La Patologia preneoplastica cervicale

M. Barbero, V. Rabino

Corso di aggiornamento in Ginecologia e Ostetricia

Bologna 29-30 Settembre 2017

Treatment

Overtreatment

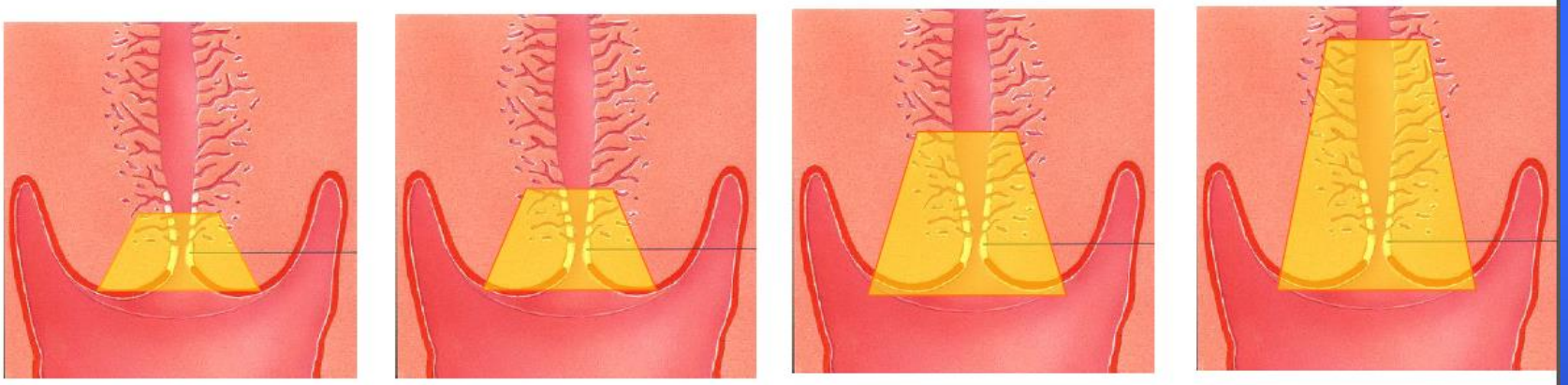
Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis

BMJ

Maria Kyrgiou,[1,2] Antonios Athanasiou,[3] Maria Paraskevaidi,[1] Anita Mitra,[1,2] Ilkka Kalliala,[1] Pierre Martin-Hirsch,[4,5] Marc Arbyn,[6] Phillip Bennett,[1,2] Evangelos Paraskevaidis[3]

2016

<10/12mm	**>10/12mm**	**>15/17mm**	**>20mm**
1.54 [1.09, 2.18]	1.93 [1.62, 2.31]	2.77 [1.95, 3.93]	4.91 [2.06, 11.68]



The treatment effect increased with increasing Tx cone length/volume…

Treatment significantly increased the risk of PTB irrespective of the comparison group used … But the magnitude of effect was different..

TRATTAMENTO DELLA CIN



TRATTAMENTO DELLA DONNA AFFETTA DA CIN

TERAPIA DELLA CIN

- < 25 anni
- > 50 anni
- in gravidanza
- nella donna immunodepressa

MANAGEMENT OF CIN

While some 60–70% of histologically spected cases will revert to normal over time, some 15% will persist.

Between 0% and 30% will ultimately reveal CIN2-3 and less than 1% will lead to invasive carcinoma.

Pertanto..

- Cautela nel decidere un trattamento
- Scegliere il trattamento meno invasivo
- Terapia efficace
- Follow up necessario

MANAGEMENT OF CIN > 50 ANNI

- La zona di trasformazione tende a ritrarsi entro l'endocervice in più del 40% delle donne sopra i 50 anni.
- L'epitelio squamoso diviene atrofico
- Viene persa la glicogenazione
- Frequente stenosi dell'OUE

