Bethesda 2014 for Gyn Cytology, An Update

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For this talk…

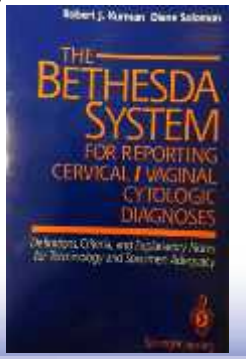
- Historical Perspective
- Understand the Rationale for Bethesda 2014
- Update the changes
- Risk stratification and management guidelines
- Review available resources

Conflict of Interest

- None for myself or Drs Nayar or Wilbur
- No royalties from publisher to anyone in order to keep price low
- Acknowledge Drs Nayar and Wilbur for their ASC Webinar (April 2015) and presentation at ASC meting in Dallas (2014)

History

- 1st Bethesda workshop 1988, chaired by Dr Robert Kurman…to address the various terminologies used for reporting Paps
- To establish terminology that would provide clear cut thresholds for management and decrease interobserver variability
- At end of 2 days, 2 tiered reporting system emerged(LSIL and HSIL) based on understanding of HPV biology (viral infection (LSIL) vs viral associated precancer(HSIL))
- Incorporated statement of adequacy
- Subsequent workshops in 1991 developed criteria for interpretive categories and adequacy
- First Bethesda atlas in 1994
- Became a worldwide reference for practice of cervical cytology



Guiding Principles for The Bethesda System (TBS)

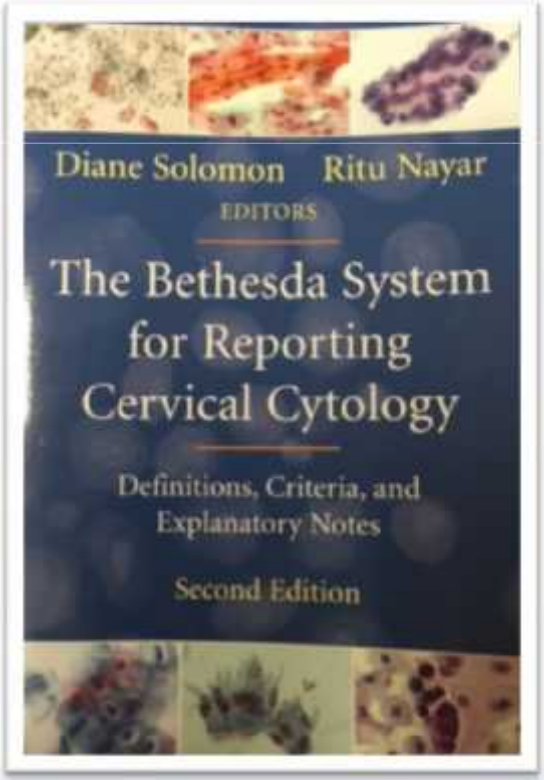
- Terminology must communicate clinically relevant information from the laboratory to the patient's health care provider
- Terminology should be uniform and reasonably reproducible across different pathologists, laboratories and yet flexible to be adapted to different lab and geographic settings
- Terminology must reflect *current understanding* of cervical neoplasia

