately described. This study describes and illustrates the cytologic artifacts introduced by the ThinPrep technique when used on fine-needle aspirates (FNAs), and evaluates these artifacts as potential diagnostic pitfalls.

We reviewed a total of 120 FNAs simultaneously processed by both conventional smears and ThinPrep. FNAs were obtained from the following sites: lymph node (27), breast (23), soft-tissue sites (20), salivary glands (13), gastrointestinal tract (10), lung (9), thyroid gland (13), liver (3), adrenal gland (1), and kidney (1).

The ThinPrep smears were consistently devoid of obscuring elements, and the cells were adequately preserved and evenly dispersed. However, we noted some cytomorphologic alterations that should be recognized to avoid erroneous diagnoses. The size of cell clusters was decreased, large branching sheets were fragmented, and there were more single cells, resulting in apparent discohesion. Small cells such as lymphocytes tended to aggregate. All cells were generally smaller and occasionally spindled, the chromatin detail was attenuated, and nucleoli were more prominent. Intranuclear inclusions were difficult to visualize. Background matrix was often altered in both quantity and quality. Extracellular particles, small mononuclear cells, red blood cells, and myoepithelial cells were markedly decreased in number.

The pathologist should be cautious in interpreting FNAs prepared using ThinPrep if that is the only methodology employed. Familiarity with artifacts is essential to avoid misinterpretations. Diagn. Cytopathol. 2000;23:6–13.

Key words: fine-needle aspirates; ThinPrep; monolayer; cytologic artifacts

The ThinPrep® (Cytyc, Malborough, MA) process is an automated slide technique designed to improve the conventional cytologic preparation and overcome many of the factors that limit the cytologic interpretation of conventional smears. These limiting factors include obscuring material such as blood, inflammatory exudate, and mucus, air-drying, and variable smear thickness. The technique involves collection of the specimen in a proprietary methanol-based solution (Cytyc CytoLyt) which contains hemolytic and mucolytic agents.[1] The specimen is then centrifuged, and the cell pellet is transferred to another methanol-based preservative (Cytyc Preservcyt). In the ThinPrep processor, a cylinder with a polycarbonate thin filter attached to one end is introduced into the specimen vial and gently rotated. This agitation creates a mild current that disperses mucus and other debris, and promotes a random distribution of cells within the fluid. A vacuum is applied to the cylinder that causes most of the erythrocytes and inflammatory cells to pass through the filter pores, while the diagnostic cells adhere to its surface. The processor software controls the cellular density. The cylinder is removed, inverted, and lightly pressed against a positively charged slide. A mild positive air pressure is applied to ensure adherence of cells to the slide. The result is a 20-mm circular smear with evenly dispersed cells.[2]

In July 1995, the ThinPrep method for nongynecologic specimens was implemented at the University of Michigan. We noted several worrisome artifacts in our ThinPrep FNAs when compared to conventional smears. Some of these artifacts proved to be easily recognized, while others caused uncertainty and resulted in either false-negative or false-positive diagnoses. This prompted us to study FNAs obtained from a wide variety of lesions, so that we could describe and illustrate the cytologic artifacts produced by ThinPrep and evaluate their potential as diagnostic pitfalls.

Materials and Methods

We reviewed a total of 120 FNAs simultaneously prepared by conventional smears and the ThinPrep process. These included a cohort of 93 FNAs obtained at the FNA clinic or

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Table I. Fine-Needle Aspirates of the Breast

Diagnosis	*Number of cases*
Adenocarcinoma	14
Fibrocystic changes	2
Diabetic mastopathy	1
Fibroadenoma/gynecomastia	3
Papilloma	1
Lactating adenoma	2
Total	23

Table II. Fine-Needle Aspirates of the Thyroid Gland

Diagnosis	*Number of cases*
Hyperplastic colloid nodule	3
Hashimoto's thyroiditis	1
Follicular/Hurthle-cell lesion	3
Papillary carcinoma	3
Lymphoma	1
Medullary carcinoma	1
Trabecular carcinoma	1
Total	13

Table III. Fine-Needle Aspirates of the Salivary Gland

Diagnosis	*Number of cases*
Pleomorphic adenoma	6
Sialadenitis	1
Adenoid cystic carcinoma	1
Acinic-cell carcinoma	1
Mucoepidermoid carcinoma	2
Poorly differentiated carcinoma	1
Squamous-cell carcinoma	1
Total	13

Table IV. Fine-Needle Aspirates of Soft-Tissue Lesions

Diagnosis	*Number of cases*
Leiomyosarcoma	2
Granular-cell tumor	1
Amyloidoma	1
Nodular fascitis	1
Enchondroma	1
Total	6

as radiologically directed aspirates. An additional 27 surgical bench FNAs were obtained as a control group for optimal cellularity and specimen representation. FNAs were obtained from the following sites: lymph node (27), breast (23), soft tissue (20), salivary glands (13), thyroid gland (13), gastrointestinal tract (10), lung (9), liver (3), adrenal gland (1), and kidney (1). Major diagnoses included: adenocarcinoma (52), squamous-cell carcinoma (13), small-cell carcinoma (6), small round cell tumors (11), melanoma (11), soft-tissue tumor (6), and benign (21). A summary of selected site-specific diagnoses is presented in Tables I–IV.

