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# The Paris System for Reporting Urinary Cytology

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*Second Edition*

 Springer

# TPS: the global experience

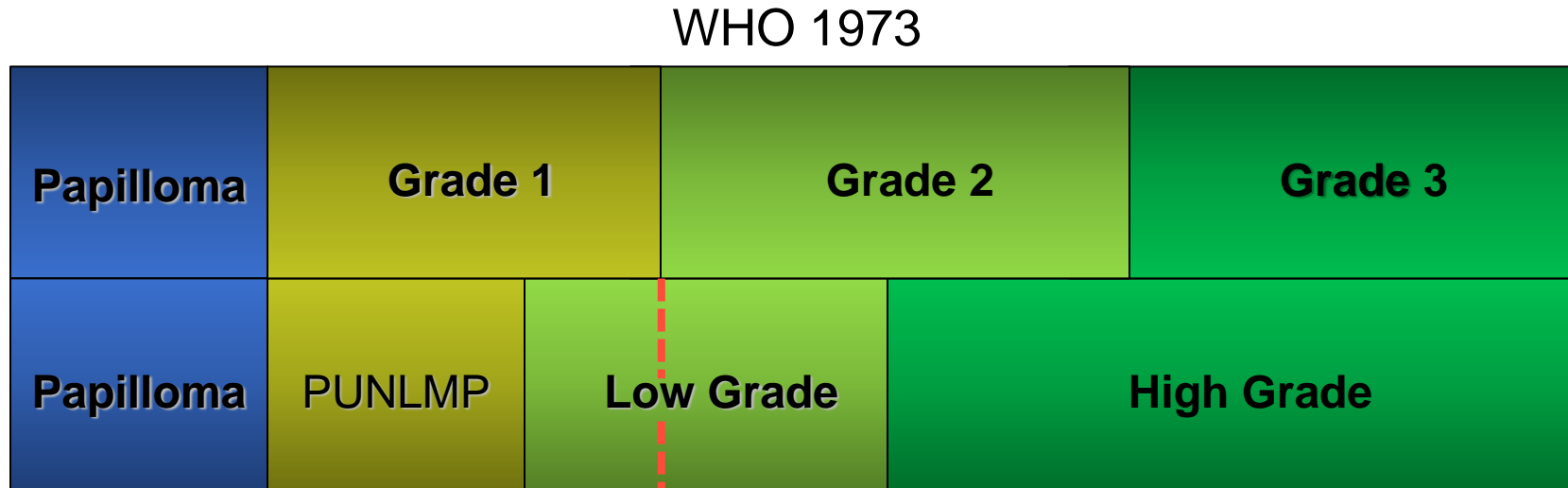
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GUY'S & ST. THOMAS' NHS  
LONDON, UK

# History of urinary cytology performance in detecting urothelial carcinoma



WHO/ISUP 2022

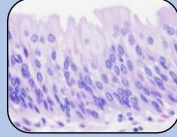
~ 10-20%

~50-60%

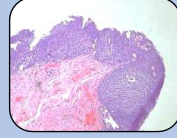
~ 80-90%

Sensitivity

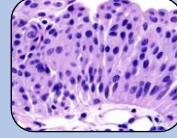
**Normal Urothelium**



**Precursors**

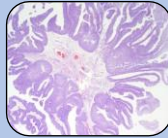


**Hyperplasi**

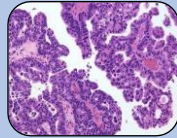


**Dysplasia**

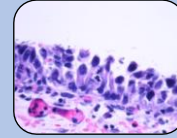
**Urothelial Carcinoma, Non-Invasive**



**Low Grade Carcinoma, Papillary**  
*FGFR, RAS*

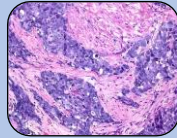


**High Grade Carcinoma, Papillary**  
*FGFR, TP53*



**Carcinoma in situ**  
*TP53, RB*

**Urothelial Carcinoma, Muscle Invasive**



*RTK/RAS/PI3K* Pathway (72%)  
*FGFR3* alterations  
*ERBB2* enrichment

Histone Modification Pathway (89%)

*SWI/SNF* Complex Alterations Pathway (64%)

*TP53/RB* Pathway (93%)

# TPS 1.0

- The Paris System for Reporting Urinary Cytology (TPS) was first published in 2016 with clear objectives to standardize cytological diagnostic criteria and provide uniform reporting, in order to improve patient stratification and associated clinical management.



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Volume 10, Issue 1, January–February 2021, Pages 79-87



## Experience on the use of The Paris System for Reporting Urinary Cytopathology: review of the published literature

Ricardo G. Pastorello MD <sup>a, b, 1</sup>, Güliz A. Barkan MD <sup>c, d, 1</sup>, Mauro Saieg MD, PhD <sup>e, f, 1</sup>  

# Following adoption of TPS -

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- Sensitivity ranged from 40% to 84.7%
  - Specificity from 73% to 100%
  - PPV from 62.3% to 100%
  - NPV from 46% to 90%
- 
- The application of TPS in the selected series has improved the screening and surveillance potential of urine cytology, while reducing high rates of indeterminate diagnoses, improving sensitivity and providing proper risk stratification for patients.

# Results of user survey Dec 2020

- A total of 523 participant responses from 55 countries was collected and 451 passed initial screening
- 82% (218/266) of responding participants use TPS
- 168 of people who responded regarding their urinary cytology atypia rates reported an average decrease from 21.6% to 16%
- Of those who use TPS (218) a majority responded that the same criteria should be used for voided and instrumented samples (72%, 158/218) as well as upper and lower urinary tract specimens (78%, 169/218)
- There were varied opinions on addressing atypical squamous cells and suggestions for new features to be included in Paris 2.0



# What's new in TPS 2.0 (2022)

- The key changes in the second edition are in the form of more detailed discussion and the addition of numerous new images, sample reports and up-to-date references
- There are new chapters on the upper urinary tract and on Risk of high grade malignancy (ROHM) as a better indicator of clinical outcome than Risk of Malignancy (ROM)

# Diagnostic categories in TPS 2.0

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*The focus remains on high grade urothelial carcinoma!*

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1. Non-diagnostic or unsatisfactory

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2. Negative for high grade urothelial carcinoma

Low grade urothelial neoplasia included here in TPS2.0

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3. Atypical urothelial cells

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4. Suspicious for high grade urothelial carcinoma

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5. Low grade urothelial neoplasia

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5. High grade urothelial carcinoma

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6. Other primary and metastatic malignancies & miscellaneous lesions

## LGUN included under NHGUC

- One of the notable changes is the incorporation of Low Grade Urothelial Neoplasia (LGUN) within the Negative for HGUC (NHGUC) category
- This strengthens the message that the focus of urinary cytopathology is on HGUC while LGUN remains a mainly cystoscopic finding, only occasionally detected on cytology due to their bland appearance and the rare finding of fibrovascular cores
- Specimens where these features are seen should be reported as NHGUC with a comment stating that LGUN is possible and should be confirmed by cystoscopy and biopsy.

# Fibrovascular cores in HGUC

- There is also a clarification offered that fibrovascular cores may also be seen in HGUC and that its established diagnostic criteria should be sought within these cores as well as in other groups and dispersed urothelial cells
- The spectrum of N/C ratios, the observation of hypochromasia, degenerative changes and HGUC sub-types are also covered in this edition

# More highlights of TPS2.0

- There is a streamlined discussion of atypical vs. benign-appearing urothelial tissue fragments, further characterization of degenerative changes in benign specimens and updated performance data for the NHGUC category.
- Illustrations of different preparations such as cytopspin, ThinPrep and SurePath images have been significantly increased.
- Cytopreparatory methods including the role of cell blocks in selected cases have also been addressed.

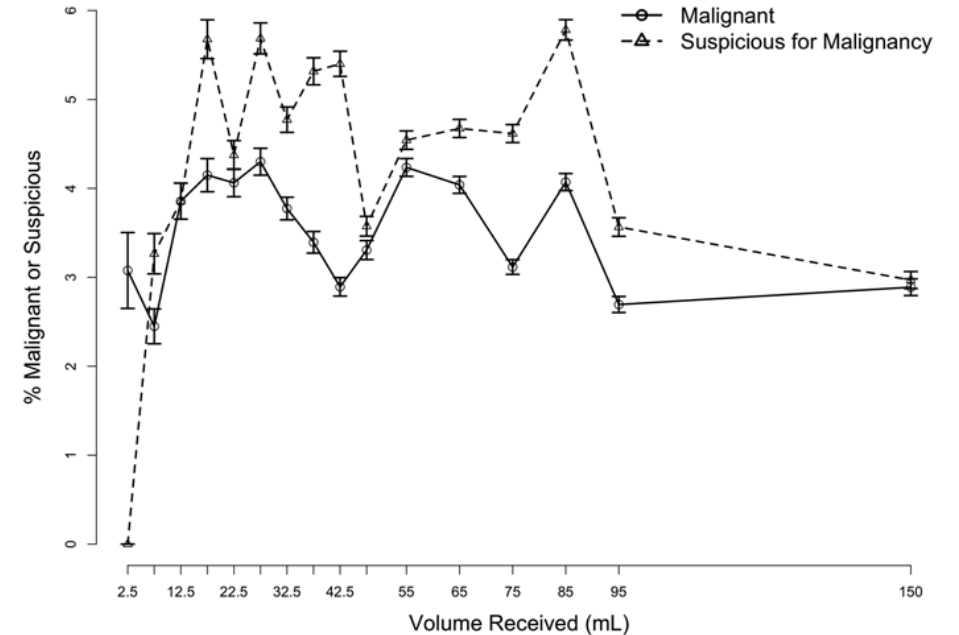
# Adequacy

The adequacy of urine specimens for the diagnosis of urothelial carcinoma is determined by the interplay of four specimen characteristics:

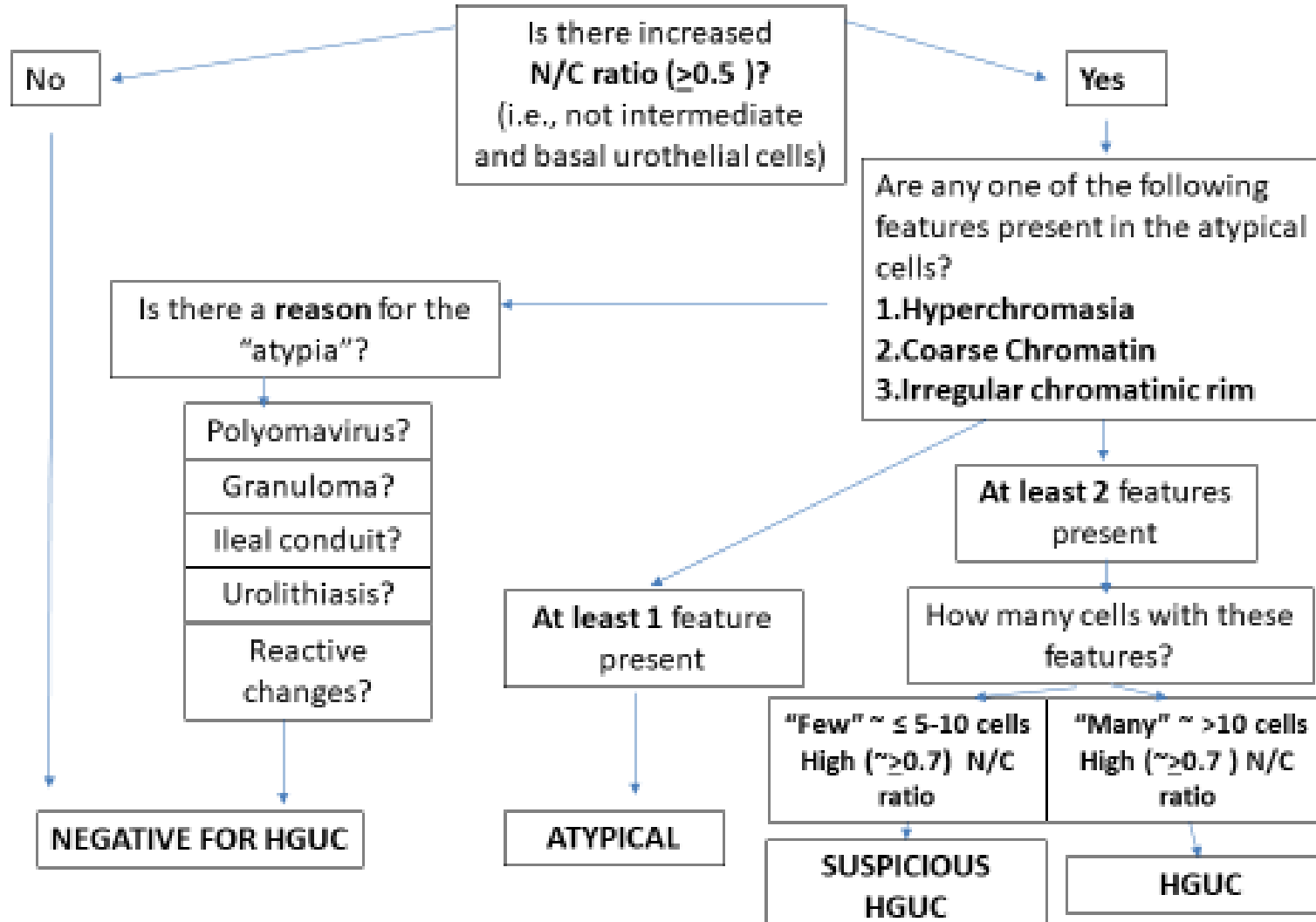
- Collection type- voided, catheterized, cystoscopy, upper tract
- Cellularity
- Volume
- Cytomorphological findings

# Adequacy: cellularity and volume

- Volume: 30ml for SurePath; 25ml for ThinPrep
- Cellularity: urothelial cells present in variable numbers in voided urine
- 20 urothelial cells/10hpf in bladder washings on ThinPrep (10-20 suboptimal; <10 non-diagnostic)



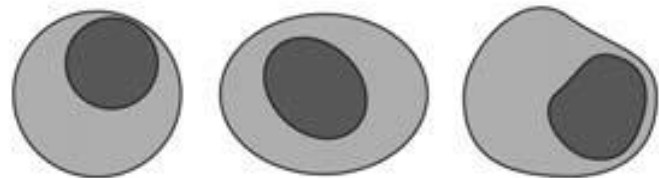
## The Paris System Approach to Diagnosis in Urinary Cytology



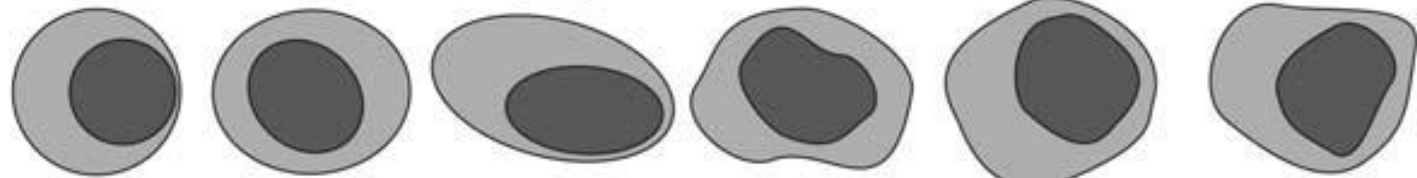


N:C

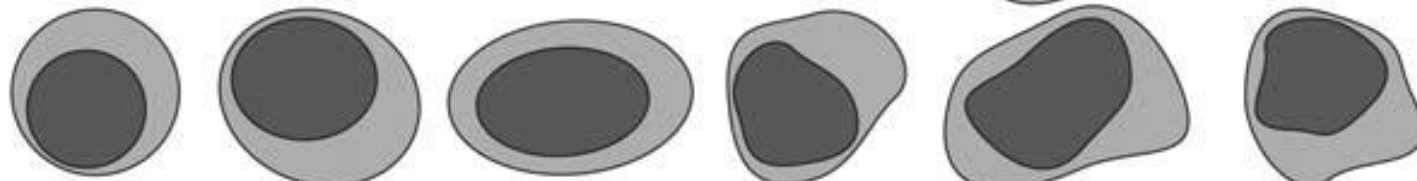
0.3



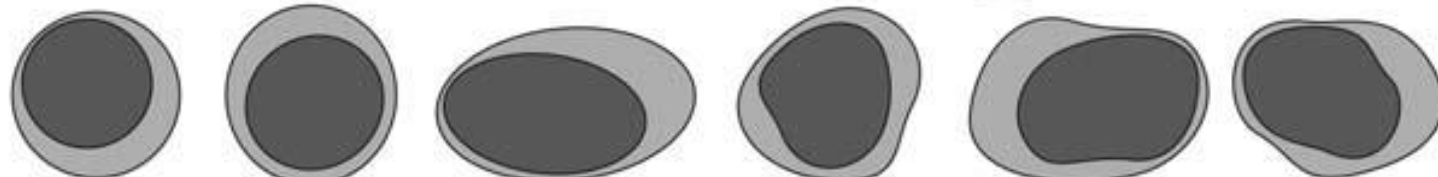
0.4



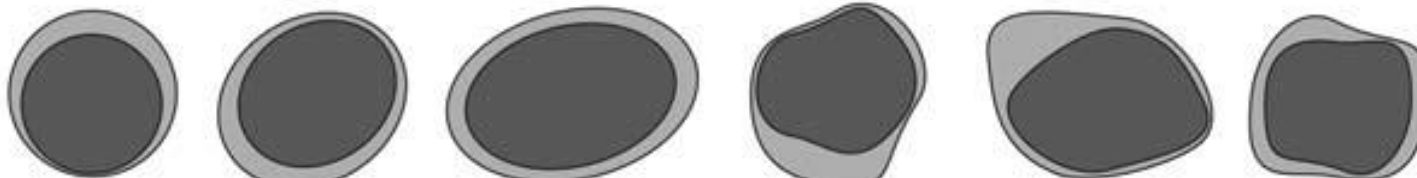
0.5



0.6



0.7

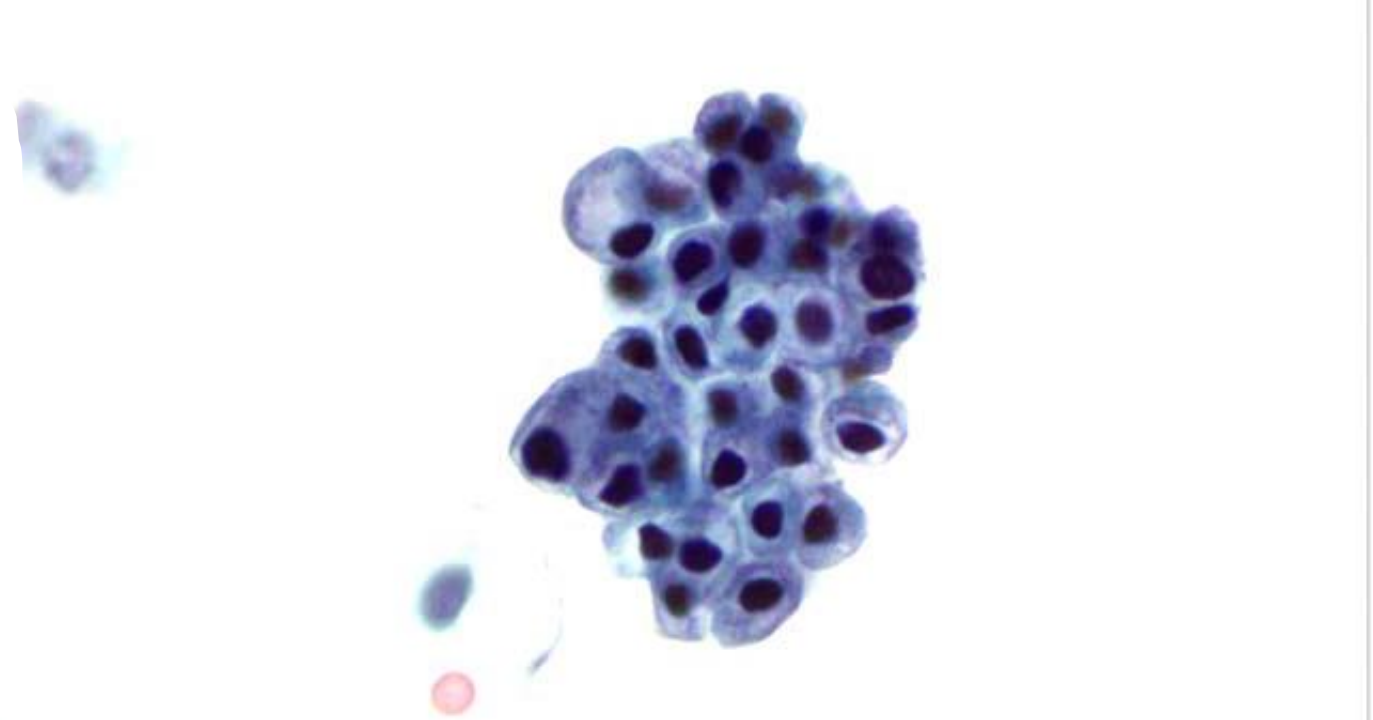
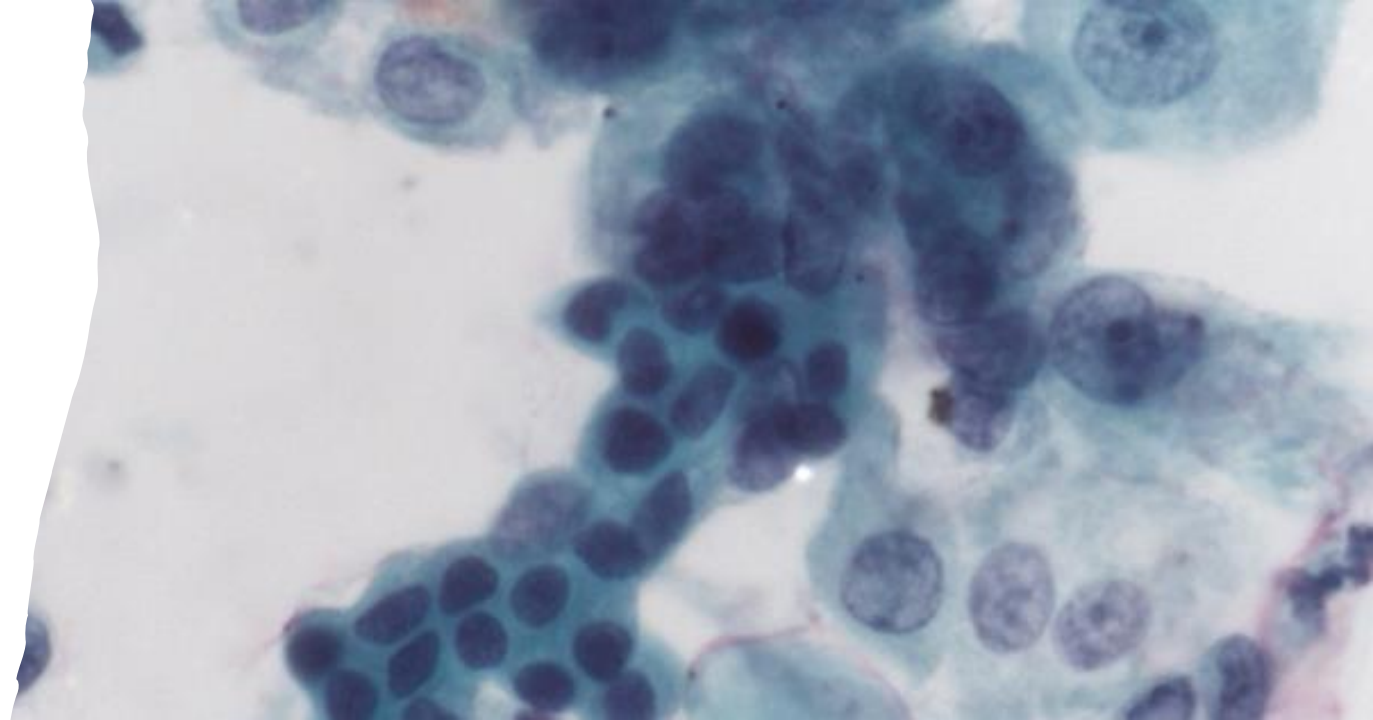