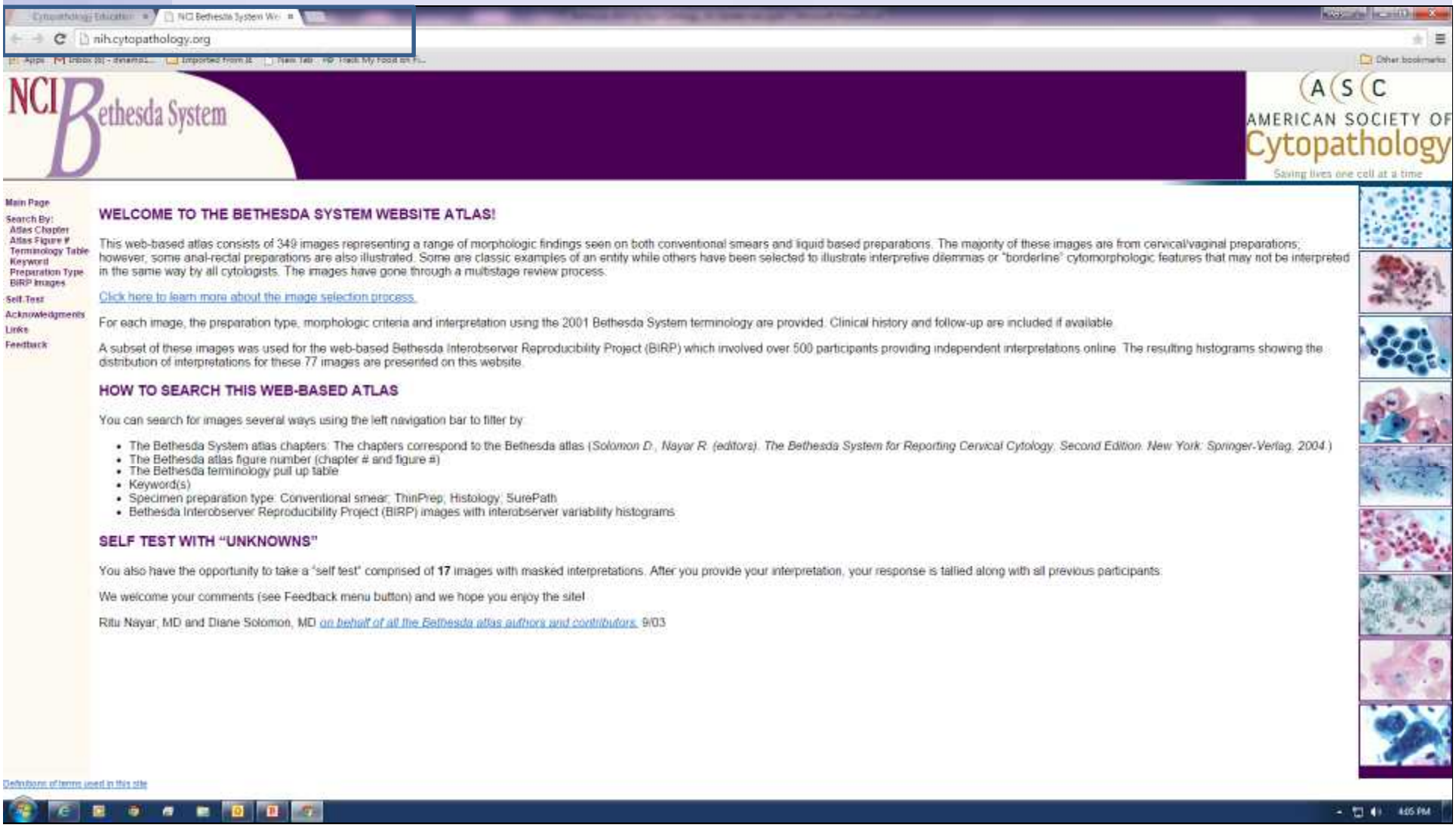
History continued…

- Bethesda 2001 workshop used the internet and provided an opportunity for the worldwide community to offer input
- Over 2000 comments, 400 participants from over 2 dozen countries met in Bethesda in May 2001 to finalize terminology
- Terms “interpretation” or “result” were recommended instead of “diagnosis” in the heading of cervical cytology report as Cervical cytology primarily a *screening test*

History continued…

- Subset of atlas images used for Bethesda Interobserver Reproducibility Study(BIRST)
- Print atlas in 2004 and Bethesda website established providing additional images, histograms from BIRST and self evaluation test (extensively used, >60,000 individuals)




nih.cytopathology.org
NCI Bethesda System
ASC
AMERICAN SOCIETY OF
Cytopathology
Saving lives one cell at a time
Main Page
Search By:
Atlas Chapter
Atlas Figure #
Terminology Table
Keyword
Preparation Type
BIRP Images
Self-Test
Acknowledgments
Links
Feedback
WELCOME TO THE BETHESDA SYSTEM WEBSITE ATLAS!
This web-based atlas consists of 349 images representing a range of morphologic findings seen on both conventional smears and liquid based preparations. The majority of these images are from cervical/vaginal preparations; however, some anal-rectal preparations are also illustrated. Some are classic examples of an entity while others have been selected to illustrate interpretive dilemmas or "borderline" cytomorphologic features that may not be interpreted in the same way by all cytologists. The images have gone through a multistage review process.
Click here to learn more about the image selection process.
For each image, the preparation type, morphologic criteria and interpretation using the 2001 Bethesda System terminology are provided. Clinical history and follow-up are included if available.
A subset of these images was used for the web-based Bethesda Interobserver Reproducibility Project (BIRP) which involved over 500 participants providing independent interpretations online. The resulting histograms showing the distribution of interpretations for these 77 images are presented on this website.
HOW TO SEARCH THIS WEB-BASED ATLAS
You can search for images several ways using the left navigation bar to filter by:
The Bethesda System atlas chapters: The chapters correspond to the Bethesda atlas (Solomon D., Nayar R. (editors). The Bethesda System for Reporting Cervical Cytology. Second Edition. New York: Springer-Verlag, 2004.)
The Bethesda atlas figure number (chapter # and figure #)
The Bethesda terminology pull up table
Keyword(s)
Specimen preparation type: Conventional smear; ThinPrep; Histology; SurePath
Bethesda Interobserver Reproducibility Project (BIRP) images with interobserver variability histograms
SELF TEST WITH "UNKNOWNS"
You also have the opportunity to take a "self test" comprised of 17 images with masked interpretations. After you provide your interpretation, your response is tallied along with all previous participants.
We welcome your comments (see Feedback menu button) and we hope you enjoy the site!
Ritu Nayar, MD and Diane Solomon, MD on behalf of all the Bethesda atlas authors and contributors, 9/03
Definitions of terms used in this site
4:05 PM

Why Bethesda 3?

- Significant changes in practice of cervical cytology since 2001
  - New screening and management guidelines
  - Primary HPV screen was FDA approved with cytology triage as one option in the USA
  - Changes in histopathology terminology (LAST)
  - HPV vaccination (Cervista, Gardasil, Gardasil 9)
- New Data and technology
  - Experience with Liquid based greater than 10 yrs.
  - New data(Anal, biomarkers, endometrial cells)
  - Automation, risk assessment
  - Pap still the standard in most settings

TBS 2014 Process

- Dr Nayar, ASC president in 2014 appointed 2 ASC Bethesda task forces-Atlas and Website
- Smaller working groups designed for speed, expertise and efficiency (cytologists, clinician, epidemiologists)
- *Chairs* David C Wilbur and Ritu Nayar
- *Advisor* Diane Solomon

TBS 2014 Process continued…

- **Members** *Fadi W Abdul- Karim, George G Birdsong, David Chelmow, David C. Chheing, Edmund S. Cibas, Teresa M. Darragh, Diane D. Davey, Michael R. Henry, Walid E. Khalbuss, Daniel F.I Kurtyz, Dina R. Mody, Ann T. Moriarty, Joel M. Palefsky, Celeste N. Powers, Donna K. Russell, Mark Schiffman, Mary K. Sidawy, Paul N. Staats, Mark H. Stoler, Sana O. Tabbara, Alan G. Waxman, Nicolas Wentzensen*

Development of Atlas Content

- *Early 2014* posted proposed draft content, changes and questions on internet bulletin board for *3.5 months*
- 2454 internet responses from 59 countries
- Comments considered and incorporated into final chapters
- >1000 images reviewed by taskforce in 2 stages

From ASC webinar by Nayar and Wilbur, April 28, 2015

Bethesda 3 Atlas (2015)

