Comparison of ThinPrep and TriPath PREP Liquid-Based Preparations in Nongynecologic Specimens:
A Pilot Study

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ThinPrep (TP) and TriPath PREP (TriP) are two liquid-based cytologic preparations that produce a thin layer of cells. This study compares the diagnostic accuracy and different cytomorphologic alterations produced by these preparations in nongynecologic specimens. Samples from 10 urines (3 urothelial carcinomas and 7 negative), 4 positive serous fluids, and 7 fine-needle aspirates (FNAs) were prepared by both techniques. FNAs represented one each of: Hashimoto's thyroiditis (HT), hyperplastic colloid nodule (HCN), Hodgkin's lymphoma, liposarcoma, chondrosarcoma, squamous-cell carcinoma (SCC) metastatic to the lymph node, and carcinoid tumor. All 5 participants, none of whom had prior knowledge of the clinical history or histologic diagnosis, reviewed and interpreted the slides.

Both techniques produced a clean background and were equally accurate in urines, serous fluids, and three FNAs. TriP was slightly more accurate in four FNAs: HCN and HT where colloid and lymphocytes were better represented, SCC where keratin and malignant cells were more readily identified among lymphocytes, and carcinoid which was easier to evaluate on TriP due to less cellular shrinkage and more dispersion of cells between aggregates. TP preparations had more cell shrinkage, and the chromatin was harder to evaluate. Both techniques produced artificial aggregations of lymphocytes, but TriP had a more evenly dispersed single-cell population between aggregates, rendering them easier to evaluate for atypia. TP produced fragmentation of large sheets that were flattened, while TriP contained larger branching sheets in a three-dimensional (3-D) configuration. TP produced a true monolayer of cells that were all spread at the same plane, while in TriP the cells were spread at slightly different planes, requiring frequent focusing of the viewed plane.

While both techniques are acceptable for diagnostic purposes, they both introduce new cytomorphologic alterations that pathologists need to recognize. TriP seems superior to TP in FNAs specimens where preservation of architecture and cellular integrity are important considerations. Diagn. Cytopathol. 2001; 25:177–184. © 2001 Wiley-Liss, Inc.

Key Words: thin layer; monolayer; cytologic artifacts; ThinPrep; TriPath PREP; AutoCyte PREP

Liquid-based cytologic preparations (LBP) for both gynecologic and nongynecologic specimens are gaining widespread support and becoming the method of choice in many laboratories. ThinPrep (CYTYC Co., Marlborough, MA) and TriPath PREP (TriPath, Inc., Burlington, NC), formerly known as AutoCyte PREP, are two new liquid-based sampling techniques currently approved by the Food and Drug Administration (FDA) for the preparation of both gynecologic and nongynecologic cytologic samples. Both techniques produce a thin layer of cells devoid of obscuring blood and inflammation. Numerous studies evaluating the efficacy of ThinPrep (TP) in gynecologic and nongynecologic samples have been published. There are fewer reports that evaluate the TriPath PREP (TriP) technique and are mainly focused on gynecologic samples, and none examine the use of TriP in fine-needle aspirates. The purpose of this study was to compare and contrast the diagnostic accuracy of both preparations in nongynecologic samples and assess the effect of the cytomorphologic alterations introduced by these techniques on screening and final interpretation.

Materials and Methods

Samples from 10 urines (3 urothelial carcinomas and 7 negative), 4 positive serous fluids (2 papillary serous adenocarcinomas of the ovary and 2 gastrointestinal tract ade-

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Table I. Comparison of ThinPrep and TriPath PREP Procedures

Preparation step	*ThinPrep*	*TriPath PREP*
Collection	1. Sample collected in CytoLyt (methanol-based) 2. Sample centrifuged, 2–3 drops transferred to PreserveCyt (methanol-based) 3. Vial introduced to ThinPrep processor	1. Sample collected in CytoRich (ethanol-based)
Preparation	Dispersion: A cylinder with a TranCyt Filter attached to one end is introduced into the vial and rotated. This produces a mild current that disperses debris and mucus. Cell collection: A gentle vacuum is created within the filter. Cells are collected on the exterior surface of the membrane.	Enrichment Process: a. Centrifuge at 600 *g* for 10 min. Aspirate the supernatant and resuspend in 10 ml of distilled water. b. Centrifuge at 600 *g* for 5 min. Aspirate the supernatant. c. Vortex the cell-pellet and introduce into the Tripath PREP system.
Transfer	The cylinder is removed and inverted. The tranCyt Filter is gently pressed against a ThinPrep slide. Slight air pressure is applied to insure adherence of cells to slide.	Cells are allowed to settle within the instrument at a rate of 1 *g* on a coated slide.
Slide appearance	A 20-mm circle	A 13-mm circle
Slide requirement	Positively charged slides provided by Cytyc Co.	In-house poly-L-lysine freshly coated and well-dried slides
Staining	The slide is removed from the processor and stained according to laboratory routine staining technique (manual or automatic).	The slides are automatically stained within the instrument.
Time required	Approximately 30 min	Approximately 60 min

