GUIDELINES OF THE CANADIAN SOCIETY OF CYTOPATHOLOGY

The Paris System for Reporting Urine Cytology

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January 25, 2019

The CSC endorses The Paris System for reporting urine cytology (2016). The following document is a short summary of the highlights of the Paris system guidelines. Further details can be found in the original Atlas and online public image bank (Refs 1 and 2).

The main objectives TPS are to standardize the terminology used in urine cytology as well as the diagnostic criteria applied with a focus on the detection of high-grade urothelial carcinoma (HGUC). The criteria which should be assessed in the intermediate cells rather than the superficial cells (umbrella) are used in voided and instrumented specimens similarly. TPS includes six diagnostic categories.

Adequacy

Although no rigid criteria were implemented it was suggested that volume and cellularity be incorporated in the assessment of sepcimen's adequacy. Volumewise, one study shows that a cutt-off of 30 ml is appropriate in *SurePath* preparation in voided and unfixed specimens. In terms of cellularity, another study showed that in instrumented specimens, a cutt-off of 20 well preserved cells per 10HPF is an adequacy criterion, with specimens showing <10 cells per 10 HPF considered inadequate. The presence of cellular atypia make the specimen adequate regardless of volume and cellularity.

Negative for HGUC

This group includes benign urothelial cells, metasplastic squamous or glandular cells, renal tubular cells, reactive changes (infection, calculi, instrumentation), chemotherapy or radiation-related changes, and viral cytopathic changes including BK virus changes. Reactive urothelial cells may show increased N/C ratio (>0.5) and prominent nucleoli but do not show hyperchromasia, irregular clumpy chromatin or irregular nuclear membranes. Also, the presence of urothelial cell fragments should not be considered an 'atypical' feature, as long as nuclear atypia is absent, and this even in voided specimens. The category of **'low-grade urothelial neoplasia (LGUN)'** is also included under the 'negative for HGUC' diagnosis. LGUN refers to the rare cases in which three dimensional cellular papillary clusters are seen admixed with either benign urothelial cells or atypical cells not fulfilling the criteria of HGUC.

Atypical urothelial cell (AUC)

This category includes cases with mild cytologic atypia falling short of a HGUC diagnosis, provided reactive atypia has been excluded. N/C >0.5 is a required criterion. In addition, cells should show one of the following: hyperchromasia, irregular clumpy chromatin, irregular nuclear membranes. In the presence of cellular degeneration, more than one of those features is allowed. Currently, there are no quantitative criteria (i,e. number of atypical cells) in the AUC category.

Suspicious for HGUC

This category refers to cases with rare cells showing both increased N/C ratio (>0.5-0.7) and moderate to severe hyperchromasia in addition to one or both of the following: irregular clumpy chromatin, irregular nuclear membranes.

Positive for HGUC

No significant cytological differences exist between this category and the 'suspicious for HGUC' with the main difference being the number of atypical cells. While TPS advocates for at least 5-10 severely atypical cells in order to establish a 'positive for HGUC' diagnosis (i,e. a 'positive for HGUC' diagnosis should not be made with <5 atypical cells) a rigid threshold was not established and pathologists are encouraged to incorporate the clinical context as well as the specimen type in that distinction. While it is suggested that a threshold of 5 atypical cells is sufficient in voided specimens or in patients with known history of urothelial carcinoma, a cut-off of 10 atypical cells is advocated in upper tract specimens.

Other malignancies (primary and metastatic)

Those include primary non-urothelial tumors (squamous cell carcinoma, adenocarcinoma, neuroendocrine tumors, sarcoma, melanoma, lymphoma) as well as direct extension from tumors of adjacent organs (colorectal, cervix, prostate) or metastases. Clinical information is crucial in this context and immunohistochemical studies are important to perform if sufficient material is available.