- 66% greater page count
- Addressed issues raised post TBS 2001 on adequacy and terminology
- No major terminology changes
- Updated and refined criteria
- Added to pitfalls and images
- Management and references updated
- Risk stratification

Journal of the American Society of Cytopathology (2015) 4, 170–180

Available online at www.sciencedirect.com

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journal homepage: www.jascyto.org/

COMMUNICATION

The Pap Test and Bethesda 2014

"The reports of my demise have been greatly exaggerated." (after a quotation from Mark Twain)

Ritu Nayar, MD[a,*], David C. Wilbur, MD[b]

Published simultaneously in May issue of Acta Cytologica (IAC), Cancer Cytopathology, Journal of the American Society of Cytopathology (ASC)
and Journal of Lower Genital Tract Disorders (ASCCP)

JASCyto May 2015

Chapter 1: Adequacy

George G. Birdsong and Diane D. Davey

- Important quality assurance of TBS
- TBS 2014 adds guidance
  - Clarified cellularity criteria for vaginal/post radiation samples and Anal Paps
  - Added data on lubricant/blood interference
  - HPV testing in unsatisfactory specimens
  - TZ component/2012 ASCCP

From ASC webinar by Nayar and Wilbur, April 28, 2015

Journal of the American Society of Cytopathology (2014) 3, 256–260

Available online at www.sciencedirect.com

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journal homepage: www.jascyto.org/

ORIGINAL ARTICLE

Common causes for unsatisfactory Pap tests in a high-risk population: insights into a yet unresolved problem in gynecologic cytology

Gabriela Quiroga-Garza, MD[a], Laura S. Satrum, BS, CT (ASCP)[b], Crystal J. Trujillo, MD[c], Dina R. Mody, MD[b], Yimin Ge, MD[b,*]

Should Adequacy Criteria in Cervicovaginal Cytology Be Modified After Radiotherapy, Chemotherapy, or Hysterectomy?

Chien-Hsing Lu, MD[1,2,3]; Chia-Che Chang, PhD[2]; Esther Shih-Chu Ho, MD[1]; Su-Ju Chen, MS[4]; Shu-Jiuan Lin, BS[4]; Tsai-Feng Fu, PhD[5]; and Ming-Chen Chang, MD[4]

BACKGROUND. The general criterion of an unsatisfactory Papanicolaou (Pap) test in the 2001 version of the Bethesda system is not applicable to patients after treatment with radiotherapy, chemotherapy, or hysterectomy. The current study was performed to determine whether specimen adequacy criteria for Pap tests should be modified for these conditions. **METHODS.** Consecutive patients who underwent conventional Pap tests between March and August 2006 were reviewed. The original reports were done according to the 2001 Bethesda system, with cellularity criteria modified in patients with a history of radiotherapy, chemotherapy, or hysterectomy. The slides of these patients were reviewed again. The degrees of cellularity, obscuring red blood cells, and inflammation were recorded. **RESULTS.** The final analyses included 7033 patients for which there were complete data. The original interpretation was unsatisfactory in 4.4% of all samples. When the 1337 slides obtained from patients with a history of radiotherapy, chemotherapy, and/or hysterectomy were reviewed using the general satisfactory threshold of >8000 squamous cells/slide and

1.2 Minimum Squamous Cellularity Criteria

1.2.1 Cellularity

There is no further evidence since the last Bethesda System update in 2001, to support adjustment of the minimum cellularity requirements for routine cervical cytology screening and follow-up. However, published literature and laboratory practice experience since the 2001 Bethesda workshop demonstrates ongoing confusion regarding the minimum cellularity estimates in special circumstances. Cytologists have often applied rigid minimum cellularity estimates to vaginal and postradiation or post-chemotherapy specimens, leading to a high unsatisfactory rate in these settings [9]. Quiroga-Garza found that almost half of 276 women with unsatisfactory results were over 50, and 85 % of these women had a history of gynecologic cancer. The most common cause for the unsatisfactory specimens was low squamous cellularity [10]. Women who have received radiation, chemotherapy, hysterectomy, or trachelectomy for invasive cancer often develop atrophic and reparative cellular changes, and when a cervix remains, there is frequently stenosis and altered anatomy [11]. There is little scientific evidence that a minimum cell threshold of 5,000 is required in these circumstances; some investigators recommend a lower threshold of 2,000 cells in these patients [12]. The 2001 Bethesda atlas stated that minimum cellularity criteria were developed for use with all cervical cytology specimens, but it is emphasized in this update that a 5,000 cell threshold should not be rigidly applied in vaginal and post-therapy specimens.