nocarcinomas), and 7 fine-needle aspirates (FNAs) were prepared using both techniques. Separate aliquots were submitted in the CytoLyt and CytoRich collecting media for all specimens. The urines and serous fluids were obtained from our routine laboratory samples. FNAs were performed on surgical bench specimens to insure adequate cellularity and included: Hashimoto's thyroiditis, hyperplastic colloid nodule, Hodgkin's lymphoma, liposarcoma, chondrosarcoma, carcinoid tumor, and squamous-cell carcinoma metastatic to a lymph node.

Sample Collection and Fixation

In both techniques, large specimens such as body fluids are first well-agitated to ensure random distribution of the sample. The specimens are then concentrated by centrifugation of two 50-ml tubes before the cell pellets are transferred to the specific collecting media. Urines obtained in operating rooms are split and directly collected in the specific media. For fine-needle aspirates, at least two separate passes are dedicated to each technique, and the needle and hub are immediately rinsed several times into the specific collecting media. Specimens prepared by TP method were processed in our laboratory within 24 hr. The CytoRich vials were batched and sent by express mail to TriPath, Inc., where TriP are prepared and stained. All slides were stained by Papanicolaou stain. A comparison of the actual procedures of both techniques is summarized in Table I. The following is a summary of sample processing and staining for each method.

Sample Processing and Staining

ThinPrep. The specimen is collected in CytoLyt (methanol-based solution that contains mucolytic and hemolytic agents). The sample is centrifuged, and 2–3 drops of the cell pellet are transferred to PreservCyt (methanol-based preservative). The specimen vial is placed in the ThinPrep processor, and the sample is processed as follows.[1,2]

Cell dispersion. 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 random distribution of the cells within the fluid.

Cell collection. A vacuum is applied to the cylinder that causes most of the broken erythrocytes and debris to pass through the filter pores, while the diagnostic cells adhere to the filter's exterior surface. The processor software controls the cell density and assesses the rate of filtration, to avoid overlapping of cells.

Cell transfer. The cylinder is removed, inverted, and lightly pressed against a positively charged slide. A slightly positive air pressure is applied to ensure adherence of cells to the slide. The result is a 20-mm circular smear with even distribution of cells and minimal overlap.

Staining of slide. The slide is removed from the processor and may be stained either manually or by an automatic stainer.

TriPath PREP. The sample is collected in CytoRich (an ethanol based solution) and processed as follows.[3,4]

Cell enrichment process.

1. The fixed specimen is concentrated by centrifugation at 600*g* for 10 min.
2. The supernatant is decanted, and 10 ml of distilled water are added.
3. The cell pellet is vortexed to resuspend it, prior to its transfer to a CytoRich centrifuge tube.

Table II. Comparison Between ThinPrep and TriPath Slide Preparations

Feature	*ThinPrep*	*TriPath PREP*
Background		
Clean	Yes	Yes
PMN/lymphs	Markedly reduced	Reduced, present as small clumps
Red blood cells	Markedly reduced	Reduced
Proteinateous debris	Markedly reduced	Reduced, present as small clumps
Urine crystals	Rarely seen	Present
Cell shrinkage	Very apparent	Not apparent
Monolayer of cells	True monolayer	Cells at slightly different planes
Cellular display	Flattening of cells and clusters	3-D appearance
Artificial pooling of cells	Present	Present
	May be difficult to interpret	Cells evenly dispersed between aggregates are easier to interpret
Papillary structures and sheets	Markedly fragmented	Architectural integrity preserved
	Flattened	3-D appearance
Extracellular material	Reduced quantity, and altered in quality	Quantity and quality not affected

4. The specimen is centrifuged at 600*g* for 5 min.
5. The supernatant is aspirated; the cell pellet is vortexed, and the specimen is placed in the TriPath PREP System.

Sample transfer and monolayer preparation. The tubes containing the pellets are placed in racks of 12 on the PREP automated instrument. The cells are allowed to settle at 1*g* on slides freshly coated with poly-L-lysine. The result is a monolayer of cells in a 13-mm circle.

Staining of slides. The slides are automatically stained within the PREP instrument.