FNAs were obtained with a minimum of four passes through the lesion. A small droplet was deposited on a slide, and the remaining material was rinsed in CytoLyt. At least one pass was dedicated to ThinPrep. With the surgical bench aspirates, two passes were prepared by conventional smears and another two were rinsed in CytoLyt. Conventional smears were prepared by the two-slide pull technique. One slide was air-dried and stained by Diff-Quik (Baxter Scientific Products, McGraw Park, IL) for immediate interpretation; the other slide was alcohol-fixed and stained by the Papanicolaou method. One ThinPrep slide was prepared for each aspirate according to the manufacturer's directions, and stained by the Papanicolaou method.

Table V. Comparison of ThinPrep and Conventional Smears[a]

Indicator	*Study group (N = 93)*	*Control group (N = 27)*	*Total (N = 120)*
Quality			
TP = CS	54 (58%)	11 (41%)	65
TP > CS	11 (12%)	3 (11%)	14
TP < CS	28 (30%)	13 (48%)	41
Cellularity			
TP = CS	82 (88%)	18 (67%)	100 (83%)
TP > CS	8 (9%)	5 (18%)	13 (11%)
TP < CS	3 (3%)	4 (15%)	7 (6%)

[a]TP, ThinPrep; CS, conventional smears; >, superior; <, inferior.

To evaluate the influence of cytologic artifacts on the final diagnosis, the ThinPrep slide was reviewed before the conventionally prepared smear without knowledge of the final diagnosis, and a diagnosis was reached by each method. A second review of the paired slides with knowledge of the final diagnosis was then performed and the findings were compared. The following features were evaluated in each case: background cells (neutrophils, lymphocytes, red blood cells, and myoepithelial cells); background particles (pigment and granules); extracellular material (mucin, colloid, myxoid, chondroid, and amyloid); architectural integrity (size and shape of cellular aggregates, degree of discohesion and single cells); and cytologic features (chromatin pattern, nuclear membranes, and nucleoli).

Results

At low magnification, ThinPrep slides appeared superior in quality to conventional smears, largely as a result of an almost total lack of obscuring elements. The cells were evenly dispersed with minimal overlap against a clean background. Screening ThinPrep slides was easier because the cells had a monolayer arrangement and were concentrated in a coin-sized area, while multiple conventional smears were reviewed, especially when excess blood or necrotic material was present. Considering all the evaluated features other than bloody background, conventional smears were equal in quality to ThinPrep in 65 cases, superior in 41 cases, and inferior in 14 cases. Table V compares the quality and cellularity between the two methods in both the study and control groups. ThinPrep was superior in cellularity in 18% of the control group vs. 9% of the study group when compared to the conventional smears. Interestingly, 4 cases

(15%) of the control group suffered of loss of cellularity, while their correlating conventional smears were richly cellular.

Background Cells and Particles

The ThinPrep technique can result in the loss of some cells. Red blood cells (RBCs) are either lysed or actually pulled through the filter except in very bloody aspirates, where a few scattered ghosts of RBCs are retained. Similarly, other small cells in the specimen such as lymphocytes, neutrophils, and myoepithelial cells may be pulled through the filter and consequently be underrepresented. In some cases with reactive epithelial changes and a few scattered inflammatory cells, it was difficult to determine whether the inflammatory cells originated from lysed peripheral blood or underrepresented true inflammation. Small loose particles such as melanin, hemosiderin, and granular debris disappeared from the background but were retained when present in the cellular cytoplasm. Necrotic debris was also diminished and tended to aggregate in small clumps, making it difficult to recognize.

Extracellular Material

Colloid (Fig. C-1), mucin (Fig. C-2), and amyloid, chondroid, and myxoid extracellular material (Fig. C-3) were all decreased in quantity and altered in quality. In ThinPreps, this material appeared as small dense droplets or acquired a filamentous and/or moth-eaten appearance that made it indistinguishable from fibrin.

Architectural Integrity

Large aggregates, branching sheets, and papillary clusters of cells traditionally seen on conventional smears were fragmented in ThinPreps and appeared as small clusters and cell aggregates with irregular borders. Papillae or branching fragments were completely broken, and only a rare cluster displayed a hint of papillary formation or branching. These architectural changes were accompanied by increased numbers of intact single cells in the background that gave a false impression of cellular discohesion, and resulted in mistaken diagnoses of malignancy in the initial phase of our review.

