MASSACHUSETTS GENERAL HOSPITAL
PATHOLOGY

HARVARD MEDICAL SCHOOL

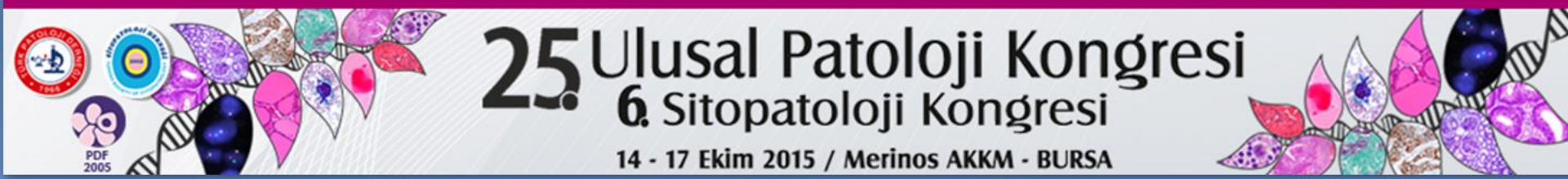
The Bethesda System: Updates for 2015

6th Cytopathology Congress
Bursa, Turkey
October 14, 2015

David C. Wilbur, M.D.

Dept. of Pathology

Massachusetts General Hospital



DISCLOSURES

- No relevant financial interests related to this presentation.

- The editors and authors of the Bethesda Cervical Cytology Atlases did not and will not receive any royalties from the publisher for this work in order to keep the price as low as possible.

WHY DID WE UPDATE TBS 2001?

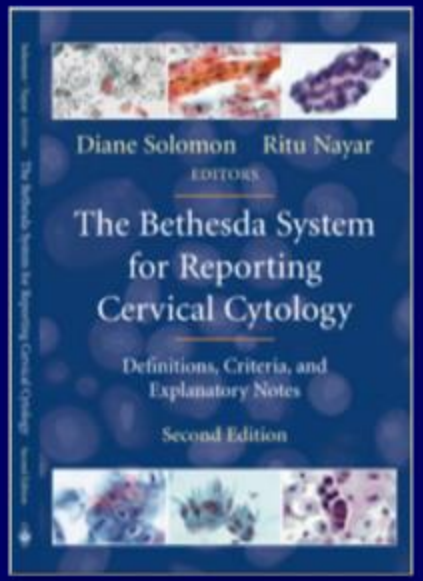
- **Significant changes in practice of cervical cytology**
  - New screening and management guidelines
  - Changes in histopathology terminology
  - Increasing uptake of HPV vaccination
  - Primary HPV screening with Pap as "diagnostic" triage
- **New data and technology**
  - Additional experience with LBP over last 10 yrs
  - New data - Endometrial cells, Anal cytology, Biomarkers, Automation, Risk assessment
- **Still a need for Pap testing in low resource areas and for standardization of terminology for trials and research**

“ In the future cervical cancer screening may well begin with HPV testing with cytology as a triage for HPV-positive samples……

On one hand, the absolute number of cervical cytology samples would decrease, but on the other hand, cytologic evaluation, in its new role as a method of triage, would become even more important and challenging. ”

Foreword by Robert Kurman, MD in

The Cervical Cytology Bethesda Atlas, 2rd Ed. Springer 2004



TBS 2014 Process

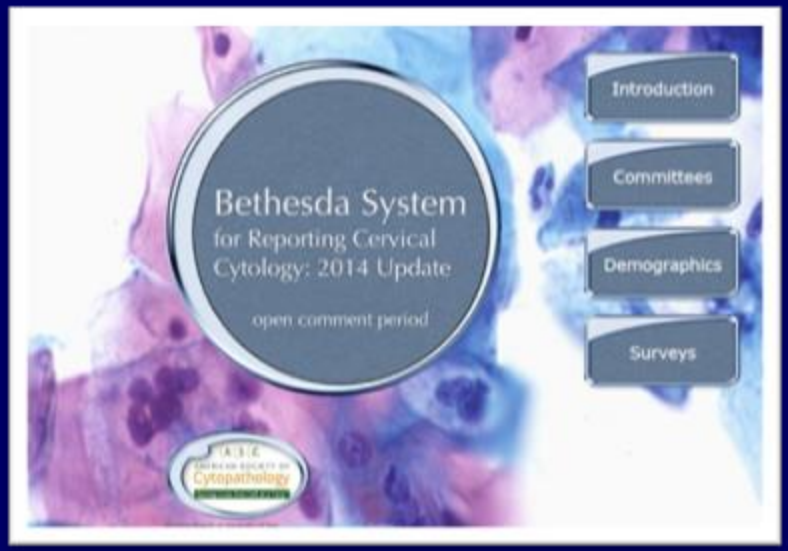
- Major changes to terminology were not anticipated
- Two Bethesda Task Forces - Atlas and Website appointed
- Smaller working groups – designed for speed, expertise, and efficiency (***included cytologists, clinicians, epidemiologists***)

- **Bethesda 2014 ATLAS TASK FORCE**

Chairs: David C. Wilbur, and Ritu Nayar
Advisor: Diane Solomon
Members: Fadi W. Abdul-Karim, George G. Birdsong, David Chelmow, David C. Chhieng, Edmund S. Cibas, Teresa M. Darragh, Diane D. Davey Michael R. Henry, Walid E. Khalbuss, Daniel F.I. Kurtycz, 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

TBS 2014 PROCESS

- Workgroups reviewed literature, posted proposed draft content, changes and questions on an Internet bulletin board for 3.5 months in early 2014
  - 2454 Internet responses from 59 countries
  - Comments considered and incorporated into final chapters

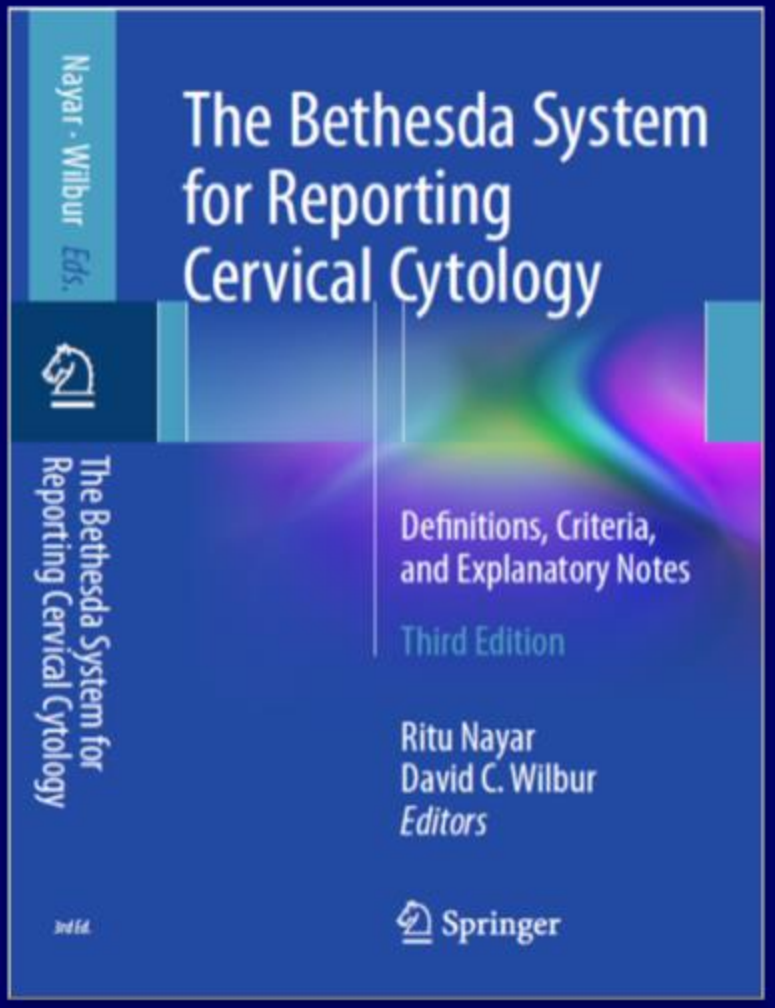


- **>1000** images reviewed by task force (2 stages)

RESULTS

- **TEXT**
  - 12 chapters: 6 correspond to major TBS interpretation categories; 6 in related areas
  - New chapter- risk assessment in cancer screening

- **IMAGES**
  - 370 in atlas (*many additional on TBS 2014 website*)
  - 52% new, 48% from 2nd Ed.
  - 60% LBP/ 40% conventional
  - ↑ in composites, cell blocks, IHC, histology correlation



Soft cover and eBook

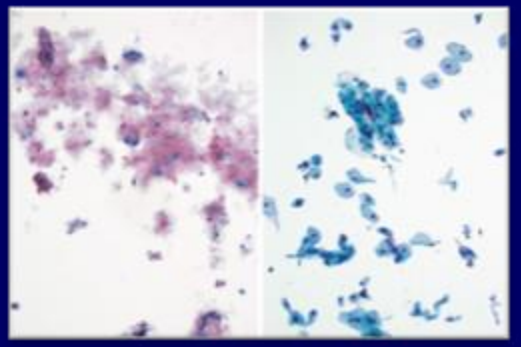
3rd EDITION OF ATLAS

- Builds on popular features of the first 2 editions
- Highlights:
  - 66% greater page count
  - Addressed issues raised in practice with some areas of TBS 2001 adequacy and terminology
  - No major changes in terminology
  - Updated and refined morphologic criteria
  - Added increased numbers of pitfalls & mimics
  - Updated management and references

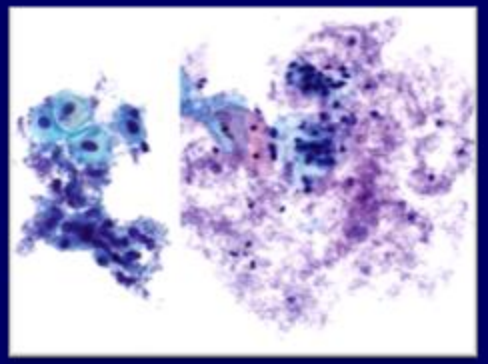
Chapter 1: ADEQUACY

- Evaluation of specimen adequacy is an important quality assurance component of TBS.

- TBS 2014- additional guidance
  - Clarified cellularity criteria for vaginal/ post radiation samples (2000)
  - Added data on lubricant/ blood interference (TP)
  - Section on HPV testing in unsat specimens (cellular controls)
  - TZ component /2012 ASCCP
  - New references



Unsatisfactory Reprocessing with GAA

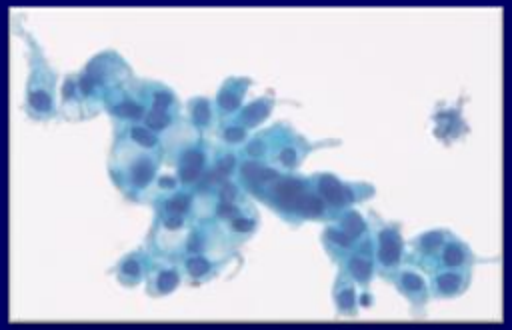


Unsatisfactory Interfering lubricant

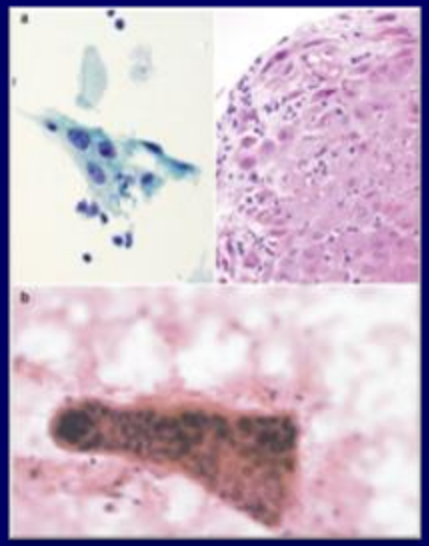
Chapter 2:
NON-NEOPLASTIC FINDINGS

- An expanded variety of "normal" findings as well as non-neoplastic mimics of classic epithelial abnormalities are included.

- Provides a more complete representation of the morphologic variations that can be encountered in cervical cytology preparations.



Squamous metaplasia



Pregnancy associated changes

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

Background

- **TBS 1988** recommended *benign-appearing exfoliated endometrial cells* reporting in **postmenopausal women.**
- **TBS 2001** recommended that this be done in all **women ≥40 yrs**.
  - Increased reporting of benign-appearing endometrial cells: 0.17% to 0.49% of Paps (3x).
  - Decreased predictive value for hyperplasia/cancer.

	Risk Associated with Reporting EMC	
	Pre-2001	**Post-2001**
hyperplasia	**12%**	**2%**
cancer	**6%**	**1%**

TBS 2014: New Recommendation

- Little evidence since 2001 to support endometrial cancer detection in women under 45yrs.
- **Raise the threshold for reporting to age 45**.
- General support for this change during public comment period.
- 2012 ASCCP management guidelines recommended that histologic endometrial assessment only be performed in postmenopausal women.

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

- Endometrial cells are reported in women ages 45 and greater - *to increase PPV and reduce unnecessary endometrial biopsies*
- The educational note specifies endometrial evaluation only in postmenopausal women

SAMPLE REPORT: CERVICAL PAP TEST

Endometrial cells are present in a woman ≥ 45 years of age.

Negative for squamous intraepithelial lesion.

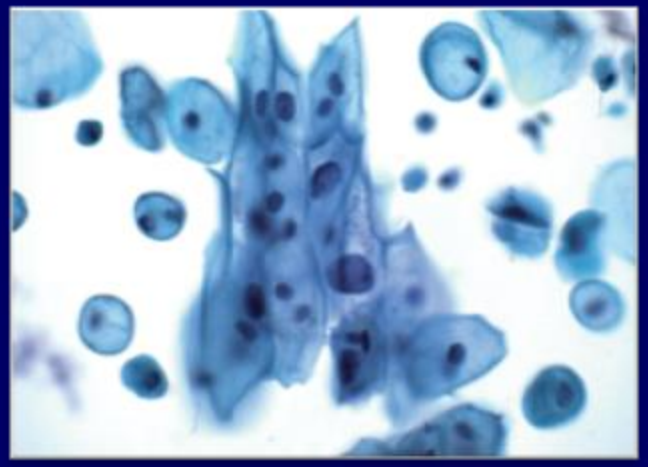
or

Endometrial cells correlate with the menstrual history provided

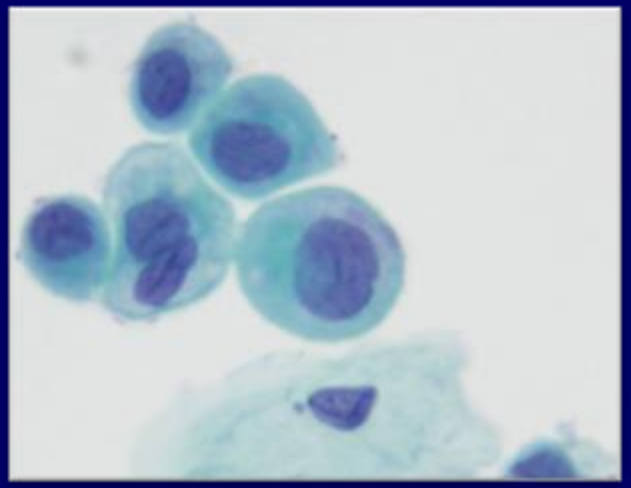
NOTE: Endometrial cells in women 45 years or older may be associated with benign endometrium, hormonal alterations, and, less commonly, endometrial or uterine abnormalities. *Endometrial evaluation is recommended in postmenopausal women.*

Chapter 4:
ATYPICAL SQUAMOUS CELLS

- The category of ASC is by far the most commonly reported abnormal cervical cytology interpretation.
- ASC remains the general category; subcategorization as ASC-US / ASC-H.
- ASC-US and ASC-H patterns are reviewed.
- Guidance on use of ASC with HPV test results to monitor quality and consistency among practitioners and laboratories.