Slide Review

To assess diagnostic accuracy, slides of both preparations were separated and reviewed independently by each of the 5 authors. Each participant was asked to submit his/her diagnosis and comment on the two preparations for each specimen. None of the reviewers had any prior knowledge of the clinical history or histologic diagnosis. Two participants (C.W.M. and J.P.) had previous experience with ThinPreps; none had any experience with TriPath PREPs. Once these reviews were completed, a paired review by one of the authors (C.W.M.) with knowledge of the final diagnoses was performed. In the second review, the comments submitted by all reviewers were tabulated and the slides were reevaluated for the following features: 1) monolayer quality, 2) background clarity and presence of inflammatory and red blood cells, 3) extracellular material, 4)architectural integrity, and 5) cellular morphology.

Results

Both techniques provided a uniform cellular spread in a thin layer without cellular overlap or obscuring elements. Considering all reviewed features, TriPs were similar in quality to TPs in 12 cases (9 urines, 3 FNAs), superior to TPs in 7 cases (3 serous fluids, 4 FNAs), and inferior to TPs in 2 cases (1 urine, 1 serous fluid). Despite the apparent similarity, the two preparations showed several significant differences (Table II).

Table III. Correct Cytologic Interpretation of Specimens Prepared by ThinPrep and TriPath PREP Issued by 5 Reviewers[a]

Site	*Final diagnosis*	*ThinPrep*	*TriPath PREP*
1. Bladder wash	Negative	4	4
2. Instrumented urine	Urothelial carcinoma	5	4
3. Bladder wash	Urothelial carcinoma	5	4
4. Instrumented urine	Urothelial carcinoma	5	5
5. Instrumented urine	Negative	2	2
6. Instrumented urine	Negative	4	4
7. Bladder wash	Negative	5	5
8. Bladder wash	Negative	4	5
9. Instrumented urine	Negative	5	5
10. Bladder wash	Negative	4	4
11. Thyroid	H. thyroiditis	1	3
12. Soft tissue	Chondrosarcoma	3	3
13. Thyroid	Colloid nodule	3	4
14. Lymph node	Hodgkin's lymphoma	4	4
15. Soft tissue	Liposarcoma	5	5
16. Lymph node	Squamous-cell Ca	3	4
17. Small bowel	Carcinoid	3	4
18. Pleural fluid	Esophageal Ca	4	4
19. Pleural fluid	P.S. Ca of ovary	5	5
20. Pleural fluid	Adenocarcinoma	3	4
21. Peritoneal fluid	P.S. Ca of ovary	5	5

[a]H, Hasimoto's; P.S., papillary serous; Ca, carcinoma.

The diagnostic accuracy of the two techniques was equal in urines, serous fluids, and 3 FNAs. The diagnostic accuracy was slightly better in 4 FNAs prepared by TriP than by TP: Hashimoto's thyroiditis, hyperplastic colloid nodule, carcinoid tumor, and metastatic squamous-cell carcinoma to a lymph node. Table III summarizes the frequency of correct interpretations issued, based on the two preparation techniques for all samples evaluated.

Monolayer Quality

Both preparations resulted in an evenly dispersed smear. The TP produced a true monolayer, with all cells spread in the same plane of focus, requiring minimal adjustment of the fine focus during examination. The TriP produced cells at slightly different planes of focus, requiring frequent fine