Cellular Changes

The cells in a ThinPrep appeared smaller than the same cells in conventional smears. The nucleoli were more prominent and acquired a red color. The chromatin detail was generally well-preserved but did not appear as vesicular as in conventional smears. General features of malignancy such as nuclear pleomorphism and membrane irregularity were well-preserved. The cytoplasm was denser and more easily seen in small cells such as lymphocytes and small-cell carcinoma. Occasionally the cytoplasm appeared spindled or frayed, especially in the cells along the aggregates' borders. Intranuclear inclusions were less visible in ThinPrep while easily detected on conventional smears. Mononuclear cells such as lymphocytes, which are traditionally singly dispersed in conventional smears, were artificially aggregated and formed tight clusters in ThinPreps, resulting in some difficulty in evaluating their nuclear features (Fig. C-4).

Myoepithelial (bipolar) cells were decreased in number and tended to localize at the periphery of the ThinPrep, making it difficult to subclassify some benign breast aspirates (Fig. C-5). Some myoepithelial cells had intact spindled cytoplasm that made it difficult to differentiate them from the fibrous stromal cells of an invasive carcinoma.

In small-cell carcinoma, the cellular aggregates were smaller and more fragmented than typically seen on a conventional smear. Nuclear molding was present in ThinPrep, but considerably less so than in conventional smears. Chromatin smearing was almost nonexistent in ThinPreps. The nucleoli in ThinPreps were more conspicuous than traditionally observed in conventional smears, which resulted in initially misdiagnosing some cases as poorly differentiated carcinomas of the nonsmall-cell type (Fig. C-6).

Relation of Cellularity to Artifacts on ThinPrep

The quantity and/or quality of elements such as extracellular material, myoepithelial cells, and evidence of branching were directly proportional to the number of passes performed and the original cellularity of the aspirate. This relation was evident by the higher percentage of superior ThinPreps among the control group than the study group (18% vs. 8%). Similarly, among the study group we noticed better quality ThinPreps in cases performed by the pathologists than in the radiology or ultrasound-guided aspirates, where we only provided assistance.

Discussion

Most cytology laboratories utilize more than one technique to prepare nongynecologic specimens. The decision of which technique to use depends on the type of specimen and the advantages offered by the particular preparation method. Conventional smears are most commonly used for FNA to best evaluate architecture, cellular arrangements, and extracellular material. In contrast, centrifugation is preferred for specimens such as urine and other body fluids, where a large specimen is concentrated and a representative cytospin can be produced.

The improvement in quality of the cytologic smear with the use of the ThinPrep methodology has made this new technique the procedure of choice in many institutions. ThinPrep insures the presence of well-preserved cells spread in a uniformly thin layer with minimal overlap, in a background devoid of obscuring blood or inflammatory exudate. In suboptimal FNAs, the cells have a better chance of being represented on the slide. This should result in a decrease in the number of unsatisfactory diagnoses. Fischler