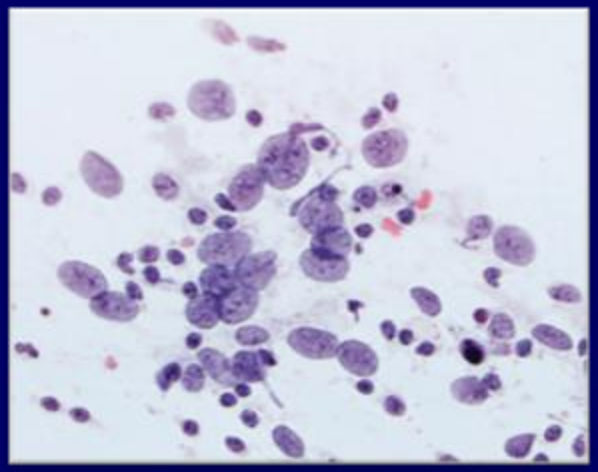
Postmenopausal "Atypia"



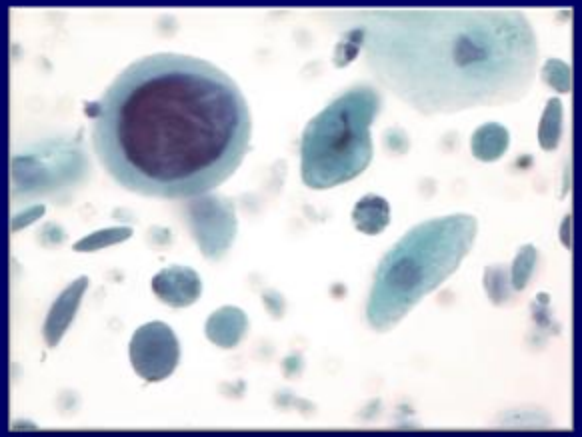
ASC-H

Chapter 5:
Squamous Epithelial Lesions

- HSIL is the focus of cervical cancer screening
- Expanded substantially
- Added problematic, less common HSIL patterns
- Illustrate mimics of LSIL and HSIL
- More examples of squamous cell carcinoma, tumor diathesis and their look-alikes



HSIL- stripped nuclei



ASC-US in atrophy

Chapter 5:
Squamous Epithelial Abnormalities

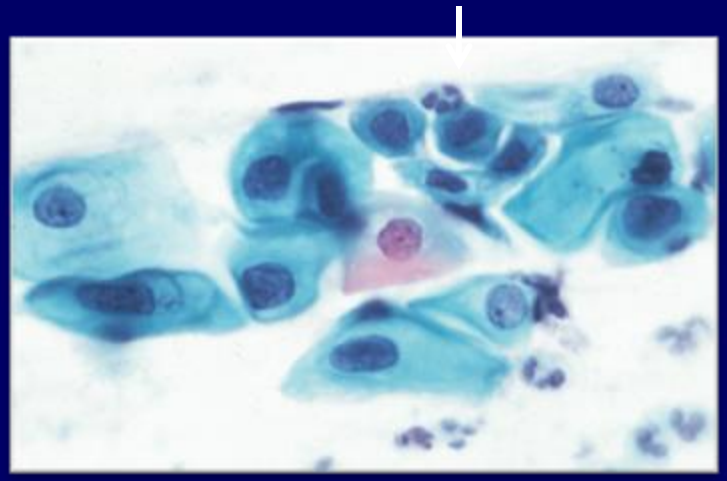
- **TBS 2014 maintains the dichotomous reporting terminology of LSIL/HSIL**
  - This reflects our current understanding of the natural history of HPV related infections.
  - Low-grade changes represent productive, largely transient HPV infection, and high-grade morphology represents a precancerous lesion.

- **"LSIL with some features suggestive of the presence of HSIL"**

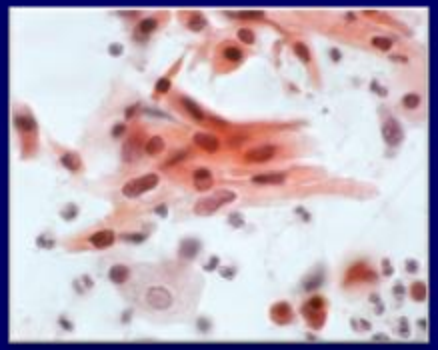
- LSIL-H would create a defacto 3-tier system.
- Would not correlate with biology/management.
- Poor reproducibility.
- Histology also LSIL/HSIL.

How To Report Equivocal SIL in TBS 2014

- In occasional equivocal cases options are
  - **ASC-H + LSIL** when definite LSIL in background (preferred)
  - SIL of uncertain grade with comment as to why
- Should occur in only a small % of cases.



ASC-H + LSIL



Keratinizing SIL. *Comment*:..

Chapter 6:
Glandular Epithelial Abnormalities

- This update includes many more images of glandular lesions and differential diagnostic considerations.

- Tables illustrating differences in criteria are included for quick reference.

Shed endometrium vs. AIS/p16

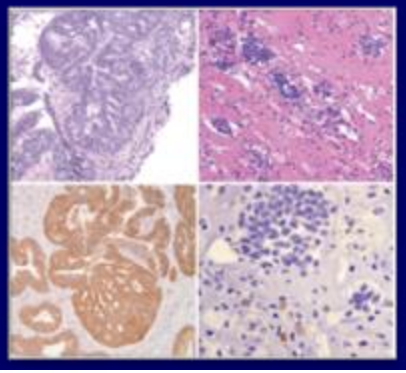


Table 6.2 Cytologic distinction between endocervical, endometrial, and extrauterine cancers

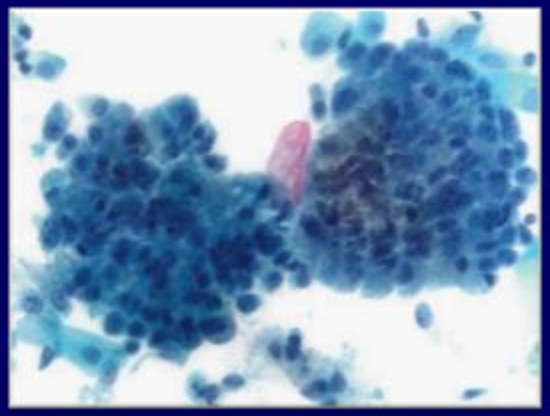
Features	Endocervical Ca	Endometrial Ca	Extrauterine Ca
Cellularity	Hypercellular	Low cellularity usually	Rare cells (unless direct extension/mets)
Pattern	Strips, rosettes, sheets with feathering, single malignant cells	Small clusters, rarely papillae, single cells	Varies depending upon primary and mode of spread
Diathesis	Visible, type varies by preparation	Variable, watery or subtle or absent	Usually absent unless direct spread or mets
Cell shapes	Oval, columnar, pleomorphic	Round, irregular, usually smaller	Variable, do not belong
Nuclei	Oval, elongated, pleomorphic, vesicular	Round, irregular in higher grade	Variable
Cytoplasm	Mucin +	Degenerative vacuoles	Variable
SIL or Sq Ca	Present in >50 %	Absent	Absent
High-risk HPV	Positive in most	Negative	Negative
p16	Block positive	Patchy/focal except in high grade/serous	Variable, depends on type

Adapted from Mody [11]

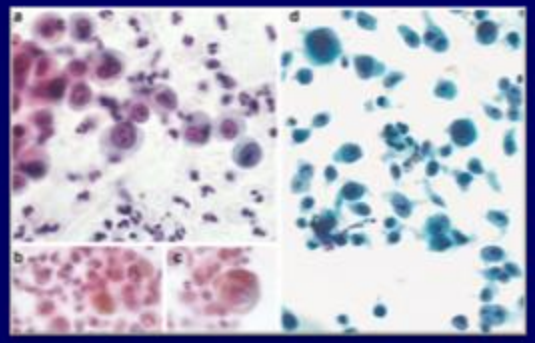
Chapter 7:
OTHER MALIGNANT NEOPLASMS

- Special variants of cervical carcinoma/ uterine or adnexal tumors and metastasis from other primaries may be seen on cervical cytology.

- May be diagnostically challenging.
- Increased numbers of such cases are now illustrated.



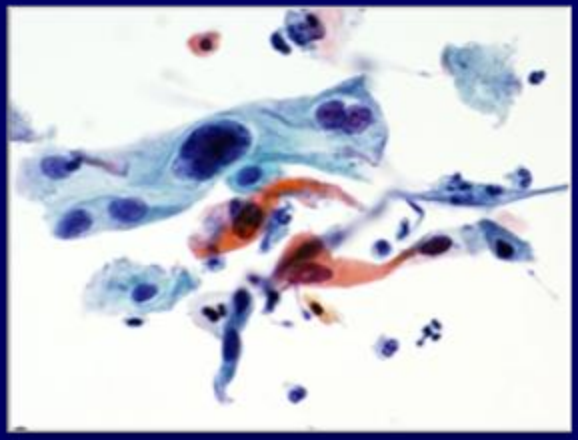
Adenoma malignum



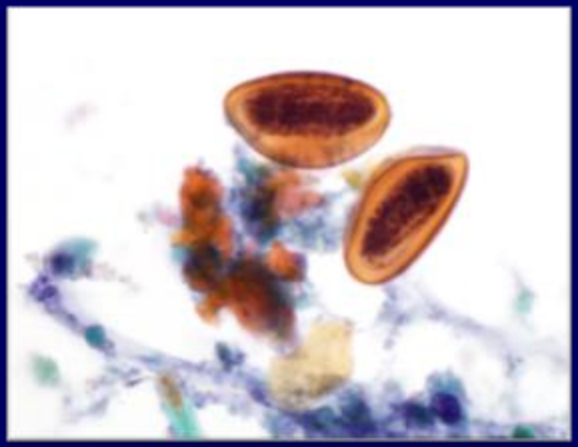
Metastatic melanoma

Chapter 8:
ANAL CYTOLOGY

- Anal cancer - significant increase in high risk groups.
- Anal cytology included in TBS 2001 atlas- gained acceptance as a screening tool for anal ca.
- Expanded chapter with
  - Epidemiology, performance characteristics
  - Additional images: organisms, SIL, cancer
  - Role of HPV testing /biomarkers
  - Clinical management



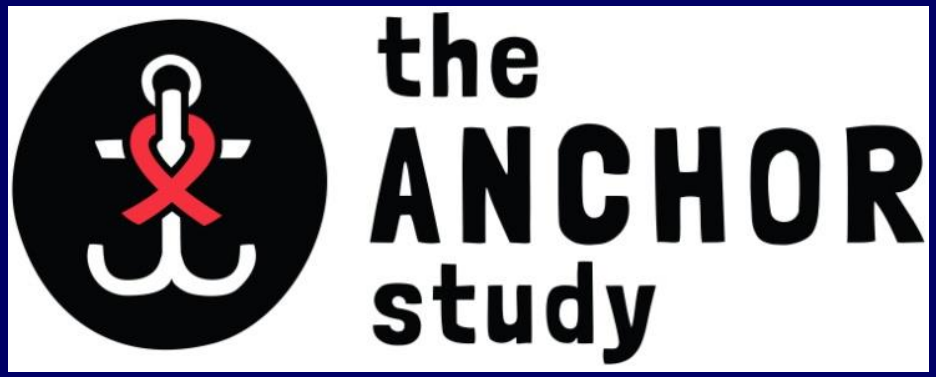
Squamous cell carcinoma



Pinworm

Anal Cancer Screening

- 15 sites in US → screen ~17K HIV+ men & women, ages 35 and older
- ~5000 with HSIL on anal biopsy
- Followed for 5+ years
- Two arms:
  - Treatment
  - Active monitoring



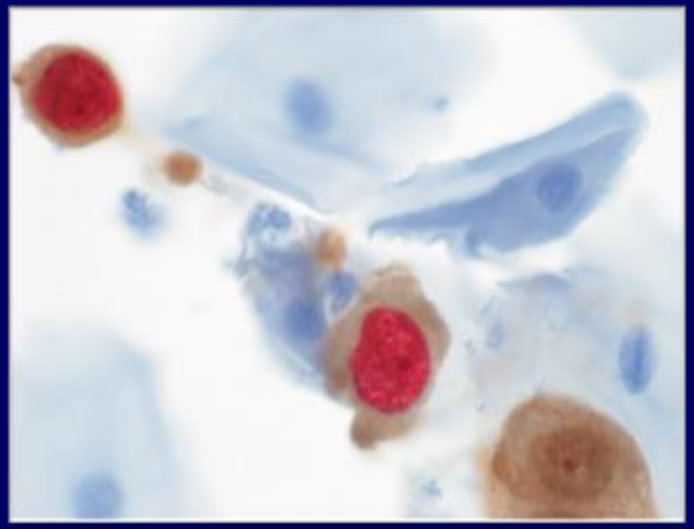
- Does treatment of anal HSIL effect natural history?
- …should we screen for anal cancer + its precursors?

Anal Cancer/HSIL Outcomes Research Study

Chapter 9:
ADJUNCTIVE TESTING

- Reporting of the results from ancillary studies has evolved since the 2nd ed, and this chapter updates reporting schemes.

- Data concerning use and reporting for the current HPV testing schemes and adjunctive immuno-cytochemistry procedures (eg, p16) are included.



Immunocytochemstry **for p16/Ki67 dual stain**) p6 stains both cytoplasm & nucleus (*brown; Ki67 stains the nucleus (red). Cells with combined staining are a strong predictor of the presence of HSIL. (LBP, ThinPrep)*

Chapter 10: COMPUTER ASSISTED INTERPRETATION OF CERVICAL CYTOLOGY

- Several new US FDA approvals in the field of automated cervical cytology screening have occurred in the past decade.

- The 3rd ed. provides an overview of the currently used systems and updates recommendations and reporting items for "location-guided screening"

- **Automated Review Summary**

  If a cervical cytology case is examined by an automated device, the report should specify the following:

  1. ***Device utilized***
  2. ***Type of review***
  3. ***Result of the automated review process***
  4. ***The individual(s) involved in the process and their role stipulated***

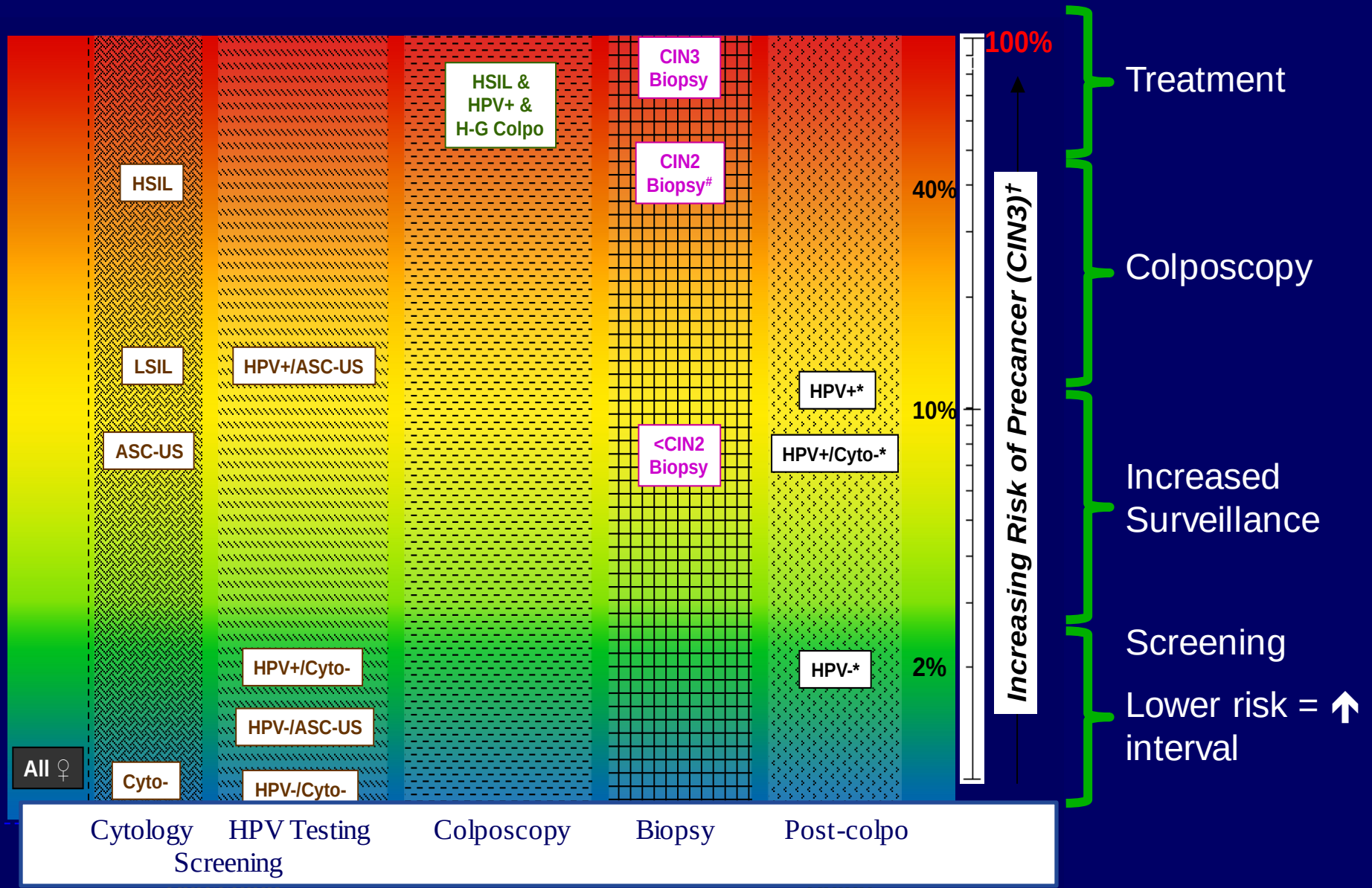
Chapter 11: EDUCATOINAL NOTES AND COMMENTS

- In keeping with TBS guiding principles, improving communication from the laboratory provider to the physician caring for the patient is important.
- The use of written recommendations and/or comments in cervical cytology reports is optional;
  - When used, they must be worded carefully and relay clear, concise, current, evidence-based information.
- 3rd edition
  - Discusses implications of new access rules for patients and electronic health record (EHR) mandates.