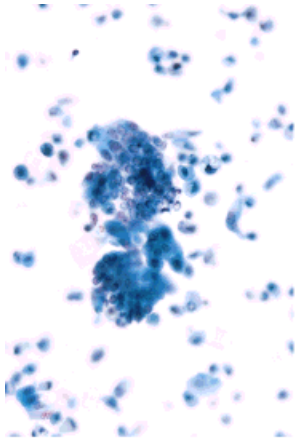

Fig. C-1A

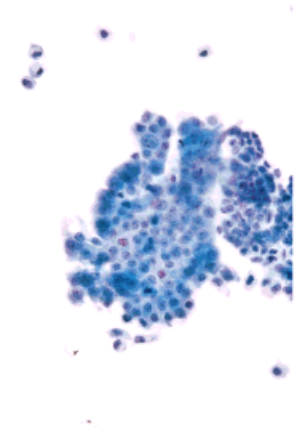

Fig. C-1B

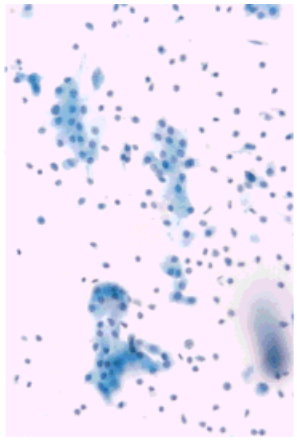

Fig. C-2A

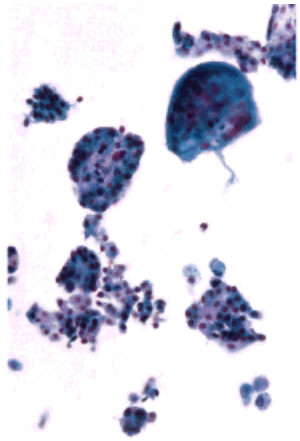

Fig. C-2B

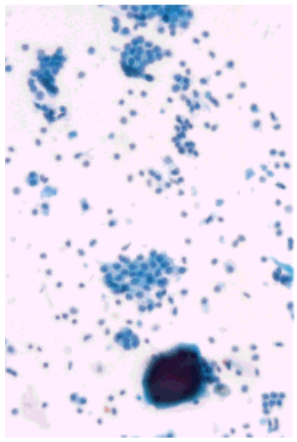

Fig. C-3A

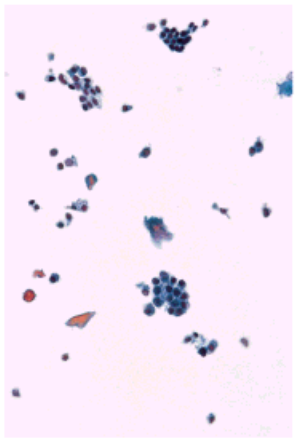

Fig. C-3B

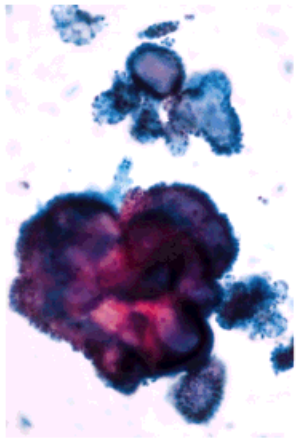

Fig. C-4A

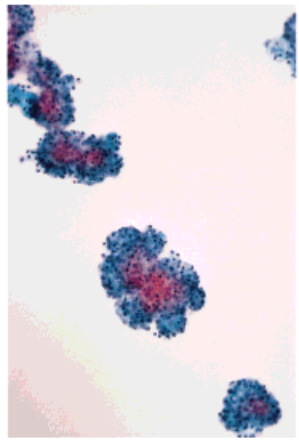

Fig. C-4B

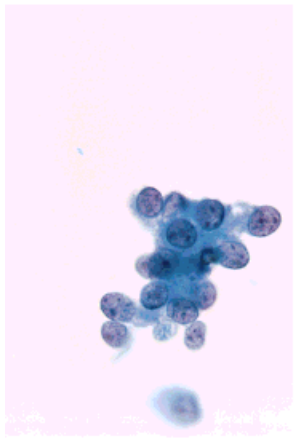

Fig. C-5A

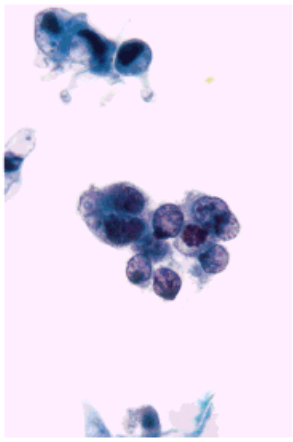

Fig. C-5B

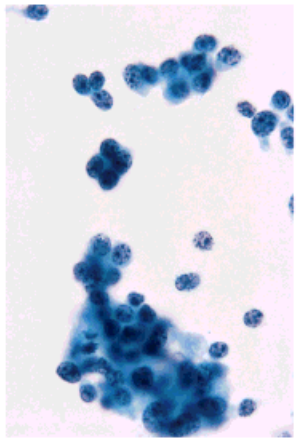

Fig. C-6A

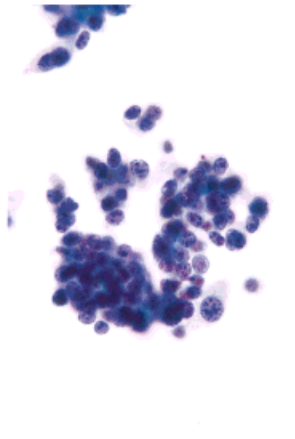

Fig. C-6B

Figs. C-1–C-6.

focusing of the viewed field. Generally, the cellular density in the center was less than that towards the periphery of the ring in both techniques, but this finding was more pronounced in TP, where the cells tended to collect in pools with empty spaces in between. In highly cellular specimens, both techniques produced smears with cohesive cellular aggregates interspersed by single cells. In TP, the single cells are usually spaced away from the clusters, while in TriP they are spread adjacent to the clusters without any spacing.