↓

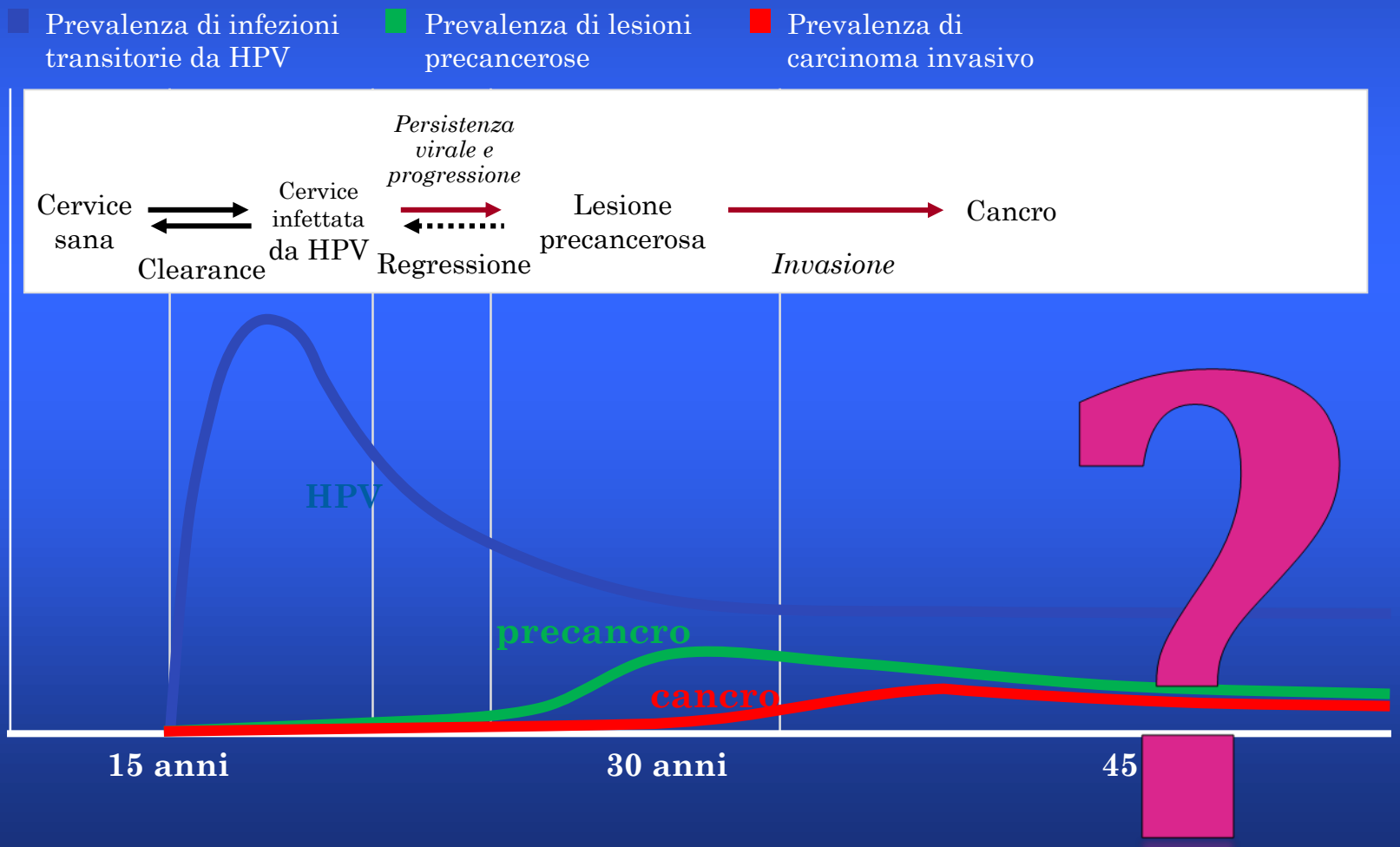
COLPOSCOPIA NON CONCLUSIVA



Pertanto..

- Ripetizione PAP TEST
- Colposcopista esperto
- Terapia estrogenica locale
- Trattamento escissionale
- Ago
- Follow-up intensivo

STORIA NATURALE DEL CERVICOCARCINOMA



Cochrane Database of Systematic Reviews

The Cochrane Library, Copyright 2010,

The Cochrane Collaboration

Surgery for cervical intraepithelial neoplasia

2014 The Cochrane Collaboration

Types of intervention

1) Laser Ablation
2) Laser Conisation
3) LLETZ
4) Knife Conisation
5) Cryotherapy

Conclusions

Implications for practice

The evidence from the 29 RCTs identified suggests that there is no obvious superior surgical technique for treating cervical intraepithelial neoplasia in terms of treatment failures or operative morbidity.

LLETZ appeared to provide the most reliable specimens for histology with the least morbility

Characteristics and Morbidity

1) Duration of treatment
2) Peri-operative severe pain
3) Peri-operative severe bleeding, primary and secondary haemorrhage
4) Depth and presence of thermal artifact
5) Adequate colposcopy at follow-up
6) Cervical stenosis at follow-up