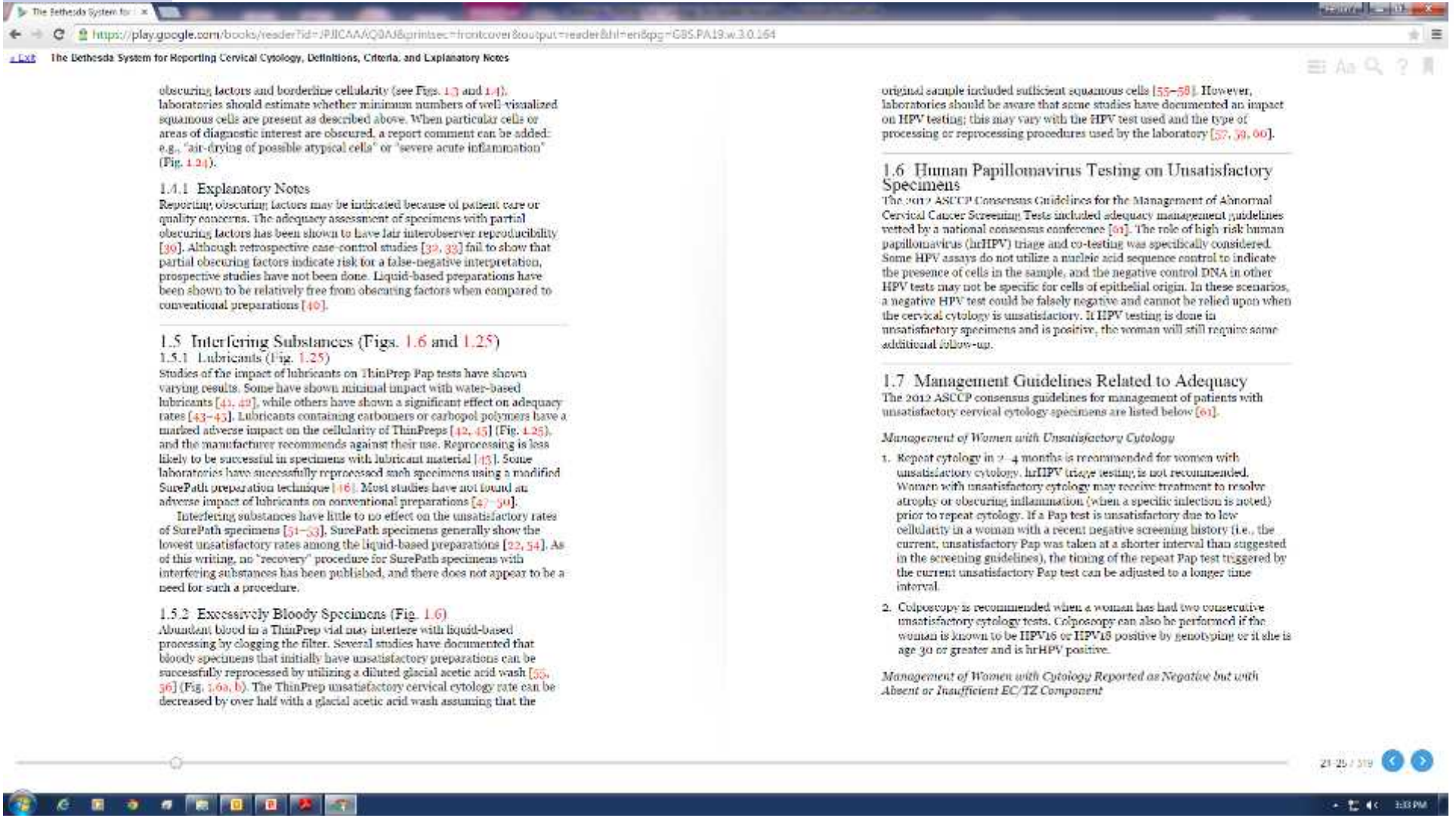
Adequacy

- Conventional Smears: 8000-12000 well preserved well visualized squamous or squamous metaplastic cells
- 5000 squamous cells minimum for liquid based for cervicovaginal specimens
- This works out to 8-9cells/HPF on SP and 3-4on TP, 10 fields across
- Mention endocervical/TZ component
- 2000 squamous cells is the absolute minimum for vaginal or s/p XRT/Rx smears*, anything less is Unsat
- *See Bethesda 2014 for details

Adequacy Issues with Blood

- Especially problematic with Thin prep specimens
- Filter clogged
- Glacial acetic acid wash and reprocessing
- Wash may affect HPV testing using some HPV platforms

Screen Shot of TBS 3 Book…..



obscuring factors and borderline cellularity (see Figs. 1.3 and 1.4), laboratories should estimate whether minimum numbers of well-visualized squamous cells are present as described above. When particular cells or areas of diagnostic interest are obscured, a report comment can be added: e.g., "air-drying of possible atypical cells" or "severe acute inflammation" (Fig. 1.24).

1.4.1 Explanatory Notes

Reporting obscuring factors may be indicated because of patient care or quality concerns. The adequacy assessment of specimens with partial obscuring factors has been shown to have fair interobserver reproducibility [39]. Although retrospective case-control studies [32, 33] fail to show that partial obscuring factors indicate risk for a false-negative interpretation, prospective studies have not been done. Liquid-based preparations have been shown to be relatively free from obscuring factors when compared to conventional preparations [40].

1.5 Interfering Substances (Figs. 1.6 and 1.25)

1.5.1 Lubricants (Fig. 1.25)

Studies of the impact of lubricants on ThinPrep Pap tests have shown varying results. Some have shown minimal impact with water-based lubricants [41, 42], while others have shown a significant effect on adequacy rates [43–45]. Lubricants containing carbomers or carbopol polymers have a marked adverse impact on the cellularity of ThinPreps [42, 45] (Fig. 1.25), and the manufacturer recommends against their use. Reprocessing is less likely to be successful in specimens with lubricant material [45]. Some laboratories have successfully reprocessed such specimens using a modified SurePath preparation technique [46]. Most studies have not found an adverse impact of lubricants on conventional preparations [47–50].

Interfering substances have little to no effect on the unsatisfactory rates of SurePath specimens [51–53]. SurePath specimens generally show the lowest unsatisfactory rates among the liquid-based preparations [22, 54]. As of this writing, no "recovery" procedure for SurePath specimens with interfering substances has been published, and there does not appear to be a need for such a procedure.

1.5.2 Excessively Bloody Specimens (Fig. 1.6)

Abundant blood in a ThinPrep vial may interfere with liquid-based processing by clogging the filter. Several studies have documented that bloody specimens that initially have unsatisfactory preparations can be successfully reprocessed by utilizing a diluted glacial acetic acid wash [55, 56] (Fig. 1.6a, b). The ThinPrep unsatisfactory cervical cytology rate can be decreased by over half with a glacial acetic acid wash assuming that the original sample included sufficient squamous cells [55–58]. However, laboratories should be aware that some studies have documented an impact on HPV testing; this may vary with the HPV test used and the type of processing or reprocessing procedures used by the laboratory [57, 59, 60].