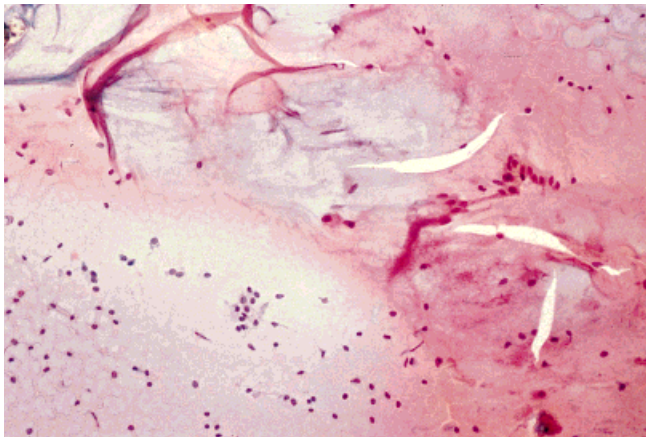

Fig. C-1A

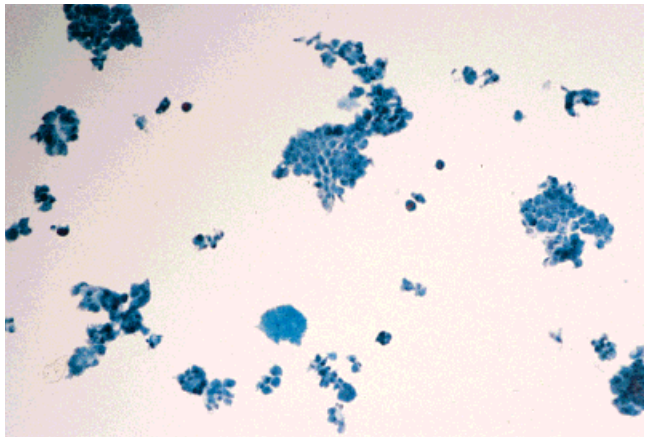

Fig. C-1B

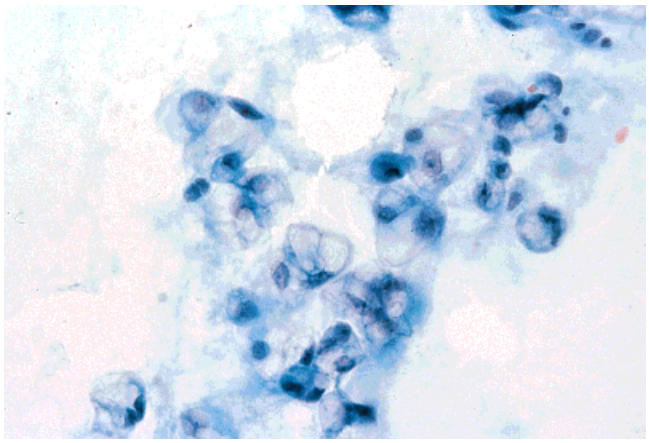

Fig. C-2A

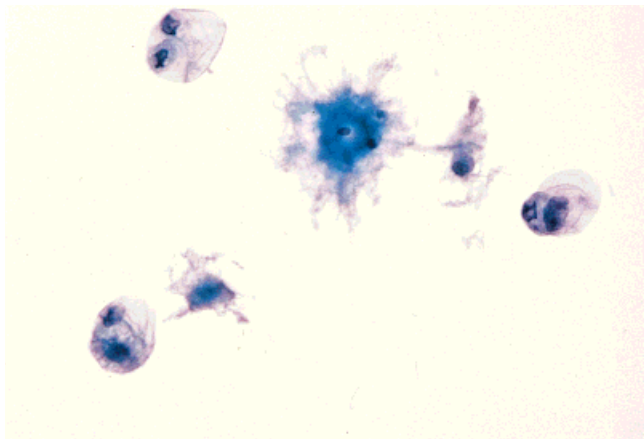

Fig. C-2B

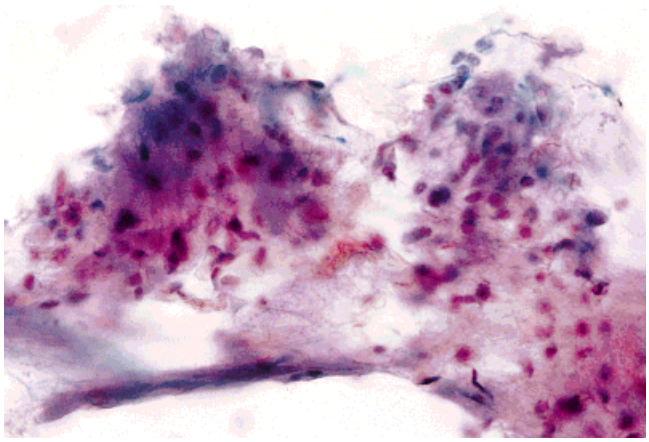

Fig. C-3A

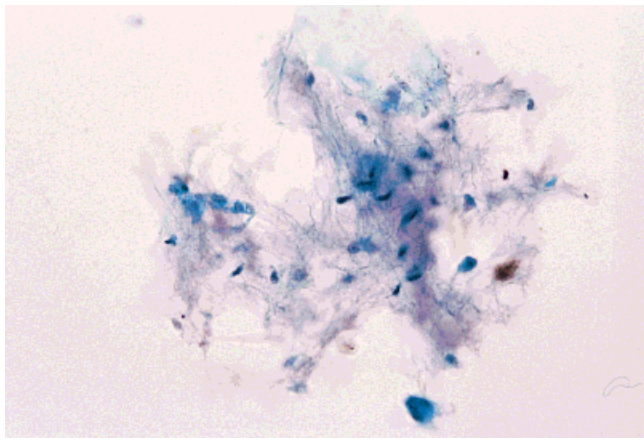

Fig. C-3B

Fig. C-1. A: Conventional smears from a colloid nodule, revealing scattered small clusters of follicular cells in a background of abundant watery colloid and numerous bare nuclei (Papanicolaou stain, ×200). **B:** Correlating ThinPrep, illustrating the relatively increased cellularity and few small droplets of dense colloid in a clear background (Papanicolaou stain, ×200).
Fig. C-2. A: Conventional smears from a metastatic colon carcinoma to the omentum, revealing malignant cells with abundant vacuolated cytoplasm in a background of abundant mucin ((Papanicolaou stain, ×400). **B:** Correlating ThinPrep, in which the mucin presented as small thick deposits with a filamentous texture (Papanicolaou stain, ×400).
Fig. C-3. A: Conventional smears from a pleomorphic adenoma, revealing clusters of myoepithelial cells enmeshed and surrounded by abundant myxoid material (Papanicolaou stain, ×400). **B:** Correlating ThinPrep, in which myxoid material presented as a few deposits with a filamentous texture (Papanicolaou stain, ×400).