Background

Both preparations had a clean background that differed in its content. The TP prepared slides had an almost complete absence of proteinaceous debris, inflammatory exudate, and red blood cells. These elements were only seen when present in considerable amounts in the original sample. Crystals were seldom seen on TP urine specimens (Fig. C-1). Inflammatory cells of all types were decreased in number in all TP smears. Similarly, benign lymphocytes, as in the case of Hashimoto's thyroiditis, were markedly reduced in number except for those entrapped within the epithelial clusters, and tended to be pushed towards the periphery of the ring (Fig. C-2). TriP prepared slides retained some of these elements: a few scattered red blood cells, neutrophils, and clumps of mucus or proteinateous debris were frequently seen. None of these elements obscured the diagnostic cellular material. Lymphocytes and intact crystals were also retained and more readily identified.

Extracellular Material

In this study, colloid and chondroid were the main extracellular materials encountered. Colloid was significantly decreased in amount and fragmented on TP, and was present in much larger and more numerous fragments on TriP (Fig. C-3). Chondroid was well-represented in both methods, although it appeared as smaller fragments on TP. Individual lacunae were well-preserved and easy to examine in both preparations.

Architectural Integrity

Papillary structures and large or branching sheets of cells remained intact using the TriP technique; these same structures were markedly fragmented into small cellular aggregates on TP. In our 2 cases of papillary serous adenocarcinoma, where papillary structures were abundant, the TP prepared slides showed two-dimensional (2-D) simple branching clusters that provided a clue to their papillary nature. In contrast, TriP slides contained more complex three-dimensional (3-D) branching fragments with obvious papillary architecture (Fig. C-4).

Cellular Morphology

Cellular features commonly examined in cytology, such as nuclear to cytoplasmic ratio, pleomorphism, irregular/hyperchromatic vs. vesicular chromatin, and a honeycomb-like orderly distribution of cells vs. loss of orientation, were all retained in both preparations (Fig. C-5). TP tended to exhibit more prominent nucleoli, even in benign cells. TPs produce more cellular shrinkage than TriP. As a consequence, TP prepared slides required examination under higher magnification more frequently and rendered evaluation of chromatin detail more difficult. In addition to the lesser amount of cellular shrinkage produced by TriP, it had a larger and more evenly dispersed single-cell population between aggregates which allowed for easier evaluation of chromatin detail in small cells, such as lymphocytes or neuroendocrine cells (Fig. C-6). Both techniques produced artificial aggregations of lymphocytes. Diagnostic cells accompanied by large numbers of lymphocytes (e.g., Reed-Sternberg cells in Hodgkin's lymphoma or malignant squamous cells in a lymph node), although present in both preparations, were more readily identified among the lymphocyte aggregates on TriP prepared slides.

TP produced flattening of single cells and clusters; TriP produced a more 3-D configuration. These 3-D cells and clusters were sometimes difficult to examine at high magnification (400×), and in cases with large clusters or papillae nearly impossible to photograph at high power.

Figs. C-1–C-6. Fig. C-1. Negative bladder washing. **A:** TriP contains a sheet of urothelial cells with a slight 3-D appearance in a background of single cells that are evenly spread adjacent to the cluster. Many single cells are at a different plane of focus. There are also several crystals present. **B:** TP contains a flattened sheet of urothelial cells and single cells in the same plane of focus. Single cells are spaced away from the cell aggregate, and no crystals are identified (Papanicolaou stain, ×400). **Fig. C-2.** Hashimoto's thyroiditis. **A:** TriP contains clusters of benign Hurthle cells in a honeycomb arrangement in a background of numerous mature lymphocytes. **B:** TP contains relatively smaller clusters of Hurthle cells, with a few entrapped lymphocytes. Lymphocytes are considerably decreased in number and are mainly identified towards the periphery of the ring. Note the difference in cells size at the same magnification (Papanicolaou stain, ×400). **Fig. C-3.** Hyperplastic colloid nodule. **A:** TriP contains several clusters of follicular cells, numerous bare nuclei, and a large fragment of colloid. **B:** TP contains relatively smaller clusters of follicular cells, no bare nuclei, and very small fragments of colloid (Papanicolaou stain, ×400). **Fig. C-4.** Papillary serous adenocarcinoma in peritoneal fluid. **A:** TriP contains intact, complex branching papillae with 3-D configuration. **B:** TP contains fragmented simple branching papillae with 2-D configuration (Papanicolaou stain, ×400). **Fig. C-5.** Transitional-cell carcinoma. TriP (**A**) and TP (**B**) show similar features diagnostic of malignancy, including loss of orientation, increased nuclear:cytoplasmic ratio, and irregular chromatin distribution (Papanicolaou stain, ×1,000). **Fig. C-6.** Carcinoid tumor. **A:** Although a diagnosis can be established by both methods, TriP shows relatively larger cells that are more loosely spread, making it easier to examine chromatin details. **B:** TP shows smaller cells with tighter arrangements, making examination of chromatin detail relatively difficult (Papanicolaou stain, ×1,000).