Chapter 12:
RISK ASSESSMENT IN CERVICAL CANCER

- Rapid evolution of cervical cancer screening options.
- Not a new concept in medicine.
- This new chapter is an important addition to the 3rd atlas- it is key to understanding how the results of various screening and triage test combinations relate to the patient's risk for cervical cancer.

Harmonizing Management According To Risk



Castle PE, Sideri M, Jeronimo J, et al.: Risk assessment to guide the prevention of cervical cancer. Am J Obstet Gynecol 197:356, 2007

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]

May 2015
Ca Cytopathol
JASC
JLGTD
Acta Cytol

Bethesda System

For Reporting Cervical Cytology 2014: Online Atlas

Bethesda System 2014 ASC Website

Please Click to advance

ASC
AMERICAN SOCIETY OF Cytopathology
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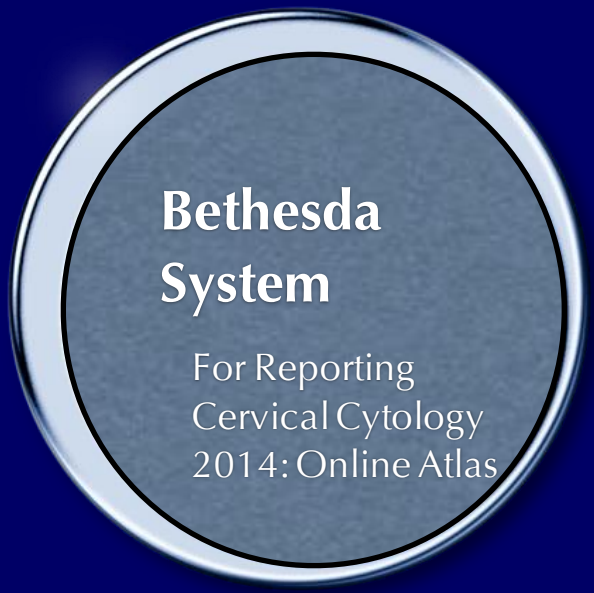
Web Project

- TBS should always be a work in progress
- Allows updates to be made in real time
- Allows for additional material to be presented
- New methods for educational dissemination
- Always adaptable to new presentation modes

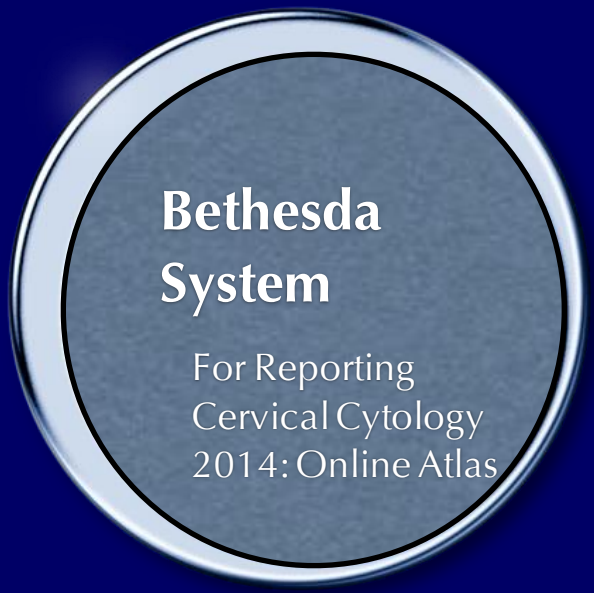
Bethesda Website Update



Cytopathology.org
Bethesda.soc.wisc.edu

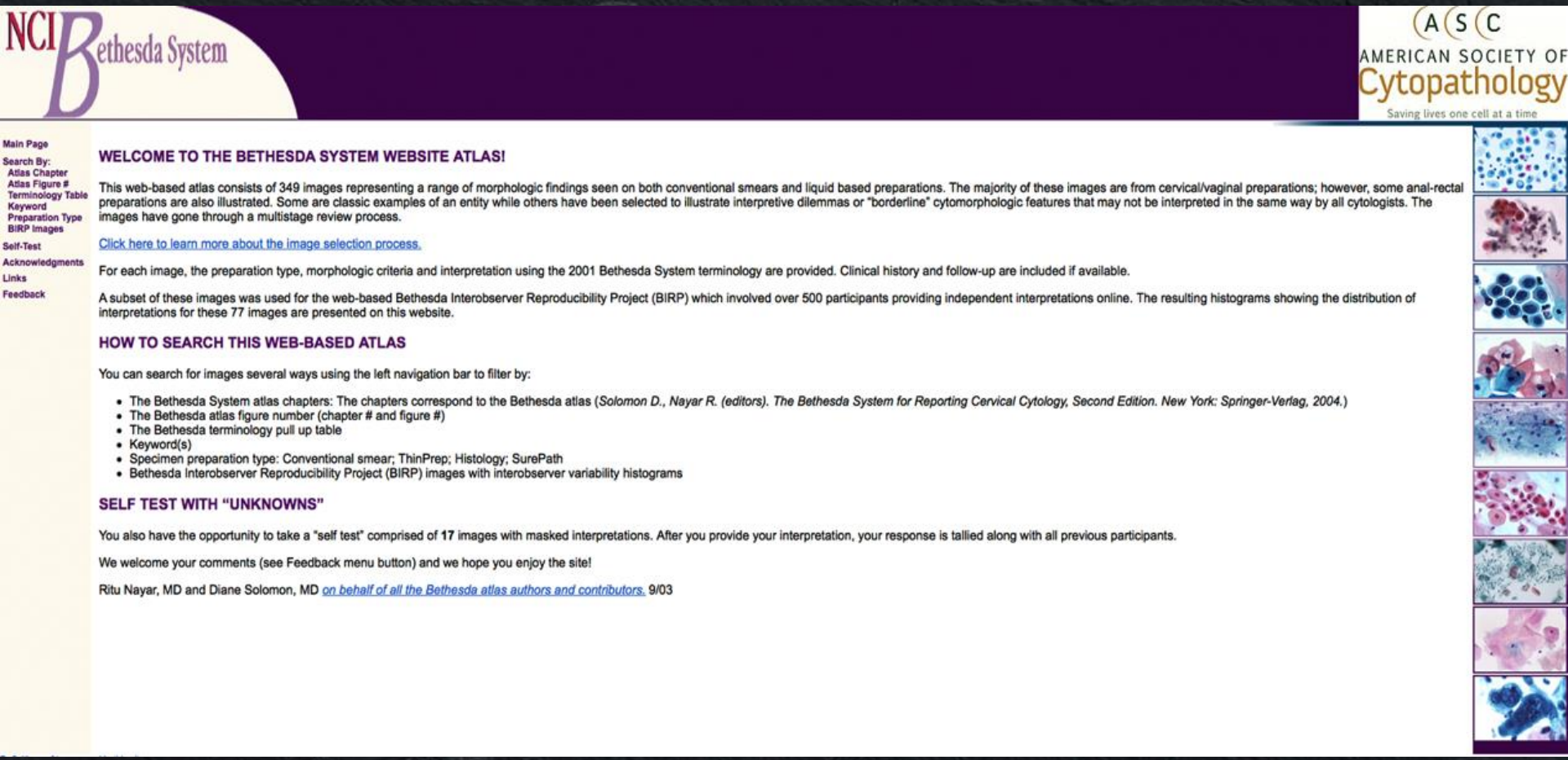
- This is the first update to the Bethesda Website in 13 years
- It incorporates the 370 new images from the new Atlas
  - Which includes material from the older editions, but 56% of the images are new
  - All images are digitally revised
- The Website is now live

Bethesda Website Update



Cytopathology.org
Bethesda.soc.wisc.edu

- The site has all the features of the previous Bethesda Website and builds on that success.
- Search Capabilities have been enhanced
- As well as displaying the current images, the site solicits images from the international cytopathology community



Original TBS Website Appearance

Bethesda System

for Reporting
Cervical Cytology
2014

Bethesda 2014 Online Atlas

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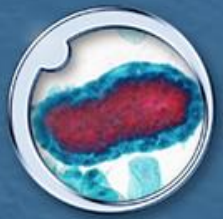
2014: Online Atlas

- Introduction
- Search
- Self Test
- Links
- Donate Image

I Adequacy

II Non-neoplastic

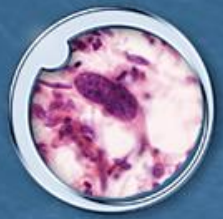


III Endometrial > 45

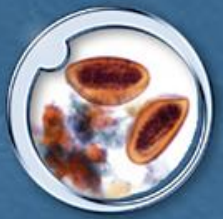
IV ASC-US/ASC-H

V Epithelial Abnormalities Squamous

VI Epithelial Abnormalities Glandular



VII Other Malignant Neoplasms



VIII Anal Cytology

IX Adjunctive Testing

AMERICAN SOCIETY OF CYTOPATHOLOGY |100 West 10th Street, Suite 605 | Wilmington, DE 19801
Phone: 302-543-6583 | Fax: 302-543-6597
Email: bjenkins@cytopathology.org
Web site: cytopathology.org

Page last updated: August 27, 2015

Bethesda System
for Reporting
Cervical Cytology
2014: Online Atlas

Introduction
Search
Self Test
Links
Donate Image

Welcome to the Bethesda System for Reporting Gynecologic Cytology Online Atlas!

The purpose of this atlas is to offer instructive images with explanatory text to illustrate the features of the Bethesda system for practitioners and trainees alike. Additionally, this site will provide an opportunity for real-time updates of terminology and criteria from previous print versions of the system. This website is a companion to the Bethesda System for Reporting Gynecologic Cytology 2014 print atlas. It includes all the images from the atlas, and more, but because of its nature as an online image atlas, it does not duplicate the text or detail of the print version.

Features:

- **Search:** Search for images by chapter, figure number, preparation type, or keyword.
- **BIRST Histograms:** Participant results are displayed for the 85 images included in the 2014 Bethesda Inter-observer Reproducibility Study (BIRST), in which over 800 participants rendered their diagnostic opinions on Atlas images. This popular feature of the prior website allows users to compare what they see in the image with the evaluations of their peers.
- **Self-test:** We invite you to participate in a self-test, which incorporates a subset of images from the atlas and additional donated images. This test will be periodically updated. The results of the self-test are only for the edification of users.
- **Online Image Donation:** We encourage you to donate images that you think are especially noteworthy. Our team will review the images and if they show features that are instructive, challenging, or are just excellent we will place them on the site alongside the images from the Atlas. Help make this atlas a truly shared resource.
- **Future growth:** We plan to continue to add images regularly, including whole slide imaging of instructional cases, and more. Visit regularly as the site continues to grow.

The site and the print atlas represents the work of a large number of people from private, public and academic facilities who are dedicated to serving our patients. We thank them and the staff of the American Society of Cytopathology for all their efforts.

Bethesda 2014 Website Committee:
Co-Chairs: Daniel F. I. Kurtycz, and Paul N. Staats
Members: Deborah Chute, Maria Friedlander, Sara Monoco, Donna Russell
Advisors: Ritu Nayar, David Wilbur

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2014: Online Atlas

Search By:

(•) Keyword ( ) Figure Number ( ) Preparation Type

Keyword

Enter keywords to search by:

koilocyte ×

☐ Show only interpretations that contain BIRST graphics

Image	Interpretation
	Fig. 2.28 Negative for intraepithelial lesion or malignancy (NILM). Pregnancy related changes.
	Fig. 2.36 Negative for intraepithelial lesion or malignancy (NILM). Reactive cellular changes.
	Fig. 5.4 Low-grade squamous intraepithelial lesion (LSIL).
	Fig. 5.5 Low-grade squamous intraepithelial lesion (LSIL).
	Fig. 5.6 Low-grade squamous intraepithelial lesion (LSIL).

1 – 5 of 5 items

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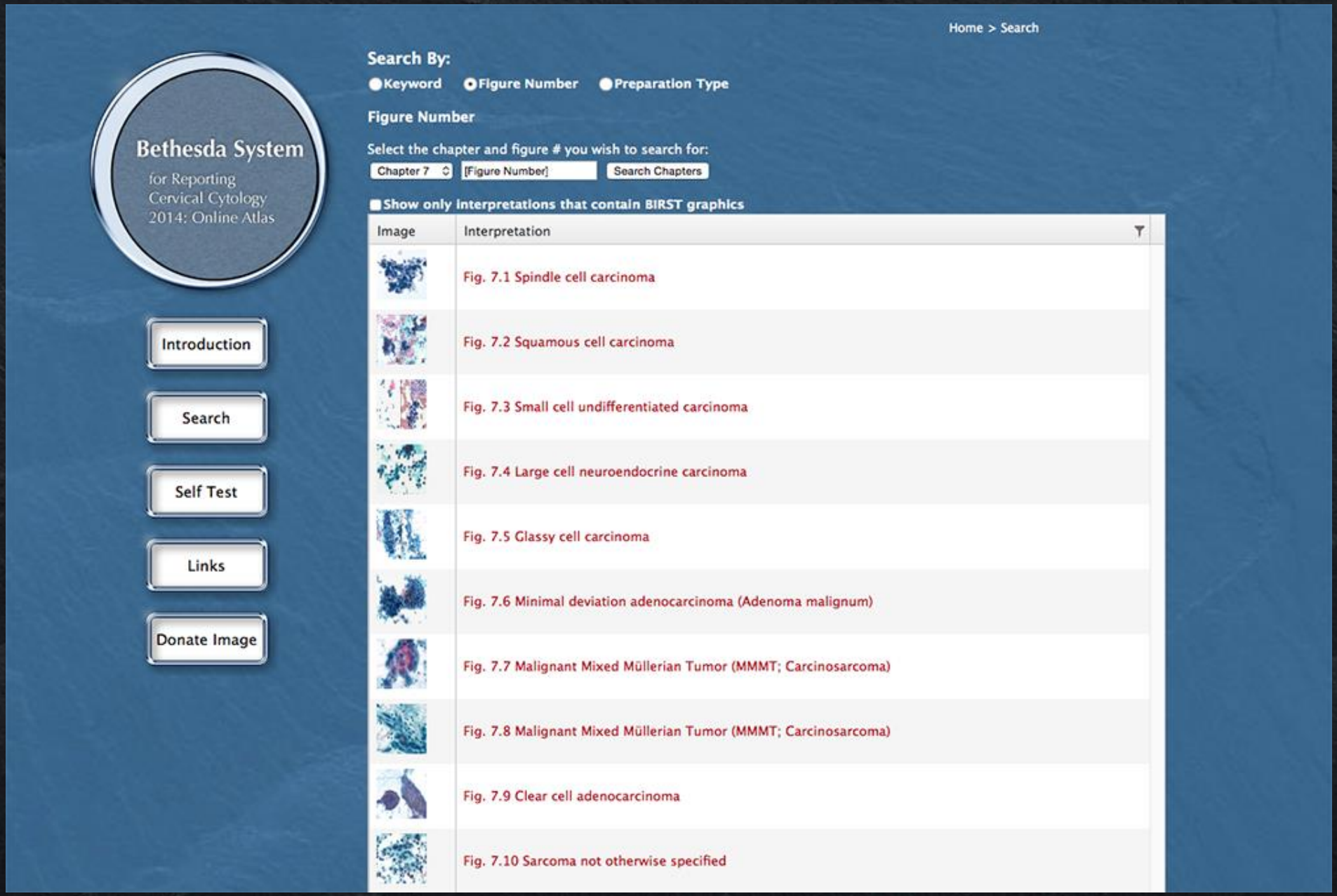


