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ThinPrep® Pap Test™

History: 50 Year Old Female Routine Pap

Specimen type: Cervical/Vaginal

This case was provided by Dr. Bruce Dziura of New England Pathology Associates, Springfield, Massachusetts.

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

Slide Description:

Slide 1: Plate E taken from Papanicolaou and Traut's book, Diagnosis of Uterine Cancer by the Vaginal Smear, reproduced with permission from The Commonwealth Fund.

Slide 2: Notice the marked variability in nuclear chromasia within the same 20x field. On the left side of the field, a more traditionally recognized hyperchromatic group is present. The cells on the right side of the field are markedly hypochromatic but their irregular nuclear outlines and high nuclear to cytoplasmic ratio are striking.

Slide 3: This photograph again illustrates that the degree of nuclear hypochromasia impacts only slightly on the ability to make a diagnosis of a High Grade Squamous Intraepithelial Lesion. Even from 20x, these cells appear clearly abnormal. They have irregularly distributed chromatin, high nuclear to cytoplasmic ratios, abnormally shaped nuclear membranes and are arranged in a loosely cohesive grouping, exhibiting a loss of polarity.

Slides 4, 5 and 6: Markedly abnormal cells are evident in these high power views (60x, 40x and 40x respectively), . Nuclear chromatin is clumped and irregularly distributed. The cells are discohesive and have high nuclear to cytoplasmic ratios. Depth of focus to the nuclei is another significant criteria that is represented by a "blurry" appearance in these two dimensional pictures. Under a microscope, the nucleus exhibits many different focal planes. Perhaps the most striking feature, however, is the extraordinary irregularity of the nuclear membranes.

Cytologic Diagnosis:

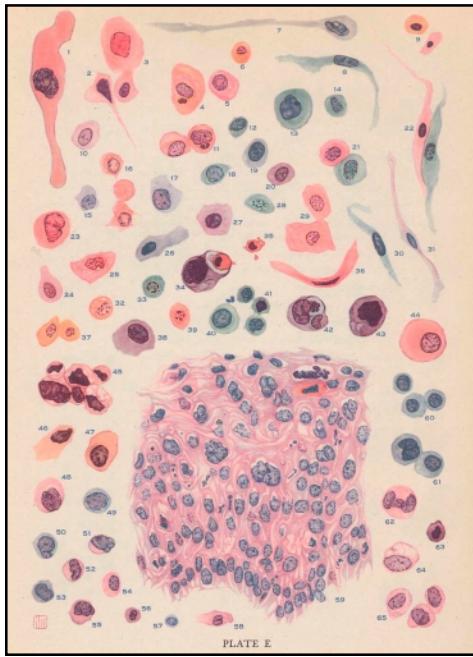
High Grade Squamous Intraepithelial Lesion: Severe Dysplasia/CIS/CIN III.

Histologic Diagnosis:

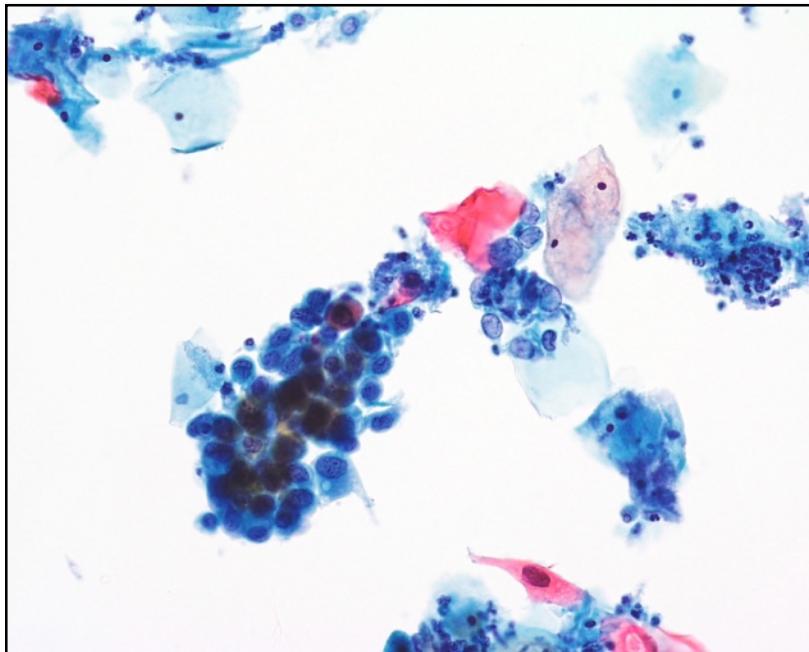
Cervical Biopsy showed CIN III with Human Papilloma Virus effect.

