The University of Michigan at the USCAP 2010
poor photographic technique? . . . or might there be some other explanation for those red, red eyes . . .
... whatever the explanation, it is a consistent finding (p < 0.05)
Morphological Findings in Upper Gastrointestinal Biopsies of Patients with Ulcerative Colitis: A Controlled Study

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Abstract

Background: Ulcerative colitis (UC) is a chronic inflammatory disease characterized by mucosal ulceration and chronic inflammation of the colon. The disease affects the mucosa and submucosa of the colon and rectum, leading to abdominal pain, diarrhea, and bloody stools. The pathogenesis of UC is multifactorial, involving genetic, environmental, and immunological factors.

Aim: The aim of this study was to evaluate the morphological findings in upper gastrointestinal biopsies of patients with ulcerative colitis compared to healthy controls and other inflammatory bowel diseases, with the goal of understanding the role of the upper gastrointestinal tract in UC.

Methods: A total of 50 patients with UC who underwent upper gastrointestinal endoscopy were included in the study. Biopsies were taken from the stomach, duodenum, and jejunum. Histological evaluation was performed using standard staining techniques. The results were compared to a control group of 25 healthy individuals and another group of 25 patients with Crohn's disease.

Results: The study found that the upper gastrointestinal tract is involved in UC, with an increased prevalence of inflammation and architectural abnormalities. The results also showed differences in the extent and severity of inflammation compared to controls and patients with Crohn's disease.

Conclusion: The findings suggest that the upper gastrointestinal tract may play a role in the pathogenesis of UC, and further research is needed to elucidate the mechanisms involved.

Materials and Methods

Patient Recruitment: Fifty patients with UC were recruited from the gastroenterology clinic at the University of Michigan. Inclusion criteria included a diagnosis of UC confirmed by histological examination of colon biopsies and endoscopic examination.

Biopsy Protocol: Upper gastrointestinal endoscopy was performed using a standard small bowel capsule endoscope. Biopsies were taken from the stomach, duodenum, and jejunum for histological evaluation.

Histological Analysis: Biopsies were stained with hematoxylin and eosin (H&E) and other standard histological stains, and evaluated for inflammation and architectural changes.

Comparison Groups: The study included a control group of 25 healthy individuals and a group of 25 patients with Crohn's disease for comparison.

Data Analysis: Statistical analysis was performed using ANOVA and Chi-square tests to compare the results between groups.

Acknowledgments: This study was supported by grant number K08AI072886-03 from the National Institute of Allergy and Infectious Diseases.
Improving Quality and Efficiency of Pap Test Processing: A Lean Approach

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Abstract

Background: In the State of Michigan, 50% of cancer cases are diagnosed in premenopausal women. Although routine screening is recommended, the American Cancer Society (ACS) guidelines updated in 2012 state that current evidence does not support screening for women ages 21-29. Women ages 30-65 should undergo annual Pap tests. Many women do not undergo routine Pap testing. Some providers do not recommend screening because of the risk of false-positive results and the fact that only a minority of women with negative Pap tests develop invasive cervical cancer. This study aimed to improve quality and efficiency of Pap test processing.

Materials and Methods

To explore opportunities for improvement in our ThinPrep Pap Test processing and scoring procedures, we created a value stream map (VSM) and performed root cause analysis.

- Team definitions: A total of 15 individuals (4 clinicians and 11 non-clinical staff) were involved. The VSM analysis was conducted and a Lean approach was utilized.
- The process was defined as follows: The start point was defined as the reception of the specimen, and the end point was defined as the reporting of the result.
- The process chain was divided into six main steps: 1) Specimen receipt and processing, 2) Centrifugation, 3) Staining, 4) Reading, 5) Reporting, and 6) Follow-up.
- In addition, we mapped the cycle time, cycle efficiency, and process capability.

Results:

Changes Implemented:

1. Single shift flow during processing.
2. Monitor processing batch in T240 and scanning, counting, and labeling steps from 6 to 2 hours.
3. Elimination of redundant steps e.g., highlighting information on requisitions, entering requisition number, etc.
4. Interchange of workflow and technologies focused on improving the quality and efficiency of testing the T240 machine and reducing variability in waiting times.

<table>
<thead>
<tr>
<th>Monitor</th>
<th>Pre-Implementation</th>
<th>Post-Implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Processing Time</td>
<td>No of subjects 137</td>
<td>Average 5 days</td>
</tr>
<tr>
<td>Cancellation errors</td>
<td>No of cancellation 12</td>
<td>Average 7%</td>
</tr>
<tr>
<td>Values reported</td>
<td>No of reported 120</td>
<td>Average 9%</td>
</tr>
</tbody>
</table>

Conclusions:

- Implementation of single shift flow and monitoring batch size allows for higher quality and greater patient safety by maximizing up-front detection of labeling errors.
- Single shift flow improved efficiency by reducing the number of times each specimen is handled during the process and eliminating re-work due to errors detected at earlier stages.
- Turnaround time was improved by eliminating several redundant steps in the process and decreasing specimen waiting time throughout the process.
- Engaging the staff in the process is essential in building the team spirit and positive attitude toward work management. They actively participated with valued critique and contributed valuable suggestions. By owning their process, they implemented many of the changes without hesitation and even incorporated these in further implementing the Plan-Do-Check-Act process for the pilot.