1.6 Human Papillomavirus Testing on Unsatisfactory Specimens

The 2012 ASCCP Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests included adequacy management guidelines vetted by a national consensus conference [61]. The role of high risk human papillomavirus (hrHPV) triage and co-testing was specifically considered. Some HPV assays do not utilize a nucleic acid sequence control to indicate the presence of cells in the sample, and the negative control DNA in other HPV tests may not be specific for cells of epithelial origin. In these scenarios, a negative HPV test could be falsely negative and cannot be relied upon when the cervical cytology is unsatisfactory. If HPV testing is done in unsatisfactory specimens and is positive, the woman will still require some additional follow-up.

1.7 Management Guidelines Related to Adequacy

The 2012 ASCCP consensus guidelines for management of patients with unsatisfactory cervical cytology specimens are listed below [61].

Management of Women with Unsatisfactory Cytology

1. Repeat cytology in 2–4 months is recommended for women with unsatisfactory cytology. hrHPV (triage testing) is not recommended. Women with unsatisfactory cytology may receive treatment to resolve atrophy or obscuring inflammation (when a specific infection is noted) prior to repeat cytology. If a Pap test is unsatisfactory due to low cellularity in a woman with a recent negative screening history (i.e., the current, unsatisfactory Pap was taken at a shorter interval than suggested in the screening guidelines), the timing of the repeat Pap test triggered by the current unsatisfactory Pap test can be adjusted to a longer time interval.
2. Colposcopy is recommended when a woman has had two consecutive unsatisfactory cytology tests. Colposcopy can also be performed if the woman is known to be HPV16 or HPV18 positive by genotyping or if she is age 30 or greater and is hrHPV positive.

Management of Women with Cytology Reported as Negative but with Absent or Insufficient EC/TZ Component

HPV testing on Unsatisfactory Paps

- Negative HPV test on Unsat Pap is unreliable
  - Some HPV testing platforms have no internal control(HCII)
  - Internal control may not be epithelial cell specific
- A positive HPV test still requires additional follow up

Management Guidelines related to Adequacy

- **Unsatisfactory cytology**…repeat in 2-4 months(may treat atrophy or inflammation prior to repeat)
- If Unsat due to low cellularity but recent negative screening history, can adjust repeat test at a longer interval than 2-4 months
- Two consecutive Unsats then colposcopy
- Women>30 with Unsat pap and +HPV then colpo
- If 16, 18 types+ then colposcopy

Management Guidelines related to TZ / Endocervical component

- Women 21-29 with no TZ/EC…routine screening
- Women 30 and over with no TZ/EC, HPV testing is preferred. If negative HPV or no HPV, then routine screening in 3 yrs.
- Women 30 and over with HPV +, repeat in 1yr
- Women 30 and over, HPV+ and genotyping 16 or 18+, then colposcopy. Other types, Pap in a year

Chapter 2: Non-Neoplastic Findings

Daniel F.I Kurtycz, paul N. Staats, Nancy A. Young, Marluce Bibbo, Terrence J. Colgan, Marianne U. Prey, Ritu Nayar

- Expanded on Normal findings and non-neoplastic mimics of classic epithelial cell abnormalities
- More comprehensive representation of morphologic variations encountered on Paps

Chapter 3: Endometrial cells: The How and When of Reporting

Edmund S. Cibas, David Chelmow, Alan Waxman* and Ann T Moriarty (* Gynecologists)*

- Exfoliated endometrial cells in post menopausal women are considered abnormal and raise possibility of endometrial hyperplasia or carcinoma
- Often menopausal status is unclear or inaccurate
- Median age in US is 51 yrs. but varies greatly
- TBS 1988 recommended reporting *benign exfoliated endometrial cells in post menopausal women*
- *TBS 2001 recommended that this be done in all women ≥ 40 yrs.*

Consequences of TBS 2001

- Increased reporting of benign-appearing endometrial cells: (0.17%-0.49% of Paps(3X)
- Decreased predictive value for hyperplasia and cancer

	Risk Associated With Endometrial Cells	
	Pre TBS 2001	Post TBS 2001
Hyperplasia	12%	2%
Carcinoma	6%	1%

From Presentation by E. Cibas at ASC 62nd annual meeting in Dallas, Nov 16th 2014

For Bethesda 2014…..

- Category re evaluated
- Recommended to raise reporting age to 45 years
- 2 cytopathologists (Cibas, Moriarty) and 2 gynecologists (Chelmow, Waxman) on the committee
- Evidence based and should increase the predictive value of this finding and reduce unnecessary biopsies
- Support for change during public comment period
- ASCCP 2012 management guidelines already recommended histologic evaluation in postmenopausal women

From Presentation by E. Cibas at ASC 62nd annual meeting in Dallas, Nov 16th 2014

Education Note for Endometrial cells

- Specifies endometrial evaluation only in post menopausal women

Sample Report:
Endometrial cells present in a woman ≥ 45 years of age
Negative for Squamous Intraepithelial Lesion or Malignancy
Or
Endometrial cells correlate with menstrual history provided

Note: Endometrial cells in a woman 45 years or older may be associated with benign endometrium, hormonal alterations and less commonly, endometrial or uterine abnormalities. *Endometrial evaluation is recommended in postmenopausal women*

Chapter 4: Atypical Squamous Cells

Fadi W. Abdul-Karim, Celeste N. Powers, Jonathan S. Berek, Mark E. Sherman, Sana O. Tabbara and Mary K. Sidawy

- No changes to definition of ASC-US and ASC-H
- Common patterns reviewed
- Guidance on use of HPV test results to monitor quality and consistency among individual practitioners and laboratories
- Additional images on Postmenopausal atypia, spontaneously exfoliated endometrials vs ASC--H