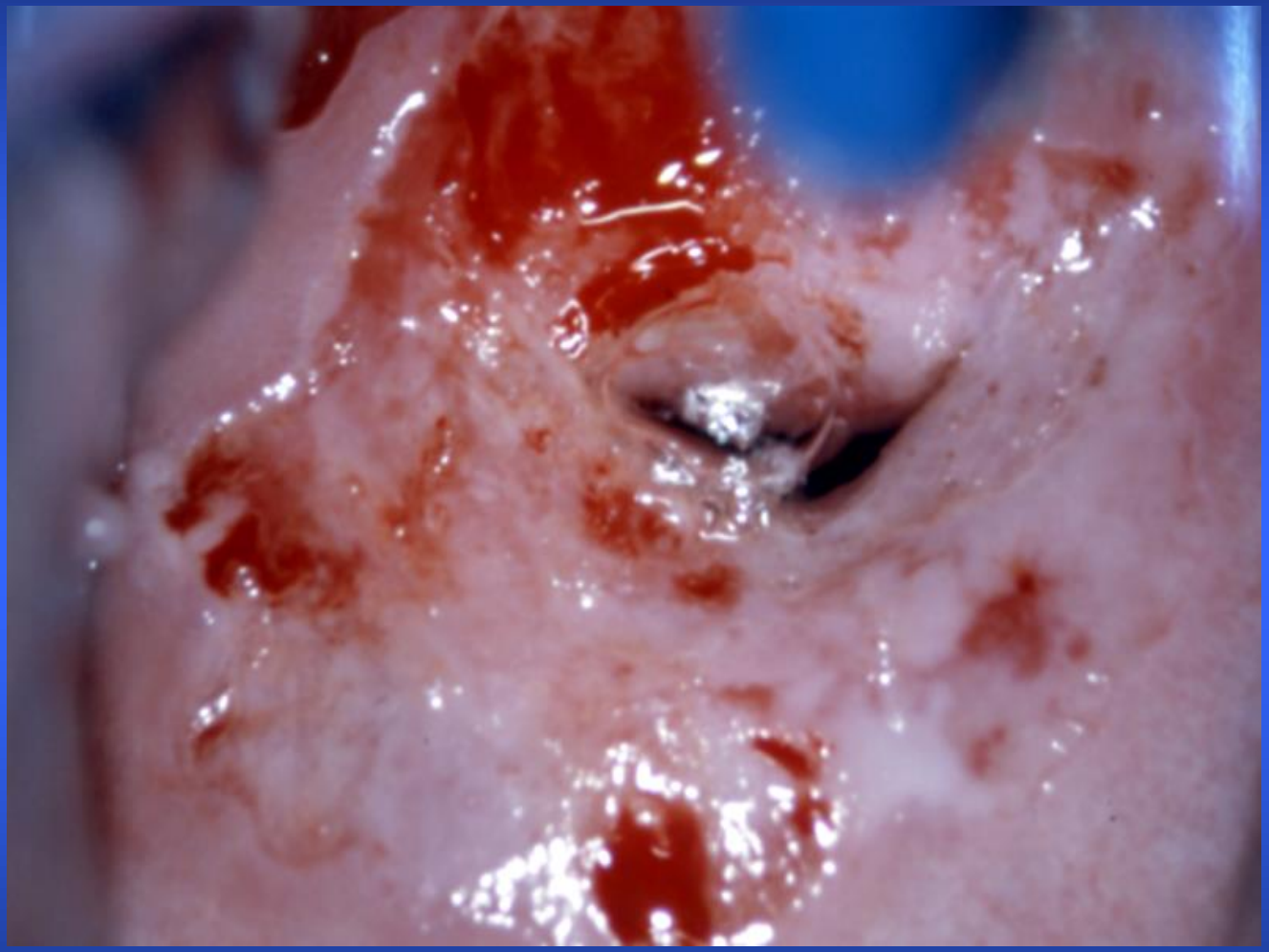
REQUISITI PER IL TRATTAMENTO DISTRUTTIVO

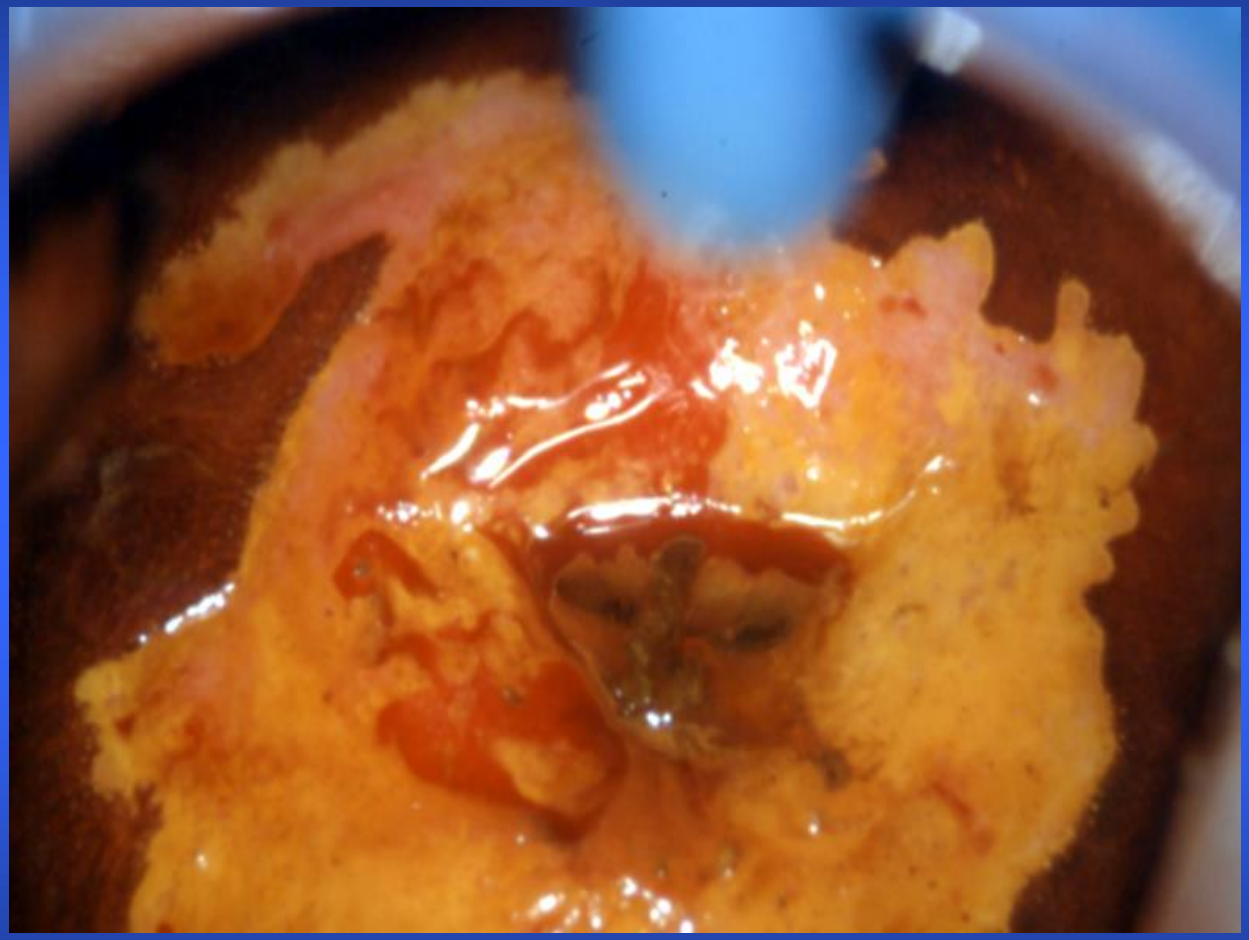
1) Zona di trasformazione interamente visibile (colposcopia soddisfacente)
2) No sospetto di microinvasione o invasione
3) No sospetto di malattia ghiandolare
4) Corrispondenza tra citologia ed istologia