Acknowledgments

We thank our colleagues and peers for their contributions and support of this project from the Michigan Quality Council.
Cytologic Parameters of Cervical Cytology Specimens Associated with "Equivocal" Hybrid Capture II High-risk HPV DNA Test Results

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1Department of Pathology, University of Michigan Health System, Ann Arbor, MI
2Providence Hospital, Southfield, MI

Background

High-risk types of human papillomavirus (hrHPV) have been implicated in the vast majority of cases of high-grade cervical dysplasia and cervical carcinoma, and hrHPV testing has emerged as a highly sensitive test for the presence of cervical neoplasia. Well-established hrHPV assays are required for optimal management of patients undergoing a pap test procedure.

The hybrid Capture II (Digene) high-risk human papillomavirus (hrHPV) DNA test is a United States Food and Drug Administration (FDA)-approved in vitro assay that performs qualitative and semiquantitative detection of hrHPV in cervical samples. Results are reported as a ratio of relative light units (RLUs) to a cut-off value (CO) or (RU/mL), with a value of 1.0 separating positive from negative results. Due to the lack of reproducibility of hrHPV tests, the manufacturer indicates that initial values falling on or above 1.0 RU/CO but less than 2.5 RU/CO (i.e., 1.0 RU/CO and 2.5 RU/CO) are deemed initial "equivocal" values and must be reviewed. These specimens are retested and must show a value above 1.0 or need to be retested as a final positive specimen. If both of these subsequent tests fall below 1.0 RU/CO, the final result of these initial "equivocal" specimens is negative. While the practice of repeated testing of samples showing values within the "equivocal" range is indicated in FDA labeling, some have suggested that each laboratory establish its own set-points for the establishment of initial "equivocal" specimens that necessitate further repeat testing. Many laboratories, including our own, have found that the lack of reproducibility of hrHPV tests encompasses a wide range of RU/CO less than 1.6 to 2.5 RU/CO stated by the manufacturer in its laboratory. The hrHPV tests performed on ThinPrep specimens show problematic reproducibility over a range of 0.8 RU/CO to 3.5 RU/CO (i.e., tests falling below 1.0 RU/CO but above 0.8 RU/CO are regarded as positives, and tests falling on or above 3.5 RU/CO less than 5.0 RU/CO are regarded as negative). For this reason, we currently report hrHPV test results in this range as "equivocal" for hrHPV, and recommend another sample be sent for definitive hrHPV testing.

Results: Prevalence of "Equivocal" Specimens

Of 10,157 hrHPV tests reviewed, 930 (9.2%) were unequivocal positive or negative tests, 811 (8.0%) were equivocal equivocal tests, and 151 (1.5%) were equivocal equivocal hrHPV tests (Figure 1).

Results: Cytodens of "Equivocal" vs. Controls

The average cytoldens of ThinPrep slides associated with equivocal hrHPV tests was lower (5.84, p = 0.041) than those associated with unequivocal positive or negative hrHPV tests. Five ThinPrep slides associated with equivocal hrHPV tests showed 4 or fewer squamous cells per 1,200 cells, with 92 of the slides considered unsatisfactory tests, defined as fewer than 2,000 cells. None of the unequivocal positive cases showed such low cytoldens (Table 1 and Figure 2).

Results: Corresponding Cytologic Diagnoses

Forty-six ThinPrep slides associated with 91 discordant equivocal equivocal hrHPV tests were available for review. The corresponding cytologic diagnoses of these 46 pap tests, as well as of hrHPV negative and hrHPV positive control groups are shown in Table 1.

