

Convegno on-line



20 • 21 • 22 ottobre 2021

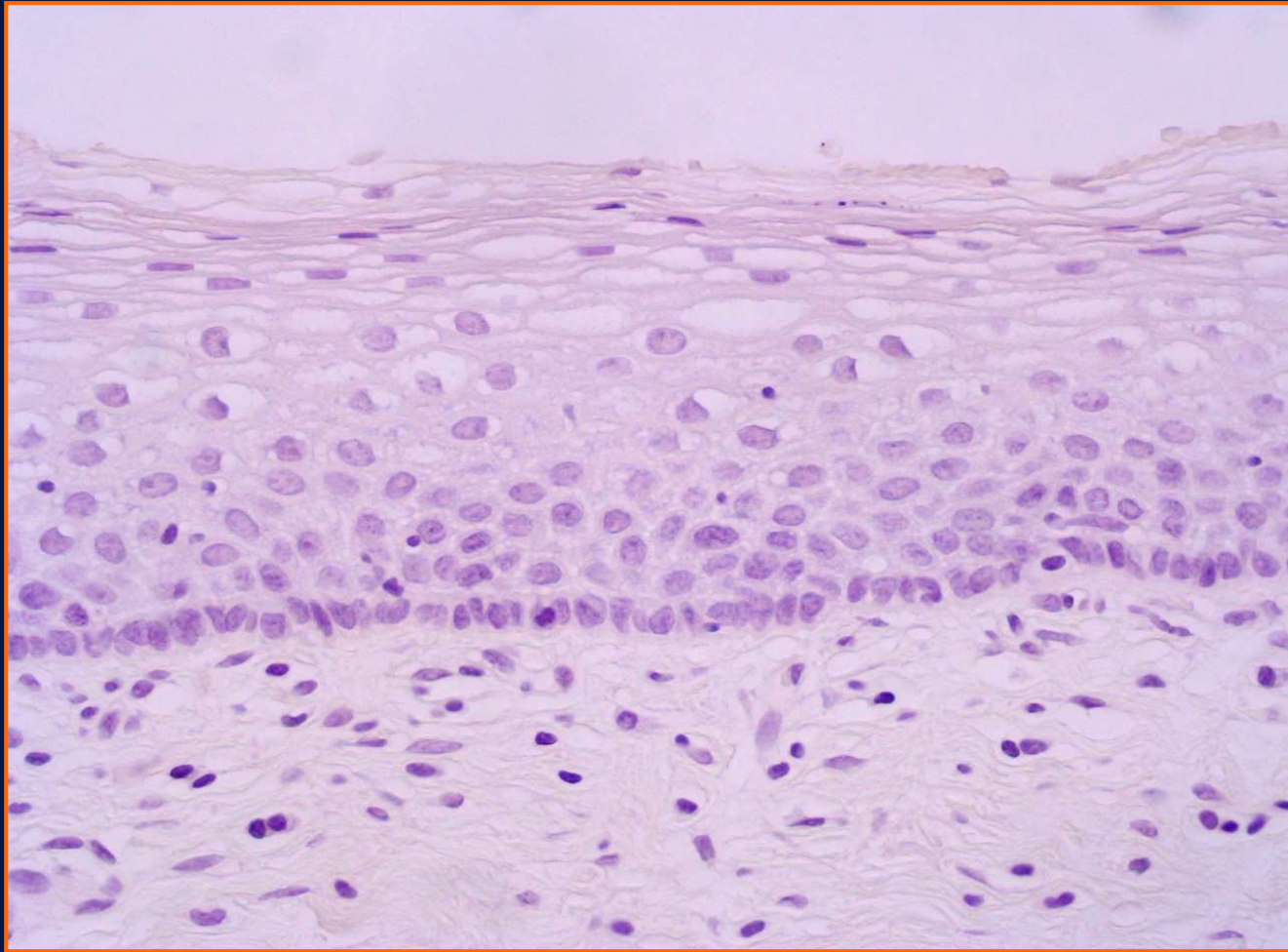
**CONVEGNO  
NAZIONALE  
GISCI 2021**

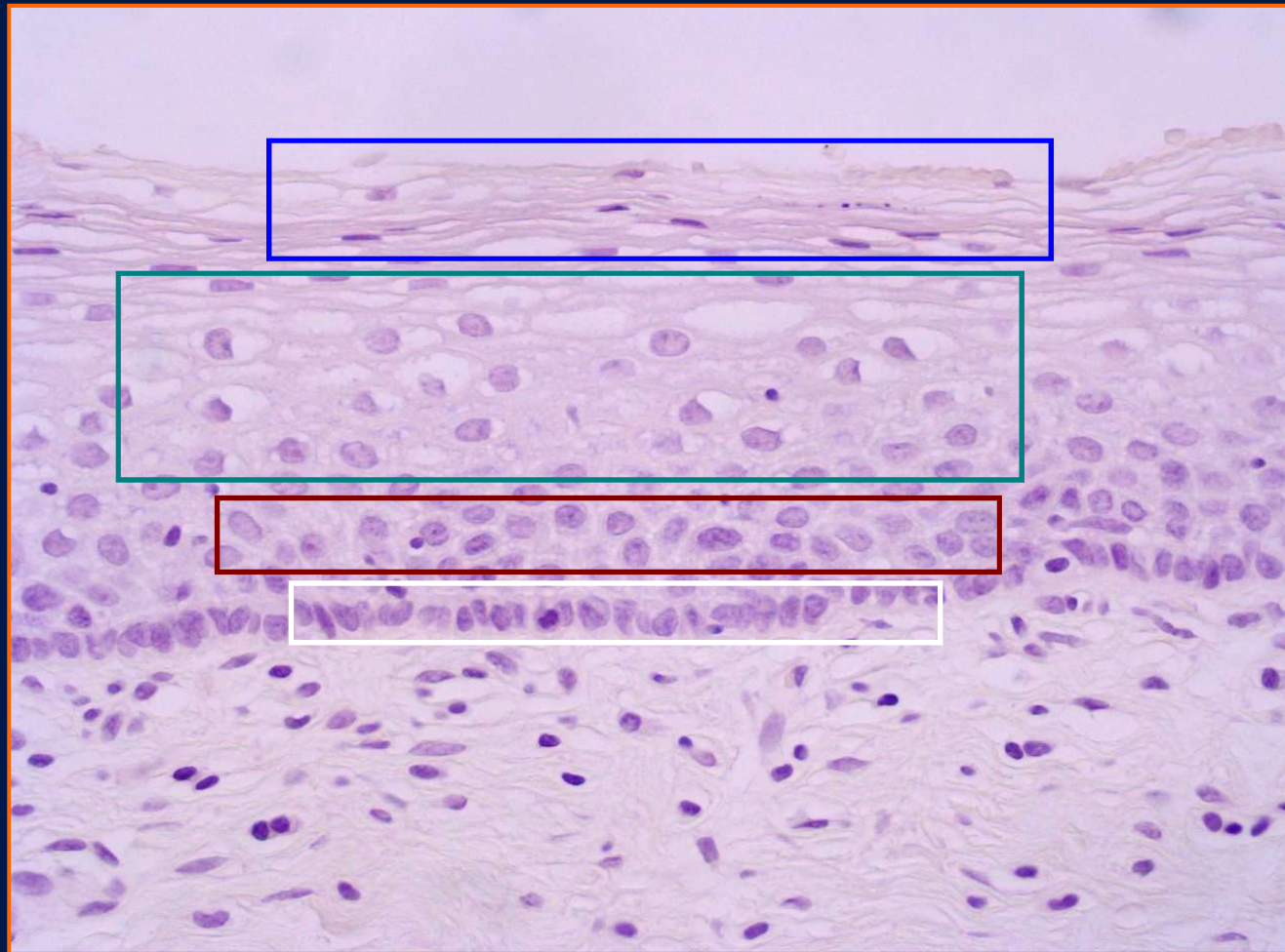
Screening con test HPV primario:  
riflessioni sui percorsi e gli effetti della pandemia