Small cells shed from moderate and severely dysplastic squamous intraepithelial lesions can pose diagnostic difficulty to even the most experienced cytologist. With the public's pursuit of legal action against laboratorians in recent years, these cells have been dubbed "litigation cells". However, a review of Papanicolaou's early color plates reveals that these cells have plagued diagnosticians for more than fifty years. Not only are they small, but very often, they can also be "pale" or hypochromatic. Contrary to what many believe, the so called "hypochromatic high-grade dysplastic cell" is not a new phenomenon. Dr. Papanicolaou's illustrations show great chromatinic and morphologic variability among dysplastic nuclei (see Slide 1). These cells present challenges to both our diagnostic and locator skills. This is of great significance, as the potential these lesions have for progressing and, ultimately, invading is substantial.

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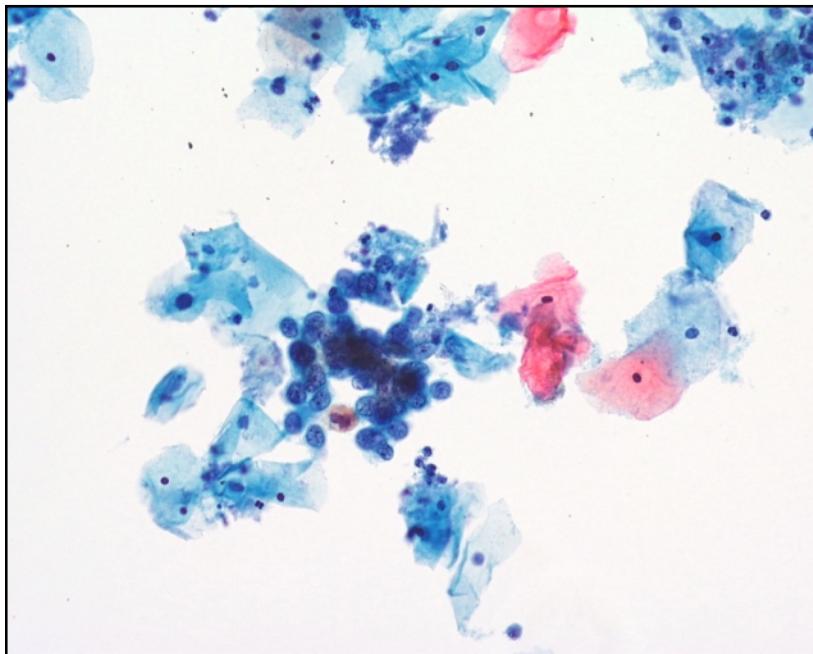