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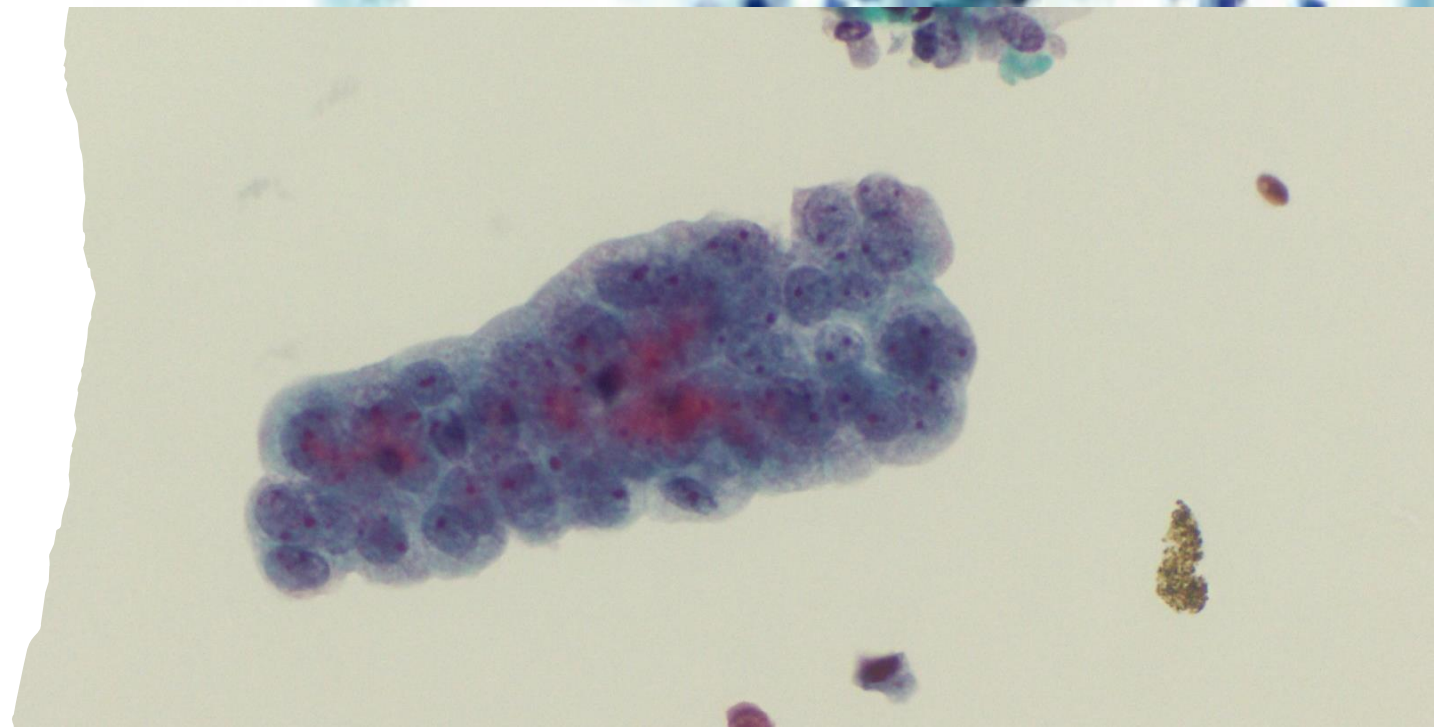
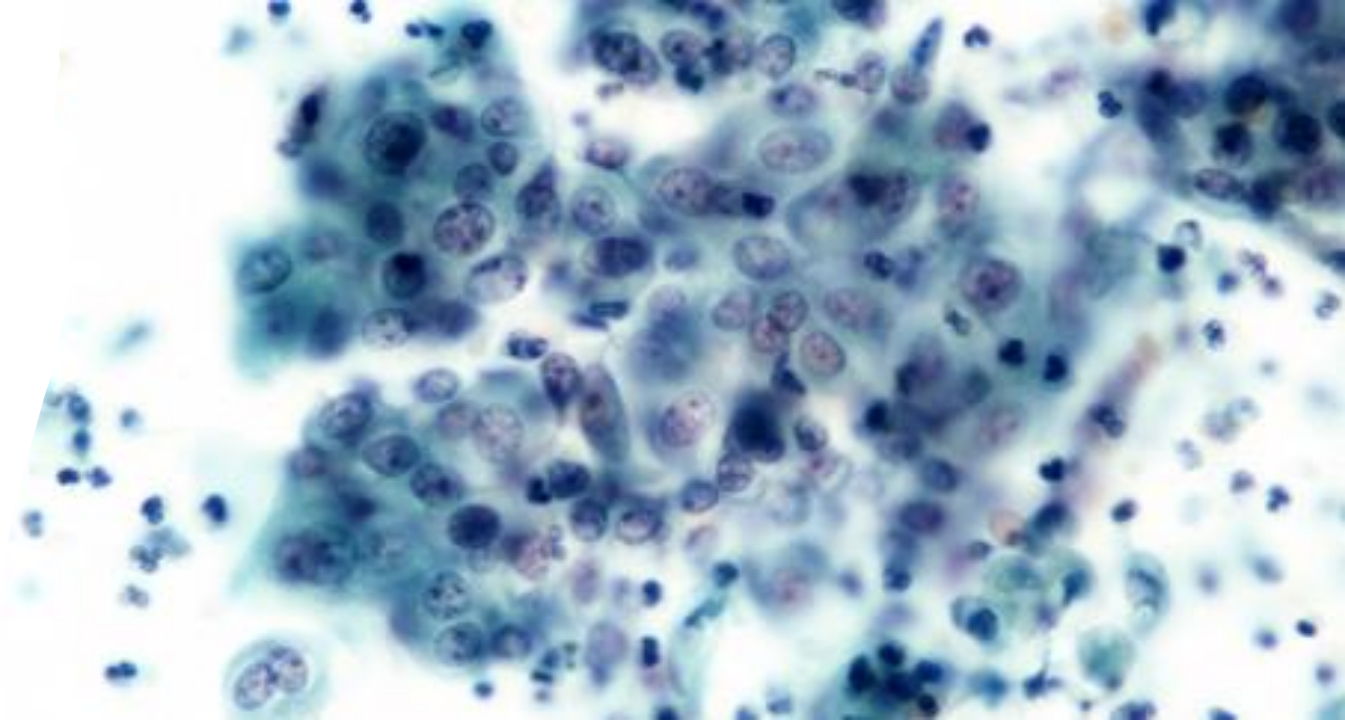
- **Negative for HGUC (NHGUC)**

- Normal urothelial cells
- Non-degenerated
- Non-superficial
- No deep hyperchromasia
- N:C ratio  $< 0.5$  but taking basal cells into account