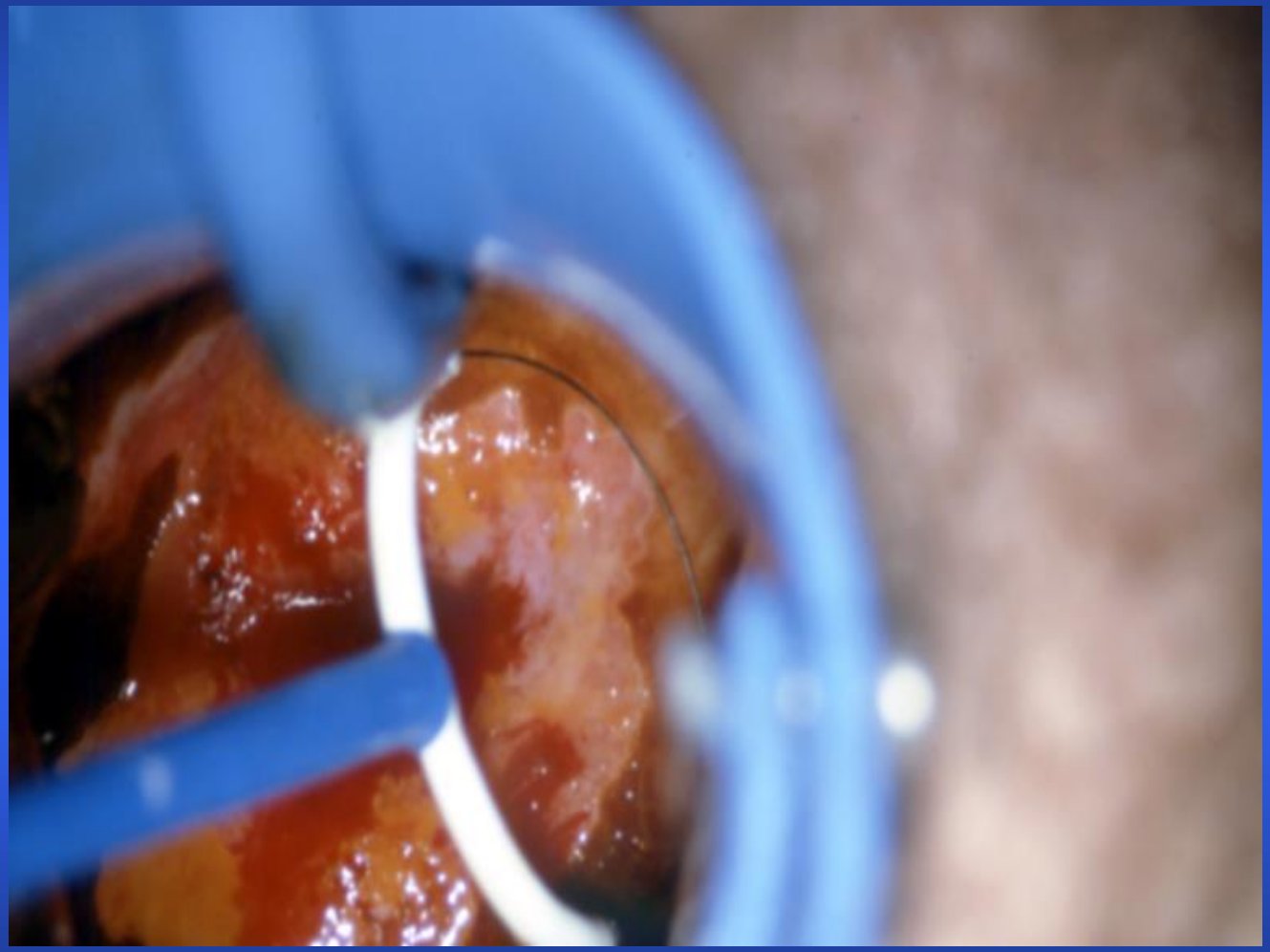
The Cochrane Database of Systematic Reviews, 2004