Discussion

There are several important considerations when a laboratory is choosing between two techniques for the preparation of cytologic material. The diagnostic accuracy, cost-effectiveness, demand on technical support, and special training required for examination and interpretation are all factors that need to be considered. While both TP and TriP are thin-layer preparations based on liquid-based sampling, they differ in methodology, reagent cost, and time of preparation. More importantly, each method introduces its own set of unique cytologic alterations that must be recognized. Numerous studies evaluated the efficiency and pitfalls of TP for nongynecologic samples and FNAs.[5–12] With the exception of one report,[13] very few studies tangentially evaluated TriP use for nongynecologic samples,[14,15] and none evaluated it for FNAs. There is no literature to date that compares the results obtainable from TP vs. TriP. In this pilot study we compared and contrasted the diagnostic accuracy, cytologic presentation, and artifacts in 21 nongynecological samples prepared by both TP and TriP

The diagnostic accuracy of TriP was similar to TP in both urines and serosal fluids. TriP was slightly superior in FNAs (4/7). Both techniques introduced their own unique cytologic artifacts related to their methodology. TriP produced a 3-D configuration for both single cells and clusters as a result of the simple sedimentation of cells on the slide surface without any applied pressure. This 3-D configuration occasionally caused difficulty, particularly when trying to evaluate some single urothelial cells for atypia at 400×. Clusters of adenocarcinoma were easy to recognize, but evaluation of the nuclear features was sometimes obscured by large, overlying cytoplasmic vacuoles. These situations required frequent fine focusing of the viewed plane. TriPath, Inc. advises diluting the sample or increasing the sedimentation time to reduce this 3-D effect (personal communication). In contrast, the TP technique produced considerable flattening of both cells and clusters, induced by the positive air pressure applied to the cylinder during the cell transfer stage. This flattening did not have any significant impact on the evaluation of cellular morphology, although at times the flattening of thick papillary clusters rendered them difficult to evaluate for features such as fibrovascular cores. However, the flattening could be exaggerated towards the circumference of the ring "compression artifact" and gives the appearance of air-drying artifact. If this artifact becomes consistent in the laboratory, the cylinder cap should be inspected for possible wear and tear in the rubber ring "O-ring." Such deterioration in the rubber may alter the air pressure and consequently the desired compression of the filter against the slide surface.

TriP produces a smear that is more reminiscent of the conventional smear, with minimal cellular shrinkage, no fragmentation of large tissue aggregates, and adequate representation of most elements of the original specimen, including blood, inflammatory cells, and extracellular material. This feature of TriP resulted in a slightly higher diagnostic accuracy for FNAs than can be obtained by TP. This higher accuracy is mainly due to the easier recognition of some cellular and extracellular elements such as colloid (hyperplastic colloid nodule) and lymphocytes (Hashimoto's thyroiditis). In addition, TriP preparations produce less cellular shrinkage, and more evenly spread individual cells between aggregates. Both these features are particularly helpful in FNAs such as lymphomas, neuroendocrine tumors, and metastatic tumors to lymph nodes. It is difficult to explain with certainty the differences between the two LBP. Wet fixation is a common factor and therefore cannot solely explain why cells appear relatively smaller in TP than in TriP. The fact that methanol may cause more cellular shrinkage than ethanol is debatable, and some literature attests to the opposite.[16] Unfortunately, we are dealing with proprietary media for which we do not know all constituents. A more plausible explanation is perhaps that the TP media may contain a trace amount of formaldehyde. This assumption is further supported by the fact that studies performing immunoperoxidase stains on TP slides have reported better performance with pretreatment of slides, in a manner similar to formalin-fixed and paraffin-embedded sections.[17] Similarly, the alteration of extracellular material may be related to mucolytic or similar agents in the TP media. It is clear that the TP methodology may severely alter loose material such as watery colloid and myxoid, but not denser material such as chondroid that was completely preserved in this study. Perhaps such agents are not sufficient to alter denser material, or else the density of the material exceeds the threshold of the processor. Fragmentation of large cellular clusters is another interesting artifact that is most probably related to the technique of cell dispersion on TP rather than centrifugation, since TriP involves two vigorous centrifugation steps and yet the clusters escape such fragmentation. During homogenization of the sample, the cylinder moves up and down within the vial simultaneously with an electric current that causes the specimen to form a layer of foam. While this causes excellent randomization of the sample and dispersion of clumps, it also breaks down the large sheets to smaller and simpler forms. While due to positive air pressure the TP is more of a monolayer preparation than TriP, it is probably that air pressure that causes most of the small cells such as lymphocytes to migrate towards the circumference of the ring and away from the clusters. This also imparts the unique appearance of a clearer center with widely scattered cell pools and a more cellular periphery on TP.

