Cytyc Corporation - Case Presentation Archive - January 2002

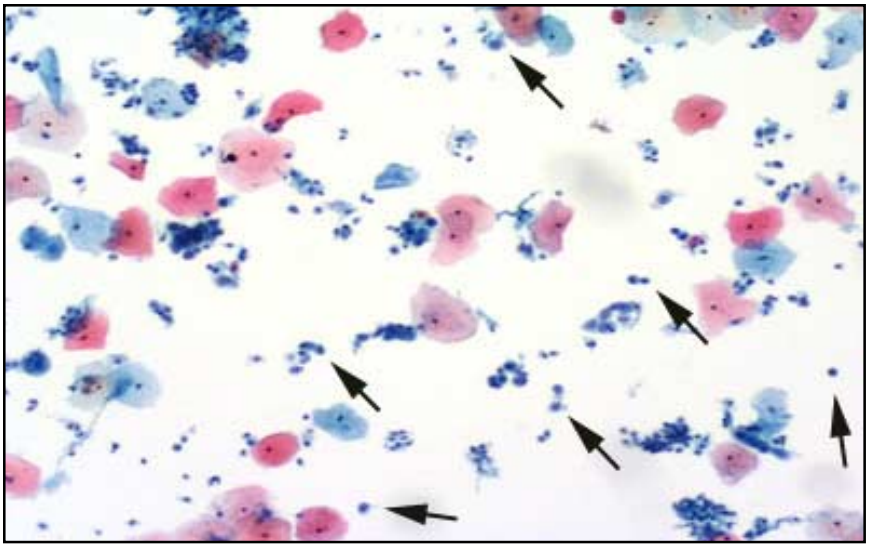
ThinPrep® Pap Test™

History: 44 Years Old

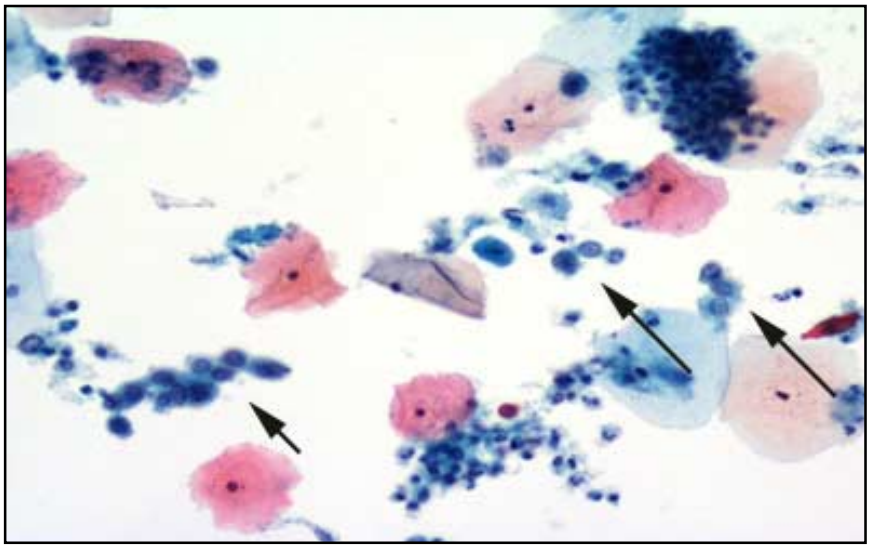
LMP: Unknown

Case provided by an independent physician who wishes to remain anonymous. Tissue follow-up for case provided by Rodolfo Laucirica, MD, Chief of Anatomic Pathology, Ben Taub General Hospital, Houston, TX.

*The images, analysis and diagnosis for this case study were provided to Cytyc by an independent physician. All conclusions and opinions are those of the physician and not Cytyc Corporation.



Slide 1 - 10x



Slide 2 - 20x

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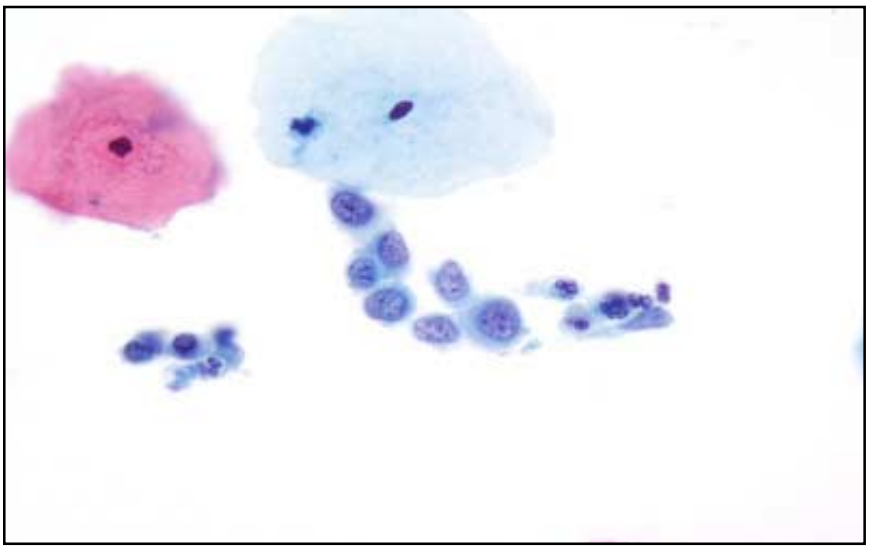