Clicking on figure number will also allow for search by Chapter

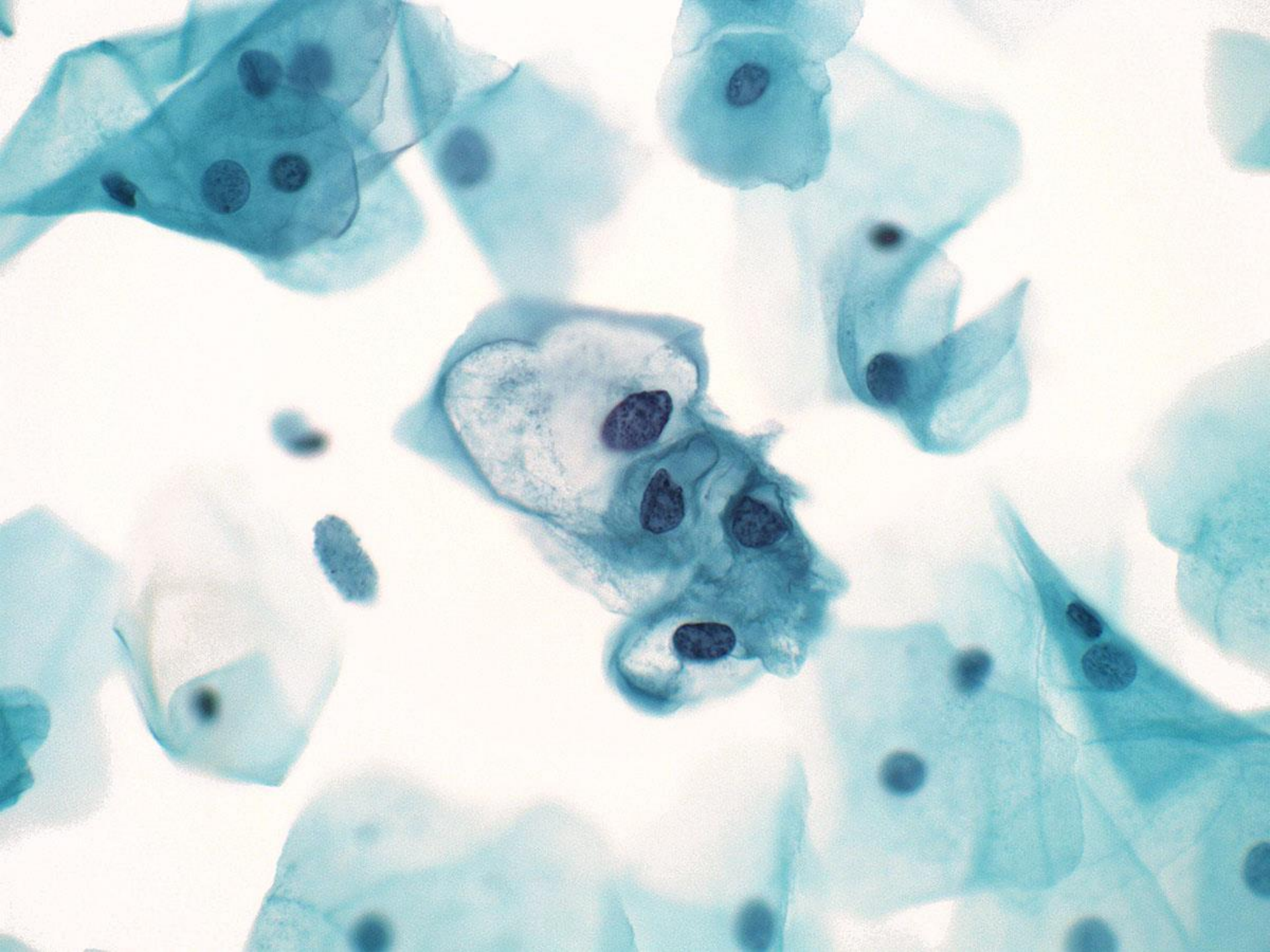
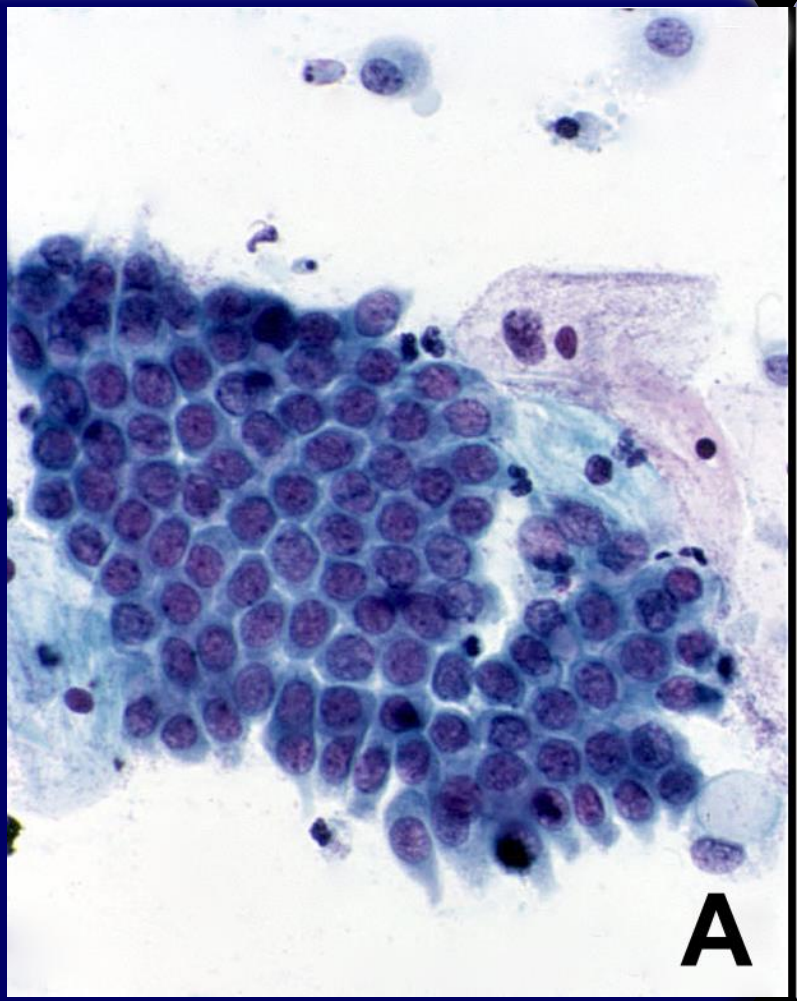
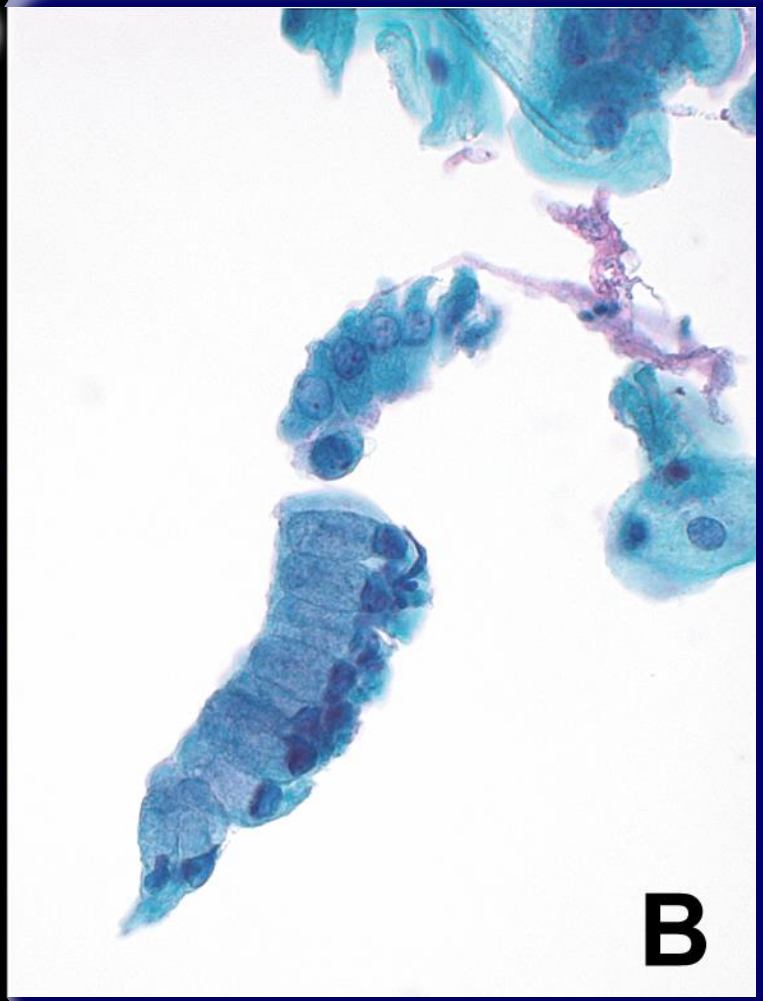


Image Display





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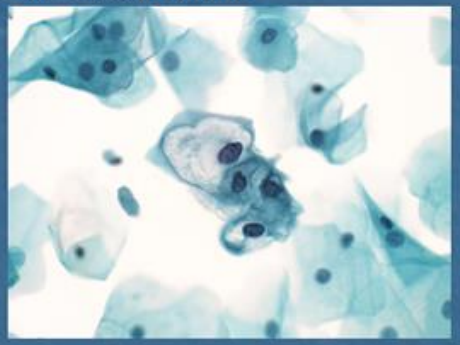

Type of Preparation:
Surepath

Magnification:
H

Interpretation:
Fig. 5.5 Low-grade squamous intraepithelial lesion (LSIL).

Cytomorphologic Criteria:
Perinuclear cavitation, nuclear enlargement, nuclear membrane irregularity

Explanatory Notes:
Sharply defined perinuclear cavity with abnormal nuclear features including nuclear enlargement and nuclear membrane irregularity are diagnostic features of LSIL.

BIRST Statistics (please Click to enlarge)

#	Answer	Bar
1	Negative for Intraepithelial Lesion or Malignancy (NILM)	
2	Endometrial cells shed by a woman aged 45 or older	
3	Atypical squamous cells of uncertain significance (ASC-US)	
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)	
5	Low-Grade squamous intraepithelial lesion (LSIL)	
6	High-Grade squamous intraepithelial lesion (HSIL)	
7	Squamous cell carcinoma (SCC)	
8	Atypical endocervical cells (AEC)	
9	Atypical endometrial cells (AEmC)	
10	Endocervical adenocarcinoma in situ (AIS)	
11	Adenocarcinoma (ADC)	
12	Other malignant neoplasm	
	Total	

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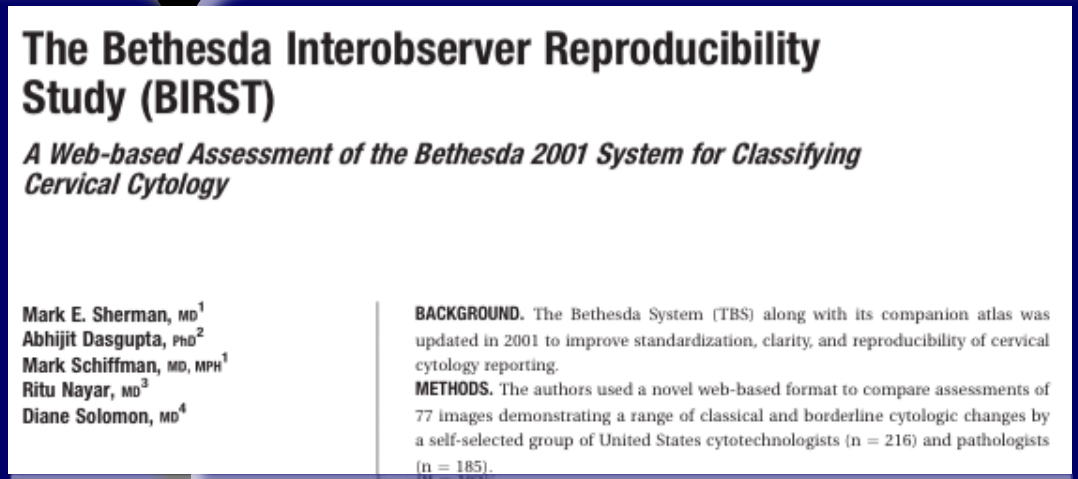
Bethesda Interobserver reproducibility Study (BIRST)

After the 2001 update to the Bethesda System a reproducibility study was performed, 401 pathologists and cytotechnologists participated.

In concert with the new revision of the system a new study was performed, BIRST-2 to evaluate reproducibility and to compare results with the earlier study.



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]

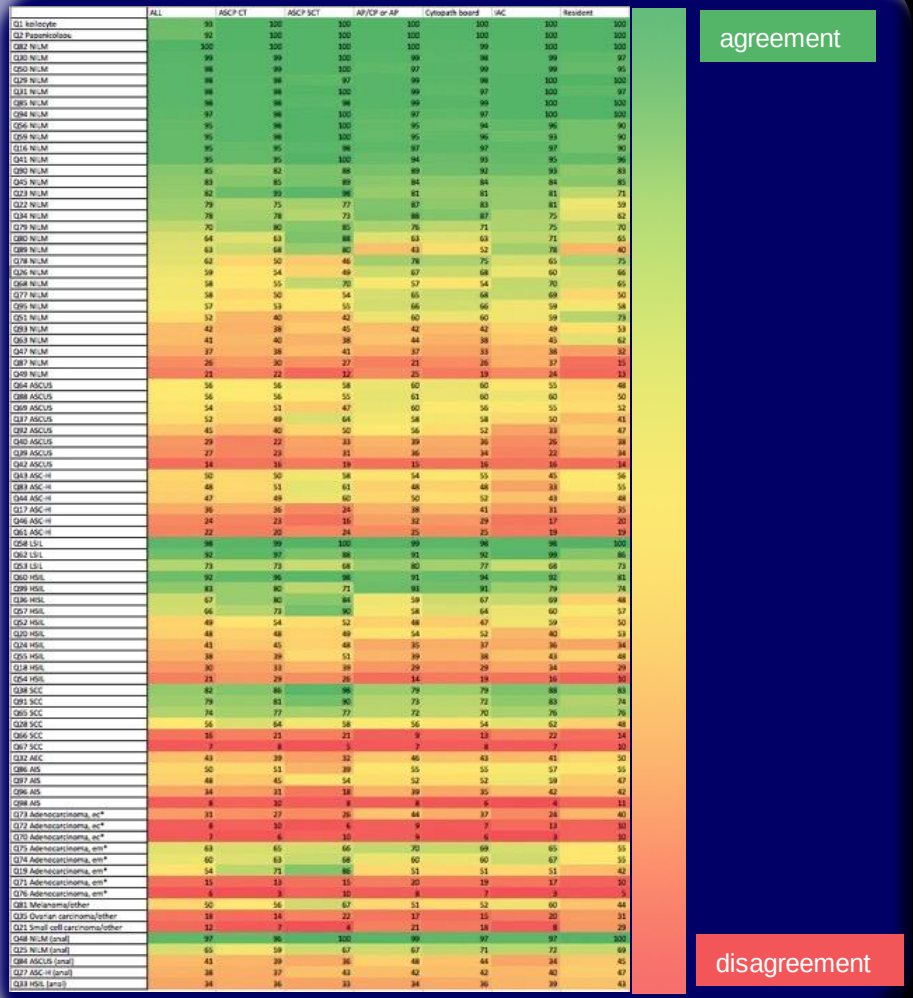
BACKGROUND. The Bethesda System (TBS) along with its companion atlas was updated in 2001 to improve standardization, clarity, and reproducibility of cervical cytology reporting.