Slide 1

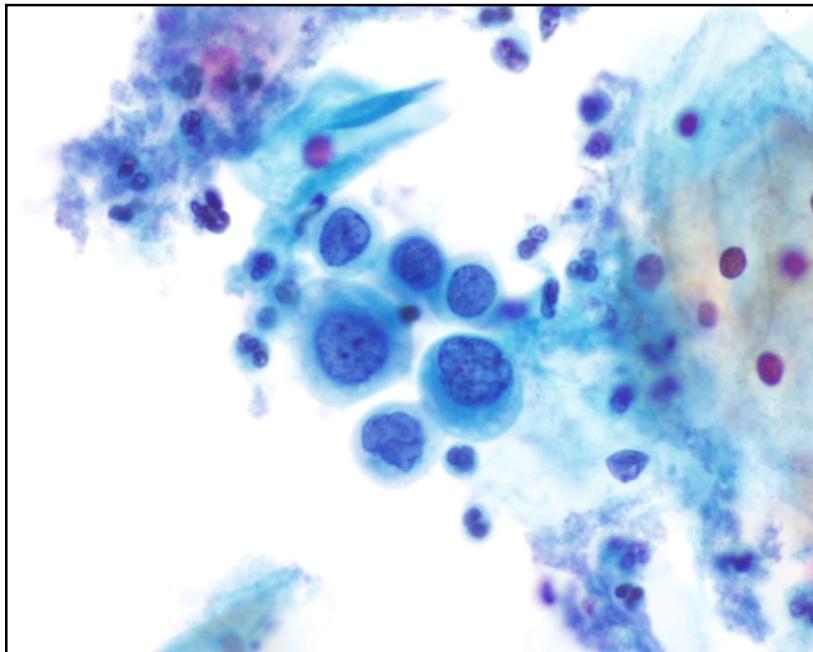


Slide 2 - 20x

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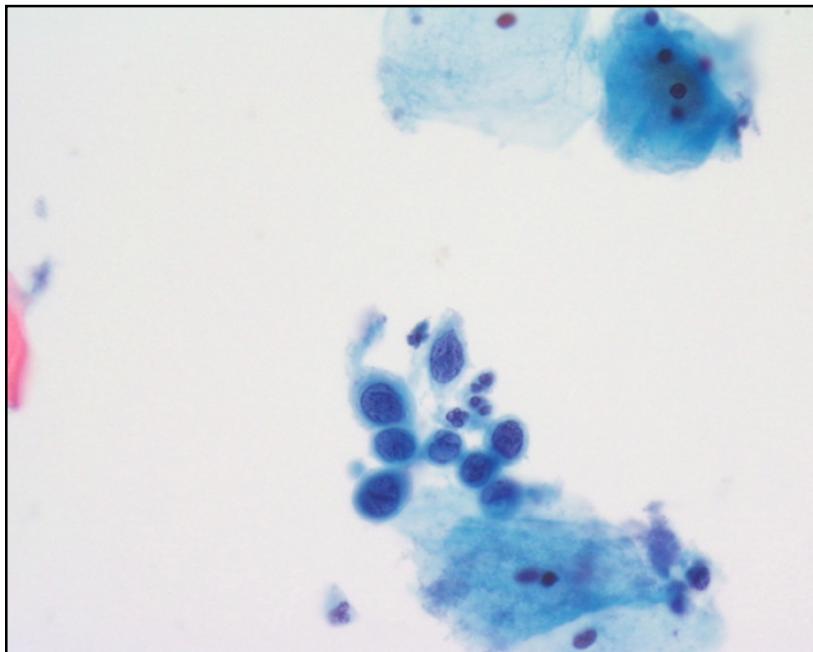