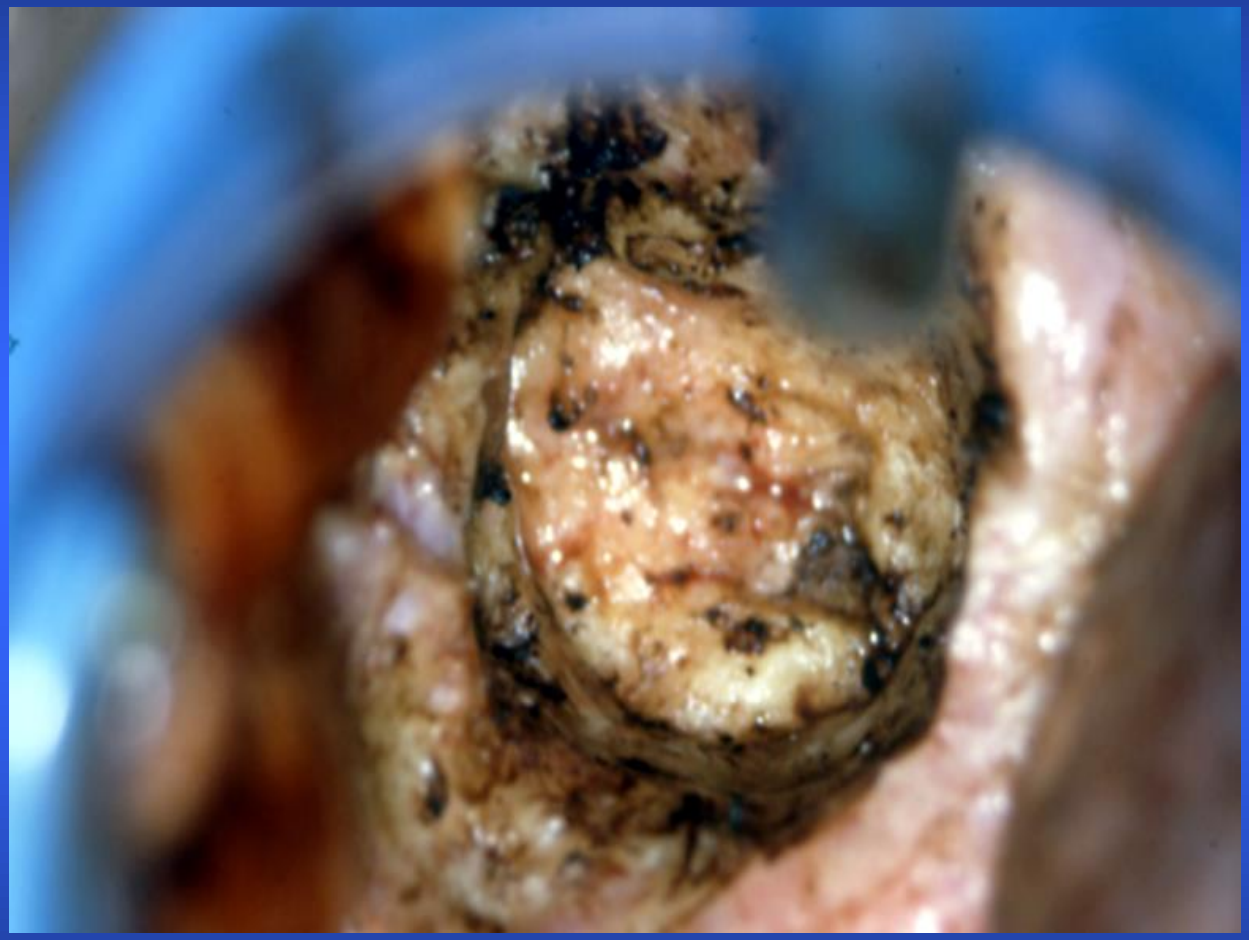
Surgery for cervical intraepithelial neoplasia