Table 1: Corresponding cytologic diagnoses of cervical samples, ASCUS, LSL, LSIL, HSIL, NILM

<table>
<thead>
<tr>
<th></th>
<th>ASCUS</th>
<th>LSL</th>
<th>LSIL</th>
<th>HSIL</th>
<th>NILM</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV Negative</td>
<td>33.3% (37)</td>
<td>3.4% (1)</td>
<td>0.0% (0)</td>
<td>3.4% (1)</td>
<td>0.0% (0)</td>
<td>46.2%</td>
</tr>
<tr>
<td>HPV Positive</td>
<td>66.7% (75)</td>
<td>20.7% (2)</td>
<td>3.4% (1)</td>
<td>0.0% (0)</td>
<td>3.4% (1)</td>
<td>96.8%</td>
</tr>
<tr>
<td>HPV Equivocal</td>
<td>31.6% (37)</td>
<td>12.7% (1)</td>
<td>0.0% (0)</td>
<td>4.3% (1)</td>
<td>10.0% (1)</td>
<td>48.0%</td>
</tr>
</tbody>
</table>

Results: Follow-up Histology of "Equivocal" Specimens

Available follow-up histologic cervical biopsies from patients discordant equivocal HPV (n=22) were examined and showed high-grade CIN (CIN 2 or CIN 3) in 21.2% of cases, and CIN 1 in 50.0% of cases (Figure 3).
Retrospective Evaluation of Instituted Standard Adequacy Criteria for On-Site Adequacy Assessment of Thyroid Fine Needle Aspiration (FNA)

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University of Michigan, Department of Pathology, Ann Arbor, Michigan

INTRODUCTION:
Criteria for specimen adequacy of thyroid fine needle aspiration (FNA) on permanent smears are still controversial. To the best of our knowledge, there are no criteria set forth for on-site adequacy assessment. In our institution, the vast majority of thyroid FNAs has been performed with on-site cytopathologist’s assistance. The lack of uniform criteria for assessing specimen adequacy resulted in diagnostic inaccuracy among the cytopathologists and difficult communications with clinicians. Thus, a standard criteria for on-site adequacy assessment was developed, distributed and explained to all involved parties including pathologists, radiologists, radiologists and surgeons, and then implemented in our practice in 2005. On-site assessment reports of specimen adequacy have been incorporated into our final cytology reports since 2005. The current retrospective study was conducted to assess the impact of using standard criteria on FNA diagnosis of thyroid nodules.

METHODS:
Computer SNOMED Search from the file at our institution between 07/06 and 12/09 retrieved a total of 1031 thyroid FNAs with on-site adequacy assessments that was performed based on instituted standard criteria. Standard criteria defined specimen adequacy as the presence of at least 100 follicular cells in total on Diff-Quik stained smears with a minimum 40x magnification in each group. Adequacy was calculated by the number of passes, number of passes performed, status of adequacy along with provisional (for adequate specimens) diagnosis.

RESULTS AND CONCLUSIONS:

Table 1. Agreement on assessments of specimen adequacy

<table>
<thead>
<tr>
<th>Final</th>
<th>Adequate</th>
<th>Inadequate</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Adequate</td>
<td>853 (99.8)</td>
<td>70 (39.3)</td>
<td>923 (99.3)</td>
</tr>
<tr>
<td>Inadequate</td>
<td>2 (0.2)</td>
<td>108 (60.7)</td>
<td>110 (10.7)</td>
</tr>
<tr>
<td>Totals</td>
<td>855 (100)</td>
<td>178 (100)</td>
<td>1033 (100)</td>
</tr>
</tbody>
</table>

Table 2. Distribution of cytologic diagnoses and cyto-histologic concordance

<table>
<thead>
<tr>
<th>Cytologic Diagnosis</th>
<th>N</th>
<th>Surgical F/U N (%)</th>
<th>Concordant Case N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate</td>
<td>921</td>
<td>221 (24.0)</td>
<td>139 (62.9)</td>
</tr>
<tr>
<td>Nodencleriosis</td>
<td>722</td>
<td>66 (9.1)</td>
<td>62 (92.9)</td>
</tr>
<tr>
<td>NH</td>
<td>638</td>
<td>62 (9.3)</td>
<td>58 (93.5)</td>
</tr>
<tr>
<td>LT</td>
<td>84</td>
<td>4 (100)</td>
<td></td>
</tr>
<tr>
<td>FL/HL</td>
<td>116</td>
<td>87 (75.0)</td>
<td>21 (24.1)</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>83</td>
<td>68 (81.9)</td>
<td>56 (82.3)</td>
</tr>
<tr>
<td>FN/HN</td>
<td>29</td>
<td>19 (65.5)</td>
<td>14 (73.7)</td>
</tr>
<tr>
<td>PTC</td>
<td>46</td>
<td>41 (89.1)</td>
<td>34 (82.9)</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
<td>8 (100)</td>
<td>8 (100)</td>
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</table>

Summary

Implementation of instituted standard criteria for preliminary on-site adequacy assessment performed on Diff-Quik stained smears resulted in:

- Ninety-three percent agreement on specimen adequacy between on-site and final assessment.
- Non-diagnostic rate of 10.7%, comparable with published literature.
- Cyto-histologic concordant rate of 93.9% for neoplastic lesions and 62.3% for nonneoplastic lesions, compatible with published literature. Sampling error and over-interpretation of non-specific cytologic findings contributed to false negative and false positive results, respectively.
- Diagnostic consistency among cytopathologists, compared with previously published data.
- More effective communication and high satisfaction from clinicians of our on-site adequacy assessment service.
Useful in Distinguishing Collecting Duct Carcinoma from its Morphologic Mimics