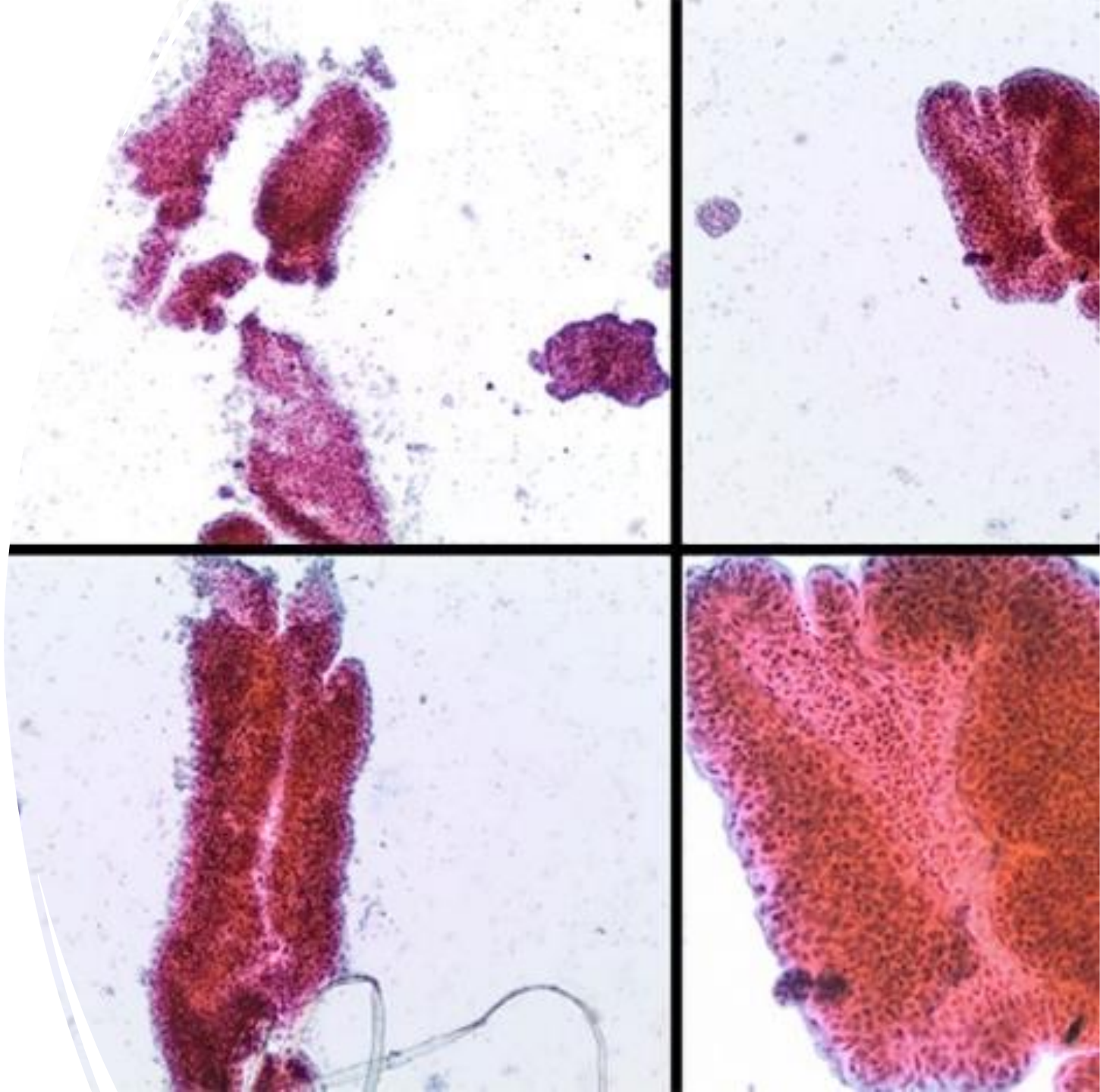
## Reactive Urothelial Cells (NHGUC)

- Uniform size
- Fine chromatin
- Round nuclei
- Smooth borders
- Small nucleoli

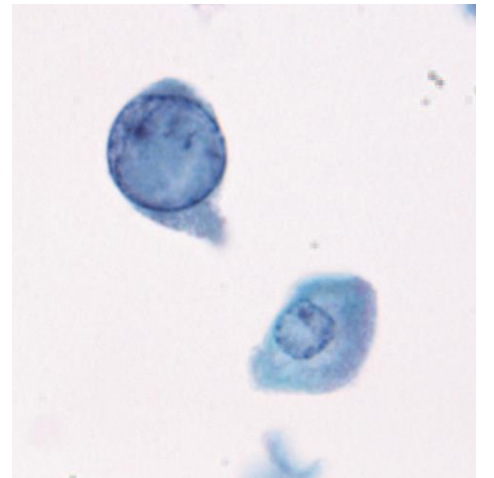


# Low grade urothelial neoplasm (LGUN) included under NHGUC

- Papillary structures with fibrovascular cores
- Cell blocks may be helpful
- Diagnosis of LGUN may be suggested in correlation with cystoscopic and biopsy findings



- *NOT ATYPIA! Report as negative for HGUC*
- Reactive urothelial cells
- “Degenerative” changes
- True tissue fragments
- Changes 2<sup>0</sup> stones
- Viral cytopathic effect eg. Polyoma virus
- Post-Rx for bladder cancer esp. BCG
- Post-Rx for pelvic malignancies
- Systemic chemotherapy
- Enteric epithelium, conduits & neobladders
- Seminal vesicle cells



# Criteria for Atypia

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Non-superficial and non-degenerated urothelial cells with a **high N/C ratio > 0.5 (required)**

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*and one of the following:*

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**Hyperchromasia** (compared to the umbrella cells or the intermediate squamous cell nucleus)

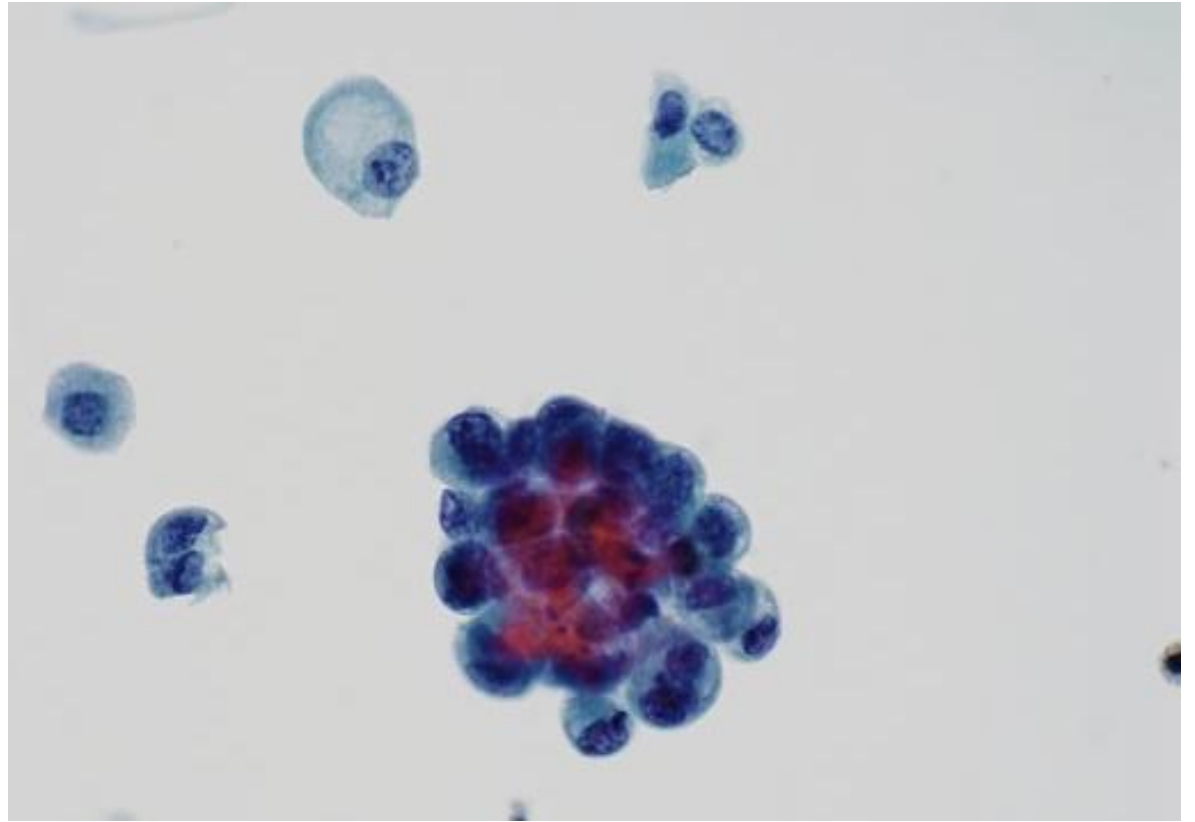
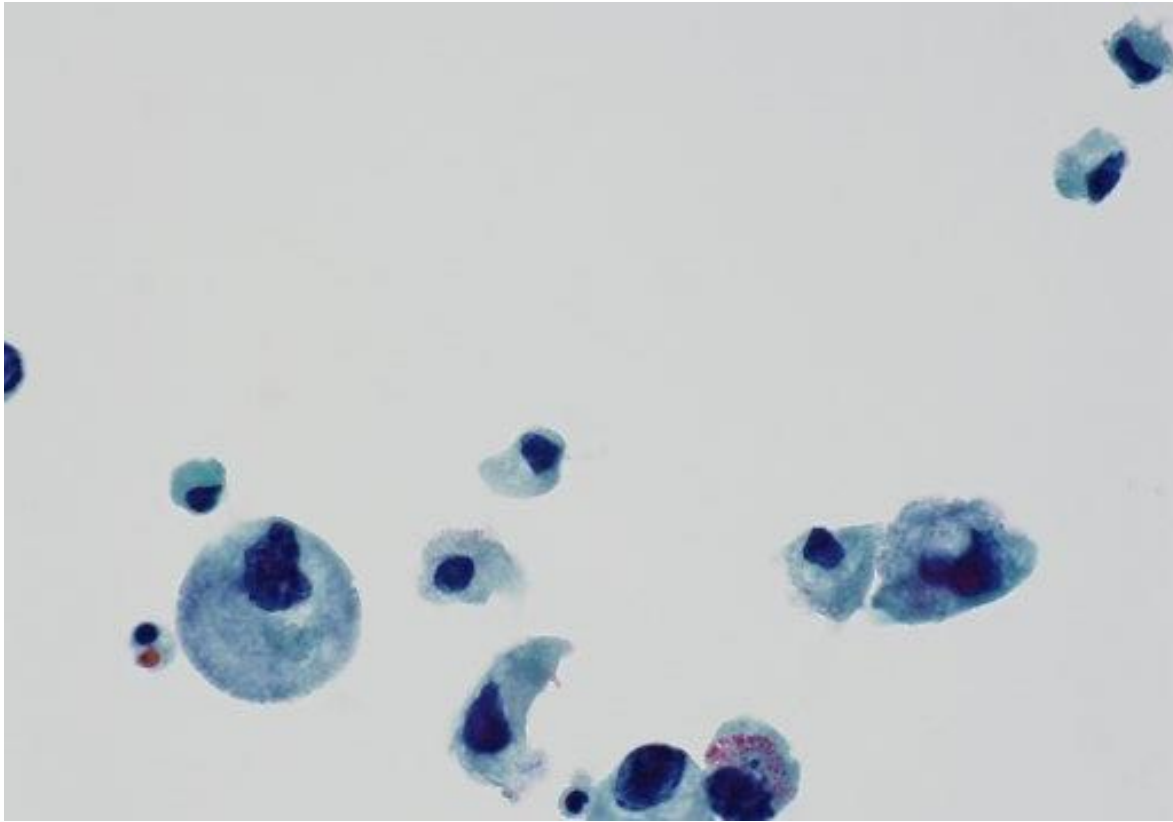
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**Irregular clumped chromatin**

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**Irregular nuclear membranes**

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**Atypia**

# Suspicious for HGUC

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Non-superficial and non-degenerated urothelial cells with a high **N/C ratio > 0.7 (required)**

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**Hyperchromasia** (compared to the umbrella cells or the intermediate squamous cell nucleus) **(required)**