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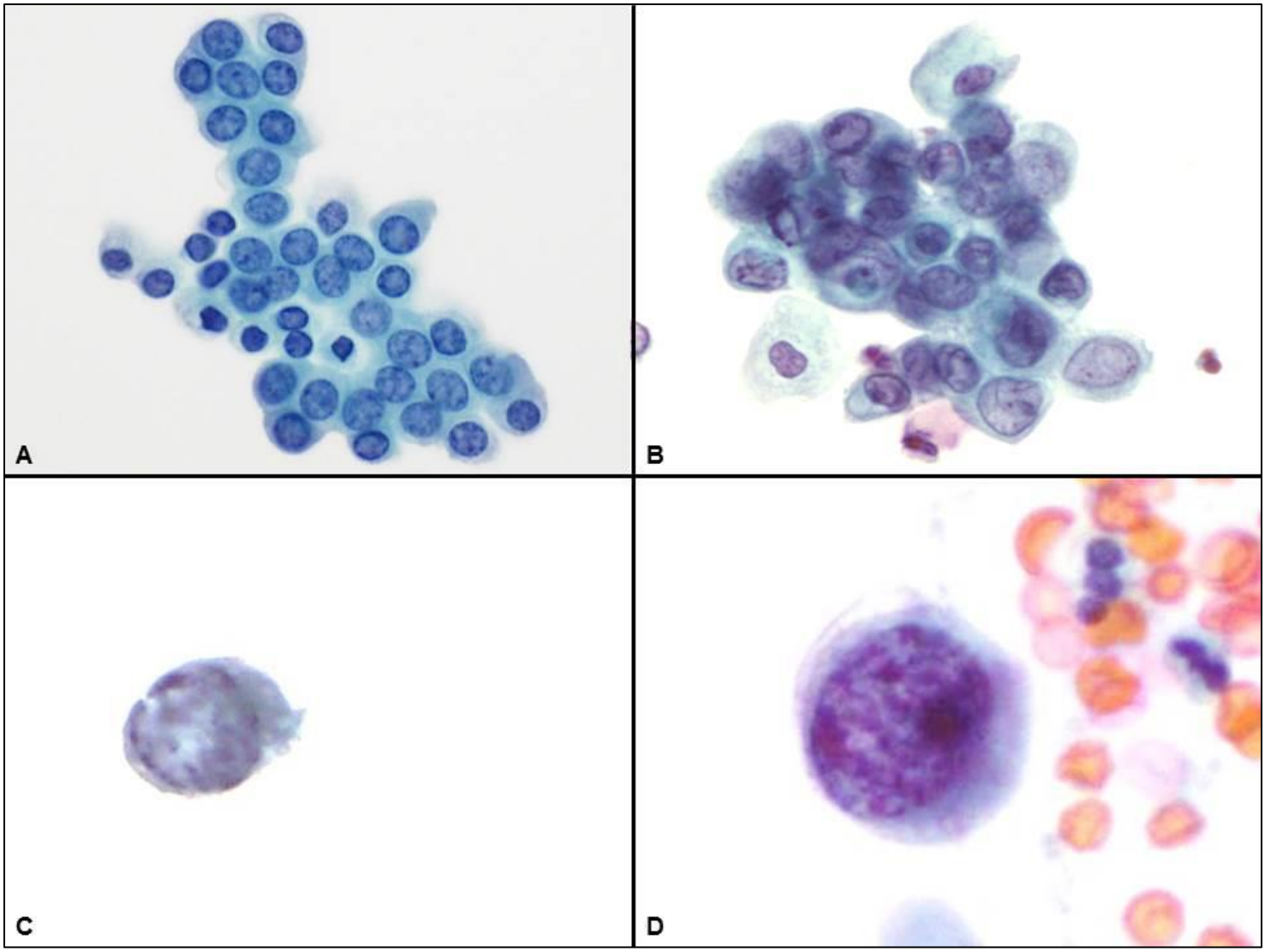

Figure 1. ***A. Negative for HGUC:*** urothelial cell cluster showing increased N/C ratio but no hyperchromasia, irregular chromatin nor irregular nuclear membranes. This example of instrumentation artifact illustrates that increased N/C ratio alone is not sufficient to label a case as 'atypical' in the Paris system. ***B. atypical urothelial cells:*** well preserved urothelial cell cluster showing increased N/C ratio, fine chromatin pattern but severely irregular nuclear membranes. ***C. Atypical urothelial cells:*** one degenerated cell showing increased N/C ratio, hyperchromasia and coarse clumpy chromatin. **D. *Suspicious for HGUC:*** one well preserved urothelial cell showing increased N/C ratio and severe hyperchromasia with irregular coarse chromatin.