We previously described the cytologic artifacts introduced by TP in FNAs and emphasized the need to develop experience in interpreting these specimens to avoid errors in diagnoses.[12] Similar artifacts have been noted in other stud-

ies on FNAs as well as with other nongynecological specimens.[6,9,11] The most significant alterations seen with the TP technique include the selective loss of extracellular material and small cells, the fragmentation of large sheets and papillae, and the lack of familiar artifacts produced by manual spreading of cells, e.g., chromatin smearing in small-cell carcinoma. These alterations particularly impacted FNAs of the thyroid, parotid gland, breast, and small-cell carcinoma. Artifacts such as cellular shrinkage and artificial aggregation rarely cause diagnostic problems. Other artifacts such as the alteration and/or loss of extracellular material and fragmentation of cell aggregates and papillae can easily lead to an incorrect diagnosis. The difficulty in distinguishing between small-cell carcinoma, when nuclear smearing and molding are lost and cells are less cohesive, and lymphoma, when cells are artificially aggregated, was previously reported.[12] In this study, we found the artifacts common to TP lacking in TriP. TriP tended to retain architectural integrity and provided a more representative sample. Although we did not have a case of small-cell carcinoma in this study, it has been our experience from our consultation files that similar loss of diagnostic features occurs when this particular lesion is prepared using TriP, due to lack of manual spreading. However, since TriP results in less shrinkage of cells and less fragmentation of clusters, these malignant cells are easier to recognize. Similarly fibroadenoma, the most problematic breast lesion on TP, will more likely have intact branching sheets and more myoepithelial cells on TriP.

Based on this pilot study, it appears that TriP is easier to evaluate and requires less training than TP. Comparing the performance of the 5 participants in this study, those with prior experience with TP performed better on TP preparations. The performance was equal among all participants on TriP preparations. The true monolayer presentation of TP vs. the multiple focal planes and 3-D presentation of TriP allowed for easier screening of the former, because minimal adjustment of focus is required. Although only of academic interest, it is easy to obtain a photograph with the entire field in focus from a TP slide. This also renders it an ideal preparation for digital microscopy and image analysis. It is very difficult to obtain a similar photograph with TriP slides because only the object of interest can be focused upon; the remaining field will be out of focus, especially at low magnifications. However, this 3-D configuration and depth of focus render it an ideal preparation for 3-D microscopy and 3-D reconstruction studies.

Both methodologies utilize automation. However, they differ in the automated portion of their procedure. TP requires minimal handling and skill by laboratory personnel, except for the initial centrifugation to concentrate the specimen. The slide is consequently stained outside the CYTYC ThinPrep processor, either manually or using an automated stainer. Although the multislide processor contributes significantly to the "hands-off" philosophy of TP for gynecologic slides, nongynecological slides still must be prepared individually and require constant attention. TriP requires far more handling during the initial steps of the process, because repeated centrifugation is required. Only the last steps of the process, namely the sedimentation and staining, are automated in TriP. Up to 48 samples can be centrifuged at one time by the batch centrifuge provided with the PREP instrument. However, the process still requires manual decanting and resuspension. According to a recent study evaluating over 800 nongynecologic samples prepared by TriP,[13] significant alterations in the TriP protocol were made constantly to improve the preparation. This constant modification requires highly skilled technical support that can perform problem-solving during sample processing. The TP process requires only 1–2 min to prepare the slide plus the time to stain it (15–20 min). The TriP process takes significantly longer: approximately 60 min for the entire procedure, including staining. This preparation time does not differ by type of sample for both techniques.