Atypical Squamous cells

- Bethesda 3 expands on criteria for diagnosis
- Common patterns classified as ASC
  - Atypical Parakeratosis
  - Atypical repair
  - Atypia in Post menopausal women with atrophy
  - Other patterns
  - Expands on explanatory notes and HPV testing and strategies
  - Quality Assurance tool using ASC reporting rates, ASC:SIL, hrHPV positivity rates and benchmarking

CAP LAP Cytology Checklist 2014

**Includes ThinPrep and ThinPrep with imaging cases in laboratories with a ThinPrep cytology volume of >300 per year.

***Includes SurePath and SurePath with FocalPoint cases in laboratories with SurePath cytology volume >300 per year.

CONVENTIONAL*
Laboratory Percentile-Reporting Rate

CATEGORY	5th	10th	25th	50th	75th	90th	95th
ASC-US (%)	0.5	0.6	1.5	2.6	4.5	6.5	7.5
ASC-H (%)	0.0	0.0	0.0	0.1	0.3	0.5	0.7
LSIL (%)	0.0	0.2	0.5	1.0	1.7	2.6	3.4
HSIL (%)	0.0	0.0	0.1	0.2	0.4	0.8	1.0
ASC/SIL	0.4	0.8	1.5	2.2	3.2	4.5	6.0
AGC (%)	0.0	0.0	0.0	0.1	0.3	0.6	0.8
UNSATISFACTORY (%)	0.0	0.2	0.6	1.2	2.2	3.7	5.7

ThinPrep**
Laboratory Percentile-Reporting Rate

CATEGORY	5th	10th	25th	50th	75th	90th	95th
ASC-US (%)	1.9	2.5	3.7	5.1	6.8	9.2	12.0
ASC-H (%)	0.0	0.1	0.2	0.3	0.4	0.7	1.0
LSIL (%)	1.1	1.4	2.0	2.7	3.6	4.7	5.5
HSIL (%)	0.1	0.2	0.3	0.4	0.7	1.0	1.3
ASC/SIL	0.8	1.0	1.3	1.7	2.2	3.1	3.8
AGC (%)	0.0	0.0	0.1	0.1	0.3	0.5	0.7
UNSATISFACTORY (%)	0.3	0.4	0.7	1.1	1.8	2.9	3.6

SurePath***
Laboratory Percentile-Reporting Rate

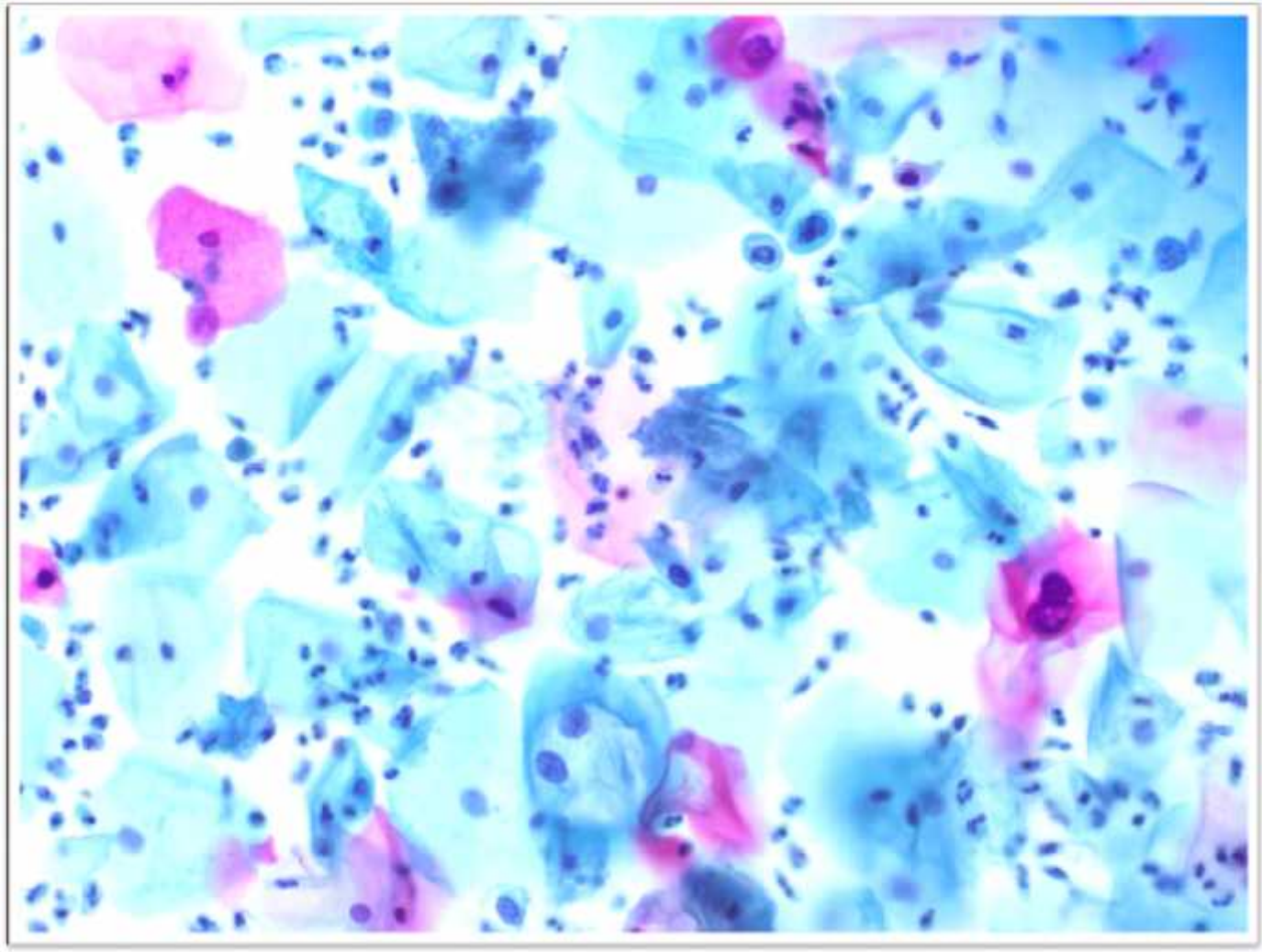
CATEGORY	5th	10th	25th	50th	75th	90th	95th
ASC-US (%)	1.7	2.2	3.3	4.5	6.2	8.7	11.3
ASC-H (%)	0.0	0.1	0.1	0.2	0.4	0.6	0.8
LSIL (%)	1.2	1.4	2.0	2.6	3.5	4.8	6.1
HSIL (%)	0.1	0.1	0.2	0.3	0.5	0.8	1.2
ASC/SIL	0.7	0.8	1.3	1.6	2.0	2.7	3.2
AGC (%)	0.0	0.1	0.1	0.2	0.3	0.5	0.8
UNSATISFACTORY (%)	0.0	0.1	0.1	0.2	0.4	0.6	0.9