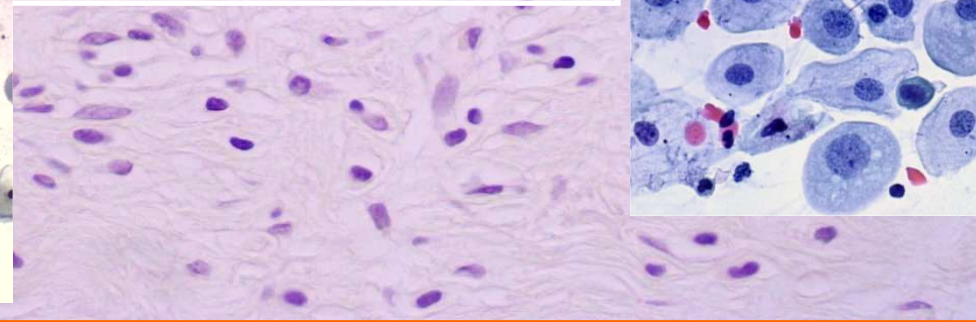
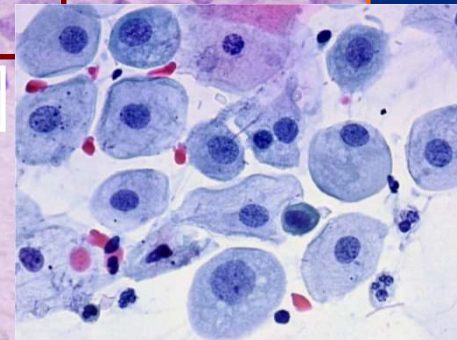
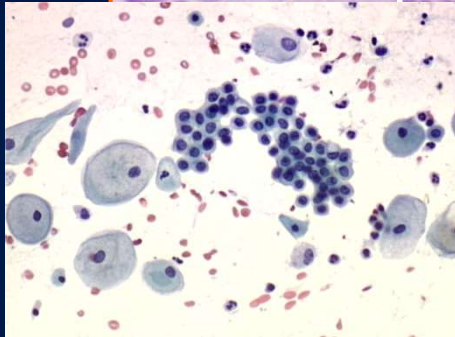
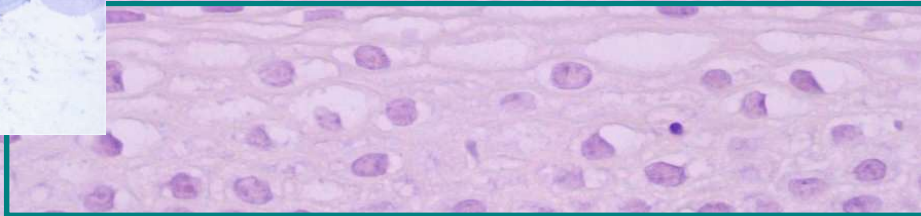
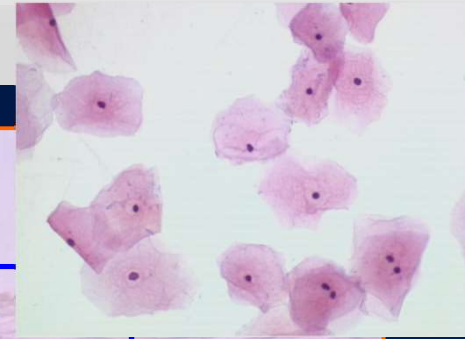
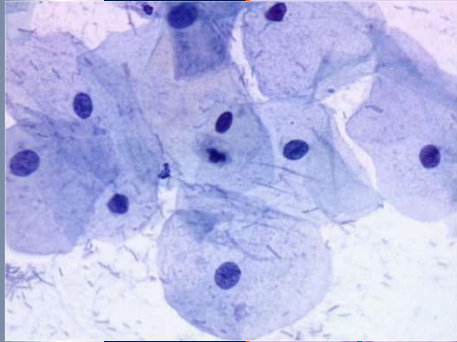
**GISCI**  
Gruppo Italiano Screening del Cervicocarcinoma

CIN 2 e regressione spontanea

*Galliano Tinacci*

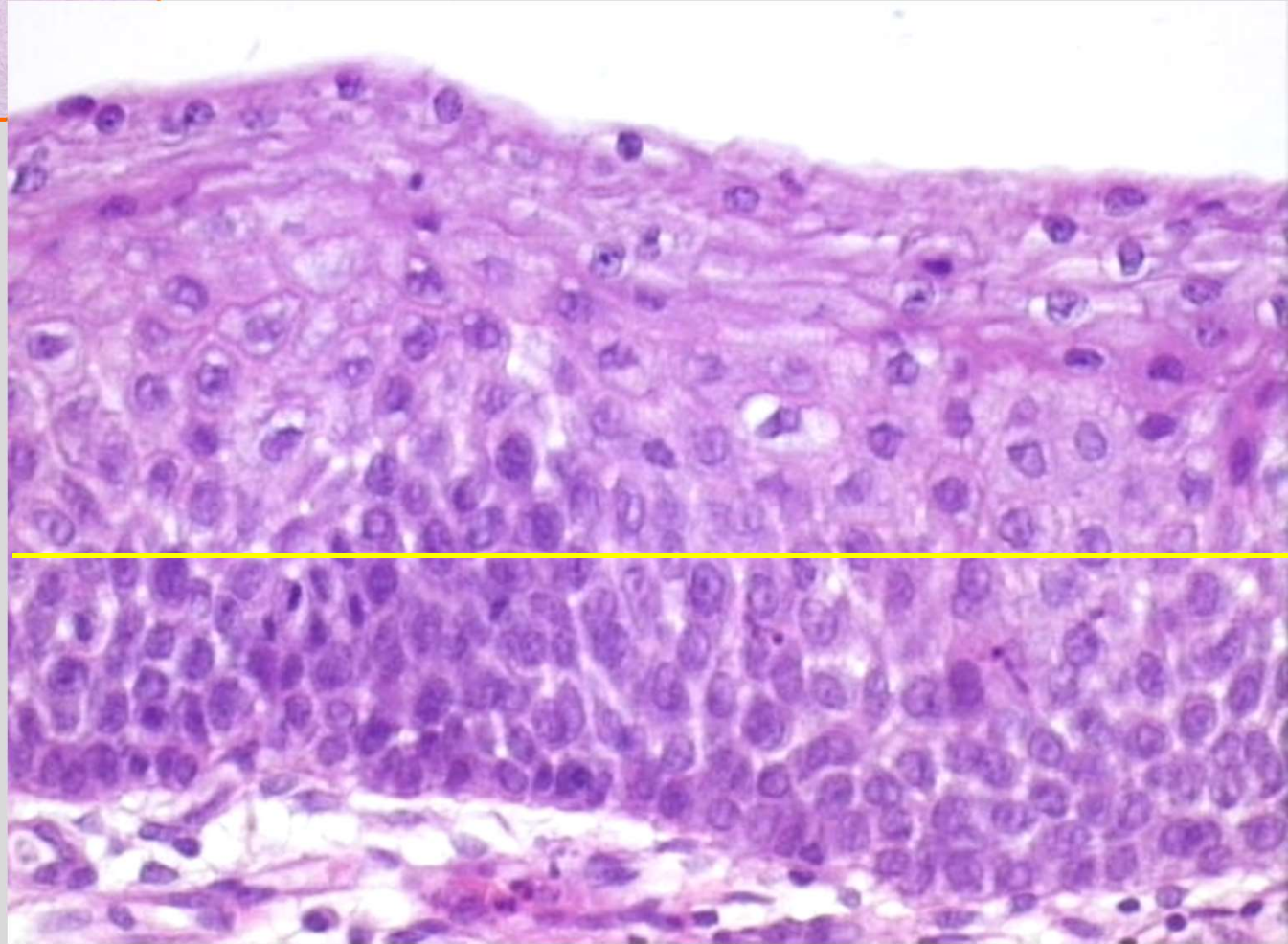
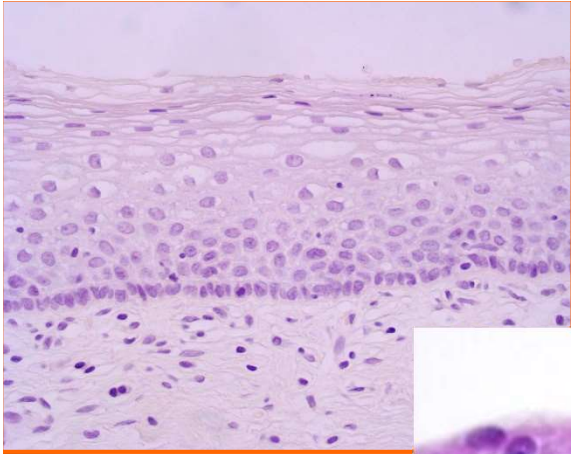