Table VI. Comparison of Conventional Smears and ThinPrep in Selected Lesions[a]

Site	*Conventional smear*	*ThinPrep*
Adenocarcinoma	Sheets and 3-D clusters of abnormal cells.	Abnormal cells in small aggregates and flattened 3-D clusters.
	Crisp nuclear detail, with coarse hyperchromatic or vesicular chromatin and prominent nucleoli.	Attenuated chromatin detail and prominent nucleoli; however, basic features of malignancy are detectable.
	Vacuolated cytoplasm.	Cytoplasm appears denser and less vacuolated.
	Abundant background mucin in mucinous carcinomas.	Mucin is decreased and appears as droplets.
Squamous-cell carcinoma	Keratinizing abnormal cells in sheets and as single cells with bizarre shapes.	Small aggregates and single abnormal cells. Keratin well-preserved.
	Hyperchromatic nuclei.	Hyperchromatic nuclei.
	Background of necrosis and tumor diathesis.	Necrosis appears as small patches of granular material with entrapped debris and neutrophils.
Small-cell carcinoma	Cohesive sheets, loosely cohesive aggregates, short chains, and numerous single cells.	Small aggregates and numerous single cells. Short chains are decreased.
	Marked nuclear molding and chromatin smearing.	Subtle nuclear molding. No chromatin smearing.
	Salt-and-pepper chromatin and inconspicuous nucleoli.	Salt-and-pepper chromatin and small nucleoli.
Breast		
Fibroadenoma	Large cohesive folded and branching sheets.	Small-cell aggregates.
	Numerous myoepithelial cells.	Reduction in numbers of myoepithelial cells.
	No discohesion.	Increase in numbers of single intact cells.
Adenocarcinoma	Sheets and 3-D clusters of abnormal cells.	Small aggregates and flattened clusters.
	Numerous single abnormal cells.	Numerous single abnormal cells.
	Occasional fragments of fibrous tissue.	Single fibroblasts (mimicking myoepithelial cells).
Thyroid		
Hyperplastic colloid nodules	Abundant watery colloid.	Decreased colloid, appearing as small droplets.
	Clusters and sheets of follicular cells. Numerous small follicles.	Small aggregates of follicular cells. Cellularity may appear relatively increased.
	Cells arranged in an ordered honeycomb.	Cells arranged in an ordered honeycomb.
	Histiocytes common.	Histiocytes present.
Follicular cell neoplasms	Scanty or absent colloid.	Few droplets or absent colloid.
	Syncytial tissue fragments with occasional follicles.	Small syncytial aggregates.
	Honeycomb with altered polarity.	Honeycomb with altered polarity.
	Cells are uniformly increased in size.	Uniformly increased cell size.
Papillary carcinoma	Papillary or large syncytial tissue fragments.	Fragmented papillae and small syncytial aggregates.
	Uniformly enlarged nuclei with crowding.	Uniformly enlarged nuclei with crowding.
	Nuclear grooves and intranuclear cytoplasmic inclusions.	Nuclear grooves present. Intranuclear inclusions are more difficult to find.
	Hard colloid, giant cells, and psammoma bodies.	Colloid droplets, giant cells, and psammoma bodies.
	Cystic degeneration and histiocytes.	Cystic degeneration and histiocytes.
Hashimoto's thyroiditis	Sheets of Hurthle cells with or without atypia.	Small aggregates of occasionally atypical Hurthle cells.
	Scant or absent colloid.	No colloid.
	Numerous mature lymphocytes, plasma cells, and transformed lymphocytes around epithelial fragments.	Fewer mononuclear cells, mostly seen in pools or towards the periphery of the smear.
Salivary glands		
Pleomorphic adenoma	Admixed mesenchymal and epithelial elements.	Admixed elements apparent only in cellular aspirates.
	Watery myxoid to chondroid stroma	Myxoid is decreased and appears as small droplets or acquires a fibrin-like or moth-eaten appearance.
	Monomorphic population of epithelial cells in branching fragments.	Small aggregates of uniform cells with no particular pattern.
Warthin's tumor	Sheets of oncocytic cells admixed with numerous lymphocytes.	Small aggregates of oncocytic cells. Lymphocytes are decreased and best seen at the periphery.
	Background with amorphous cellular debris.	Loss of amorphous background.
Benign acini	Small acinar structures with finely vacuolated cytoplasm and sheets of ductal cells. In hyperplasia, there are increased cytoplasmic vacuoles and numerous bare nuclei.	Acini are well-preserved, with vacuolated cytoplasm. Hyperplastic acini appear as "bunches of grapes" admixed with ductal cells. No bare nuclei.
Acinic-cell carcinoma	Sheets of cells with uniform nuclei.	Small aggregates of cells with uniform nuclei.
	Cytoplasm vacuolated or granular.	Cytoplasm denser in quality.