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).

BIRST 2

833 individuals participated in the study, results were stratified by occupation, type of practice and region. A manuscript is being developed and image results are included in the website.

Initial Analysis of BIRST-2 Data



	ALL	ASCP CT	ASCP SCT	AP/CP or AP	Cytopath board	IAC	Resident
Q1 koilocyte	93	100	100	100	100	100	100
Q2 Papanicolaou	92	100	100	100	100	100	100
Q82 NILM	100	100	100	100	99	100	100
Q30 NILM	99	99	100	99	98	99	97
Q50 NILM	98	99	100	97	99	99	95
Q29 NILM	98	98	97	99	98	100	100
Q31 NILM	98	98	100	99	97	100	97
Q85 NILM	98	98	98	99	99	100	100
Q94 NILM	97	98	100	97	97	100	100
Q56 NILM	95	98	100	95	94	96	90
Q59 NILM	95	98	100	95	96	93	90
Q16 NILM	95	95	96	97	97	97	90
Q41 NILM	95	95	100	94	93	95	96
Q90 NILM	85	82	88	89	92	93	83
Q45 NILM	83	85	89	84	84	84	81
Q23 NILM	82	93	98	81	81	81	71
Q22 NILM	79	75	77	87	83	81	59
Q34 NILM	78	78	73	88	87	75	62
Q79 NILM	70	80	85	76	71	75	70
Q80 NILM	64	63	88	63	63	71	65
Q89 NILM	63	68	80	43	52	78	40
Q78 NILM	62	50	46	78	75	65	75
Q26 NILM	59	54	49	67	68	60	66
Q68 NILM	58	55	70	57	54	70	65
Q77 NILM	58	50	54	65	68	69	50
Q95 NILM	57	53	55	66	66	59	54
Q51 NILM	52	40	42	60	60	59	73
Q93 NILM	42	38	45	42	42	49	53
Q63 NILM	41	40	38	44	38	45	62
Q47 NILM	37	38	41	37	33	38	32
Q87 NILM	26	30	27	21	26	37	15
Q49 NILM	21	22	12	25	19	24	13
Q64 ASCUS	56	56	58	60	60	55	48
Q88 ASCUS	56	56	55	61	60	60	50
Q69 ASCUS	54	51	47	60	56	55	52
Q37 ASCUS	52	49	64	58	58	50	41
Q92 ASCUS	45	40	50	56	52	33	47
Q40 ASCUS	29	22	33	39	36	26	38
Q39 ASCUS	27	23	31	36	34	22	34
Q42 ASCUS	14	16	19	15	16	16	14
Q43 ASC-H	50	50	58	54	55	45	56
Q83 ASC-H	48	51	61	48	48	33	55
Q44 ASC-H	47	49	60	50	52	43	48
Q17 ASC-H	36	36	24	38	41	31	35
Q46 ASC-H	24	23	16	32	29	17	22
Q61 ASC-H	22	20	24	25	25	19	19
Q58 LSIL	98	99	100	99	98	98	100
Q62 LSIL	92	97	88	91	92	99	86
Q53 LSIL	73	73	68	80	77	68	73
Q60 HSIL	92	96	98	91	94	92	83
Q99 HSIL	83	80	71	93	91	79	74
Q36 HSIL	67	80	84	59	67	69	48
Q57 HSIL	66	73	90	58	64	60	57
Q52 HSIL	49	54	52	48	47	59	50
Q20 HSIL	48	48	49	54	52	40	53
Q24 HSIL	41	45	48	35	37	36	34
Q55 HSIL	38	39	51	39	38	43	48
Q18 HSIL	30	33	39	29	29	34	29
Q54 HSIL	21	29	26	14	19	16	33
Q38 SCC	82	86	96	79	79	88	83
Q91 SCC	79	81	90	73	72	83	74
Q65 SCC	74	77	77	72	70	76	76
Q28 SCC	56	64	58	56	54	62	48
Q66 SCC	16	21	21	9	13	22	14
Q67 SCC	7	8	5	7	8	7	10
Q32 AEC	43	39	32	46	43	41	50
Q86 AIS	50	51	39	55	55	57	55
Q97 AIS	48	45	54	52	52	59	47
Q96 AIS	34	31	18	39	35	42	42
Q98 AIS	8	10	8	8	6	6	13
Q73 Adenocarcinoma, ec*	31	27	26	44	37	26	40
Q72 Adenocarcinoma, ec*	8	10	6	9	7	13	10
Q70 Adenocarcinoma, ec*	7	6	10	9	6	3	10
Q75 Adenocarcinoma, em*	63	65	66	70	69	65	55
Q74 Adenocarcinoma, em*	60	63	66	60	60	67	53
Q19 Adenocarcinoma, em*	54	71	86	51	51	51	42
Q71 Adenocarcinoma, em*	15	13	15	20	19	17	10
Q76 Adenocarcinoma, em*	6	3	10	8	7	3	3
Q81 Melanoma/other	50	56	67	51	52	60	44
Q35 Ovarian carcinoma/other	18	14	22	17	15	20	31
Q21 Small cell carcinoma/other	12	7	4	21	18	8	29
Q48 NILM (anal)	97	96	100	99	97	97	100
Q25 NILM (anal)	65	59	67	67	71	72	69
Q84 ASCUS (anal)	41	39	36	48	44	34	45
Q27 ASC-H (anal)	38	37	43	42	42	40	47
Q33 HSIL (anal)	34	36	33	34	36	39	43

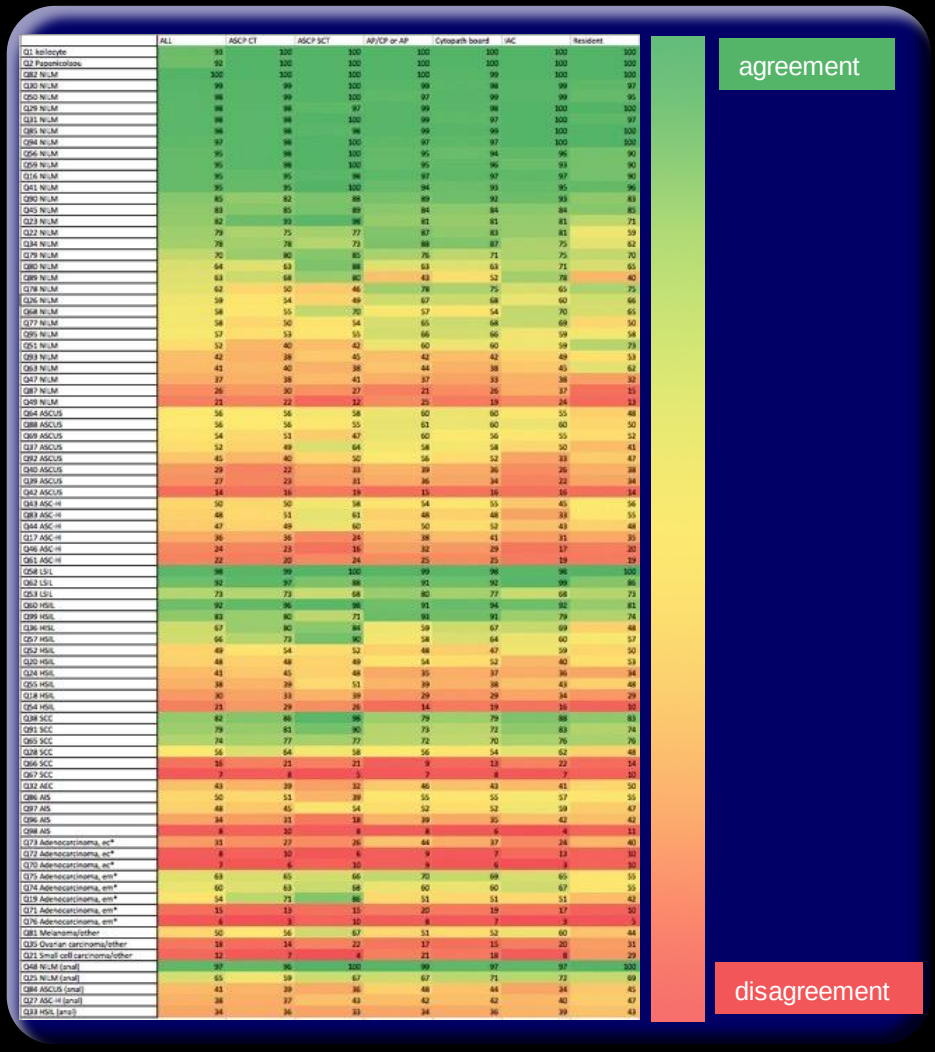
agreement

disagreement

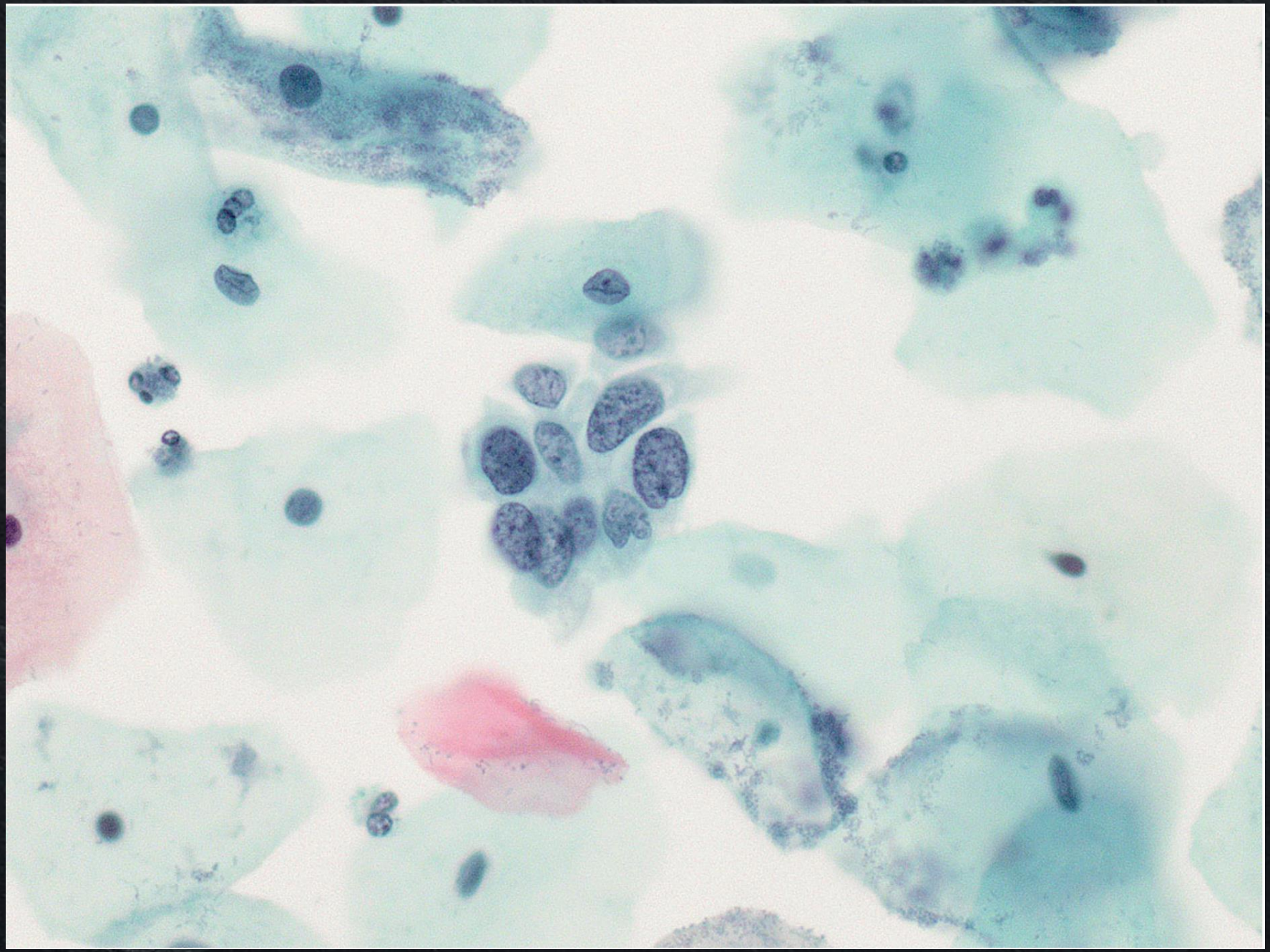
- There was consistent diagnostic agreement across certifications (CT, SCT, AP Pathologists, Cytopath Certified, IAC)
- Best agreement was found for NILM and LSIL category followed by squamous cell carcinoma.
- Agreement for ASC-US, ASC-H, Adenocarcinoma and Anal Cytology was more problematic

Thanks to D. Chute, Cleveland Clinic

Initial Analysis of BIRST-2 Data



- 41% of participants were from outside of the US (338/833).
- 64% were cytotechnologists, 37% were pathologists and 6% Other (including researchers, gynecologists and people working in commercial non -testing situations)
- 39% identified themselves as working in an academic environment, 29% private hospital, 16% commercial and 4% government (US and non-US) 72% run hrHPV testing and 80% perform it in house
- More to information to follow….



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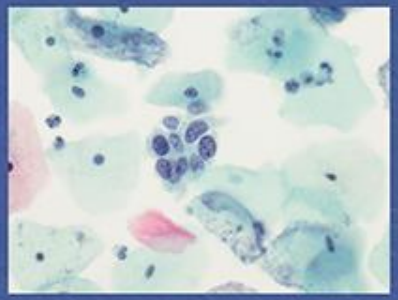

Type of Preparation:
Surepath

Magnification:
High

Interpretation:
Fig. 4.24 Atypical squamous cells, cannot exclude a High Grade Squamous Intraepithelial Lesion (ASC-

Cytomorphologic Criteria:
This cluster of small atypical cells have enlarged (2-3x) nuclei and more coarsely granular chromatin when compared to the nuclei of adjacent normal intermediate cells.

Explanatory Notes:
Cellular changes are suggestive of HSIL but lack additional criteria for definitive diagnosis.