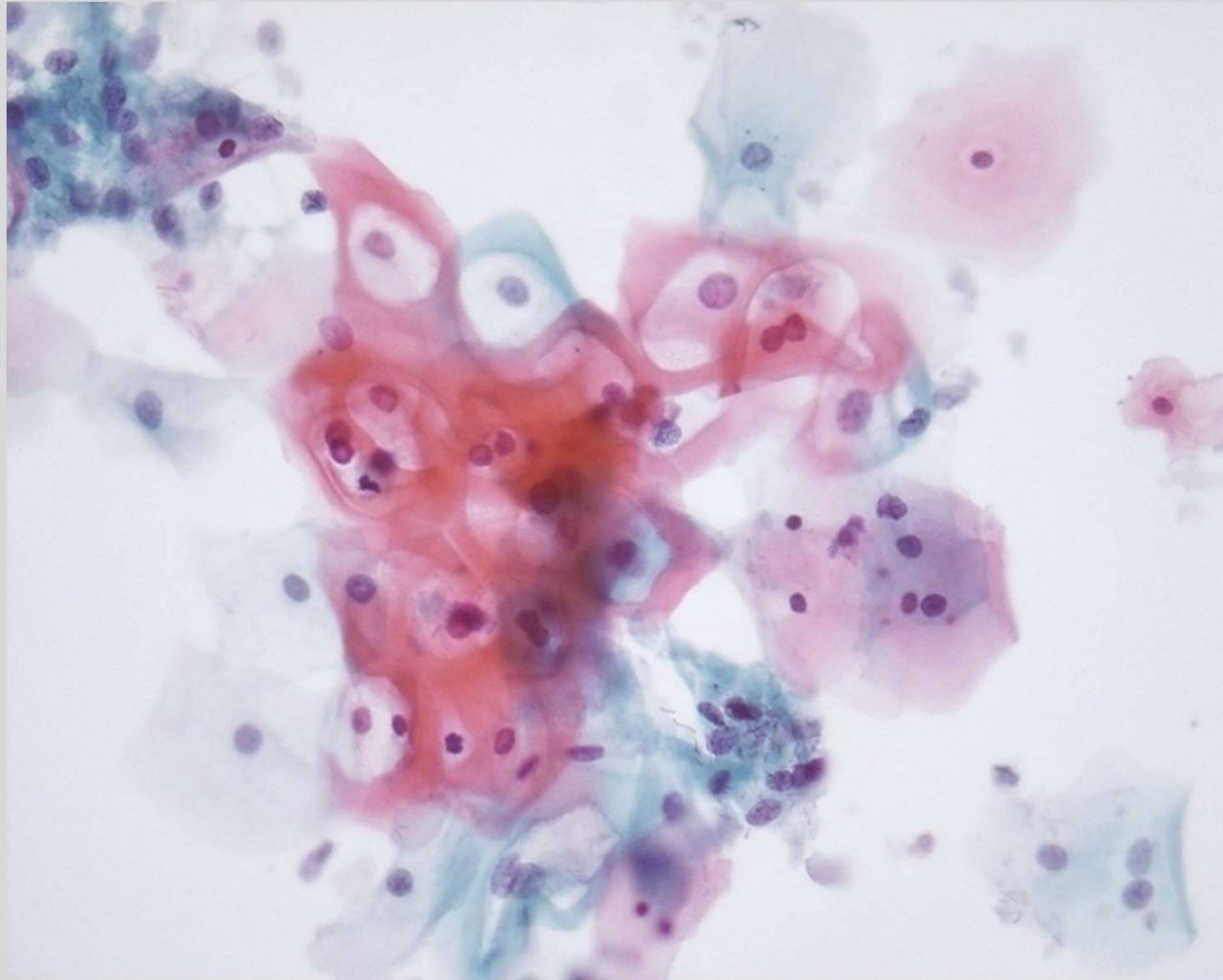


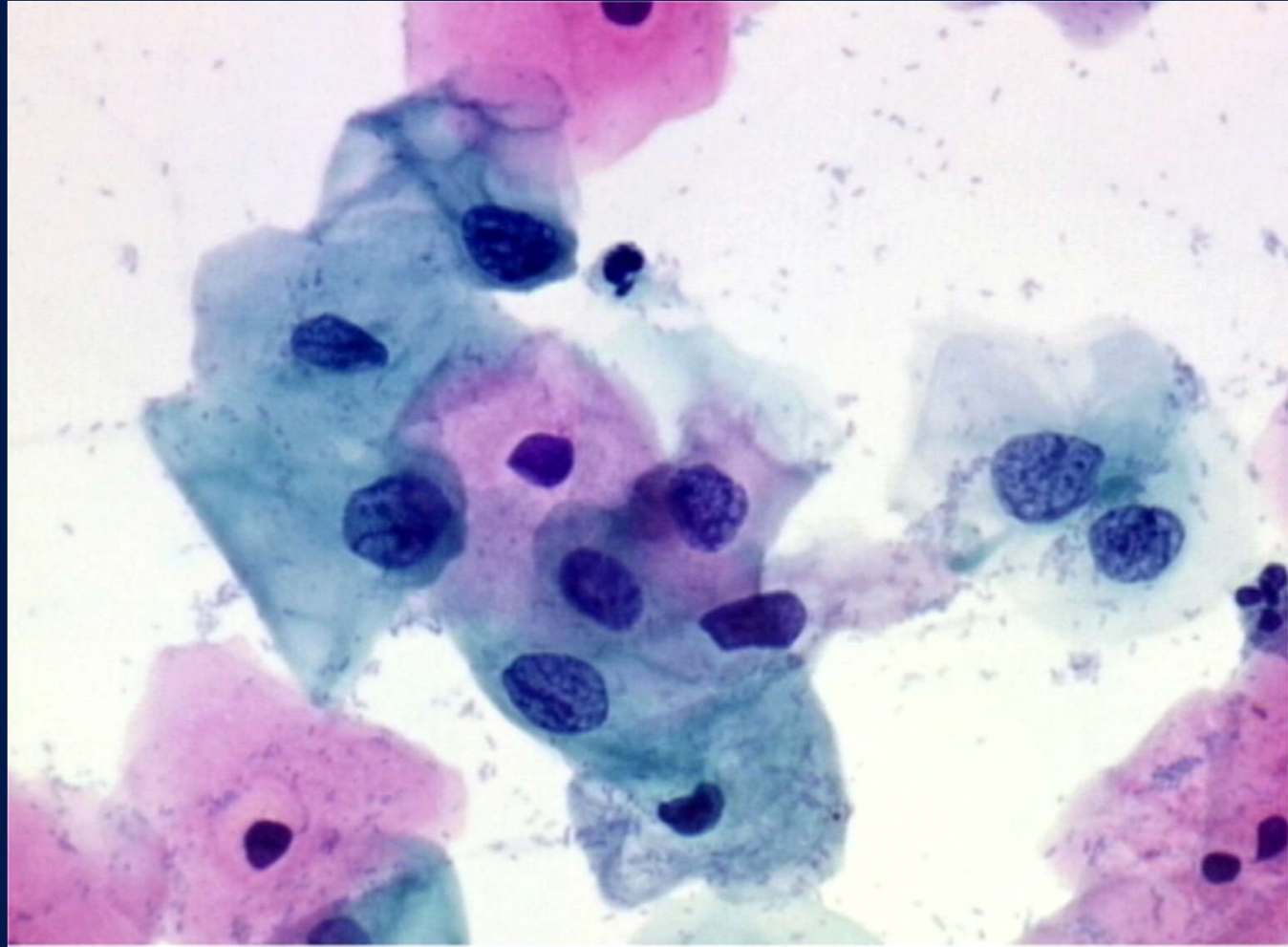


## **Definition**

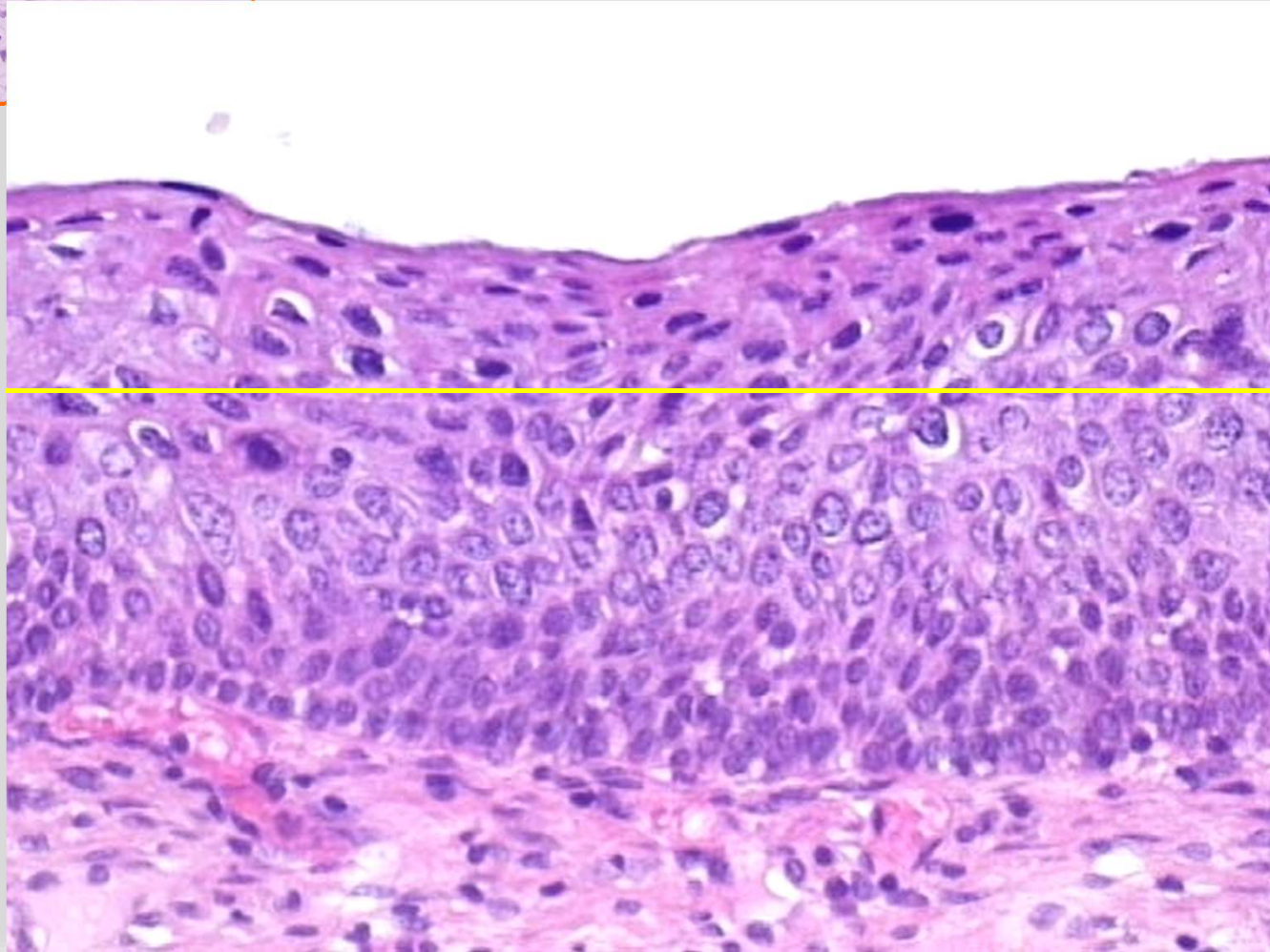
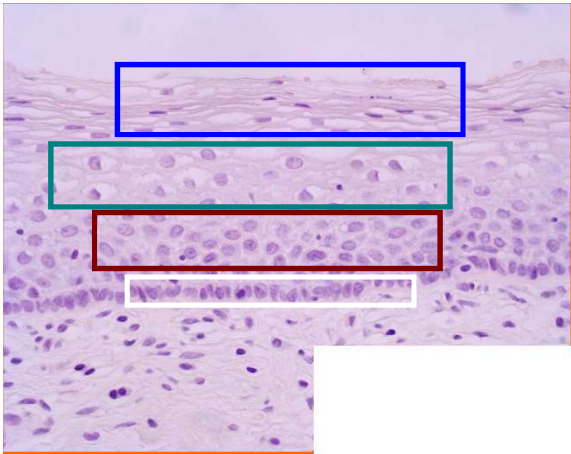
Squamous intraepithelial lesions (SILs) of the uterine cervix, also known as cervical intraepithelial neoplasia (CIN), are proliferations of squamous cells