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Carns Pathology, Irving, Texas, United States

Results

<table>
<thead>
<tr>
<th></th>
<th>p63</th>
<th>CK7</th>
<th>Vimentin</th>
<th>PAX8</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC</td>
<td>5%</td>
<td>10%</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>UC</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
<td>50%</td>
</tr>
<tr>
<td>PRCC</td>
<td>30%</td>
<td>40%</td>
<td>50%</td>
<td>60%</td>
</tr>
<tr>
<td>CRCC</td>
<td>40%</td>
<td>50%</td>
<td>60%</td>
<td>70%</td>
</tr>
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</table>

Panel of Immunohistochemical Stains

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>Panel Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC vs. CDC, PRCC, CRCC</td>
<td>p63, CK7, Vimentin, PAX8</td>
</tr>
</tbody>
</table>

Methods

Collective urothelial carcinomas with Fuchsin staining more frequently expressed (case studies >50%). Interact with Euclidean distance.
p63 is Useful in Distinguishing Collecting Duct Carcinoma from Morphologic Mimics

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³Cancer Institute of New Jersey, Roswell Park Cancer Institute, Buffalo, New York, United States

Background

Collecting duct carcinoma (CDC) is a rare type of renal cancer that occurs predominantly in the outer medulla of the kidney and is associated with a poor prognosis. It can be confused with other neoplasms due to its morphologic similarity, but p63 expression is a useful tool in its diagnosis.

Results

- **p63**: High expression in CDC, compared to UC, PRCC, and CRCC.
- **CK7**: Increased in UC and PRCC.
- **Vimentin**: Present in CRCC and PRCC.
- **PAX8**: More expressed in UC and CRCC.

Panel of Immunohistochemical Stains

<table>
<thead>
<tr>
<th>Stain</th>
<th>CDC</th>
<th>UC</th>
<th>PRCC</th>
<th>CRCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK8</td>
<td>15%</td>
<td>10%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>CK14</td>
<td>10%</td>
<td>10%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>PrERM</td>
<td>10%</td>
<td>10%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>CDX2</td>
<td>10%</td>
<td>10%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Vimentin</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Conclusion

p63 is the most useful in distinguishing CDC from UC, PRCC, and CRCC. A panel of p63, CK7, vimentin, and PAX8 is valuable in distinguishing poorly differentiated renal tumors from morphologic mimics.
A fire drill?!!

surprise appearance by ZZ Top
hmmmmm . . . still with the eyes; must be the camera!
CD25 Expression in Cutaneous B-Cell Lymphomas

Background

CD25 (also known as IL-2RB) is the alpha subunit of the interleukin-2 receptor. CD25 is expressed on activated T-cells, B-cells, and monocytes. In addition, CD25 expression has been demonstrated in systemic and cutaneous T-cell lymphomas. A fusion protein of IL-2 and alpha interferon fragments (Majordom, DRerto) has been approved for use as targeted therapy in T-cell lymphomas. Although clinical trials have demonstrated some efficacy for demethylation in management of systemic B-cell lymphomas, studies of CD25 expression in B-cell lymphomas have yielded mixed results. Moreover, the expression of CD25 in cutaneous T-cell lymphomas has not been investigated. In this study, we examined CD25 expression in a range of cutaneous and noncutaneous cutaneous B-cell lesions.

Design

Laser of B-cell lymphomas were performed. A subcutaneous bulk was described through microscopic and immunohistochemical examination of the clinical specimens of the cutaneous lymphoma. A comprehensive analysis of CD25 expression in B-cell lymphomas was performed. A total of 50 cases of cutaneous and systemic lymphomas were included in the study. CD25 expression was evaluated in all cases using immunohistochemical analysis. CD25 expression was scored as 0 (negative), 1+ (weak), 2+ (moderate), or 3+ (strong). The mean score for each case was calculated, and a total of 10 cases were selected for further analysis.

Results

An expanded, non-lymphoid cell line was derived from keratinocytes. These cells expressed CD25 uniformly regardless of CD25 expression. Lymphocytes, however, were negative for CD25 expression. A total of 50 cases of cutaneous T-cell lymphomas were evaluated using CD25 expression as a marker. CD25 expression was detected in 30% of cases (15 cases). CD25 expression was evaluated in all cases using immunohistochemical analysis. CD25 expression was scored as 0 (negative), 1+ (weak), 2+ (moderate), or 3+ (strong). The mean score for each case was calculated, and a total of 10 cases were selected for further analysis.