Follow-up:
HSIL (CIN 3) on biopsy

BIRST Statistics (please Click to enlarge)

#	Answer	Bar
1	Negative for Intraepithelial Lesion or Malignancy (NILM)	
2	Endometrial cells shed by a woman aged 45 or older	
3	Atypical squamous cells of uncertain significance (ASC-US)	
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)	
5	Low-Grade squamous intraepithelial lesion (LSIL)	
6	High-Grade squamous intraepithelial lesion (HSIL)	
7	Squamous cell carcinoma (SCC)	
8	Atypical endocervical cells (AEC)	
9	Atypical endometrial cells (AEmC)	
10	Endocervical adenocarcinoma in situ (AIS)	
11	Adenocarcinoma (ADC)	
12	Other malignant neoplasm	
	Total	

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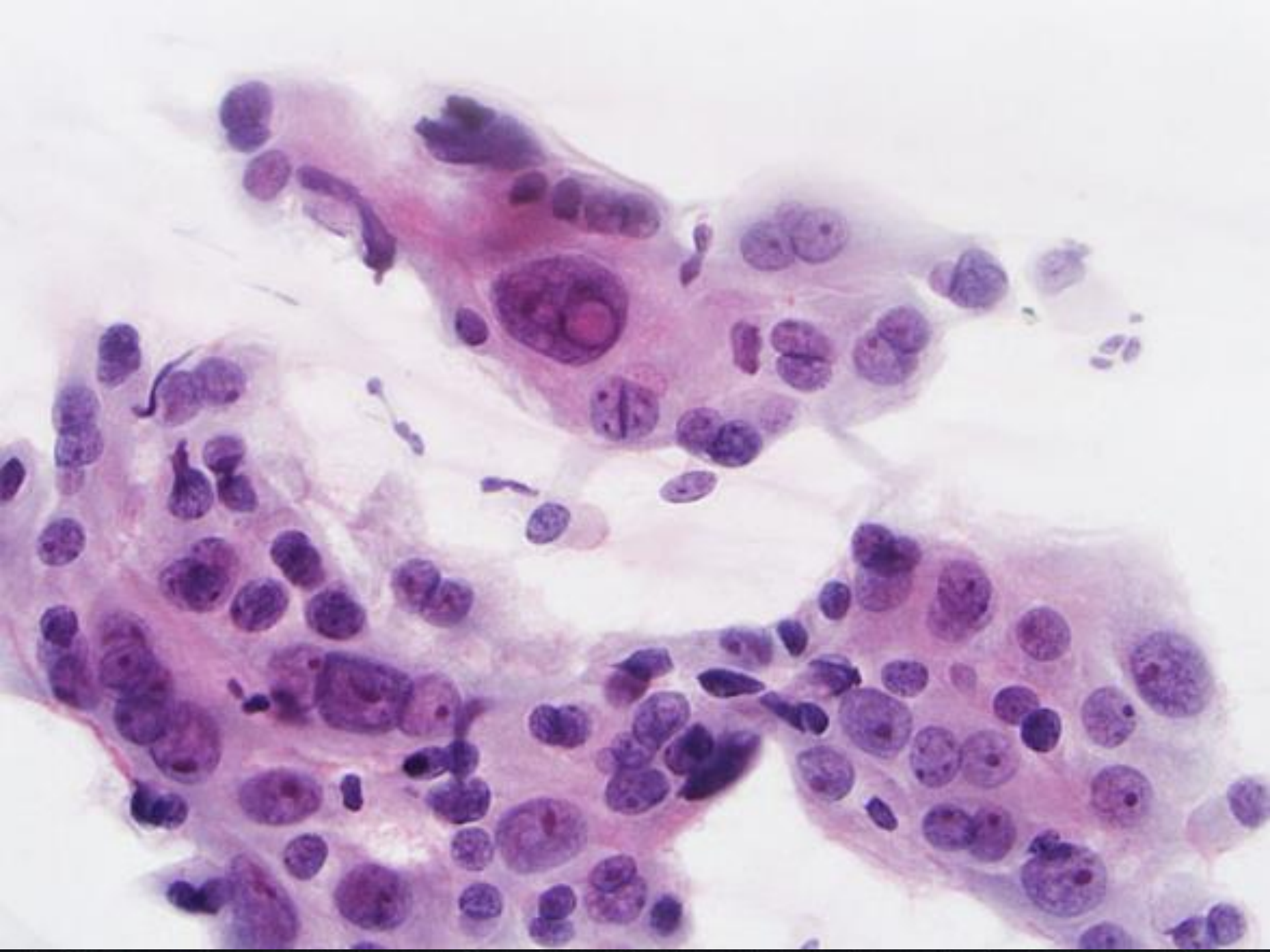
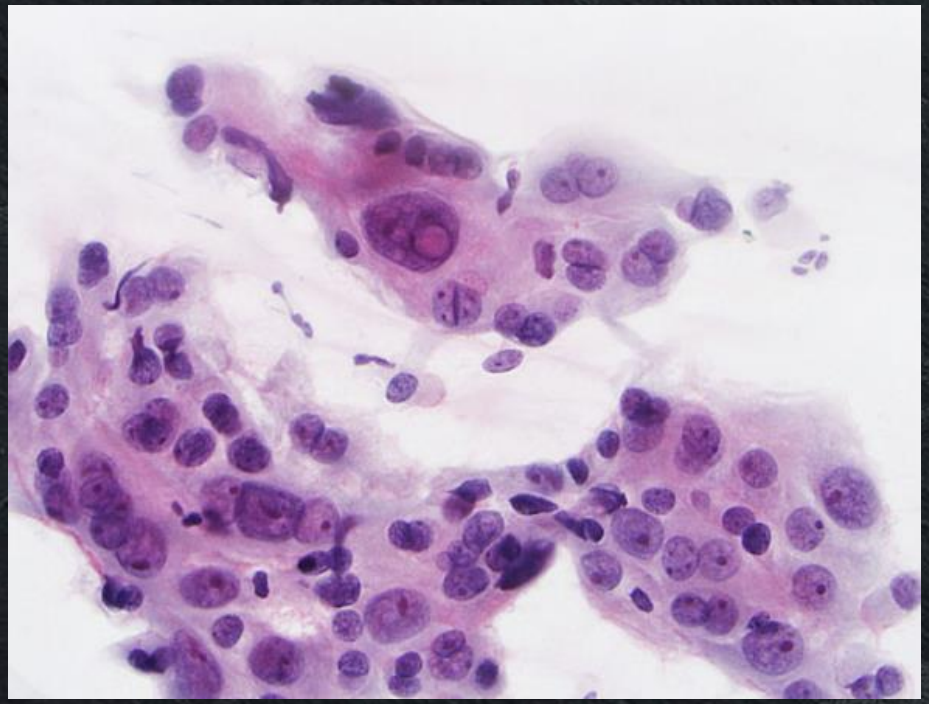
#	Answer	Bar	Response	%
1	Negative for Intraepithelial Lesion or Malignancy (NILM)		56	7%
2	Endometrial cells shed by a woman aged 45 or older		21	3%
3	Atypical squamous cells of uncertain significance (ASC-US)		65	8%
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)		279	36%
5	Low-Grade squamous intraepithelial lesion (LSIL)		13	2%
6	High-Grade squamous intraepithelial lesion (HSIL)		293	38%
7	Squamous cell carcinoma (SCC)		0	0%
8	Atypical endocervical cells (AEC)		38	5%
9	Atypical endometrial cells (AEmC)		8	1%
10	Endocervical adenocarcinoma in situ (AIS)		0	0%
11	Adenocarcinoma (ADC)		0	0%
12	Other malignant neoplasm		0	0%
	Total		773	





Bethesda Interobserver Reproducibility Data

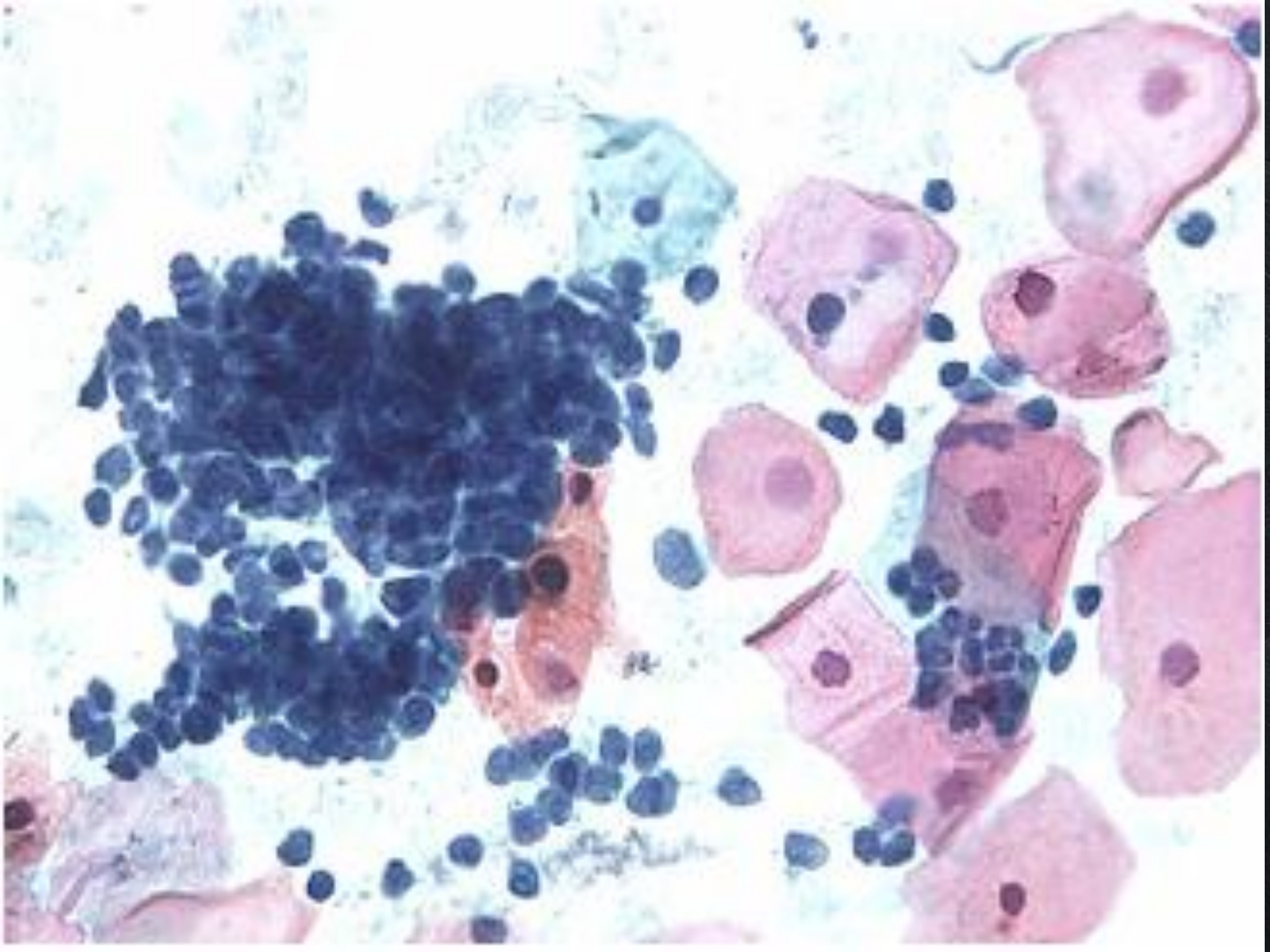
Type of Preparation:
Conventional

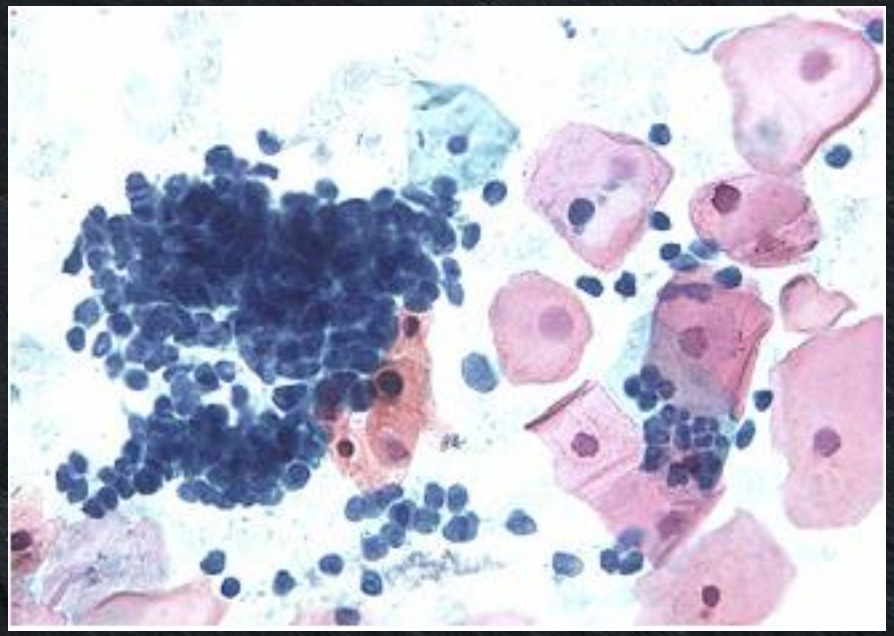
Magnification:
High

Cervical Sample: 36 year old, routine Pap test, repair

Case 27

#	Answer	Bar	Response	%
1	Negative for Intraepithelial Lesion or Malignancy (NILM)		149	25%
2	Endometrial cells shed by a woman aged 45 or older		0	0%
3	Atypical squamous cells of uncertain significance (ASC-US)		86	14%
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)		22	4%
5	Low-Grade squamous intraepithelial lesion (LSIL)		12	2%
6	High-Grade squamous intraepithelial lesion (HSIL)		48	8%
7	Squamous cell carcinoma (SCC)		51	8%
8	Atypical endocervical cells (AEC)		82	14%
9	Atypical endometrial cells (AEmC)		1	0%
10	Endocervical adenocarcinoma in situ (AIS)		12	2%
11	Adenocarcinoma (ADC)		95	16%
12	Other malignant neoplasm		45	7%
	Total		603	