Slide 3 - 20x

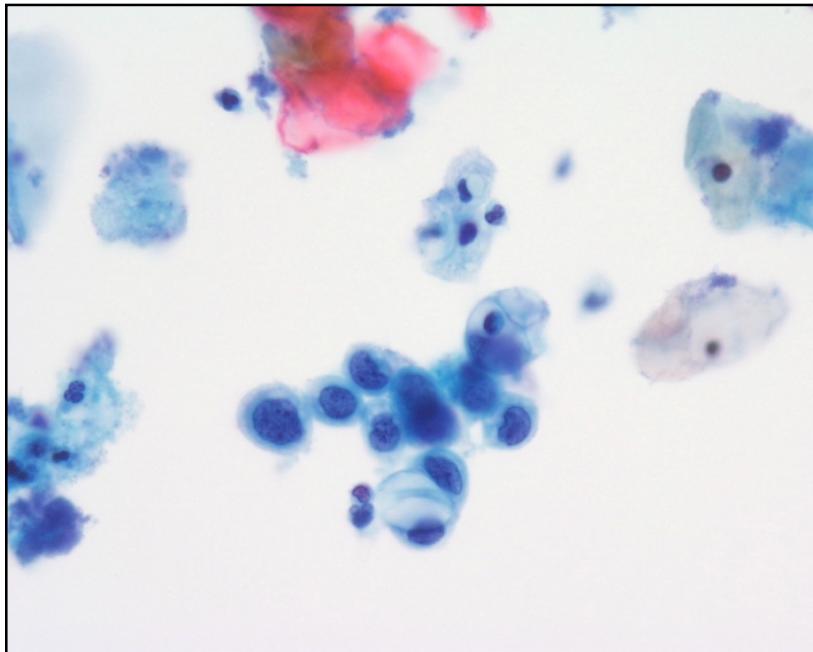


Slide 4 - 60x

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Slide 5 - 40x



Slide 6 - 40x

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As experts in light microscopy, cytologists have a vital appreciation and understanding for the visible changes within dysplastic nuclei. However, although the characterization of nuclear size, shape and chromasia are diagnostically significant, we very often fail to appreciate how these changes correspond to the processes taking place on the ultrastructural level. The nucleus is comprised of both heterochromatin and euchromatin. These two types of chromatin are intimately related, yet appear as distinct intranuclear entities. Heterochromatin is familiar to the cytologist as the dark visibly clumped material within the nucleus. It represents condensed, repressed chromosomal DNA. Its counterpart, euchromatin, is delicate and stains lightly. Euchromatin's microfibrils abound with cellular activity and represent extended DNA. Therefore, relative nuclear chromasia is more an expression of cell activity and differentiation than an artifactual anomaly. This concept is confirmed by the appearance of extremes of both hypochromasia and hyperchromasia within the same cervical sample, as illustrated in the above pictures. In a high grade squamous intraepithelial lesion, the presence of too many chromosomes within the nucleus causes enlargement and irregularity. Heterochromatin is often pushed to the nuclear margin (condensation), producing the effect we appreciate as a thickened nuclear membrane.

References:

- 1.) Childs, Gwen V. PhD. The Cell Nucleus II. <http://cellbio.utmb.edu/>
- 2.) Frenster, John H. Ultrastructure and Function of Heterochromatin and Euchromatin. <http://www.euchromatin.net>. From "The Cell Nucleus", vol. 1, pp 565-580, (1974), New York, Academic Press.
- 3.) Basic Histology. <http://www.pathguy.com>
- 4.) Sirica, Alphonse Ed. The Pathobiology of Neoplasia, Plenum Press, New York 1989.
- 5.) ThinPrep Pap Test Package Insert Rev. J.
In a multi-site, historically controlled study at ten institutions comparing 10,226 ThinPrep Pap Tests against 20,917 conventional pap smears, the ThinPrep® Pap Test™ showed a statistically significant 59.7% increase in the detection of high grade squamous intraepithelial and more severe lesions.
- 6.) Meisels, Alexander MD and Morin, Carol PhD. Cytopathology of the Uterus 2nd edition. ASCP Press, Chicago 1997.
- 7.) La Presse Médicale, Wednesday, April 11, 1928 (36: 451-454, 1928) Gynecologic Clinic of Bucharest (Professor C. Daniel) DIAGNOSIS OF CANCER OF THE UTERINE CERVIX BY SMEARS BY A. Babés Lecturer at the Faculty of Medicine of Bucharest
- 8.) Papanicolaou, George MD and Traut, Herbert MD. Diagnosis of Uterine Cancer By the Vaginal Smear. The Commonwealth Fund, New York, 1943. Plate E image used with permission by the Commonwealth Fund.