Evidence of Compliance:

- ✓ Records of statistical data for defined categories AND
- ✓ Records of data review and evaluation against benchmark data by the laboratory director or designee

Chapter 5: Squamous Epithelial cell Abnormalities

Michael R. Henry, Donna K. Russell, Ronald D. Luff, Marianne U. Prey, Thomas C. Wright Jr and Ritu Nayar



Chapter 5: Squamous Epithelial cell Abnormalities

Michael R. Henry, Donna K. Russell, Ronald D. Luff, Marianne U. Prey, Thomas C. Wright Jr and Ritu Nayar

- LSIL and HSIL stays
- No LSIL-H category
  - As it would create a defacto 3 tiered system
  - Biology does not support it
  - Anticipated poor reproducibility
  - Possible overutilization
  - Clinician confusion

Chapter 5: Squamous Epithelial cell Abnormalities

Michael R. Henry, Donna K. Russell, Ronald D. Luff, Marianne U. Prey, Thomas C. Wright Jr and Ritu Nayar

- LSIL and HSIL stays
- No LSIL-H category
  - However, CAP survey does show that most use that category
  - publications show that it has intermediate risk for HSIL on Bx between LSIL and HSIL

Should LSIL-H Be a Distinct Cytology Category?

A Study on the Frequency and Distribution of 40 Human Papillomavirus Genotypes in 808 Women

Haijun Zhou, MD, PhD; Mary R. Schwartz, MD; Donna Coffey, MD; Debora Smith, CT; Dina R. Mody, MD; and Yimin Ge, MD

BACKGROUND: The 2001 Bethesda System for gynecologic cervical cytology reporting classifies squamous intraepithelial lesions into low-grade (LSIL) and high-grade (HSIL) lesions. An intermediate term, "low-grade squamous intraepithelial lesion, cannot exclude high-grade squamous intraepithelial lesion (LSIL-H)," has been used in a small percentage of LSIL cases. To the authors' knowledge, little is known regarding the human papillomavirus (HPV) status in patients with LSIL-H. **METHODS:** A total of 808 SurePath specimens obtained between December 2009 and April 2011 were tested for 40 HPV genotypes using DNA microarray, followed by a confirmatory DNA sequencing assay. **RESULTS:** The infection rate for high-risk HPV in women with LSIL-H (92%) was strikingly close to that for women with HSIL (91%), which was higher than that for those with LSIL (74%); atypical squamous cells, cannot rule out high-grade lesion (ASC-H) (78%); or LSIL and ASC-H combined (74%). HPV type 16, the most common carcinogenic HPV genotype, was detected in 36% of women with LSIL-H, which was significantly higher than that in women with LSIL and ASC-H combined (13.8%), but less than that in women with HSIL (44.6%). Patients with LSIL-H and HSIL had similar infection rates for low-risk/intermediate-risk HPV genotypes, which were lower than those in LSIL or LSIL and ASC-H combined. **CONCLUSIONS:** Women found to have LSIL-H on a Papanicolaou test appear to have a unique HPV distribution pattern that clearly differs from LSIL and is comparable to that for HSIL, suggesting an increased risk of high-grade lesions over that of women with LSIL. Recognizing LSIL-H as an independent diagnostic category may help in the early identification of the high-risk subgroup that may require a management algorithm comparable to that for patients with HSIL. *Cancer (Cancer Cytopathol)* 2012;120:373-9. © 2012 *American Cancer Society.*

How to Report Equivocal SIL in TBS 2014

- ASC-H + LSIL when definite LSIL in background (preferred)
- Or SIL of uncertain grade with comment as to why
- Should occur only in a small % of cases
- Chapter on squamous lesions also expanded to show more problematic patterns and pitfalls and diathesis

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

Chapter 6: Glandular Epithelial Abnormalities

David C. Wilbur, David C. Chhieng, Barbara Guidos and Dina R Mody

- No Changes in reporting terminology
- More images and differentials
- Expanded on mimics
- Expanded on variants of adenocarcinomas
- Tables illustrating differences in criteria for quick reference
- Notes about HPV testing and reporting rates

TBS 2001 and 2014

Negative for Intraepithelial Lesion or Malignancy (NILM)

Epithelial Cell Abnormality

- Squamous *(ASC-US, ASC-H, LSIL, HSIL,CA)*
- Glandular (AGC, AIS, Adenocarcinomas)
- Other

Other

Atypical Glandular Cells(TBS 2001 and 2014)

Endocervical	unqualified(NOS)
	probably neoplastic/AIS/CA
Endometrial	
Glandular	NOS
	probably neoplastic

Adenocarcinoma In Situ(TBS 2001 and 2014)

Adenocarcinoma In Situ free standing entity(if all criteria) met and not under AGC (Atypical glandular cells)