Table VI. (continued)

Site	*Conventional smear*	*ThinPrep*
	Numerous bare nuclei.	No bare nuclei.
	No ductal cells.	No ductal cells.
Mucoepidermoid carcinoma, low grade	Sheets of slightly atypical cells.	Small aggregates of atypical cells.
	Admixture of mucus-secreting, goblet-like cells, intermediate, and squamous cells.	Cytoplasm is dense, and hence mucin is less apparent.
	Mucin may be seen in background.	Background mucin is absent or appears as droplets.
Lymph node		
Reactive node	Singly dispersed polymorphous population of lymphocytes.	Lymphocytes are present in pools and sometimes artificially aggregated or in short chains.
	Cytoplasm not easily detected.	A small rim of cytoplasm may be seen.
	Tingible body macrophages.	Tingible body macrophages easily found.
	Absent or rare mitotic figures.	Absent or rare mitotic figures.
Non-Hodgkin's lymphoma	Monomorphous population of atypical single lymphocytes.	Monotonous population of atypical lymphocytes in small aggregates and/or single cells.
	No tingible body macrophages (except in high-grade).	No tingible body macrophages (except in high-grade).

[a]3-D, three-dimensional.

and Toddy[3] reported a reduction in their unsatisfactory rate from 17% to 1% after ThinPrep implementation.

Despite these obvious benefits, ThinPrep has some disadvantages that need to be considered when determining which specimens are best suited for this technique. Recognition of the artifacts seen in ThinPrep aspirates becomes increasingly important as support for this technique grows. Of all cytologic specimens, FNAs require the preservation of architecture and cellular/nuclear morphology to accurately reflect the histologic picture. Several studies have reported cellular shrinkage, loss of stromal cells, altered architecture, and diminished extracellular material on ThinPreps.[4–7]

We have found several artifacts inherent to the ThinPrep process. While some of these artifacts are trivial and would not ultimately affect the final diagnosis, others could result in either misclassification of the lesion or a false diagnosis. Table VI summarizes the major cytologic artifacts observed on ThinPreps in selected sites and tumors. Pathologists can easily recognize changes induced by the wet fixation and balling up of cells, such as denser cytoplasm, prominent nucleoli, cellular shrinkage, attenuation of chromatin detail, and inconspicuous intranuclear inclusions. Lesions such as squamous-cell carcinoma and adenocarcinoma, not otherwise specified, are also easily recognized, since the pleomorphism, nuclear irregularity, and hyperchromasia that are characteristic of these lesions are obvious on ThinPrep. Other architectural or cellular changes are more problematic. For example, the loss of intestinal mucus in ultrasound-guided FNAs obtained via endoscopy is desirable, but the presence of mucin is essential for the diagnosis of mucinous cystic lesions and mucin-producing adenocarcinomas, where the cells usually exhibit only slight nuclear atypia and may be easily overlooked. The alteration of extracellular material that is essential in formulating specific diagnoses in sites such as the thyroid, salivary glands, and some soft-tissue lesions is another potential diagnostic problem. This extracellular material is diminished and altered in quality in the ThinPrep process; it may also acquire a filamentous quality that makes it indistinguishable from fibrin. In a review of 41 paired FNAs obtained from surgically resected thyroid nodules, Biscotti et al.[8] reported similar diagnostic accuracy with both techniques, although they pointed out that colloid was decreased and appeared as droplets and the cytoplasm was more disrupted on the ThinPrep. Frost et al.[9] reported a diagnostic accuracy of 85% with ThinPrep vs. 96% with direct smears of thyroid FNAs. Half of their discrepant cases with ThinPrep were adenomatoid nodules with cystic change, while the other half were chronic lymphocytic thyroiditis. They noted a decrease in lymphocytes, spherules, and colloid, which was fragmented and appeared as small droplets on ThinPrep.[9]

Malignant neoplasms of the breast are easily recognized on ThinPrep, except for those with low nuclear grade or large mucinous components. These neoplasms may be difficult to distinguish from benign mammary epithelium if ThinPrep is the only methodology employed. Fibroadenoma is the most problematic lesion on ThinPrep and is the most common cause of a false-positive diagnosis in breast aspirates. The myoepithelial cells are considerably decreased in number. The large monolayer branching and folded sheets characteristic of fibroadenoma on a conventional smear are completely fragmented and appear as small clusters. The nucleoli tend to be more prominent, and many single cells with intact cytoplasm are present in the background, features that are traditionally associated with carcinoma.