driven by HPV infection, showing maturation abnormalities and/or viral cytopathic changes that do not extend beyond the basement membrane. They are divided into low-grade SILs (LSILs) and high-grade SILs (HSILs).

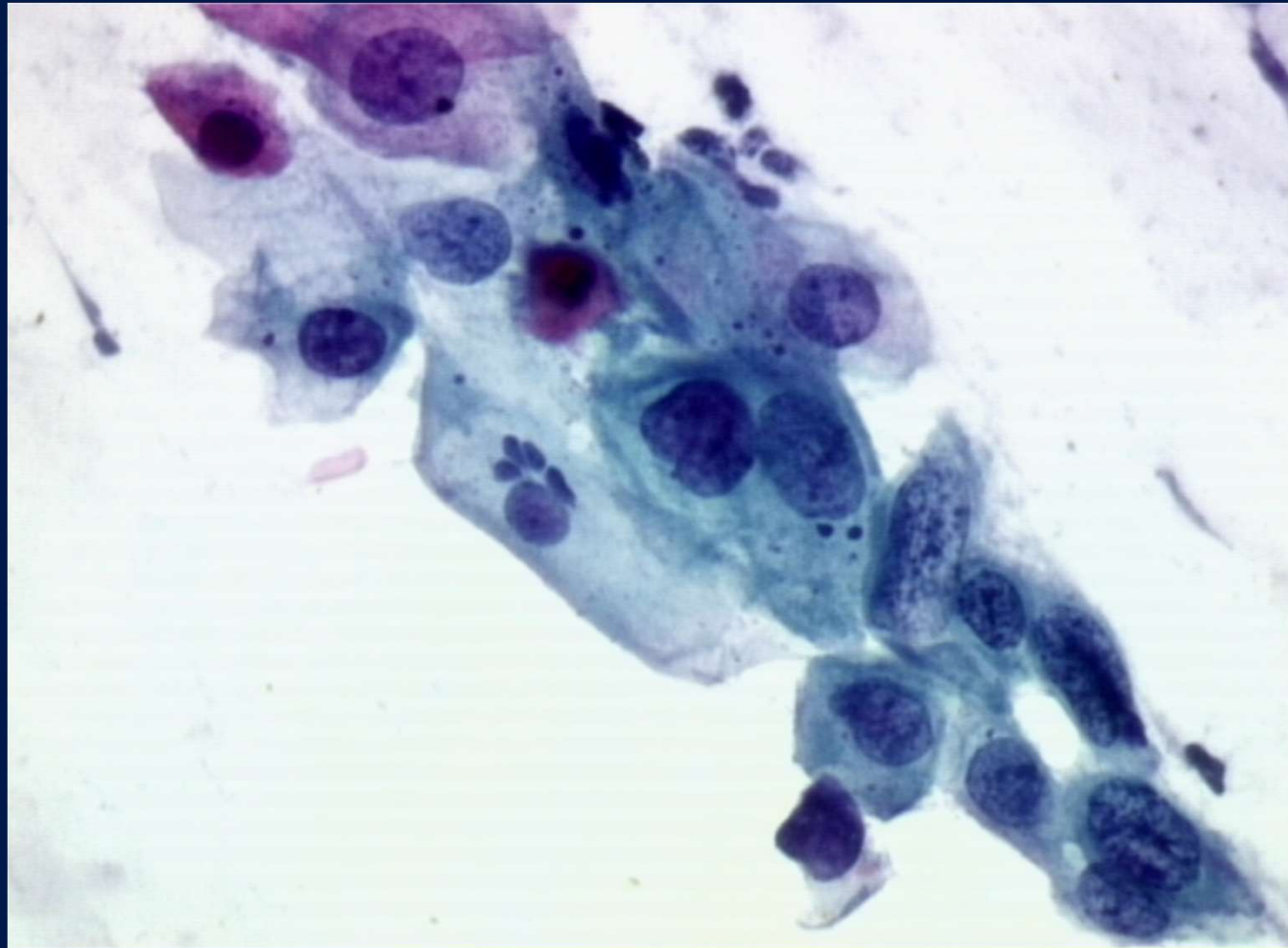


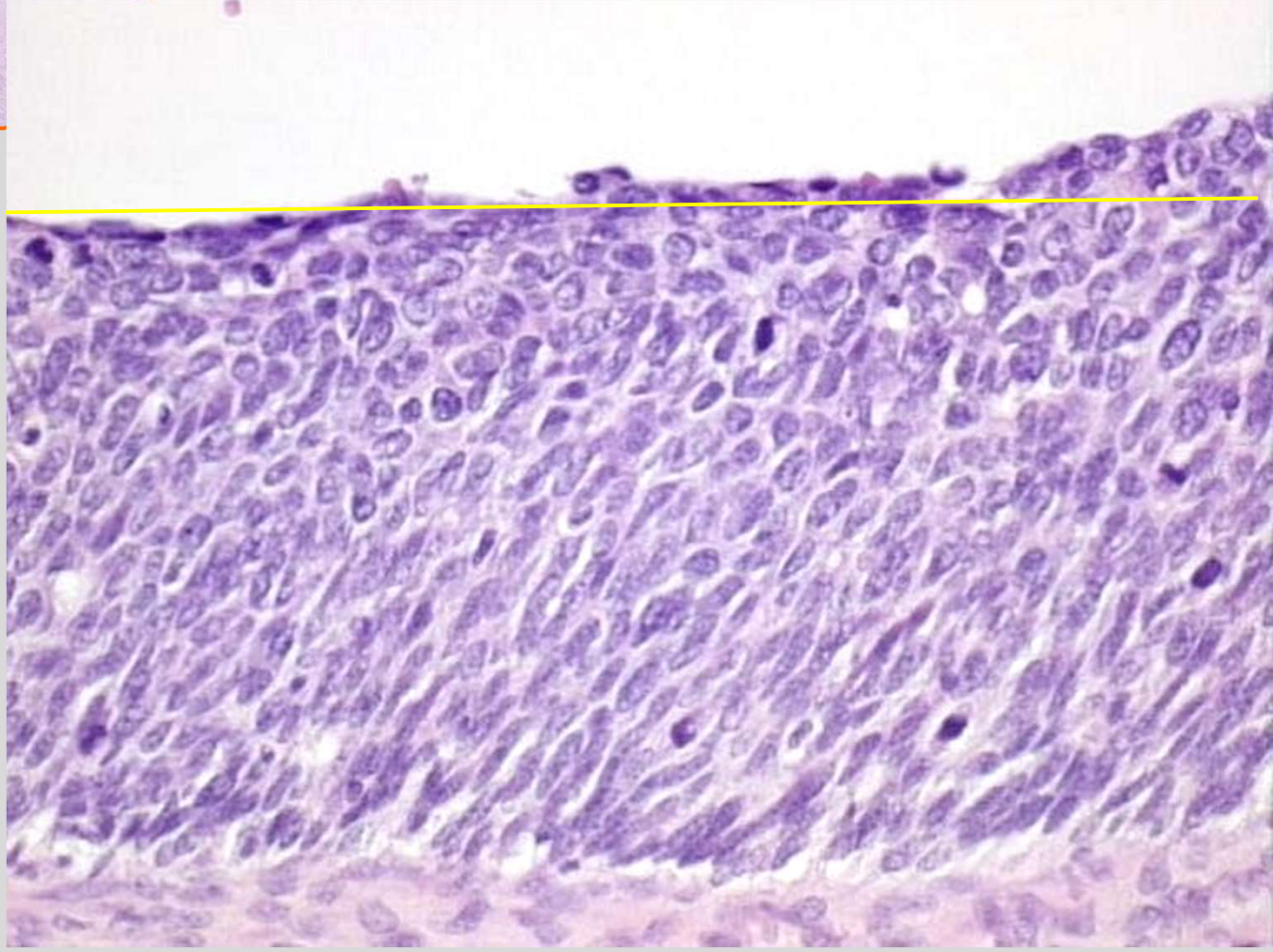
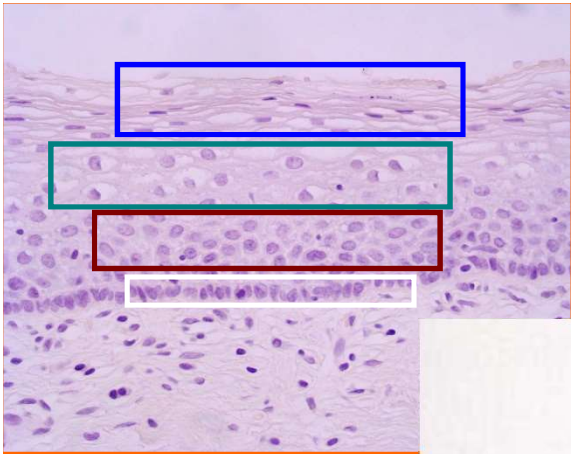