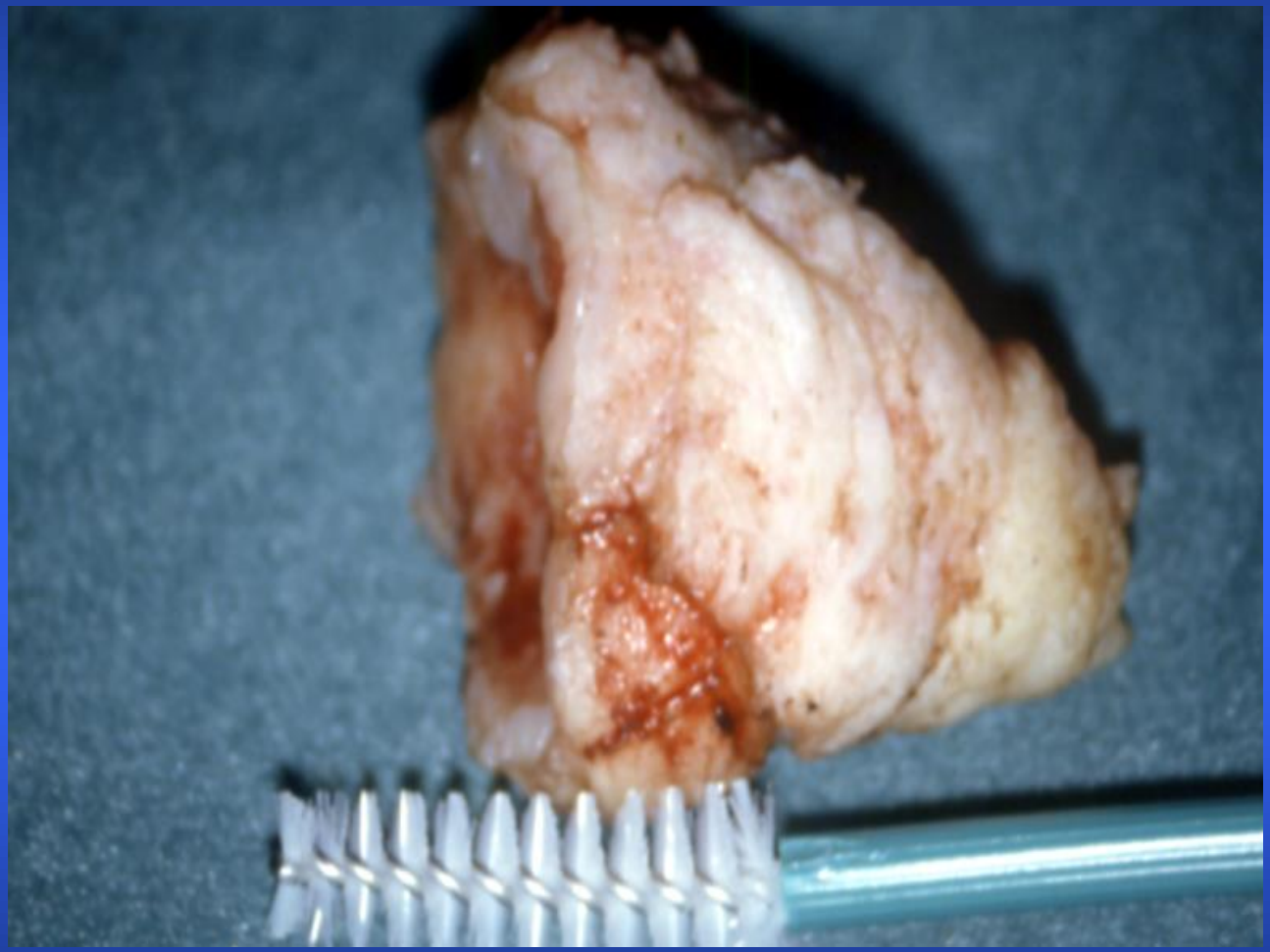




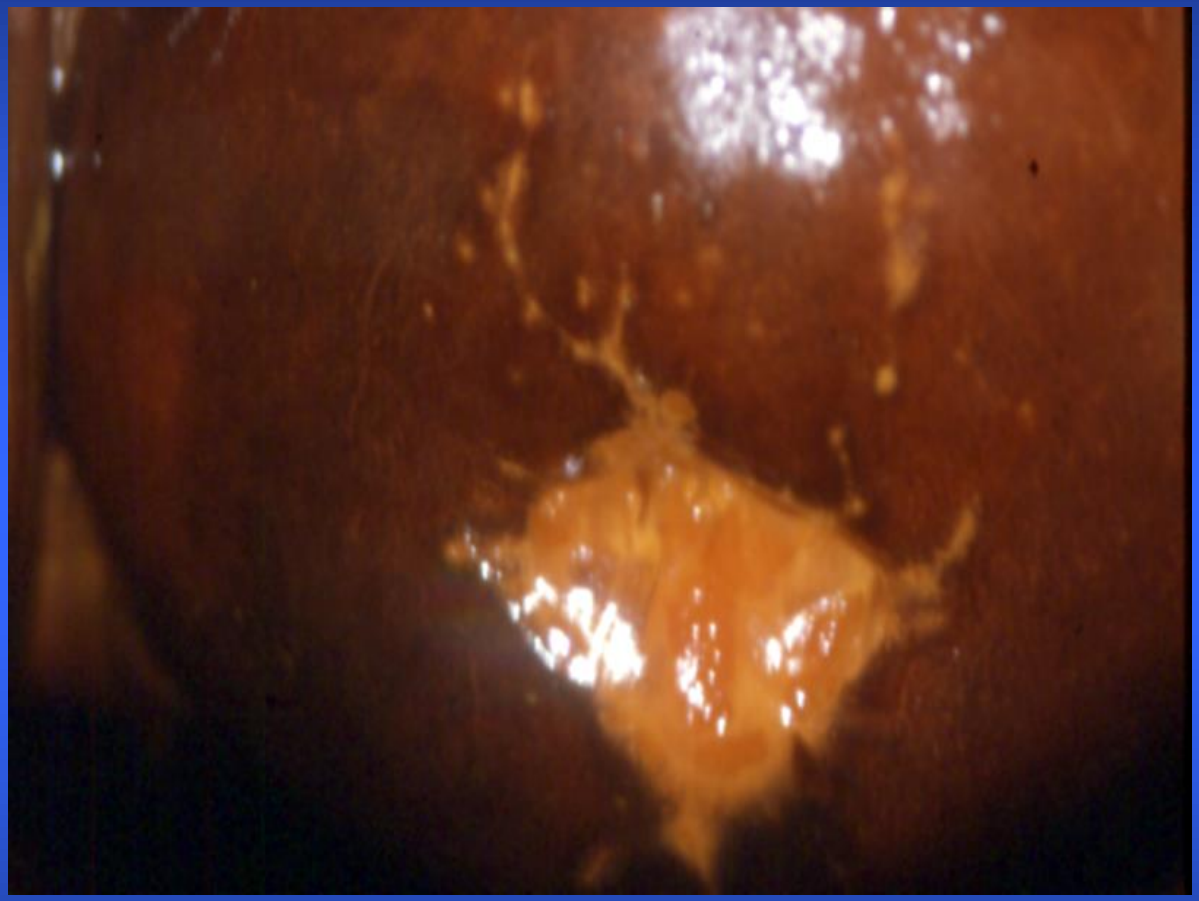