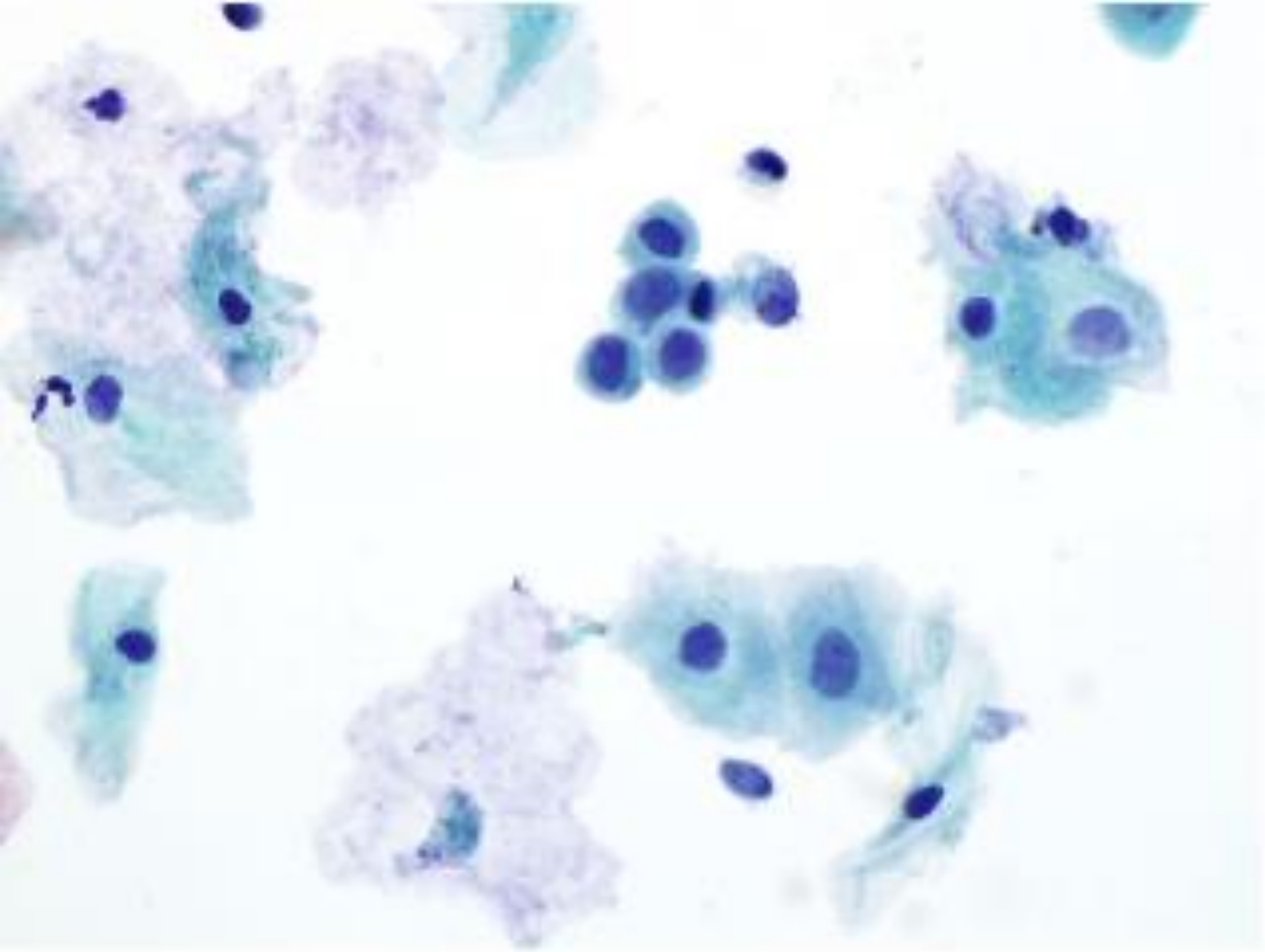


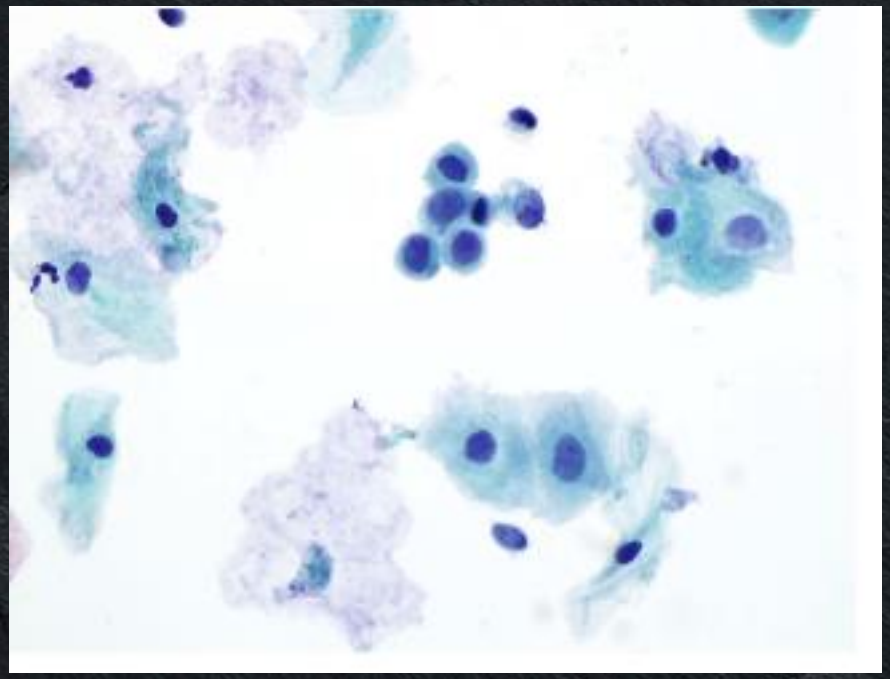


6. Cervical sample, 50 year-old with vaginal bleeding, conventional prep

Fig. 7.-3 (A and B) Small cell undifferentiated carcinoma

#	Answer	Bar	Response	%
1	Negative for Intraepithelial Lesion or Malignancy (NILM)		19	3%
2	Endometrial cells shed by a woman aged 45 or older		224	40%
3	Atypical squamous cells of uncertain significance (ASC-US)		6	1%
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)		10	2%
5	Low-Grade squamous intraepithelial lesion (LSIL)		5	1%
6	High-Grade squamous intraepithelial lesion (HSIL)		52	9%
7	Squamous cell carcinoma (SCC)		19	3%
8	Atypical endocervical cells (AEC)		15	3%
9	Atypical endometrial cells (AEmC)		102	18%
10	Endocervical adenocarcinoma in situ (AIS)		13	2%
11	Adenocarcinoma (ADC)		33	6%
12	Other malignant neoplasm		68	12%
	Total		566	

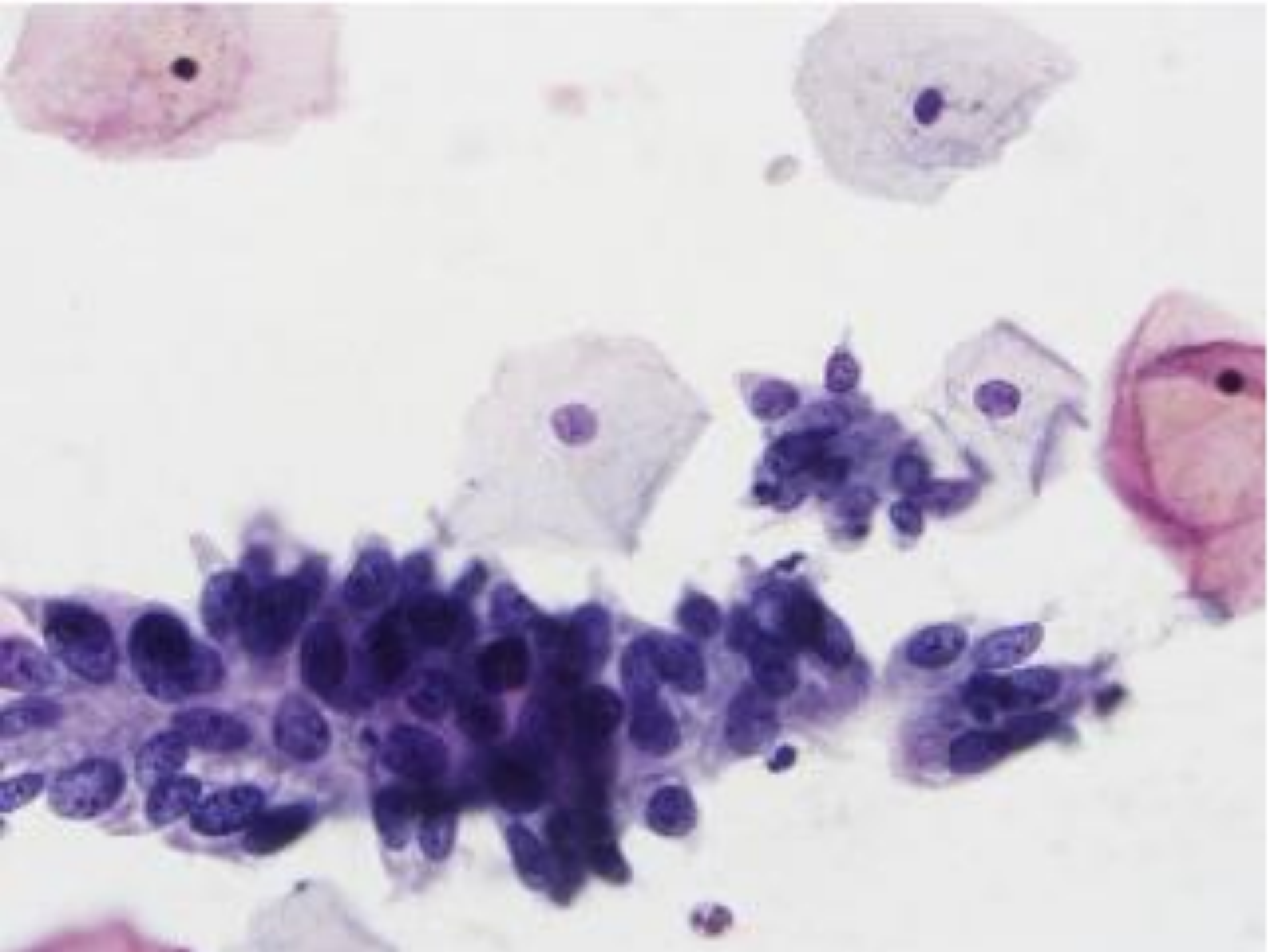


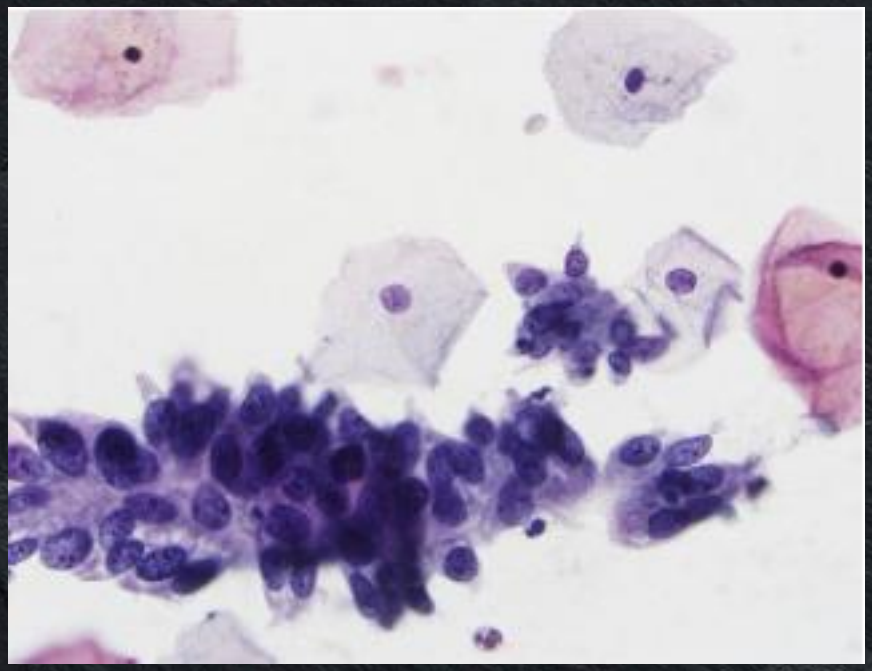


12. Anal sample, 38 year-old female, history of HPV infection, ThinPrep/LBP

Figure 8-12
ASC-H. (*liquid-based preparation, ThinPrep*).

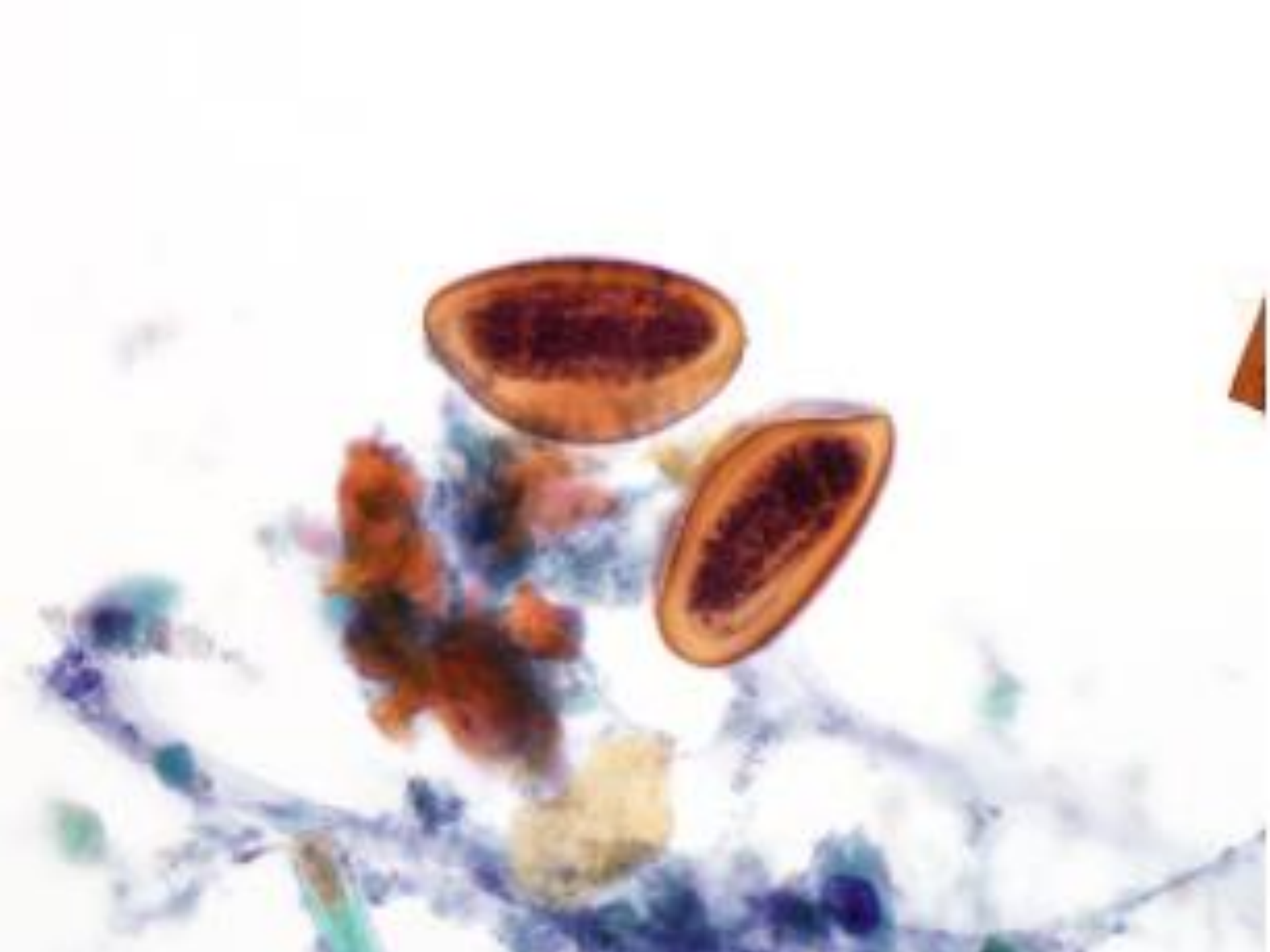
#	Answer	Bar	Response	%
1	Negative for Intraepithelial Lesion or Malignancy (NILM)		30	5%
2	Endometrial cells shed by a woman aged 45 or older		0	0%
3	Atypical squamous cells of uncertain significance (ASC-US)		38	7%
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)		225	40%
5	Low-Grade squamous intraepithelial lesion (LSIL)		17	3%
6	High-Grade squamous intraepithelial lesion (HSIL)		252	45%
7	Squamous cell carcinoma (SCC)		1	0%
8	Atypical endocervical cells (AEC)		0	0%
9	Atypical endometrial cells (AEmC)		0	0%
10	Endocervical adenocarcinoma in situ (AIS)		0	0%
11	Adenocarcinoma (ADC)		1	0%
12	Other malignant neoplasm		0	0%
	Total		564	





82. Cervical sample, 25 year old, routine screening, conventional
AIS

#	Answer	Bar	Response	%
1	Negative for Intraepithelial Lesion or Malignancy (NILM)		63	12%
2	Endometrial cells shed by a woman aged 45 or older		0	0%
3	Atypical squamous cells of uncertain significance (ASC-US)		1	0%
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)		2	0%
5	Low-Grade squamous intraepithelial lesion (LSIL)		1	0%
6	High-Grade squamous intraepithelial lesion (HSIL)		8	2%
7	Squamous cell carcinoma (SCC)		0	0%
8	Atypical endocervical cells (AEC)		190	37%
9	Atypical endometrial cells (AEmC)		2	0%
10	Endocervical adenocarcinoma in situ (AIS)		248	48%
11	Adenocarcinoma (ADC)		5	1%
12	Other malignant neoplasm		0	0%
	Total		520	

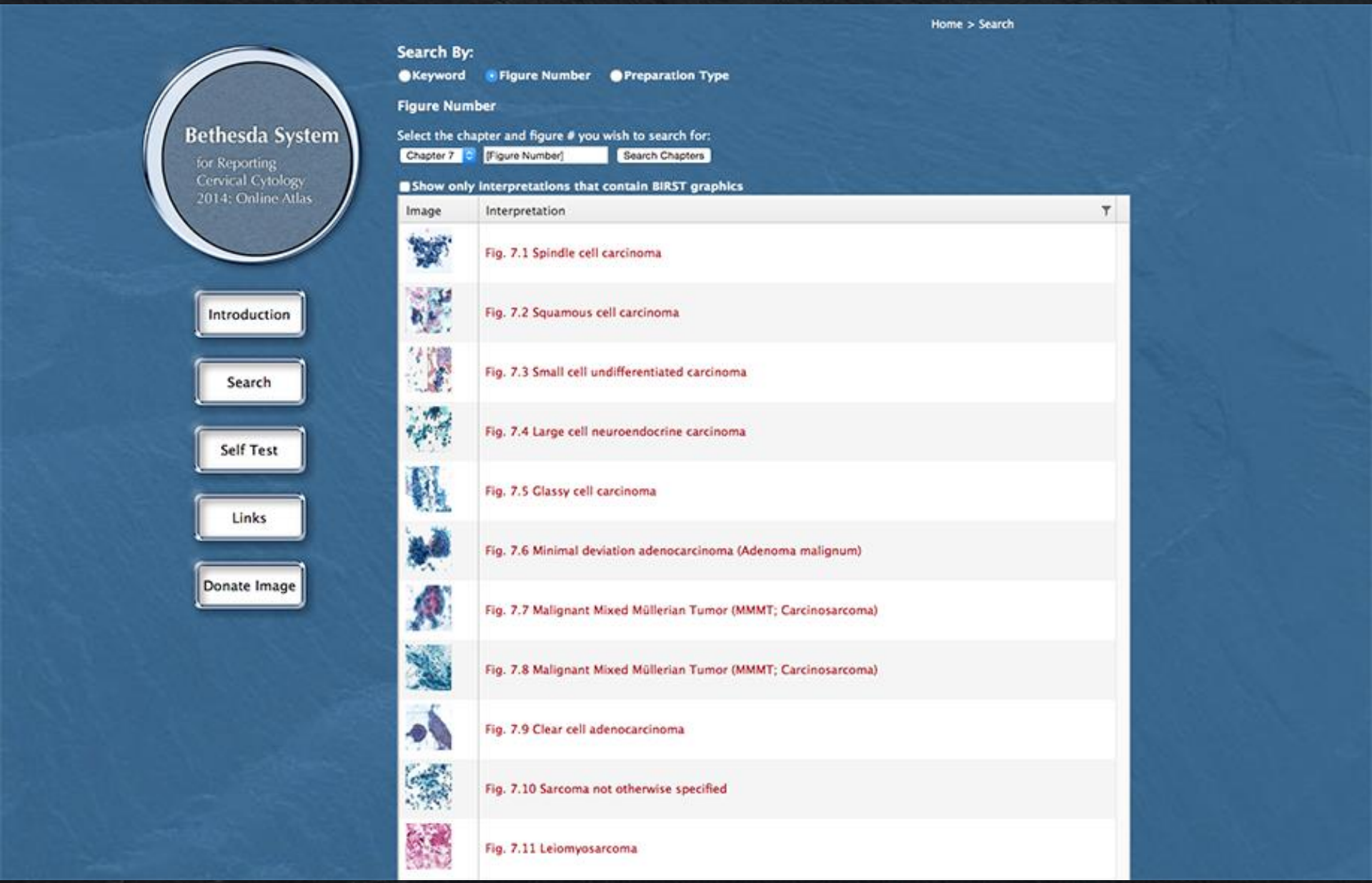


33. Anal sample, 41 year-old female, anorectal itching, Thin Prep/LBP

Figure 8.10
Pinworm eggs (*liquid-based preparation, ThinPrep*).