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*and one of the following:*

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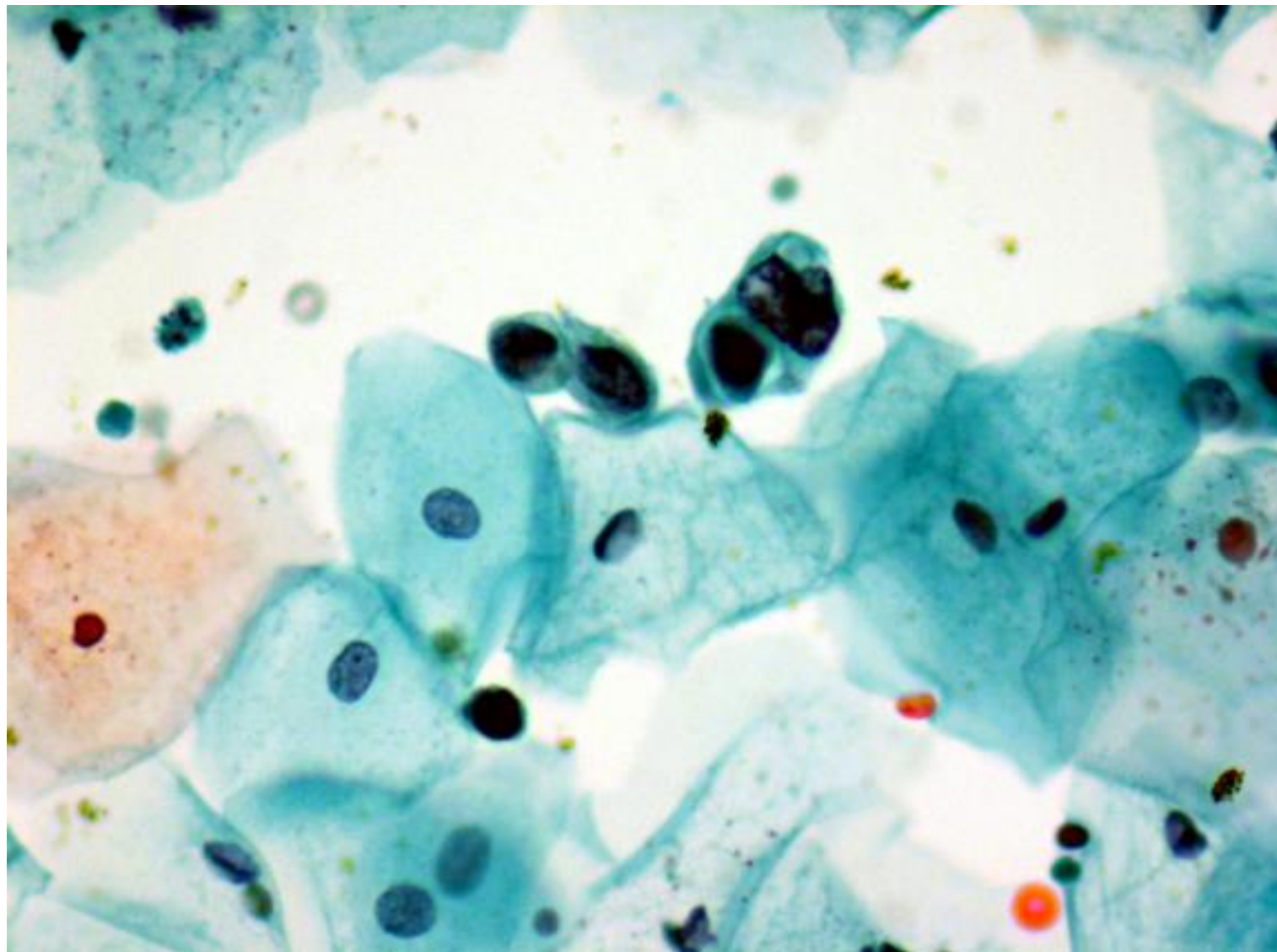
**Irregular clumpy chromatin**

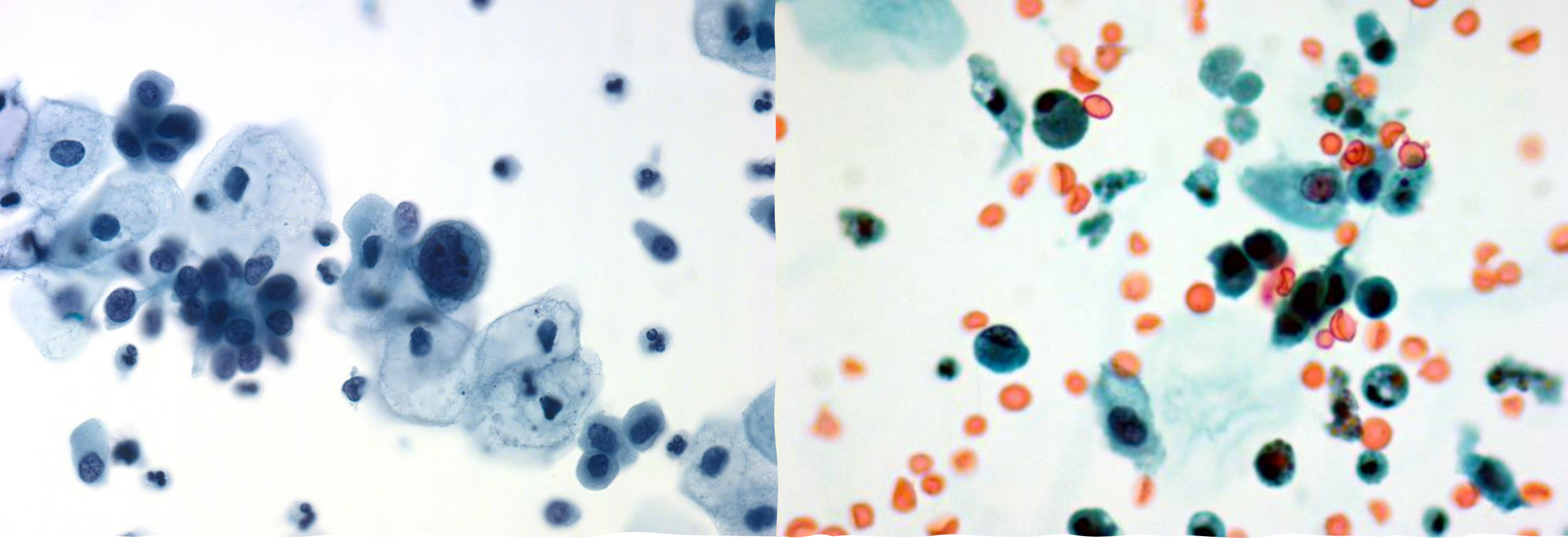
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**Irregular nuclear membranes**

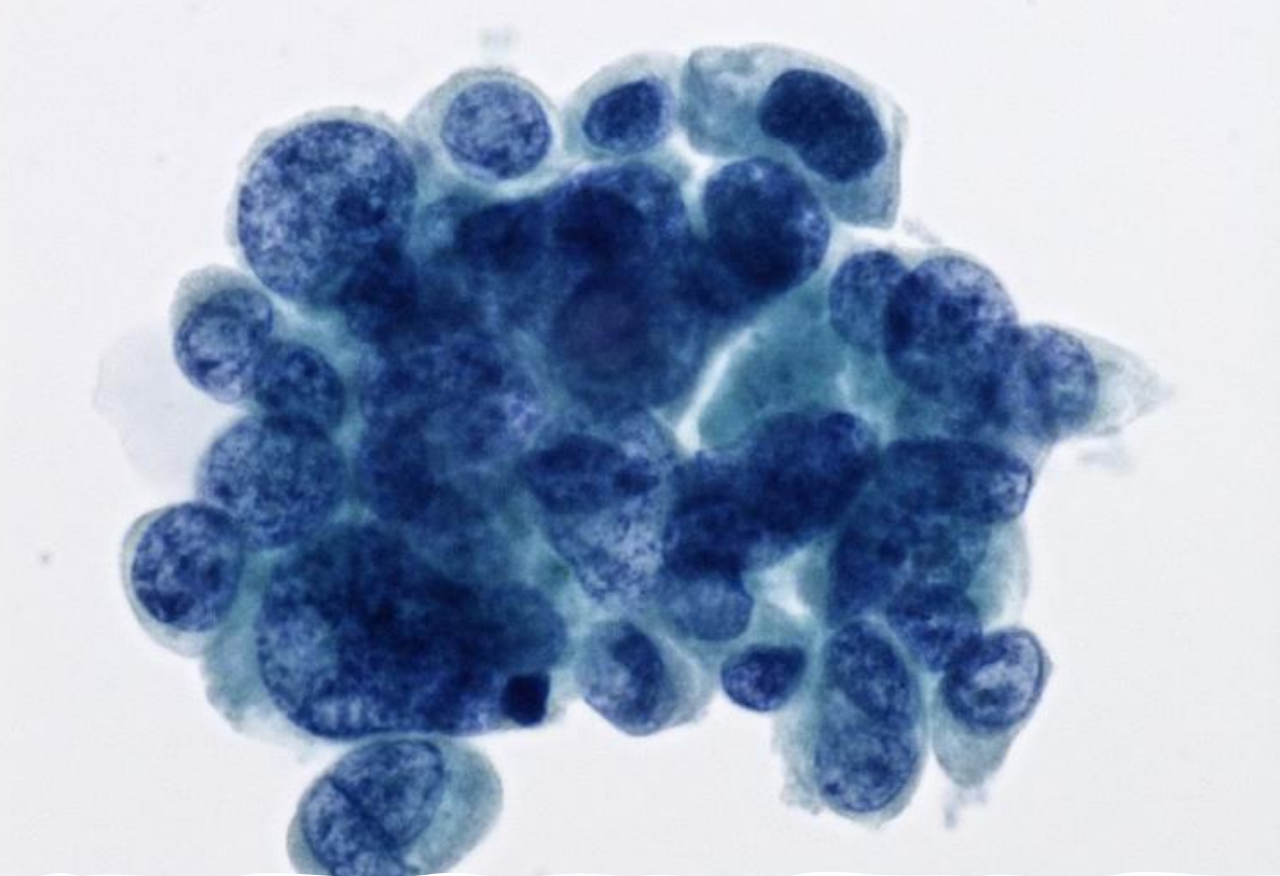
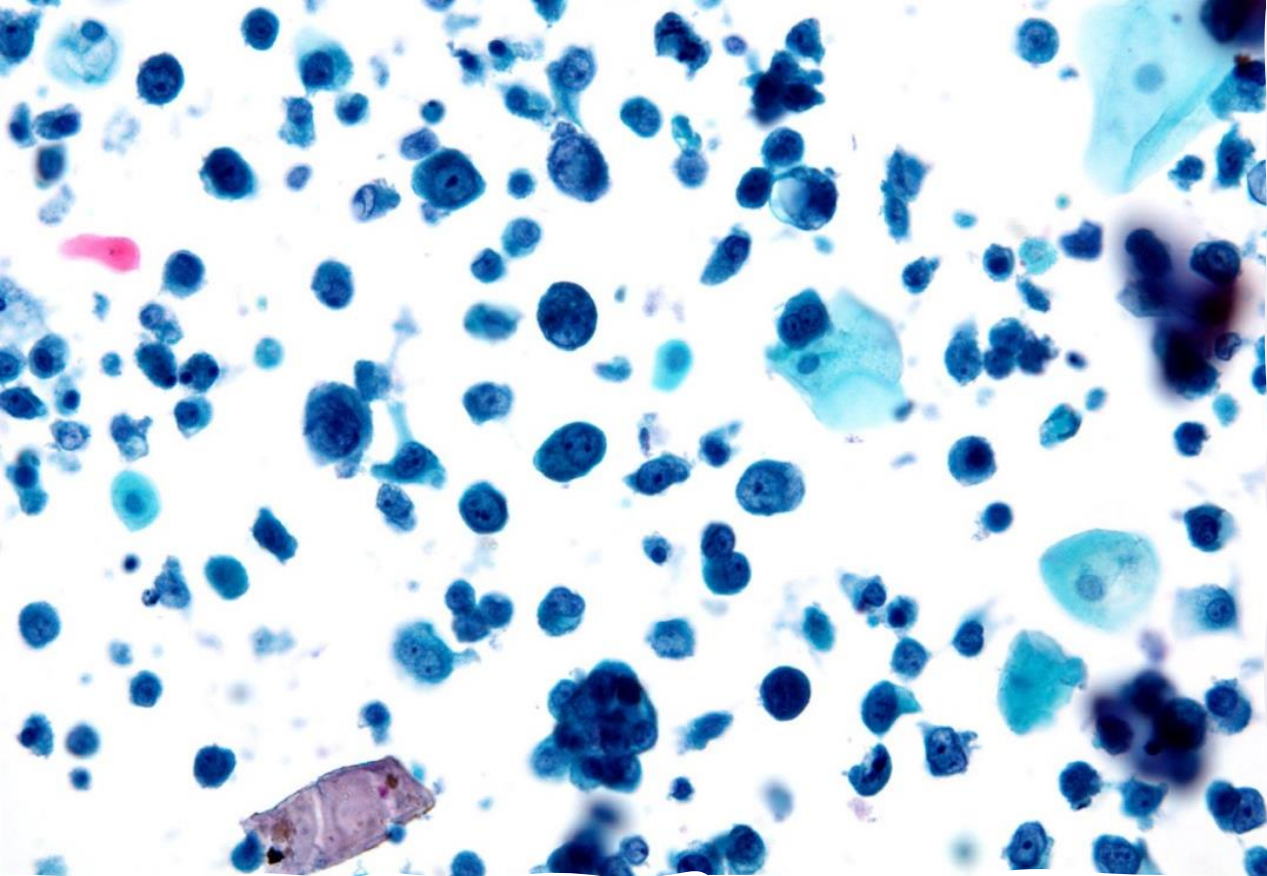