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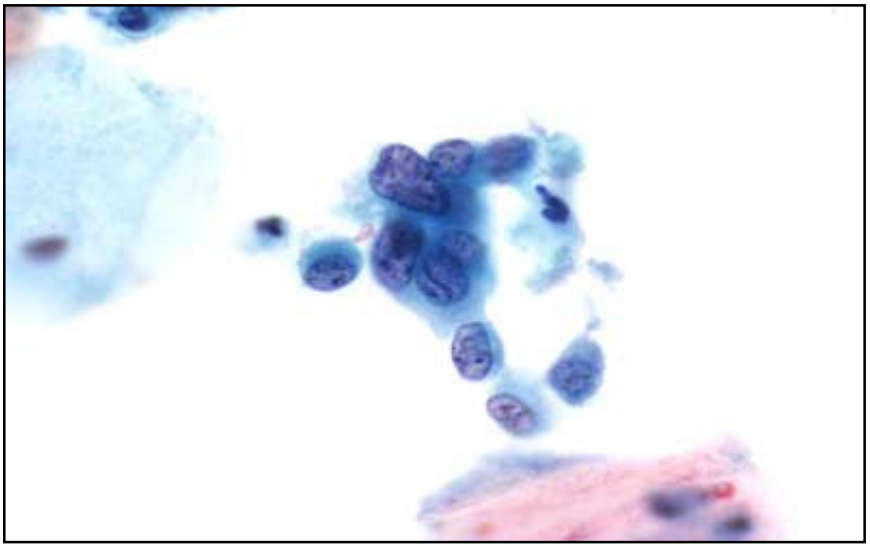

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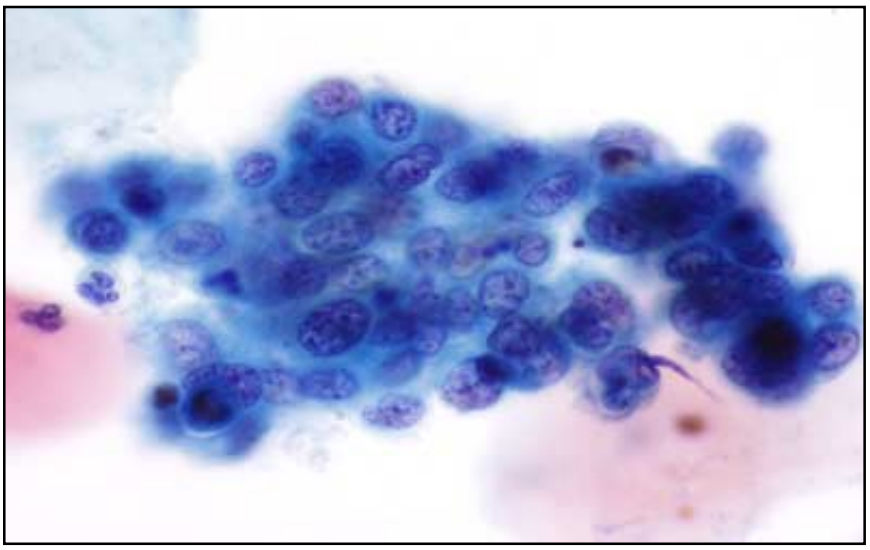