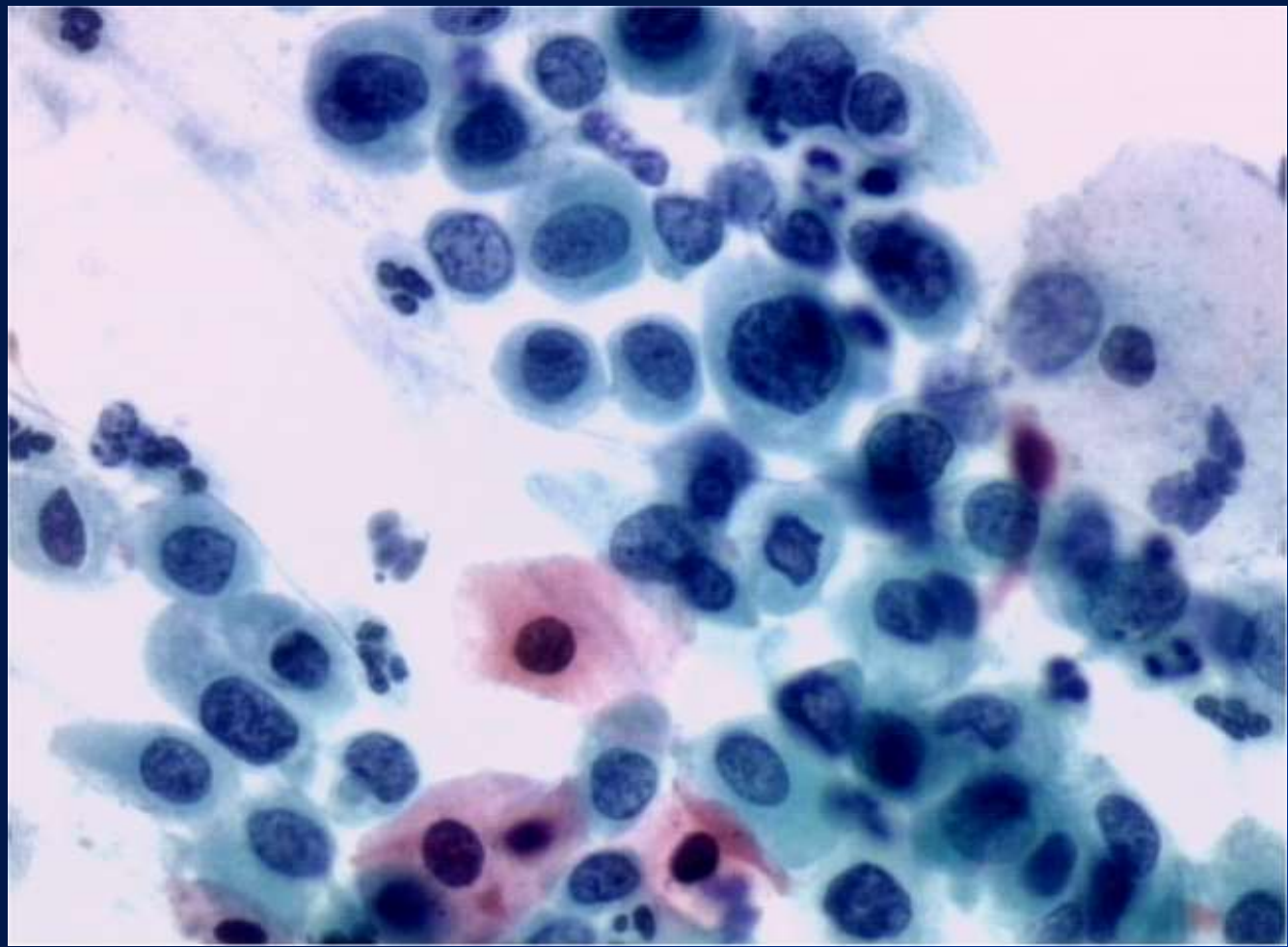


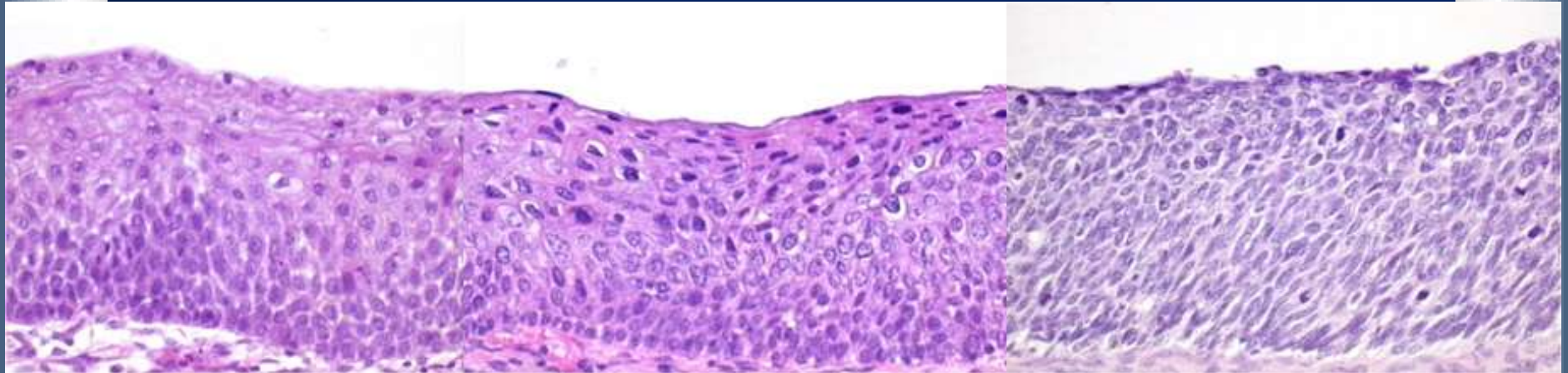















RESEARCH ARTICLE

# Conservative management of CIN2 p16 positive lesions in women with multiple HPV infection

Maria Teresa Bruno<sup>1\*</sup> , Guido Scalia<sup>2</sup>, Nazario Cassaro<sup>3</sup>, Maria Costanzo<sup>2</sup> and Sara Boemi<sup>1</sup>

**Conclusions:** With the progress of our understanding of the natural history of infection from human papillomavirus and the increasing use of colposcopy, thanks to the addition of HPV genotyping and the technique of immunohistochemistry, conservative management of these lesions is now possible.