Suspicious  
for HGUC





Suspicious for HGUC

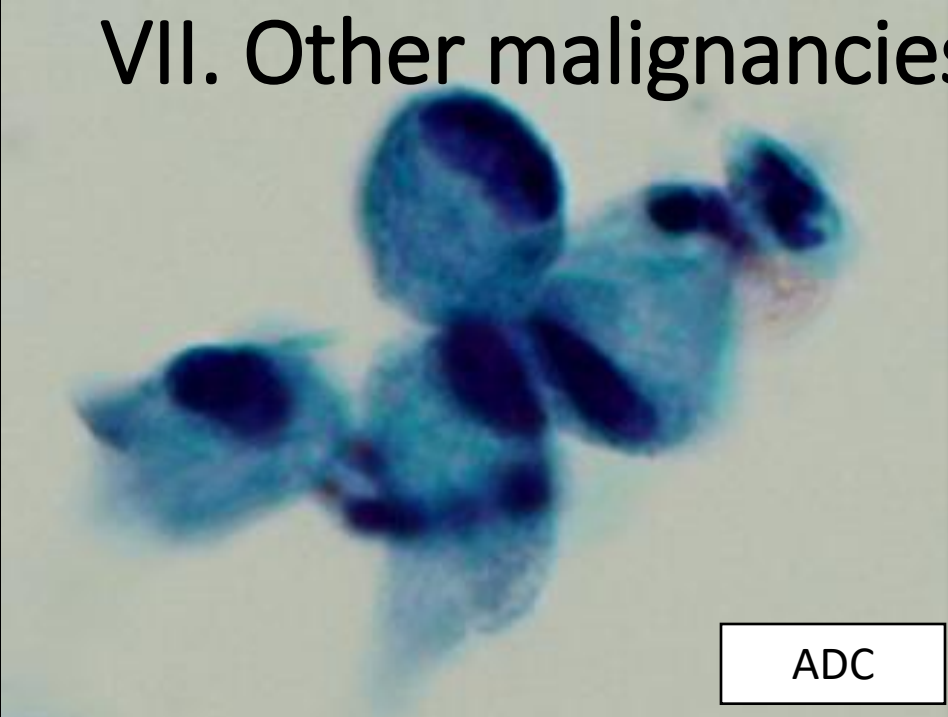


**HGUC**

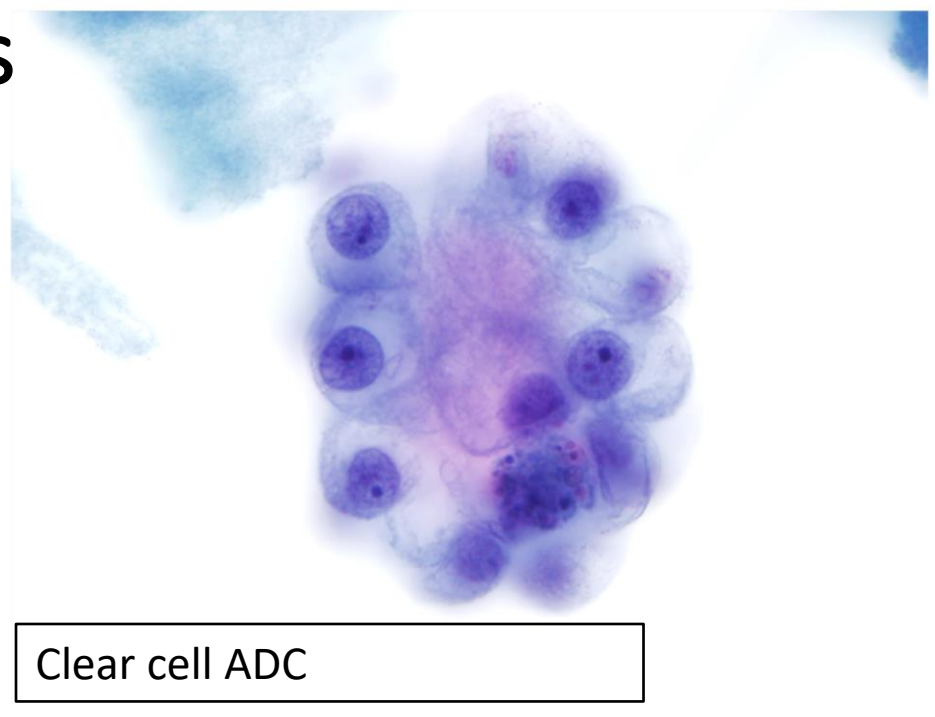
## VI. High grade urothelial carcinoma (HGUC)

- The number of atypical urothelial cells is an important criterion to classify urine cytology specimens into the 'positive' or the 'suspicious' categories.
- A cut off number of **>10 cells** to render a definitive diagnosis of HGUC seems valid from the clinical standpoint