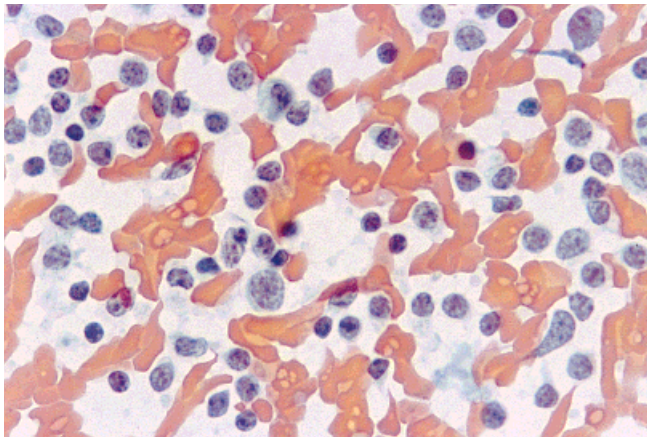

Fig. C-4A

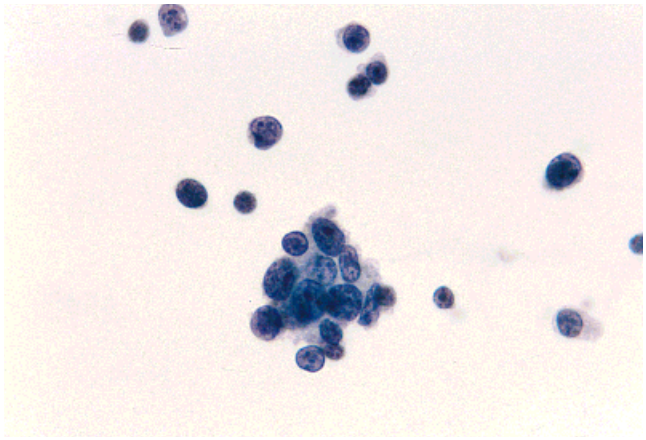

Fig. C-4B

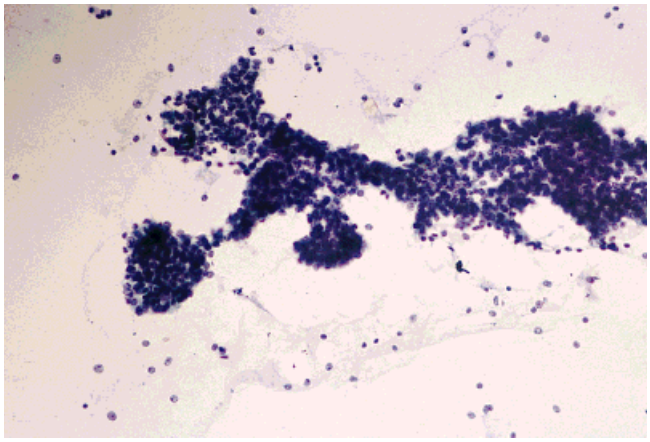

Fig. C-5A

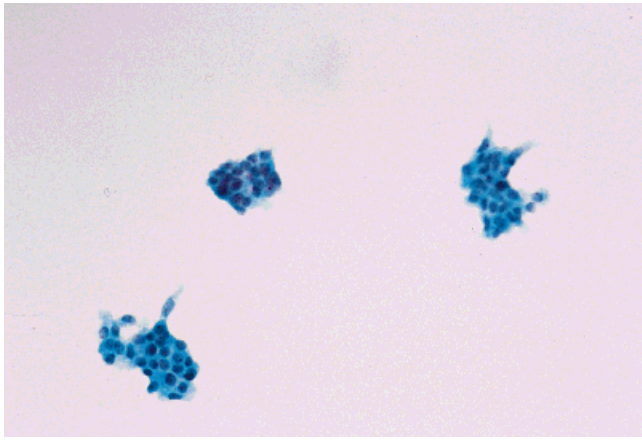

Fig. C-5B

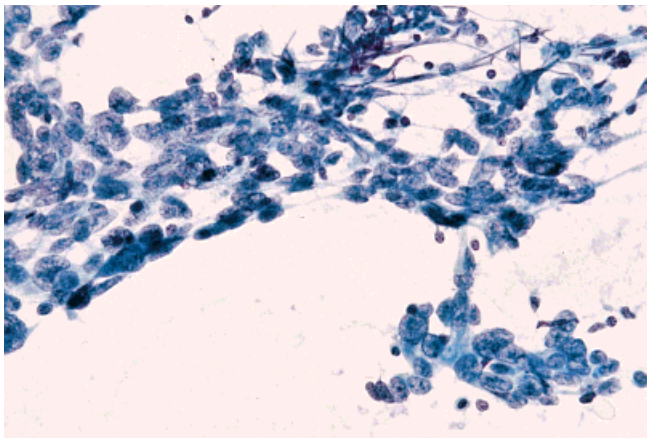

Fig. C-6A

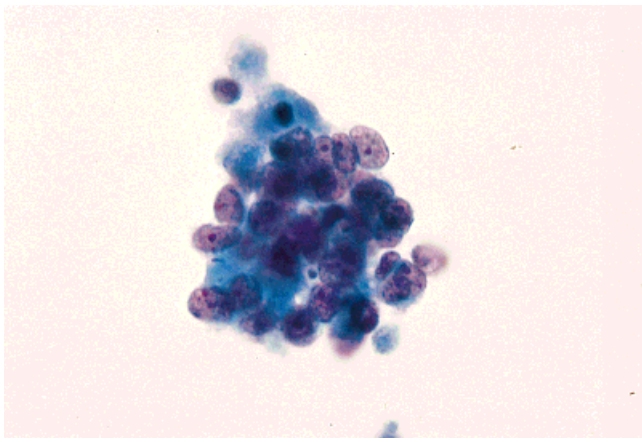

Fig. C-6B

Fig. C-4. A: Conventional smears from of a reactive lymph node, revealing a polymorphic population of singly scattered lymphocytes in a bloody background (Papanicolaou stain, ×1,000). **B:** Correlating ThinPrep, revealing lymphocytes with occasional aggregation, in a clear background (Papanicolaou stain, ×1,000).
Fig. C-5. A: Conventional smears from a fibroadenoma, revealing a large branching sheet in a background of innumerable myoepithelial cells (Papanicolaou stain, ×200). **B:** Correlating ThinPrep, revealing small epithelial fragments with irregular borders in a clear background that lacks myoepithelial cells (Papanicolaou stain, ×200).
Fig. C-6. A: Conventional smears from a small-cell carcinoma, revealing a large sheet of small blue cells with extensive molding, chromatin smearing, and single-cell necrosis (Papanicolaou stain, ×400). **B:** Correlating ThinPrep, showing a small aggregate of small blue cells with less evident molding, an occasional small rim of cytoplasm, and no chromatin smearing (Papanicolaou stain, ×1,000).

Small-cell carcinoma is difficult to recognize in a ThinPrep and requires experience. The clusters of small cells tend to be fragmented and scattered throughout the smear. The nuclear molding is subtle. The cells may exhibit conspicuous nucleoli and/or a small rim of cytoplasm as a result of the wet fixation. This is compounded by the lack of chromatin smearing introduced by the mechanical spreading in conventional smears. Based on these features, small-cell carcinoma may either be missed altogether or misdiagnosed as a poorly differentiated carcinoma or lymphoma. Hees and Lebeau[7] pointed