**Keywords:** HPV infection, Multiple HPV infection, CIN2, p16 protein, Colposcopy, Laser-therapy, LEEP

Archives of Gynecology and Obstetrics  
<https://doi.org/10.1007/s00404-020-05853-3>

GYNECOLOGIC ONCOLOGY

# Factors predicting the spontaneous regression of cervical high-grade squamous intraepithelial lesions (HSIL/CIN2)

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However, it is acknowledged that CIN2 is a mix of biological CIN1 and CIN3, resulting from colposcopic biopsy sampling and pathologic interpretive variability. Therefore, in women who want to preserve their fertility, clinicians may request that pathologists distinguish HSIL (CIN2) from



Many guidelines, such as those in the USA, recommend conservative management for women under 25 years with CIN2

Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D (2007) 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus Conference. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. *Am J Obstet Gynecol* 197:346–355

A survey has been conducted by the British Society for Colposcopy and Cervical Pathology to assess current attitudes towards conservative management of CIN2. More than half of colposcopists recommend this approach but the lack of any formal guidance

Macdonald M, Smith JHF, Tidy JA, Palmer JE (2018) Conservative management of CIN2: national Audit of British Society for Colposcopy and Cervical Pathology members' opinion. *J Obstet Gynaecol* 38:388–394

In the French guidelines, conservative management is an option for women under 30 years with a small lesion by colposcopy. However, the threshold value of a given age (25 or 30 years) has not been established on solid evidence.

French National Cancer Institute (INCa) (2016) Management of women with abnormal cervical cytology. <https://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Summary-Management-of-women-with-abnormal-cervical-cytology>, Accessed 25 March 2020

The objectives of our study were thus to determine clinical, pathological and virological factors predicting the spontaneous regression of CIN2.

**Disappearance** of CIN2 was defined as the disappearance of initial colposcopic findings, and/or a normal cytology and/or a normal histology.

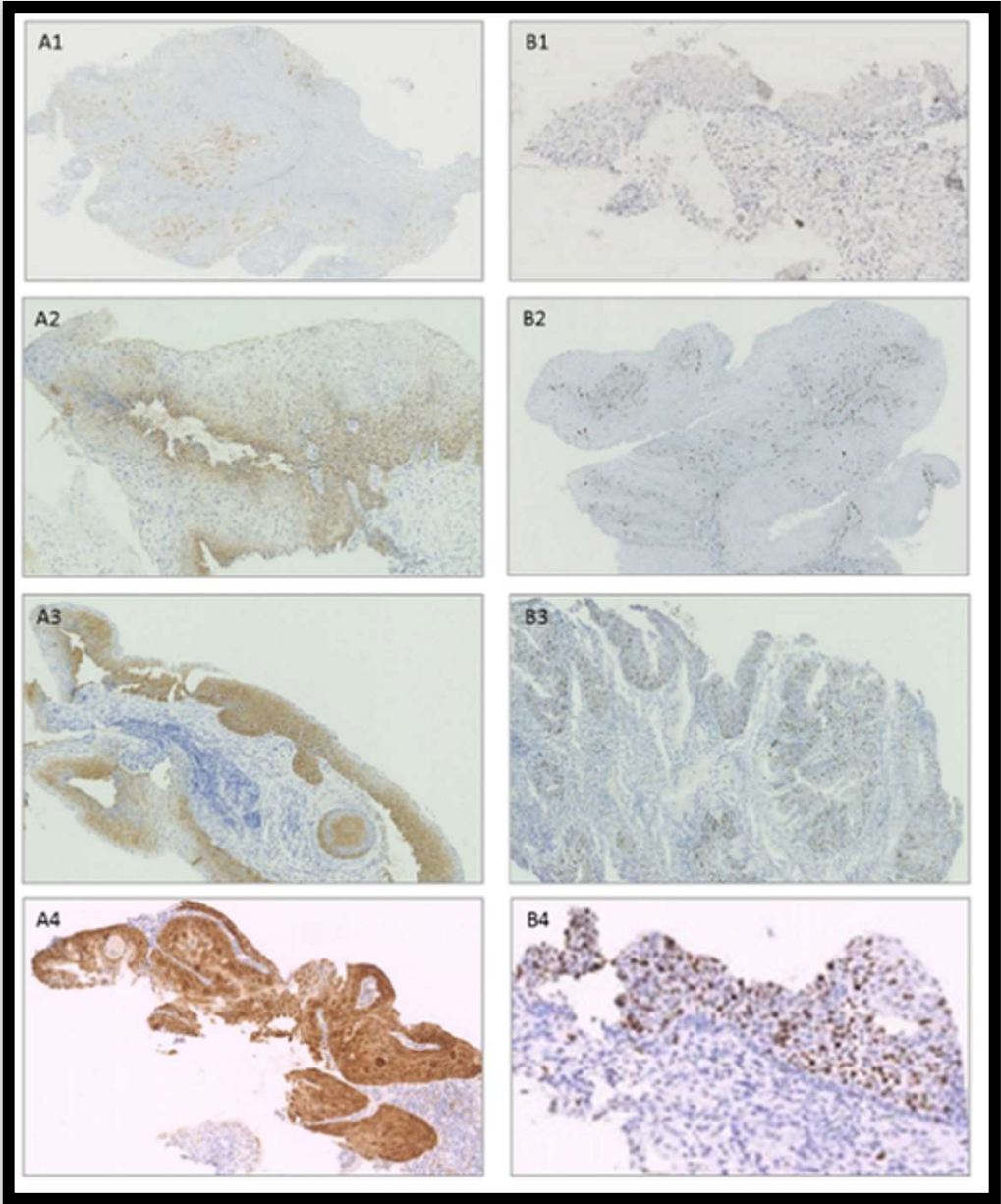
The **regression** of CIN2 was defined as the reduction in the severity of colposcopic findings (minor change or less), and/or the reduction in the severity of cytological results (low-grade squamous intraepithelial lesions (LSIL) or less) compared to the initial state and/or LSIL/CIN1 by histology.

The **persistence** of CIN2 was defined as no change by colposcopy, and/or cytology, and/or HSIL/CIN2 by histology.

The **progression** of CIN2 was defined as the diagnosis of HSIL/CIN3 + resulting from a biopsy guided by colposcopy (major change) and HSIL by cytology.

The review of all biopsies, except 3 which could not be transferred from outside, confirmed HSIL/CIN2 in 63 (90%) patients, downgraded to LSIL/CIN1 in 4 (6%) patients and upgraded to HSIL/CIN3 in 3 (4%) patients. The Cohen's kappa coefficient was  $\kappa = 90\%$  (95% CI 83–97) indicating almost perfect inter-observer agreement for the diagnosis of CIN2 performed inside or outside our institution.

P16 immunostaining scored 0 in 2 cases, 1 in 1 case, 2 in 20 cases, and 3 in 45 cases. Therefore, P16 was overexpressed (scores 2 and 3) in 65/68 (96%) of the biopsies. Ki67 immunostaining scored 0 in 1 case, 1 in 13 cases, 2 in 42 cases, and 3 in 9 cases. Therefore, Ki67 was overexpressed (scores 2 and 3) in 51/65 (78%) of the biopsies.