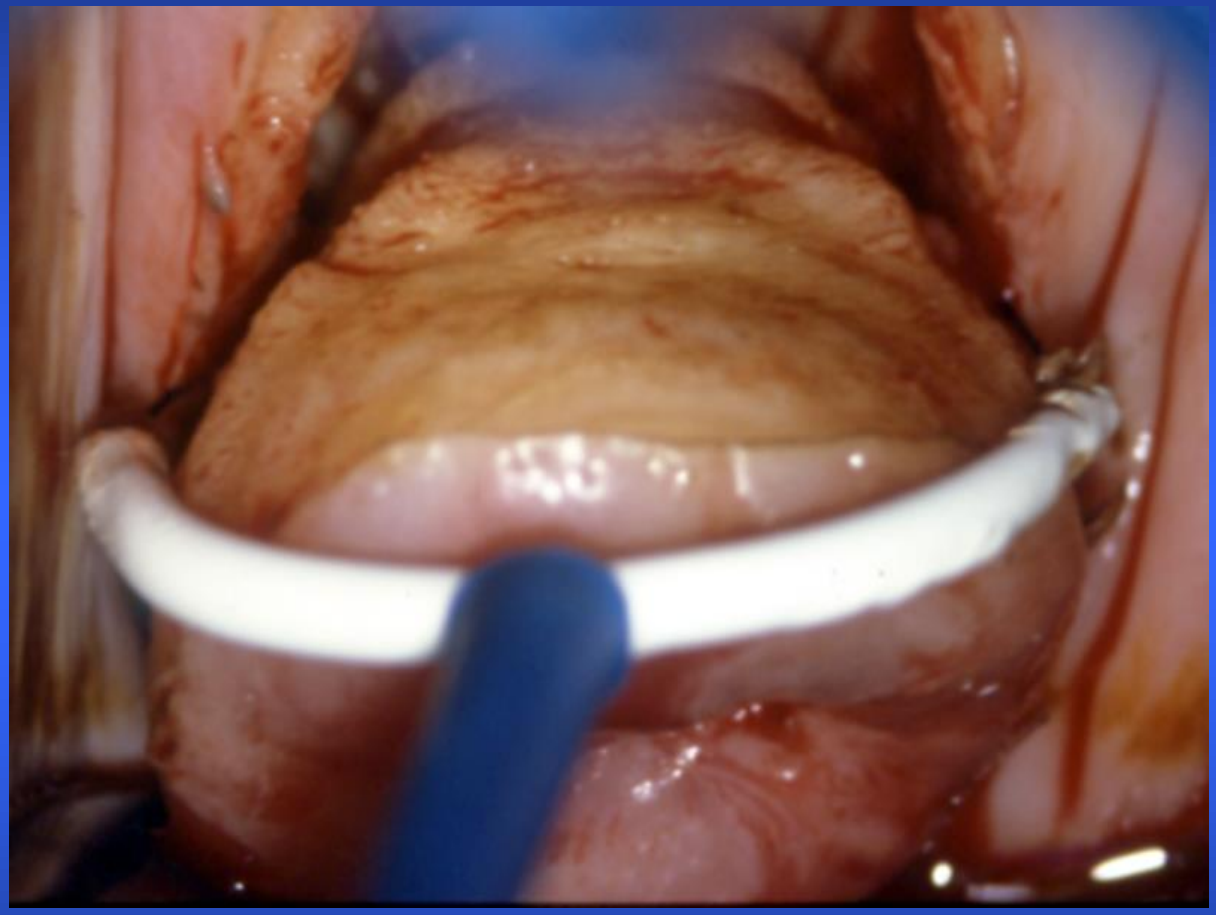