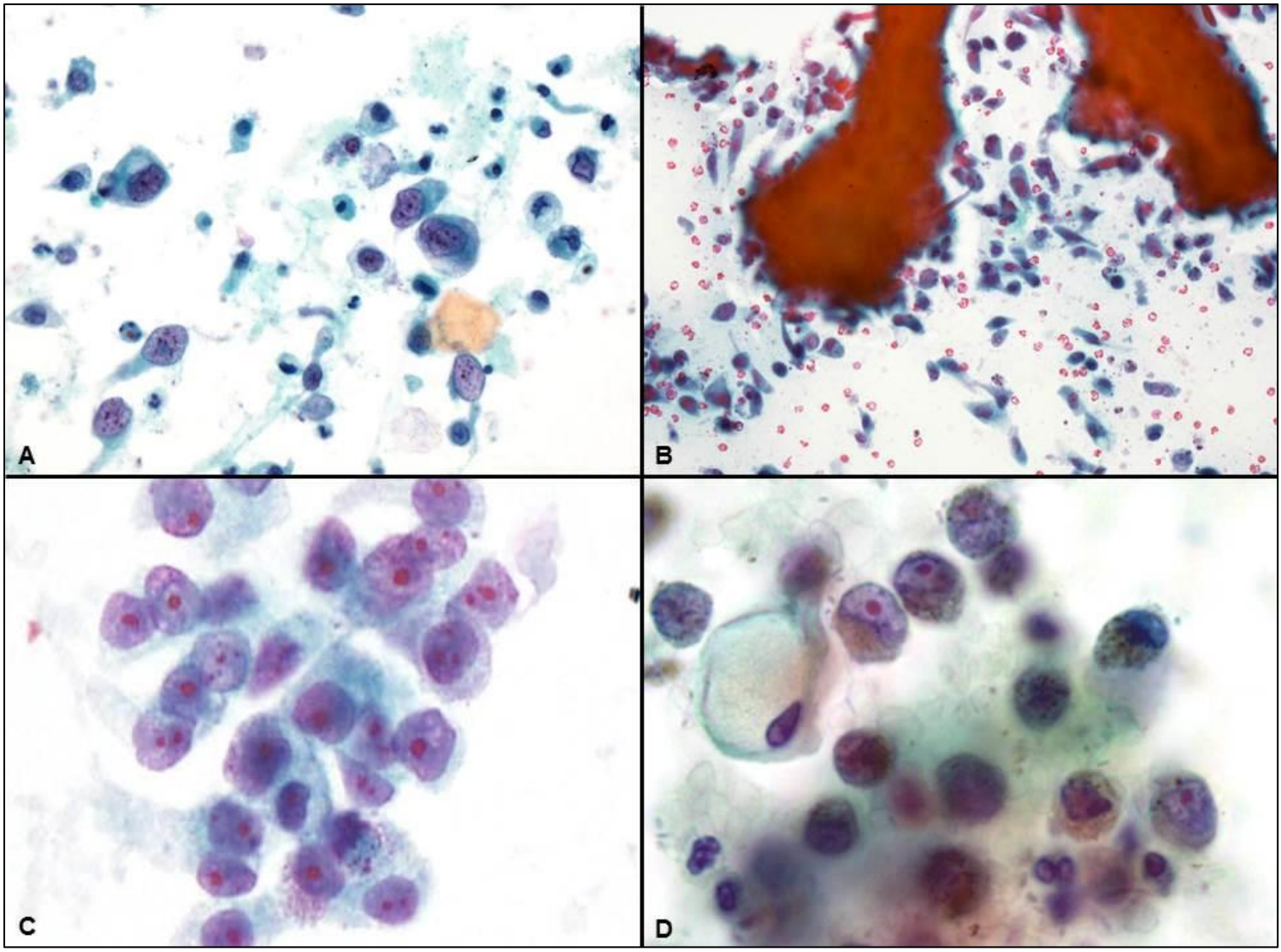

Figure 2. A. Positive for HGUC: Multiple well preserved atypical urothelial cells showing increased N/C ratio with hyperchromasia and coarse chromatin pattern. ***B. Negative for HGUC, consistent with low-grade urothelial neoplasia:*** Large three dimensional papillary structures composed of mildly atypical cells some of which show increased N/C ratio in the lack of severe hyperchromasia, coarse chromatin or irregular nuclear membranes. In this example the follow-up biopsy result was papillary urothelial neoplasm of low-malignant potential (PUNLMP). ***C. Adenocarcinoma:*** Cells cluster showing increased N/C ratio, vacuolated cytoplasm, round monotonous nuclei, finely coarse chromatin pattern and prominent cherry-red nucleoli. In this case additional material was available and the cells showed positivity for NKX3.1, a specific prostatic marker consistent with a diagnosis of prostatic adenocarcinoma. ***D. Melanoma:*** Single cells showing intracytoplasmic pigment, increased N/C ratio and prominent nucleoli. Cells showed positivity for SOX10.

Reference: 1. *Rosenthal D, Wojcik E, Kurtycz D. The Paris System for Reporting Urine Cytology. Springer, 2016,* **2.** *https://paris.soc.wisc.edu/index.htm*

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