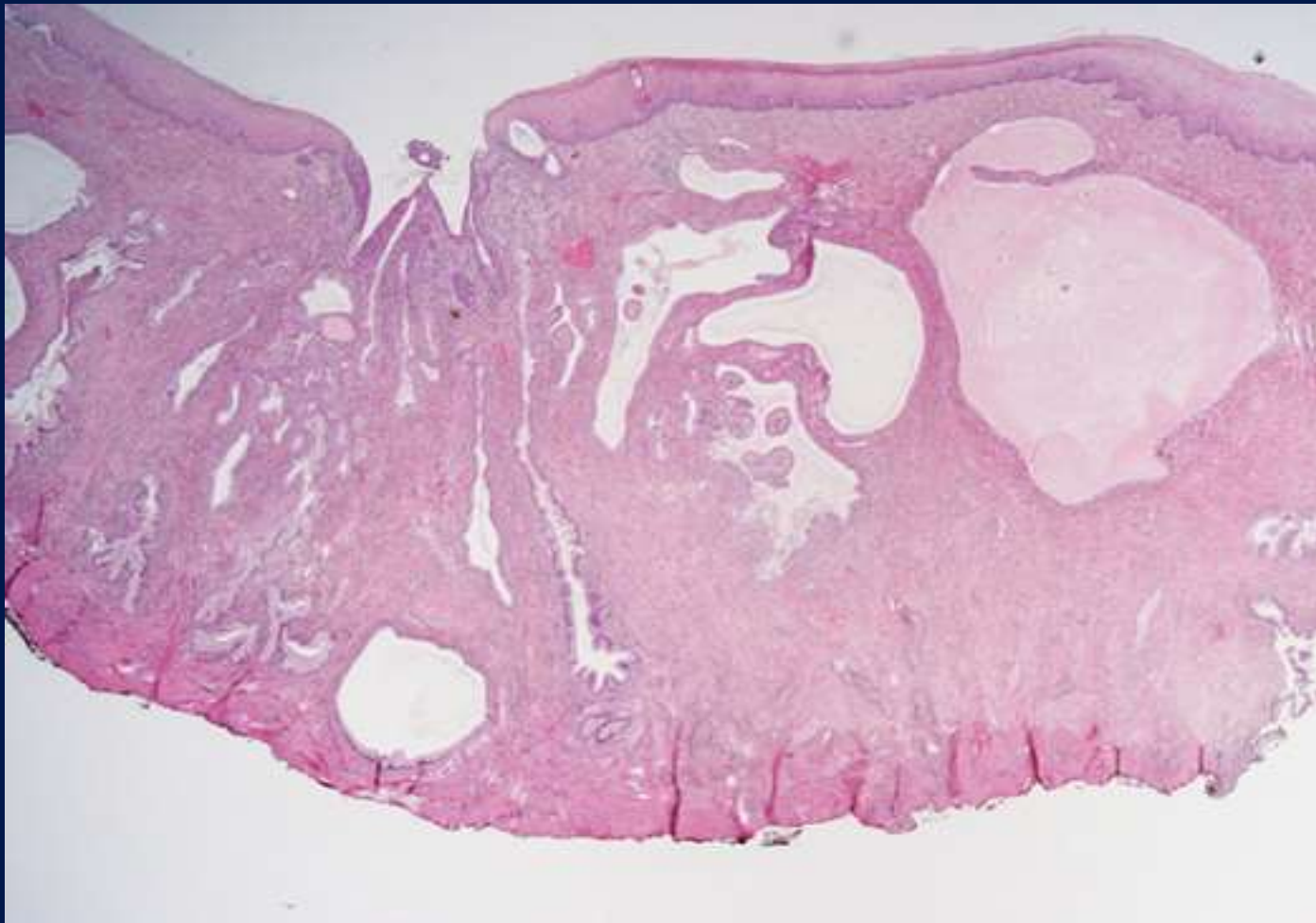


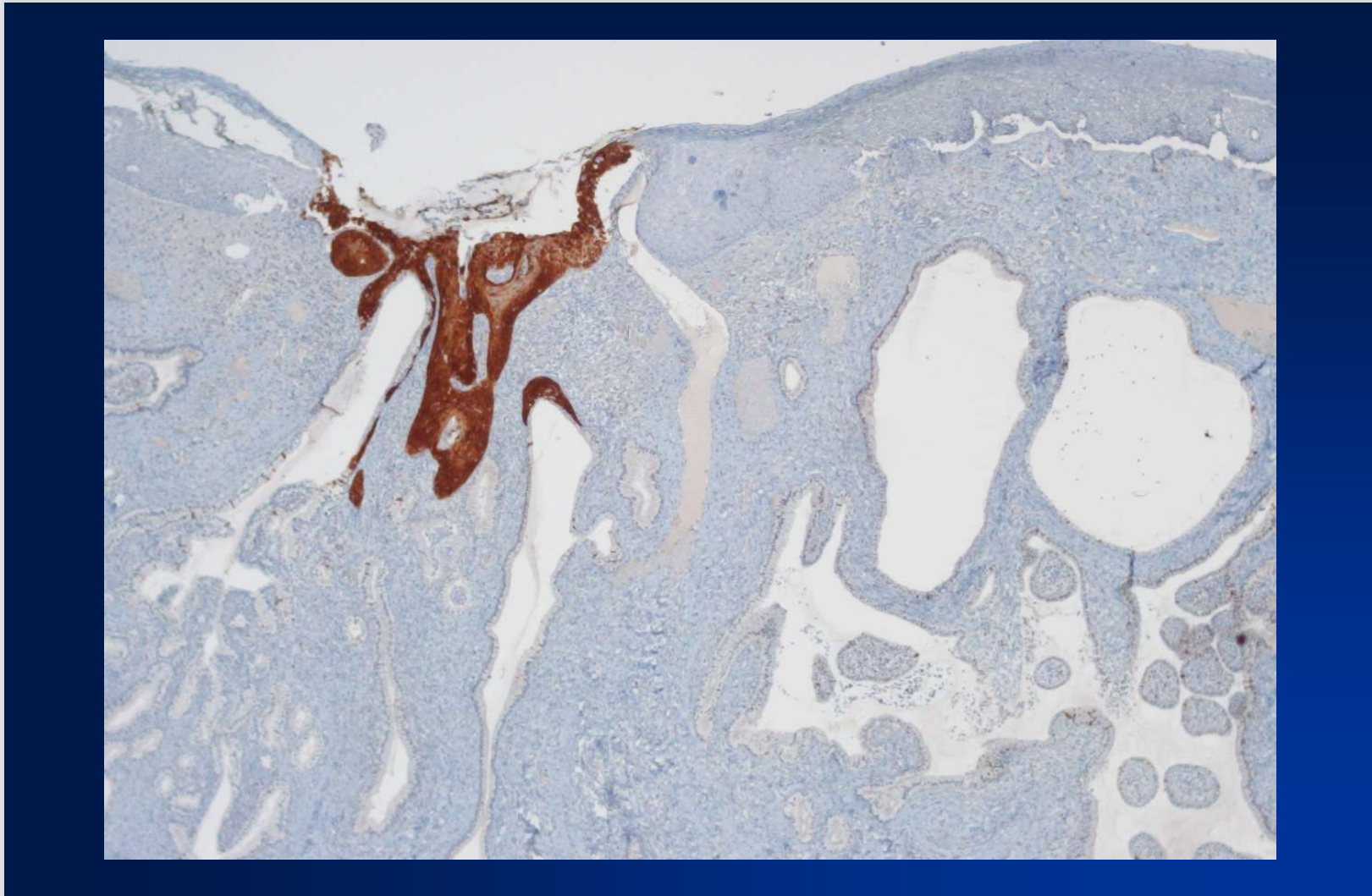


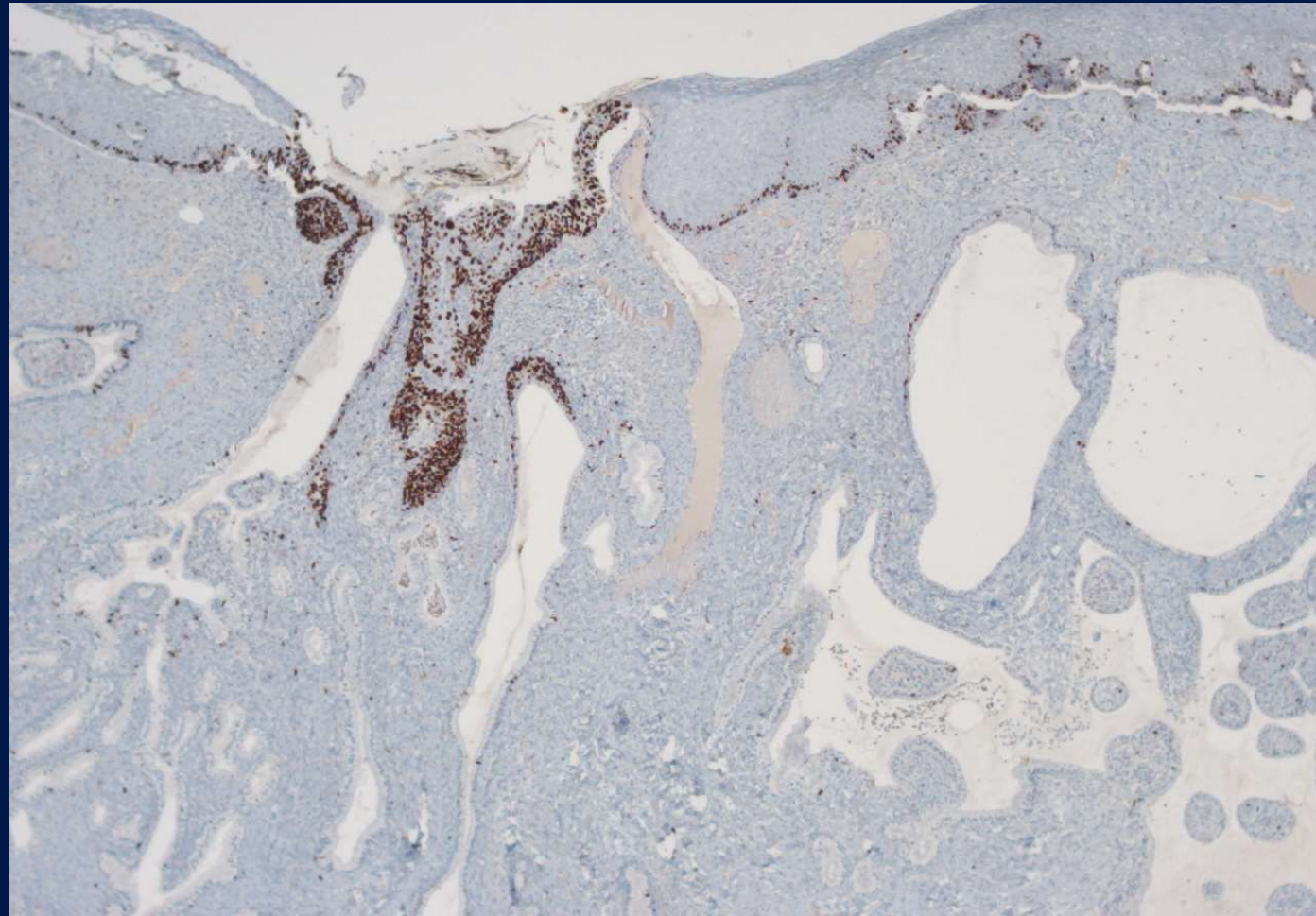
Patients with HPV 16 were less likely to respond: 42% with disappearance or regression of CIN2 vs 71% with persistence or progression ( $p = 0.027$ ). There was no difference in response rate between women with HPV-16 single infection (7/15) and women with HPV-16 multiple infections (8/17). All 4 patients with LR-HPV responded to conservative management.