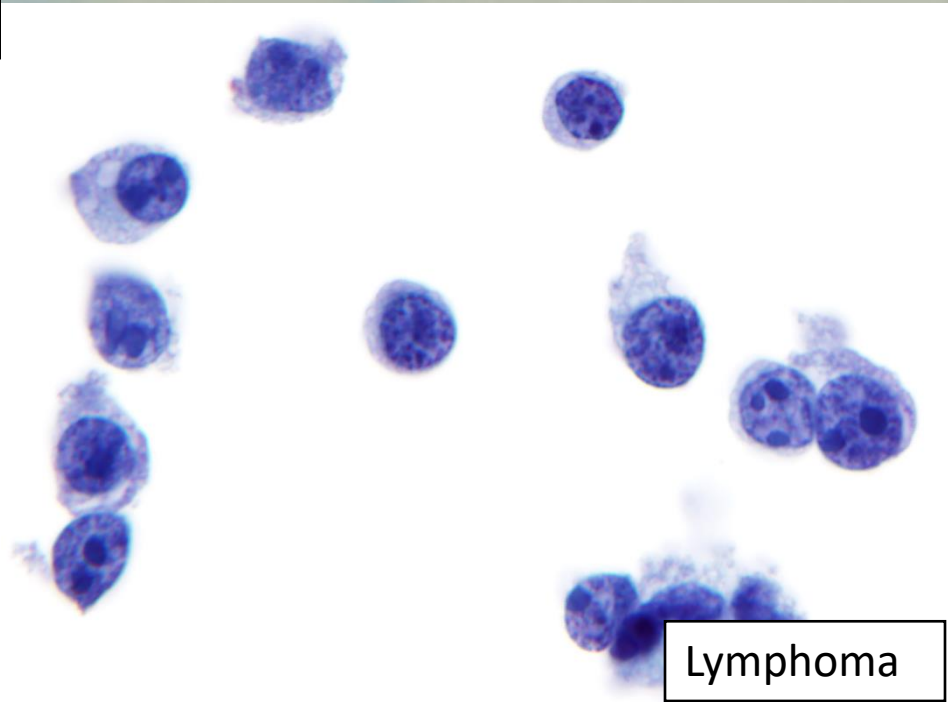
# VII. Other malignancies



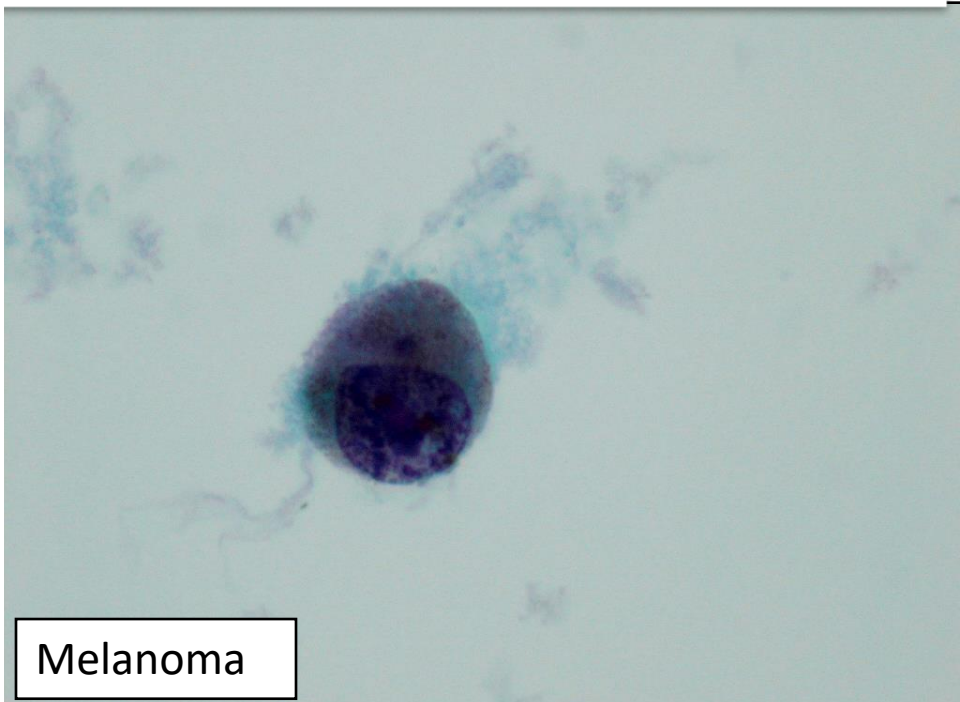
ADC



Clear cell ADC



Lymphoma



Melanoma


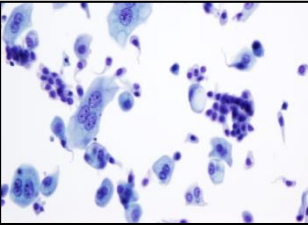
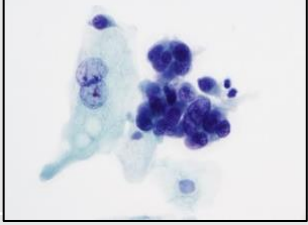
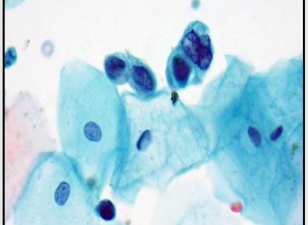
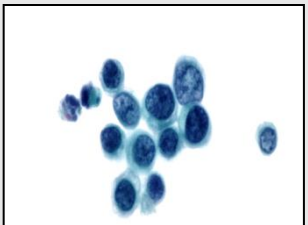
# Correlation with histology

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Bertsch EC, Siddiqui MT, Ellis CL. The Paris system for reporting urinary cytology improves correlation with surgical pathology biopsy diagnoses of the lower urinary tract. *Diagnostic Cytopathology*. 2018;00:1 –7

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20% of mismatch between HGUC vs LGUN on histology and cytology can be due to overcall on histology. Lee et al 2016 *Diagn Cytol*

Diagnostic category	Diagnostic criteria	Example	Frequency	ROHM
Unsatisfactory	Voided urine – volume (>30ml) Instrumented urine - cellularity		0% - 5%	0% - 16%
Negative for High Grade Urothelial Carcinoma (NHGUC)	Benign urothelial, glandular, squamous cells, benign tissue fragments, changes due to instrumentation, lithiasis, polyoma virus, therapy. Low Grade Urothelial Neoplasm (LGUN)		70% - 90%	8% - 24%
Atypical Urothelial Cells (AUC)	Required – increased N/C ratio ( $\geq 0.5$ ) and one of: Hyperchromasia, Irregular clumpy chromatin or Irregular nuclear contours		5% - 15%	24% - 53%
Suspicious for High Grade Urothelial Carcinoma (SHGUC)	Required – Few cells (< 5-10) with high N/C ratio (> 0.7) and hyperchromasia, and/or Irregular clumpy chromatin, Irregular nuclear contours		0.5% - 3%	59% - 94%
Positive for High Grade Urothelial Carcinoma (HGUC)	Required – Many cells (>10) with high N/C ratio (> 0.7) and hyperchromasia, Irregular clumpy chromatin, Irregular nuclear contours		0.1% - 3%	76% -100%

ROHM = Risk of High Grade Malignancy

# TPS: a continuing success story ...

- High clinical impact globally due to urine being a common specimen type
- Applicability across samples from the lower and upper urinary tract
- Useful advice to clinicians and patients on the volume of sample required
- Adaptability across conventional cytology as well as LBP
- Impact on reducing the Atypia category and improving its performance
- Correlates well with histology and ancillary tests
- Refers to low grade tumours as neoplasm rather than carcinoma
- Include in curriculum - trainees like a uniform approach to good report writing



# References

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Reynolds JP, Voss JS, Kipp BR, Karnes RJ, Nassar A, Clayton AC, Henry MR, Sebo TJ, Zhang J, Halling KC. Comparison of urine cytology and fluorescence in situ hybridization in upper urothelial tract samples. *Cancer Cytopathol*. 2014 Jun;122(6):459-67

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Dimashkieh H, Wolff DJ, Smith TM, Houser PM, Nietert PJ, Yang J. Evaluation of urovysion and cytology for bladder cancer detection: a study of 1835 paired urine samples with clinical and histologic correlation. *Cancer Cytopathol*. 2013 Oct;121(10):591-7.

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Rosenthal DL, Vandenbussche CJ, Burroughs FH, Sathiyamoorthy S, Guan H, Owens C. The Johns Hopkins Hospital template for urologic cytology samples: part I-creating the template. *Cancer Cytopathol*. 2013 Jan;121(1):15-20.



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- Owens CL, Vandenbussche CJ, Burroughs FH, Rosenthal DL. A review of reporting systems and terminology for urine cytology. *Cancer Cytopathol.* 2013 Jan;121(1):9-14.
- Rezaee N, Tabatabai L and Olson M. Adequacy of voided urine specimens prepared by ThinPrep and evaluated using The Paris System for Reporting Urinary Cytology. *JASC Volume 6, Issue 4, Pages 155–161*
- The Cancer Genome Atlas Research Network, Analysis working group: The University of Texas MD Anderson Cancer Center. Comprehensive molecular characterization of urothelial bladder carcinoma. *Nature.* 2014;507(7492):315-322. doi:10.1038/nature12965 (see diagram on next slide)

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- 1. The Paris system for reporting urinary cytology. New York, NY: Springer Science+Business Media, 2015
- 2. Barkan GA, Wojcik EM, Nayar R, et al. The Paris System for Reporting Urinary Cytology: the quest to develop a standardized terminology. J Am Soc Cytopathol. 2016;5: 177-188.
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- 4. Kurtycz DFI, Sundling KE, Barkan GA. The Paris system of Reporting Urinary Cytology: Strengths and opportunities. Diagn Cytopathol. 2020.
- 5. Stanzione N, Ahmed T, Fung PC, et al. The continual impact of the Paris System on urine cytology, a 3-year experience. Cytopathology. 2020;31: 35-40.
- 6. Torous VF, Brancely D, VanderLaan PA. Implementation of the Paris System for Reporting Urinary Cytology results in lower atypical diagnostic rates. J Am Soc Cytopathol. 2017;6: 205- 210.





*That's all Folks!*



# The global experience

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Original articles focusing on the utilization and performance of TPS in urinary cytology specimens were identified using PubMed for publications from January 2016 to July 2020

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23 relevant articles in the literature regarding the use of TPS were included in the review from a total of 30,802 urine cytology specimens, of which 21,485 (69.8%) had available diagnoses

Data from 23 articles that included at least 100 cases were analysed using SPSS software

- 10 from the United States
- 5 from India
- 2 from Canada
- 1 each from Brazil, France, Iran, South Korea, Spain and Switzerland
- 18 studies reported the distribution of cytology diagnoses both before and after TPS, allowing for comparison
- 11 studies had histological follow up within 17 months



Author, year	Type of samples	Preparation type	Country	Number of cases	Pre and Post-TPS % (n)							
					NM	NHGUC	Atypical	AUC	SM	SHGUC	M/HGUC	HGUC
Stanzione et al., 2020 <sup>5</sup>	V/I	LBP	USA (Los Angeles)	381 (87 Pre- and 294 Post-TPS†)	2.3 (2)	42.5 (125)	59.8 (52)	41.5 (122) ‡	19.5 (17)	3 (9)	18.4 (16)	12.9 (38)
Anbardar et al., 2020 <sup>2</sup>	V	CT	Iran	1842§	1732	95.3 (1757)	26	1.2 (22)	20	1.1 (20)	33	2.2 (41)
Vosoughi et al., 2020 <sup>35</sup>	V/I	CT	USA (Miami)	2192 (1588 Pre- and 604 Post-TPS)	80 (1244)	86 (519)	16 (249)¶	9 (56)	3 (47)	2 (12)	1 (18)	3 (17)
Compton et al., 2019 <sup>9</sup>	V/I	LBP	USA (Nashville)	1585#	-	80.4 (1275)	-	12.5 (199)	-	3.1 (49)	-	3.3 (51)
de Paula et al., 2019 <sup>10</sup>	V/I	LBP	Brazil	1660	-	87.1 (1446)	-	4.6 (78)	-	2.7 (45)	-	2.7 (46)
Vlajnic et al., 2019 <sup>34</sup>	V/I	CT	Switzerland	3900	-	89.7 (3496)	-	4.6 (178)	-	1.6 (61)	-	4 (155)
Bakkar et al., 2019 <sup>*3</sup>	V/I	LBP	USA (Los Angeles)	100	26 (26)	54 (54)	44 (44)	23 (23)	11 (11)	9 (9)	19 (19)	14 (14)
Rai et al., 2019 <sup>*25</sup>	V	CT	India	90	46.7 (42)	52.2 (47)	16.7 (15)	11.1 (10)	20 (18)	17.8 (16)	14.4 (13)	11.1 (10)
Vallamreddy et al., 2019 <sup>*18</sup>	NS	CT	India	74	2.7 (2)	8.1 (6)	21.6 (16)	9.5 (7)	Δ	24.3 (18)	47.3 (35)	35.1 (26)
VandenBussche et al., 2018 <sup>32</sup>	V/I	LBP/CT	USA (Baltimore)	4939 (2376 Pre- and 2563 Post-TPS)	64.9 (1543)	66.1 (1695)	23.9 (568)	23.0 (589)	5.8 (138)	4.5 (115)	3.8 (90)	5.0 (127)
Meilleroux et al., 2018 <sup>20</sup>	V/I	CT	France	3448 (1634 Pre- and 1814 Post-TPS)	82 (1340)	83.2 (1510)	6.1 (100)	5.2 (94)	0.7 (12)	2.1 (38)	4.5 (73)	4.7 (85)
Wang et al., 2018 <sup>35</sup>	V/I	LBP/CT	Canada	4764 (2371 Pre- and 2393 Post-TPS)	75.4 (1788)	80.1 (1917)	18.6 (442)	14.4 (345)	3 (70)	2.4 (57)	3 (71)	3.2 (73)
Xing et al., 2018 <sup>*37</sup>	NS	NS	USA (Pittsburgh)	300 (151 Pre- and 150 Post-TPS)	40 (60)	55 (82)	34 (52)	24 (37)	15 (23)	10 (15)	7 (11)	9 (14)
Rohilla et al., 2018 <sup>27</sup>	V	CT	India	1345	78.1 (1050)	76 (1022)	54.3 (73)	8.5 (114)	1.6 (22)	0.2 (3)	13.8 (186)	14.1 (189)
Zare et al., 2018 <sup>*38</sup>	V/I	LBP	USA (San Diego)	194	58.8 (114)	67.5 (131)	24.2 (47)	11.9 (23)	2.1 (4)	5.7 (11)	13.4 (26)	13.9 (27)
Simon et al., 2018 <sup>*013</sup>	I	NS	USA (Ann Arbor)	61	18 (11)	18 (11)	31 (19)	29 (18)	26 (16)	36 (22)	25 (15)	17 (10)
Torous et al., 2017 <sup>5</sup>	V/I	LBP	USA (Boston)	2495 (1111 Pre- and 1384 Post-TPS)	64.3 (714)	70.7 (979)	29.5 (328)	21.8 (302)	3.3 (37)	4.4 (61)	2.9 (32)	3 (42)
Granados et al., 2017 <sup>*26</sup>	V	LBP	Spain	149	69.8 (104)	51 (149)	4.7(7)	20.1 (30)	11.4 (17)	8.1 (12)	14.1 (21)	20.8 (31)
Suh et al., 2017 <sup>*25</sup>	I	LBP	Korea	142	48.6 (68)	36.6 (52)	25.4 (36)	14.8 (21)	12.7 (18)	31 (44)	14.1 (20)	17.6 (25)
Rezaee et al., 2017 <sup>26</sup>	V	LBP	USA (Baltimore + San Francisco)	744	-	64 (476)	-	14.2 (106)	-	6.6 (49)	-	11.3 (84)
Malviya et al., 2017 <sup>17</sup>	V/I	CT	India	176	-	50.5 (89)	-	5.1 (9)	-	3.9 (7)	-	13 (23)
Roy et al., 2017 <sup>*17</sup>	V	CT	India	97	19.6 (19)	6.2 (6)	41.2 (40)	11.3 (11)	-	9.3 (9)	34 (33)	49.5 (48)
Hassan et al., 2016 <sup>*20</sup>	V/I	LBP/CT	Canada	124	21.8 (27)	36.3 (45)	38.7 (48)	25.8 (32)	18.5 (23)	14.5 (18)	20.1 (26)	23.4 (29)
Mean**					73.9	80.9	23.2	10.4	3.1	2.6	4.5	4.7