Cost is another important factor. Preparing TP slides for nongynecological samples requires specially designed filters and charged slides that are provided by CYTYC Co.[18] These filters and slides are costly (approximately $4–5 per filter), and those costs are a consideration, particularly in an academic institution desiring additional slides for teaching purposes. Although TriP does not require such filters and the slides can be coated with poly-L-lysine in-house, the process tends to be more labor-intensive since all slides have to be freshly coated and well-dried on a daily basis. This may be an inconvenient task in laboratories with moderate to high workloads. Further studies are needed to evaluate whether such differences in cost could be offset by the need of highly skilled technical support for TriP.

In summary, neither ThinPrep nor TriPath PREP represents a simple replacement for the conventional smear. They both produce cytologic preparations with their own set of artifacts that need to be readily recognized, and require experience with paired slides from the same sample prior to full implementation, particularly TP. Each technique has its own advantages and disadvantages. TriP is cheaper and requires less training, but requires more laboratory space, takes longer, and requires more skilled technical support. TP is more expensive and requires more initial training, but uses less laboratory space and requires less technical support and minimal skill. It appears that both techniques may have a place in the cytology laboratory. As we have demonstrated in this pilot study, some FNAs are best examined using TriP.

References

1. CYTYC Corporation. Operator's manual. ThinPrep processor. Marlborough, MA: CYTYC Corporation; 1992.
2. Zahniser DJ, Sullivan PJ. CYTYC Corporation. Acta Cytol 1996;40: 37–44.

3. AutoCyte, Inc. Operator's manual. AutoCyte PREP. Burlington, NC: AutoCyte, Inc.; 1999.
4. AutoCyte, Inc. Procedures and protocols: non-cervical vaginal application. Burlington, NC: AutoCyte, Inc.; 1999.
5. Fischler DF, Toddy SM. Nongynecologic cytology utilizing the ThinPrep Processor. Acta Cytol 1996;40:669–675.
6. Perez-Reyes N, Mulford DK, Rutkowski MA, Logan-Young W, Dawson AE. Breast fine-needle-aspiration, a comparison of thin-layer and conventional preparation. Am J Clin Pathol 1994;102:349–353.
7. Leung CH, Chiu B, Bell V. Comparison of ThinPrep and conventional preparations: nongynecologic cytology evaluation. Diagn Cytopathol 1997;16:368–371.
8. Lee KR, Papillo JL, St. John T, Eyerer GJA. Evaluation of the ThinPrep processor for fine needle aspiration specimens. Acta Cytol 1996;40:895–899.
9. Hees K, Lebeau PB. Comparison of conventional and ThinPrep preparations of mucoid cytology samples. Diagn Cytopathol 1995;12:181–185.
10. Biscotti CV, Hollow JA, Toddy SM, Easley KA. ThinPrep versus conventional smear cytologic preparations in the analysis of thyroid fine-needle aspiration specimens. Am J Clin Pathol 1995;104:150–153.
11. Frost AR, Sidawy MK, Ferfelli M, Tabbara SO, Bronner NA, Brosky KR, Sherman ME. Utility of Thin-Layer preparations in thyroid fine needle aspiration. Diagnostic accuracy, cytomorphology, and optimal sample preparation. Cancer Cytopathol 1998;84:17–25.
12. Michael CW, Hunter B. Interpretation of fine needle aspirates processed by the ThinPrep technique: cytologic artifacts and diagnostic pitfalls. Diagn Cytopathol 2000;23:6–13.
13. Nicol TL, Kelly D, Reynolds L, Rosenthal DL. Acta Cytol 2000;44:567–575.
14. Motherby H, Nicklaus S, Berg A, Ohler S, Ross B, Sarbia M, Bocking A. Semiautomated monolayer preparation of bronchial secretions using AutoCyte PREP. Acta Cytol 1999;43:47–57.
15. Yang GC, Wan LS, Papellas J, Waisman J. Compact cell blocks. Use for body fluids, fine needle aspirations and endometrial brush biopsies. Acta Cytol 1998;42:703–706.
16. Danos M. Fixatives for cytologic use. In: Keebler CM, Reagan JW, Wied GL, editors. Compandium on cytopreparatory techniques, 4th ed. Chicago: Tutorials of Cytology; 1976. p 7–9.
17. Tabbara SO, Sidawy MK, Frost AR, Brosky KR, Coles V, Hecht S, Radcliffe G, Sherman ME. The stability of estrogen and progesteron receptor expression on breast carcinoma cells stored as PreservCyt suspensions and as ThinPrep slides. Cancer Cytopathol 1998;84:355–360.
18. Lapen DC, Jacalyn P. Performance optimization of the ThinPrep processor: effect of microscope slides. Diagn Cytopathol 1998;19:388–391.