out that for small-cell carcinoma, it is important to keep in mind that the ThinPrep process causes a reduction in number and dissociation of the cellular elements of small-cell carcinoma as compared to conventional smears. In contrast, lymphocytes may artificially aggregate or present as scattered doublets and short chains with apparent nuclear molding, features that are associated with small-cell carcinoma.

In summary, before implementing ThinPrep methodology to all FNAs, the cytology laboratory should obtain experience with and verify the artifacts described on paired slides of ThinPrep and conventional smears on a wide variety of lesions. Lee et al.[6] outlined several differences between the two preparation techniques and emphasized the importance of experience with ThinPrep for a correct interpretation. Provided that the FNA is optimal, most of the important diagnostic features are present in ThinPrep-prepared smears but are more subtle than those same features seen in conventional smears.

In our laboratory we use the ThinPrep process for vitreous FNAs with great success, since dispersing the obscuring proteinaceous background is desirable. We also use it for FNAs obtained by clinicians without our technical assistance, where conventional smears may be inappropriately prepared. Although we still have difficulty in evaluating some FNAs of the thyroid and salivary gland lesions, we think the benefits of better cellular preservation and diminished blood in the background outweigh the disadvantages of altered background matrix or tissue fragmentation. Studies are ongoing to evaluate our experience with FNAs before and after the implementation of the ThinPrep process. For FNAs performed by pathologists, we have elected to rely on conventional smears and use ThinPrep as an adjunct in cases with low cellular rinses as a cost-efficient replacement of the cell block.

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