**Table 1.** Distribution of diagnostic categories before and after the implementation of TPS across included studies.

# Distribution of cases among categories ranged from -

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- 50.5 to 95.3% for negative for high-grade urothelial carcinoma (NHGUC)
- 1.2 to 23% for atypical urothelial cells (AUC)
- 0.2 to 6.6% for suspicious for high grade urothelial carcinoma (SHGUC)
- 2.2 to 14.1% for high-grade urothelial carcinoma (HGUC)

**Table 2.** Distribution of risks of high-grade malignancy within each diagnostic category before and after the implementation of TPS across included studies

Author, year	Number of cases with available histology	ROHM Pre- and Post-TPS (%)							
		NM	NHGUC	Atypical	AUC	SM	SHGUC	M/HGUC	HGUC
Stanzione et al., 2020 <sup>5</sup>	381 (87 Pre- and 294 Post-TPS)	0	14.4	40.4	44.3*	76.5	88.9	93.8	97.4
de Paula et al., 2019 <sup>22</sup>	499	-	11	-	32.6	-	80	-	92.3
Bakkar et al., 2019 <sup>10</sup>	100	15.4	29.7	43.2	60.9	100	100	100	100
Wang et al., 2018 <sup>21</sup>	355 (188 Pre- and 167 Post-TPS)	20.3	17.7	29.6	50	81.5	76.4	89.4	89.1
Meilleroux et al., 2018	629 (330 Pre- and 229 Post-TPS)	7.3	8.7	28.2	49	83.3	87	89.4	91
Xing et al., 2018 <sup>9</sup>	300 (151 Pre- and 150 Post-TPS)	17	27	54	59	78	93	91	100
Rohilla et al., 2018 <sup>16</sup>	244	15.6	11.6	25	12.3	44.4	33.3	†	58.8
Zare et al., 2018 <sup>8</sup>	194	12.3	9.9	23.4	17.4	50	72	92	96.3
Suh et al., 2017 <sup>25</sup>	142	19.1	13.5	38.9	38.1	66.7	59.1	95	68
Granados et al., 2017 <sup>26</sup>	149	37.5	36.8	71.4	40	64.7	75	100	87.1
Hassan et al., 2016 <sup>20</sup>	124	25.9	17.8	33.3	53.1	91.3	83.3	96.2	100
Mean‡		16.4	15.7	36.2	38.5	71.5	76.2	90.5	88.8

TPS: The Paris System for Reporting Urine Cytology; ROHM: risk of high-grade malignancy; NM: negative for malignancy (pre-TPS); SM: suspicious for malignancy (pre-TPS); M/HGUC: malignant/high-grade urothelial carcinoma (pre-TPS); NHGUC: negative

# The calculated risk of high-grade malignancy (ROHM) ranged from-

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- 8.7 to 36.8% for NHGUC
- 12.3 to 60.9%% for AUC
- 33.3 to 100% for SHGUC
- 58.8 to 100 % for HGUC

**Table 3.** Diagnostic test parameter calculated before and/or after the implementation of TPS across included studies.

Author, year	Pre- and Post-TPS (%)										
	n	Sensitivity	Sensitivity	Specificity	Specificity	PPV	PPV	NPV	NPV	Accuracy	Accuracy
Bakkar et al., 2019* <sup>10</sup>	100	38	43	100	100	100	100	58	61	66	70
de Paula et al., 2019 <sup>22</sup>	449	-	40	-	99.3	-	92.3	-	88.2	-	-
Meilleroux et al., 2018 <sup>23</sup>	559 (330 Pre- and 229 Post-TPS)	82.5	84.7	94.3	92.1	92.2	91	89.1	86.4	-	-
Zare et al., 2018* <sup>8</sup>	194	72.5	74.5	72	83.9	48	62.3	88	90	74	81.4
Granados et al., 2017* <sup>26</sup>	149	49	63	91	73	93	84	42	46	-	-
Rohilla et al., 2018 <sup>16</sup>	244	66.3	-	82.9	-	95.2	-	32.2	-	69	-
Suh et al., 2017* <sup>25</sup>	142	59.4	70.8	98.2	84.9	95	68	80.9	86.5	-	-

TPS: The Paris System for Reporting Urine Cytology; PPV: positive predictive value; NPV: negative predictive value.

\*The same specimens were used to calculate diagnostic accuracy measure before and after implementation of TPS.

**Table 4.** Distribution of TPS categories initially assigned to cases ultimately reported as LGUN on histology

Author, year	Number of cases with histologic diagnosis of LGUN	TPS categories % (n)				
		NHGUC	AUC	SHGUC	HGUC	LGUN
Stanzione et al., 2020 <sup>5</sup>	58	41.4 (24)	56.9 (33) *	1.7 (1)	0 (0)	*
Anbardar et al., 2020 <sup>24</sup>	22	4.5 (1)	18.2 (4)	31.8 (7)	40.9 (9)	4.5 (1)
de Paula et al., 2019 <sup>22</sup>	88	93.2 (82)	4.5 (4)	0 (0)	2.3 (2)	0 (0)
Vallamreddy et al., 2019 <sup>18</sup>	32	18.8 (6)	21.9 (7)	6.3 (2)	0 (0)	53.1 (17)
Rai et al., 2019 <sup>15</sup>	16	37.5 (6)	12.5 (2)	25 (4)	0 (0)	25 (4)
Wang et al., 2018 <sup>21</sup>	46	69.6 (32)	23.9 (11)	4.3 (2)	2.2 (1)	†
Meilleroux et al., 2018 <sup>23</sup>	62	72.6 (45)	16.1 (10)	1.6 (1)	0 (0)	8.1 (5)
Xing et al., 2018 <sup>9</sup>	27	85.2 (23)	14.8 (4)	0 (0)	0 (0)	0 (0)
Zare et al., 2018 <sup>8</sup>	52	80.8 (42)	9.6 (5)	3.8 (2)	1.9 (1)	3.8 (2)
Roy et al., 2017 <sup>17</sup>	34	14.7 (5)	23.5 (8)	5.9 (2)	11.8 (4)	29.4 (10)
Granados et al., 2017 <sup>26</sup>	40	60 (24)	25 (10)	7.5 (3)	7.5 (3)	0 (0)
Malviya et al., 2017 <sup>19</sup>	5	40 (2)	20 (1)	20 (1)	20 (1)	0 (0)
Suh et al., 2017 <sup>25</sup>	27	33.3 (9)	11.1 (3)	37 (10)	18.5 (5)	0 (0)
Hassan et al., 2016 <sup>20</sup>	25	72 (18)	28 (7)	0 (0)	0 (0)	0 (0)
Mean‡		59.8	20.4	6.5	4.9	9.1

TPS: The Paris System for Reporting Urine Cytology; LGUN: low-grade urothelial neoplasm; ND/U: nondiagnostic/unsatisfactory; NHGUC: negative for high-grade urothelial carcinoma; AUC: atypical urothelial cells; SHGUC: suspicious for high-grade urothelial carcinoma; HGUC: high-grade urothelial carcinoma

# LGUN

- Only three series in the literature reported more than ten LGUN cytology cases with histological follow-up within their cohorts
- In these series, the risk of low-grade neoplasm (RLGN) associated with this cytologic diagnosis was actually high, ranging from 45.5 to 100% (weighted mean =  $78.1\% \pm 22.3\%$ )
- Fourteen studies had available cytological data for cases ultimately reported as LGUN on surgical specimens, a total of 534 cases
- The distribution of TPS categories initially assigned to these cases consisted primarily of NHGUC
- These data support the decision of TPS to include any diagnosis of LGUN within the NHGUC category as a secondary diagnosis

# More highlights of TPS2.0

- Significant changes in clinical guidelines for microscopic haematuria and reflex testing of atypical urine cytology as well as the expansion of surgical investigative techniques have been contributed to the book by the urologist co-authors
- TPS2.0 honours the late Dr Stefan Pambuccian through a touching tribute by the editors and by the inclusion of a chapter on the history of urinary cytology, one of his many illuminating works



# Genetics and further research

- The Cancer Genome Atlas molecular characterization has been incorporated into the pathogenesis of low-grade and high-grade urothelial carcinomas
- There is a literature review on ancillary testing including new markers and assays including recent data on ancillary testing in the era of TPS and a new section on next-generation sequencing (NGS) in urinary cytology
- A number of research questions have been listed from all areas of urinary cytopathology in a separate section of the book and should provide ideas for suitable projects that may be of interest and relevance to clinical practice

Atypia