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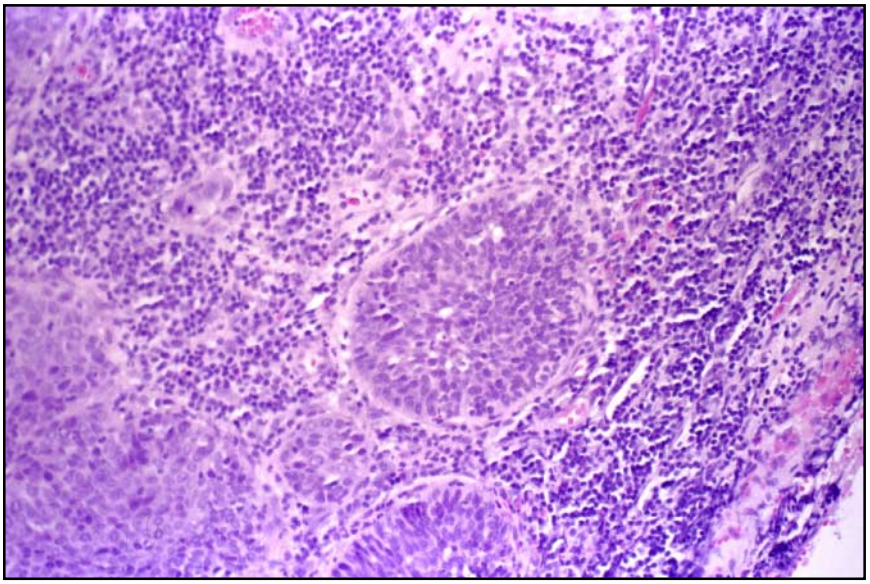

Slide 6 - 10x

Discussion:
Slide 1: At screening power, attention is drawn to the small single cells in the white spaces where high N/C ratios are observable.

Slide 2: An overview showing hypochromatic (long arrows) and hyperchromatic (short arrow) abnormal cells with high N/C ratios, irregular nuclear membranes and scarce polygonal cytoplasm lying singly or in flat sheets.

Slide 3: A loose grouping of cells with high N/C ratios and pale nuclei. Note that even though the nuclei are hypochromatic, large chromocenters are evenly distributed, still giving the nuclei an abnormal chromatin pattern.

Slide 4: A syncytia of cells with scarce, polygonal, dense cytoplasm and markedly irregular nuclei. Cells at the "bottom" of the cell group are hypochromatic and cells at the "top" of the group are hyperchromatic.

Slide 5: A syncytial group of cells giving the appearance of hyperchromasia in dense areas. On the outer edges some individual cells with pale nuclei are apparent.

Slide 6: Tissue section showing HSIL in glands and microinvasion with a lymphocytic proliferative background.

Adequacy: Satisfactory for evaluation**.**

Cytologic Diagnosis: Squamous cell abnormalities: High grade squamous intraepithelial lesion, severe dysplasia/CIS**.**

Tissue Diagnosis: Cone biopsy: Microinvasive squamous cell carcinoma; followed by a hysterectomy.

Hypochromasia, or pale staining cells, is a phenomenon that has been well illustrated in Dr. Papanicolaou's text "Diagnosis of Uterine Cancer by the Vaginal Smear", Plate E, illustration numbers 64 and 65, published in 1943. Since then it has plagued diagnosticians, not only with its pale staining nucleus, but also its "hide-and-seek" status on conventional paps, especially when it is present in "third type" or "litigation" cells. On ThinPrep, these cells are now "spotlighted" in the "white spaces" in between larger cells and cell groupings. On a gynecological prep where cells are either thick, obscured, or have no space in between cells, pale staining cells can easily be overlooked. The eye must learn to pick out criteria at screening power other than hyperchromasia, such as N/C ratio, irregular chromatin pattern, multi-focal nuclei and nuclear membrane irregularities.

The nucleus is composed of two types of chromatin: inactive heterochromation, which is acidic and therefore readily takes up hematoxylin, and active euchromation, which does not readily take up stain and is represented by pale areas. Heterochromatin can appear as rather large dark particles seen as chromocenters. Euchromation, active in the synthesis of RNA, is seen as pale spaces between the chromatin particles and referred to as parachromatin as it lies within or beside (para-) the condensed chromatin…thus parachromatin clearing.

The intensity of basophilic staining of the nucleus is roughly proportional to the amount of DNA present, but nuclear hyper- or hypochromasia depends on three factors: the amount of stainable material, the size of the nucleus and Beer's Law of Absorption; which can be read in more detail in Dr. Demay's text, page 41 (see references). Due to the variability of any one of these three factors in any given cell, hypo and hyperchromatic cells may be seen in the same specimen.

Hyperchromatic nuclei have more (inactive) heterochromatin, while hypochromatic nuclei have more (active) euchromatin. Therefore, surprisingly, darker nuclei are associated with fewer cell activities than paler ones. This is why dyskaryotic or malignant cells may occasionally have hypochromatic rather than hyperchromatic nuclei.

References:

Demay, Richard. The Art and Science of Cytopathology. 1996:41

McKee, Grace T. Cytopathology. 1997:2

Bibbo, Marluce, MD. Comprehensive Cytopathology. 1990:76-78

Papanicolaou, George, MD., Ph.D. et al. Diagnosis of Uterine Cancer by the Vaginal Smear. 1943:Plate E, #64 and #65