#	Answer	Bar	Response	%
1	Negative for Intraepithelial Lesion or Malignancy (NILM)		578	97%
2	Endometrial cells shed by a woman aged 45 or older		0	0%
3	Atypical squamous cells of uncertain significance (ASC-US)		6	1%
4	Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)		6	1%
5	Low-Grade squamous intraepithelial lesion (LSIL)		1	0%
6	High-Grade squamous intraepithelial lesion (HSIL)		0	0%
7	Squamous cell carcinoma (SCC)		5	1%
8	Atypical endocervical cells (AEC)		0	0%
9	Atypical endometrial cells (AEmC)		0	0%
10	Endocervical adenocarcinoma in situ (AIS)		0	0%
11	Adenocarcinoma (ADC)		0	0%
12	Other malignant neoplasm		1	0%
	Total		597	

6	High-Grade squamous intraepithelial lesion (HSIL)		0	0%
7	Squamous cell carcinoma (SCC)		5	1%
8	Atypical endocervical cells (AEC)		0	0%
9	Atypical endometrial cells (AEmC)		0	0%
10	Endocervical adenocarcinoma in situ (AIS)		0	0%
11	Adenocarcinoma (ADC)		0	0%
12	Other malignant neoplasm		1	0%
	Total		548	



A checkbox will restrict image display to those with BIRST stats.

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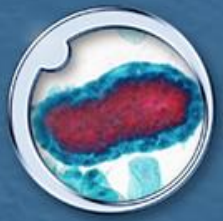
I Adequacy

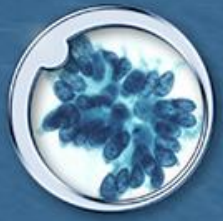
II Non-neoplastic



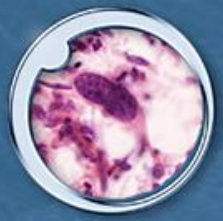
III Endometrial > 45

IV ASC-US/ASC-H

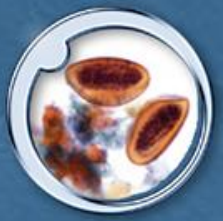
V Epithelial Abnormalities Squamous



VI Epithelial Abnormalities Glandular



VII Other Malignant Neoplasms



VIII Anal Cytology

IX Adjunctive Testing

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Web site: cytopathology.org

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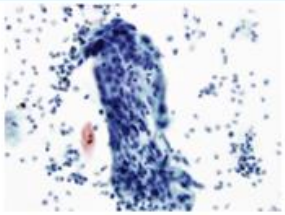
Image 1 of 21

Self-Test Image:



(Click on image to zoom in)

Type of Preparation:
Surepath

Clinical History:
32 year old woman, screening pap test

Select Your Interpretation:

- ○ Negative for intraepithelial lesion or malignancy (NILM)
- ○ Endometrial cells shed by a woman aged 45 or older
- ○ Atypical squamous cells of uncertain significance (ASC-US)
- ○ Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)
- ○ Low-grade squamous intraepithelial lesion (LSIL)
- ○ High-grade squamous intraepithelial lesion (HSIL)
- ○ Squamous cell carcinoma (SCC)
- ○ Atypical endocervical cells (AEC)
- ○ Atypical endometrial cells (AEmC)
- ○ Endocervical adenocarcinoma in situ (AIS)
- ○ Adenocarcinoma (ADC)
- ○ Other malignant neoplasm

Submit | End Test

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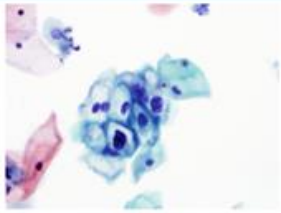
Image 2 of 21

Self-Test Image:



(Click on image to zoom in)

Type of Preparation:
ThinPrep

Clinical History:
27 year old woman, screening pap test

Interpretation:
Low-grade squamous intraepithelial lesion (LSIL)

Explanatory Notes:
Note the large (greater than 3 times) and hyperchromatic nuclei with coarse chromatin and nuclear membrane irregularities, in cells with a preserved low nuclear to cytoplasmic ratio. Koilocytic cytoplasmic halos are also present. These features should be interpreted as low grade squamous intraepithelial lesion (LSIL).

Participant Interpretation:

Low-grade squamous intraepithelial lesion (LSIL)	2	100.00 %
Negative for intraepithelial lesion or malignancy (NILM)	0	0.00 %
Endometrial cells shed by a woman aged 45 or older	0	0.00 %
Atypical squamous cells of uncertain significance (ASC-US)	0	0.00 %
Atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H)	0	0.00 %
High-grade squamous intraepithelial lesion (HSIL)	0	0.00 %
Squamous cell carcinoma (SCC)	0	0.00 %
Atypical endocervical cells (AEC)	0	0.00 %
Atypical endometrial cells (AEmC)	0	0.00 %
Endocervical adenocarcinoma in situ (AIS)	0	0.00 %
Adenocarcinoma (ADC)	0	0.00 %
Other malignant neoplasm	0	0.00 %

2 interpretations were submitted.

Next Image End Test

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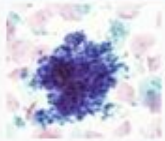
Self Test Results

Results: 17 of 21 Correct (81.0 %)

	Your Answer
 Negative for intraepithelial lesion or malignancy (NILM)	Correct
 Low-grade squamous intraepithelial lesion (LSIL)	Correct
 Other malignant neoplasm	Correct
 High-grade squamous intraepithelial lesion (HSIL)	Correct
 Endometrial cells shed by a woman aged 45 or older	Correct
 High-grade squamous intraepithelial lesion (HSIL)	Incorrect
 Negative for intraepithelial lesion or malignancy (NILM)	Correct
 Atypical squamous cells of uncertain significance (ASC-US)	Correct

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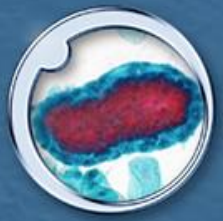
I Adequacy

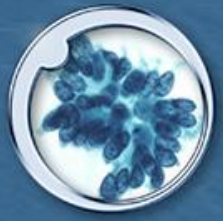
II Non-neoplastic



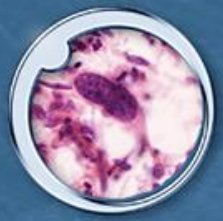
III Endometrial > 45

IV ASC-US/ASC-H

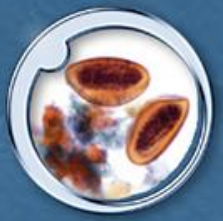
V Epithelial Abnormalities Squamous



VI Epithelial Abnormalities Glandular



VII Other Malignant Neoplasms



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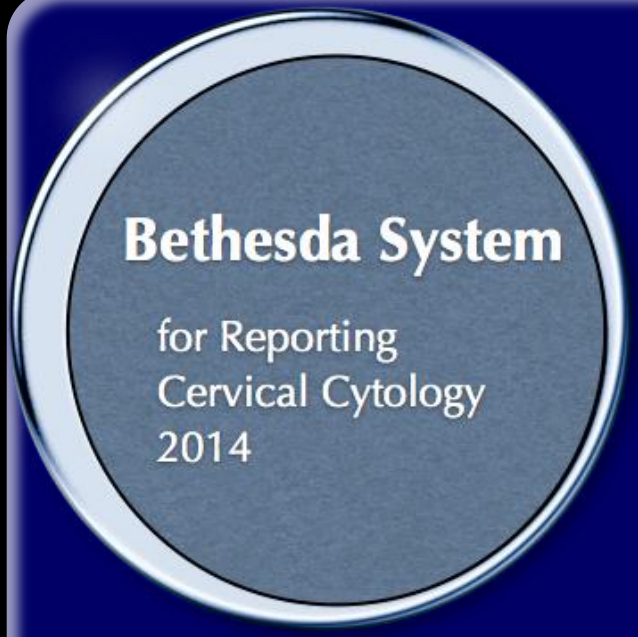
Links to Additional Resources



- ASC: American Society of Cytopathology
- ASCCP: American Society for Clinical Colposcopy and Cervical Pathology
- ASCP: American Society for Clinical Pathology
- ASCT: American Society for Cytotechnology
- CAP: College of American Pathologist Cytopathology Committee
- IAC: International Academy of Cytopathology
- NCI: National Cancer Institute
- PSC: The Papanicolaou Society
- Bethesda Website Atlas 2001
- Springer Publishing: The Bethesda System of Cytopathology

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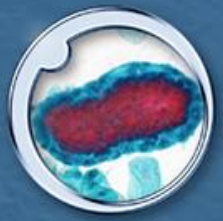

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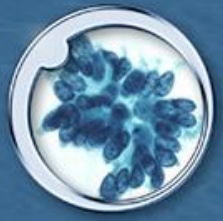

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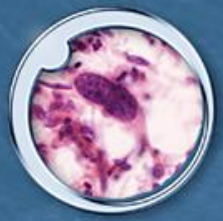

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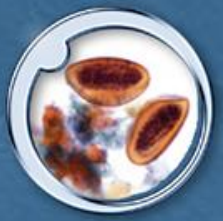

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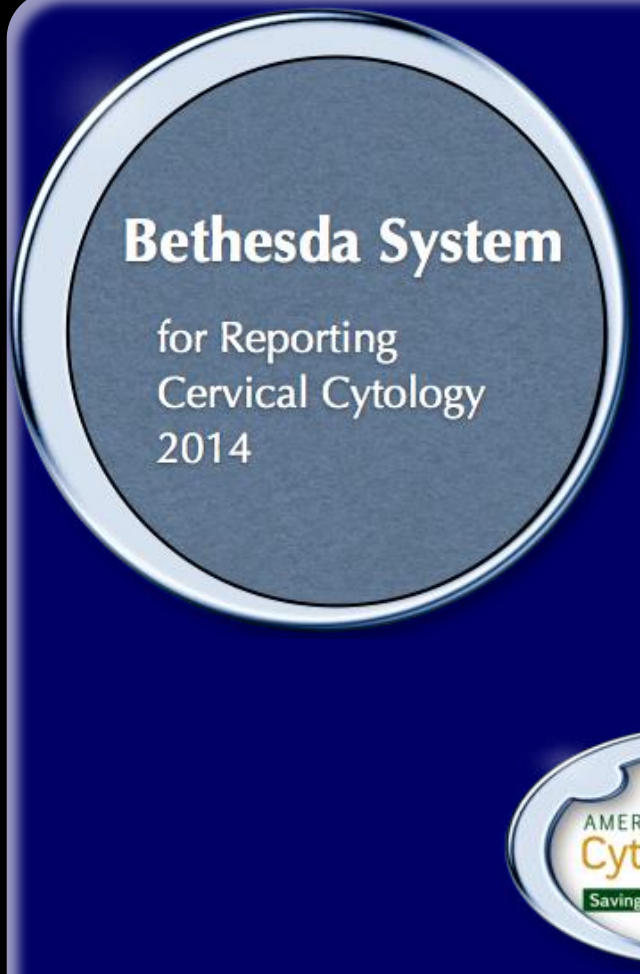


- Preparation type
- Magnification
- Patient Age
- Clinical History
  Interpretation
- Cytomorphologic Criteria
- Explanatory Notes
- Keywords

Tablet Use

- The software used to generate the website works with tablets

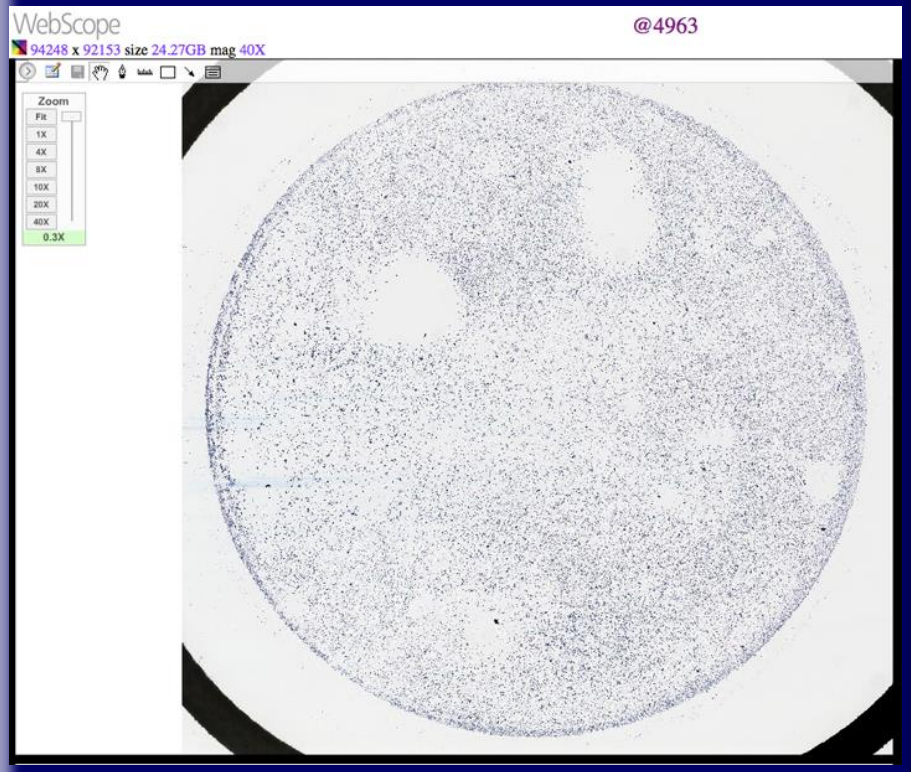
Smart Phone

The website can be displayed on smart phones.

So we provide a service that allows you to visit at any time with any reasonable device.

Invasive Technology

Virtual Microscopy Addition



- We have generated a set of virtual slides covering the major Bethesda diagnostic entities and will place them on the web site sometime in the next year.

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- We will be looking for your feedback in order to make useful tools for the cytology community.