If all criteria not met then under Atypical Endocervicals, probably AIS/neoplastic

Hyperchromatic Crowded Groups (HCGs)

- AIS
- HSIL
- ACA Cx
- Sq ca cx
- ACA endometrium
- Other Carcinomas
- Exodus ball
- Aggressive endocervical sample
- Follicular cervicitis
- LUS endometrium
- Tubal metaplasia
- MGH
- Atrophy

Chapter 7: Other Malignant Neoplasms

Sana O. Tabbara and Walid Khalbuss

- Special variants discussed
- Additional images
- Diagnostically challenging

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

Chapter 8: Anal Cytology

Teresa Darragh and Joel M. Palefsky

- Significant increase in certain high risk groups
- Chapter expanded and includes
  - Epidemiology, performance characteristics
  - Additional images of benign, SIL and carcinoma
  - HPV testing and Biomarkers
  - Clinical management

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

Chapter 9: Adjunctive Testing

Mark H. Stoler, Stephen S. Raab and David C. Wilbur

- Reporting evolved since TBS 2001.
- Chapter updates reporting schemes
- Data re use and reporting for HPV testing schemes and IHC(P16) included
- Emphasizes the importance of clinical validation of test performance vs analytic sensitivity
- Sample reports and educational notes

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

HPV Testing Notes

- For triage of abnormal Pap result
- Co-testing
- Primary HPV screening
- HPV genotyping (selective reporting of individual HPV types in conjunction with a positive pooled HrHPV test..i.e... 16, 18 or non 16/18)
  - Basically expanded TBS 2001 4 page chapter to 11 pages with addition of P16

Chapter 10: Computer Assisted Interpretation of Cervical Cytology

David C. Wilbur, Marianne U. Prey and Ritu Nayar

- In USA several FDA approved automated cervical screening devices since TBS 2001
- Overview of systems and updated recommendations for use and reporting for “location-guided screening” devices in addition to those covered in 2001

Abbreviated from ASC webinar on April 28 2015 by Wilbur and Nayar

Chapter 11: Educational Notes and Comments

Ritu Nayar, Dennis. O'Connor and Teresa M. Darragh

- Guiding principle of TBS has always been to improve communication from laboratory provider to the physician caring for the patient
- The use of written recommendations and/or comments in cervical cytology reports is optional(patient access and EHR in USA)
  - When used, they must be worded carefully and relay clear, concise, current, evidence-based information

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

Chapter 12: Risk Assessment in Cervical Cancer

Nicolas Wentzensen, Mark Schiffman, David Chelmow, Teresa Darragh and Alan G. Waxman

- New chapter
- Risk stratification based on Pap and HPV testing and reasons and types of triage and management
- Concept of "equal management for equal risk" along with *balancing benefits and harms of screening*

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

TBS 2014 Website Project Task Force

- Chairs:
  - *Daniel F.I. Kurtycz and Paul N. Staats*
- Advisors
  - *Ritu Nayar and David C. Wilbur*
- Members
  - *Deborah Chute, Maria Freidlander, Sara Monaco, Donna K. Russell*

Bethesda Interobserver Reproducibility Study(*BIRST*) of 2001

- Evaluated concordance amongst participants with different training and experience levels
- Identified features and sources of poor interobserver agreement
- Highlighted issues re reproducibility of various TBS 2001 categories
- Progress in education
- Acceptance of ancillary studies to improve predictive value of screening process

CANCER
CYTOPATHOLOGY

The Bethesda Interobserver Reproducibility Study (BIRST)

A Web-based Assessment of the Bethesda 2001 System for Classifying Cervical Cytology

Mark E. Sherman, MD[1]
Abhijit Dasgupta, PhD[2]
Mark Schiffman, MD, MPH[1]
Ritu Nayar, MD[3]
Diane Solomon, MD[4]

[1] Hormonal and Reproductive Epidemiology Branch, Division of Cancer Epidemiology and

BACKGROUND. The Bethesda System (TBS) along with its companion atlas was updated in 2001 to improve standardization, clarity, and reproducibility of cervical cytology reporting.

METHODS. The authors used a novel web-based format to compare assessments of 77 images demonstrating a range of classical and borderline cytologic changes by a self-selected group of United States cytotechnologists (n = 216) and pathologists (n = 185).

RESULTS. Participants were highly experienced, with 71.2% of cytotechnologists

Cancer Cytopathology 2007

Initial Analysis of BIRST-2 Data

- Consistent agreement across certifications
- Best agreement for NILM, LSIL and Squamous Carcinoma
- ASC-US, ASC-H, Glandulars and Anal cytology more problematic
- Continue to build new features and delivery methods
  - Virtual microscopy, cloud sourcing, solicit images from international cytology community

From ASC webinar by Wilbur and Nayar. April 28 2015. www.cytopathology.org

TBS Contributions

- Initiation of research and clinical trials
- Alignment of management with terminology
- Prototype for standardized reporting terminology in pathology
  - Thyroid Bethesda, Urinary Paris, Pancreaticobiliary, Milan for salivary
  - Histopathology LAST/WHO

Summary of Best-Practice Advice for Cervical Cancer Screening
Don't screen average-risk women younger than 21 years
Start screening average-risk women at age 21 with cytology (without HPV testing) once every 3 years
Don't screen average-risk women with cytology more often than once every 3 years
Use a combination of cytology and HPV testing once every 5 years in average-risk women 30 years and older who prefer screening less often
Don't perform HPV testing in average-risk women younger than 30 years
Stop screening average-risk women older than 65 years if they have had negative results on three consecutive cytology tests or on two consecutive cytology plus HPV tests in the previous 10 years, with the most recent test performed in the previous 5 years
Don't screen average-risk women of any age for cervical cancer if they have had a hysterectomy with removal of the cervix

Screening guidelines in the USA
ACP internal medicine 2015 press release (based on 2012 guidelines)