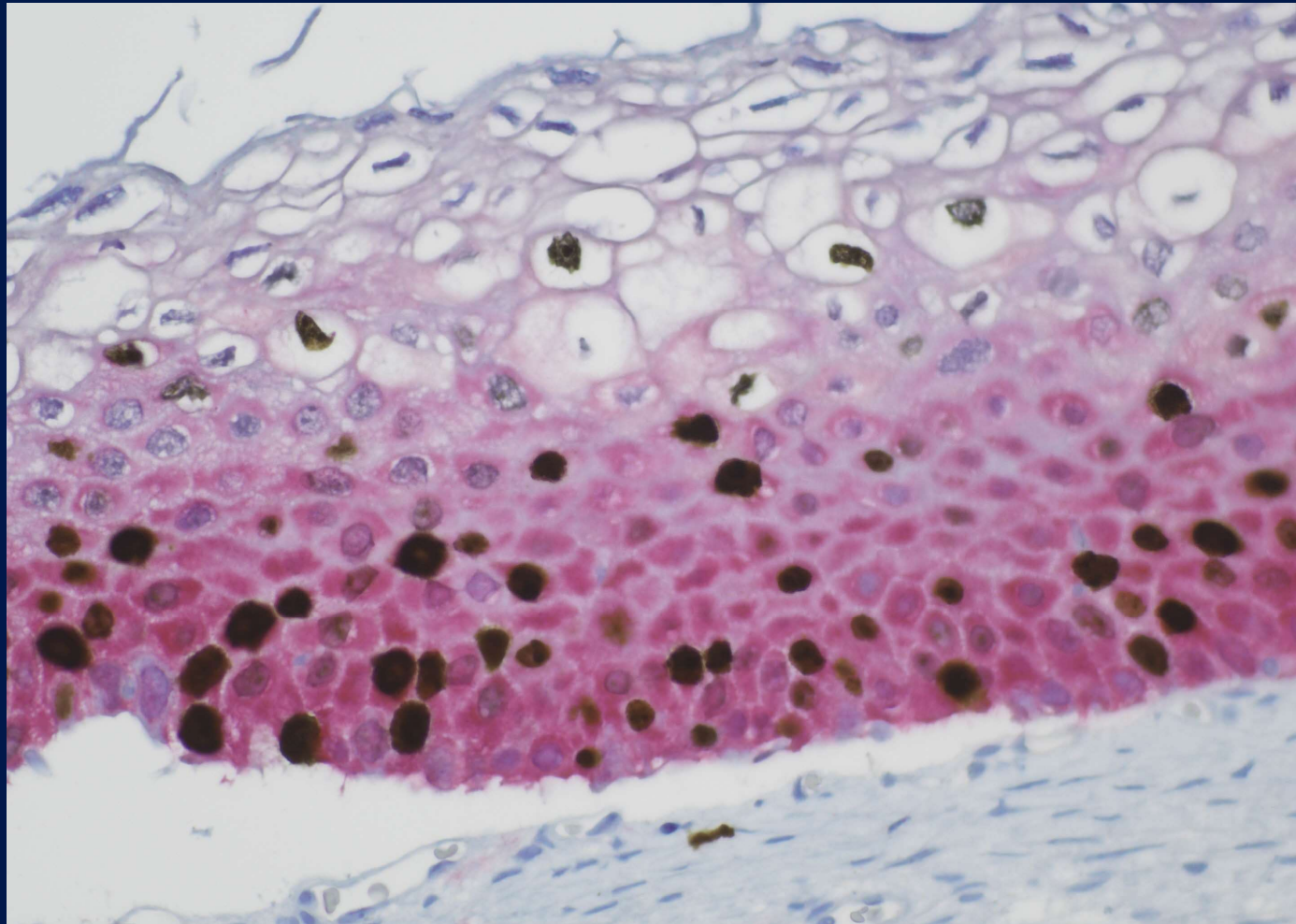
The lesion spontaneously disappeared in 11 (18%, 95% CI 10–30) patients, regressed in 25 (42%, 95% CI 29–55) patients, persisted in 15 (25%, 95% CI 15–38) patients and progressed in 9 (15%, 95% CI 7–27) patients. Thus the response rate to conservative management was 60% (95%

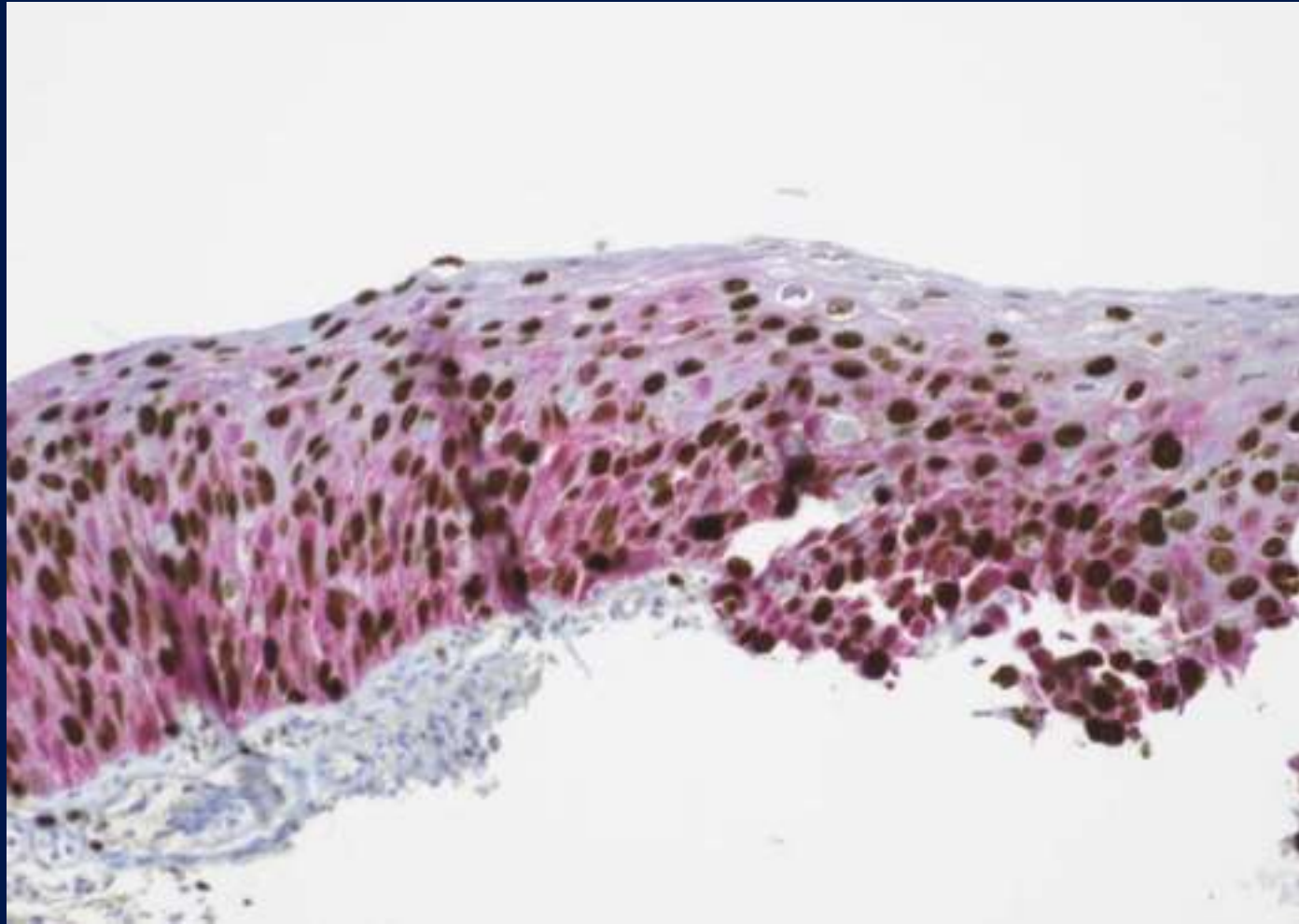
This study supports the practice of conservative management in women up to age 39 with CIN2, as the lesion will spontaneously regress in more than half of them. The colposcopist must be aware of clinical, pathological or virological prognostic factors which may predict the spontaneous regression of CIN2 or inversely the persistence or the progression. There is no risk of CIN2 progressing into cancer in women managed in colposcopy centers providing they respect the follow-up program.















Grazie