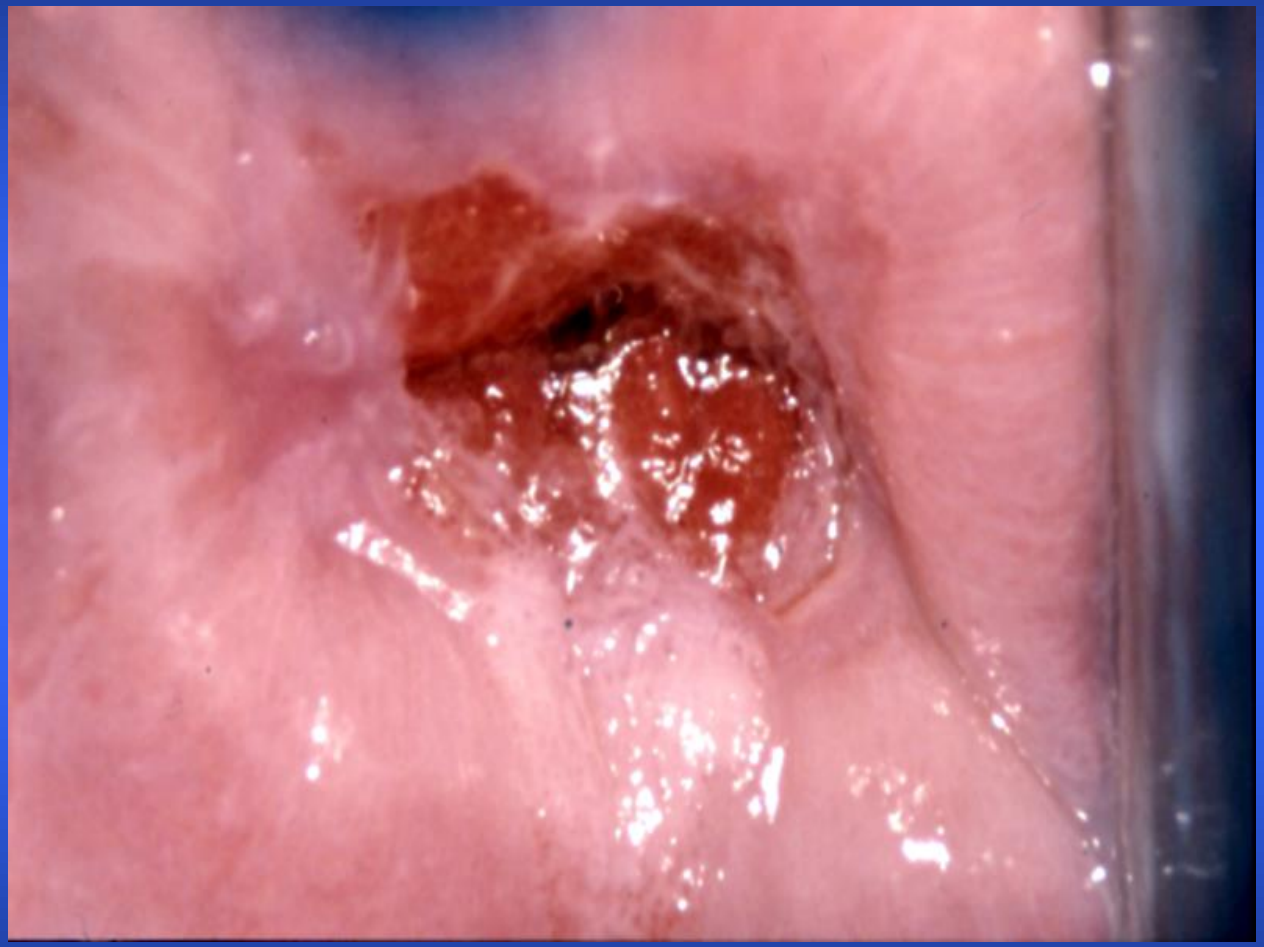


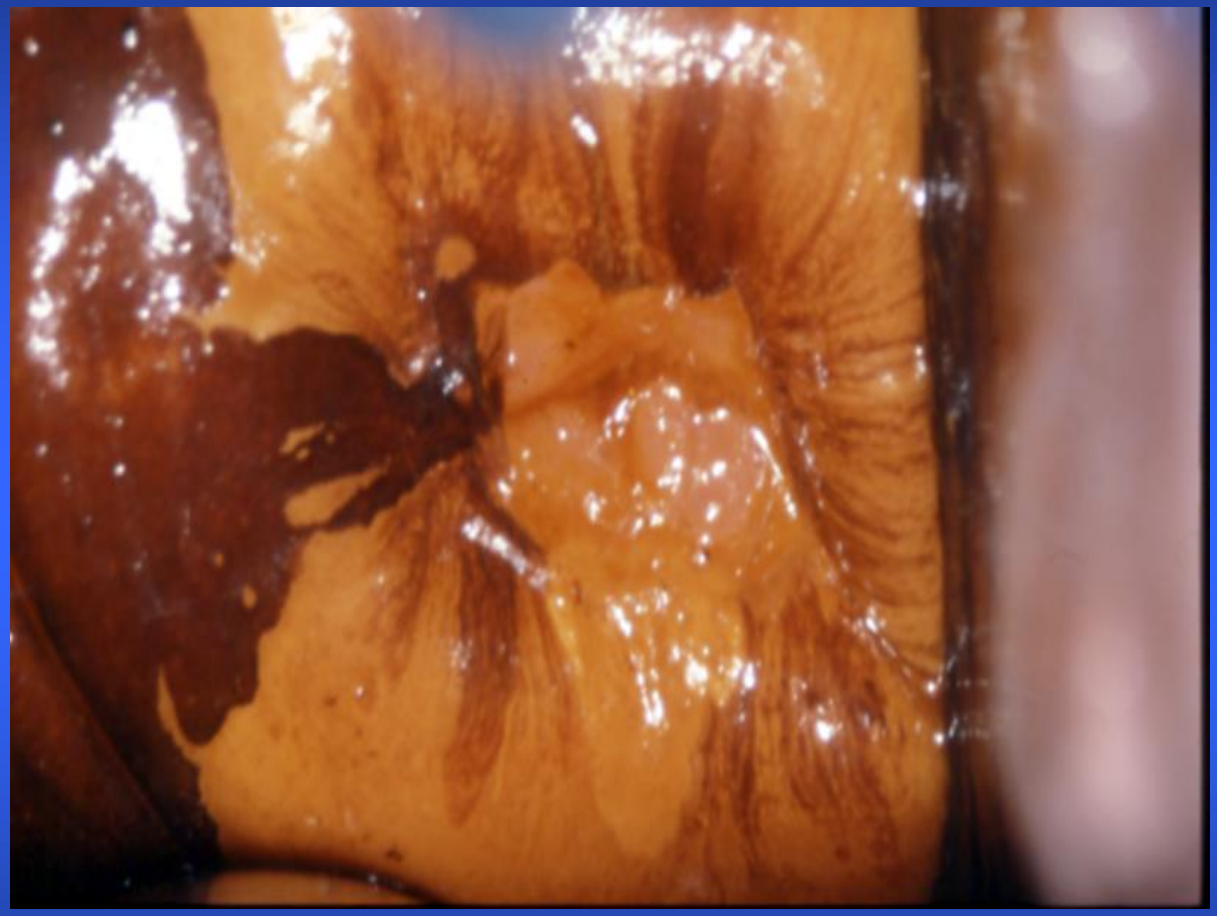


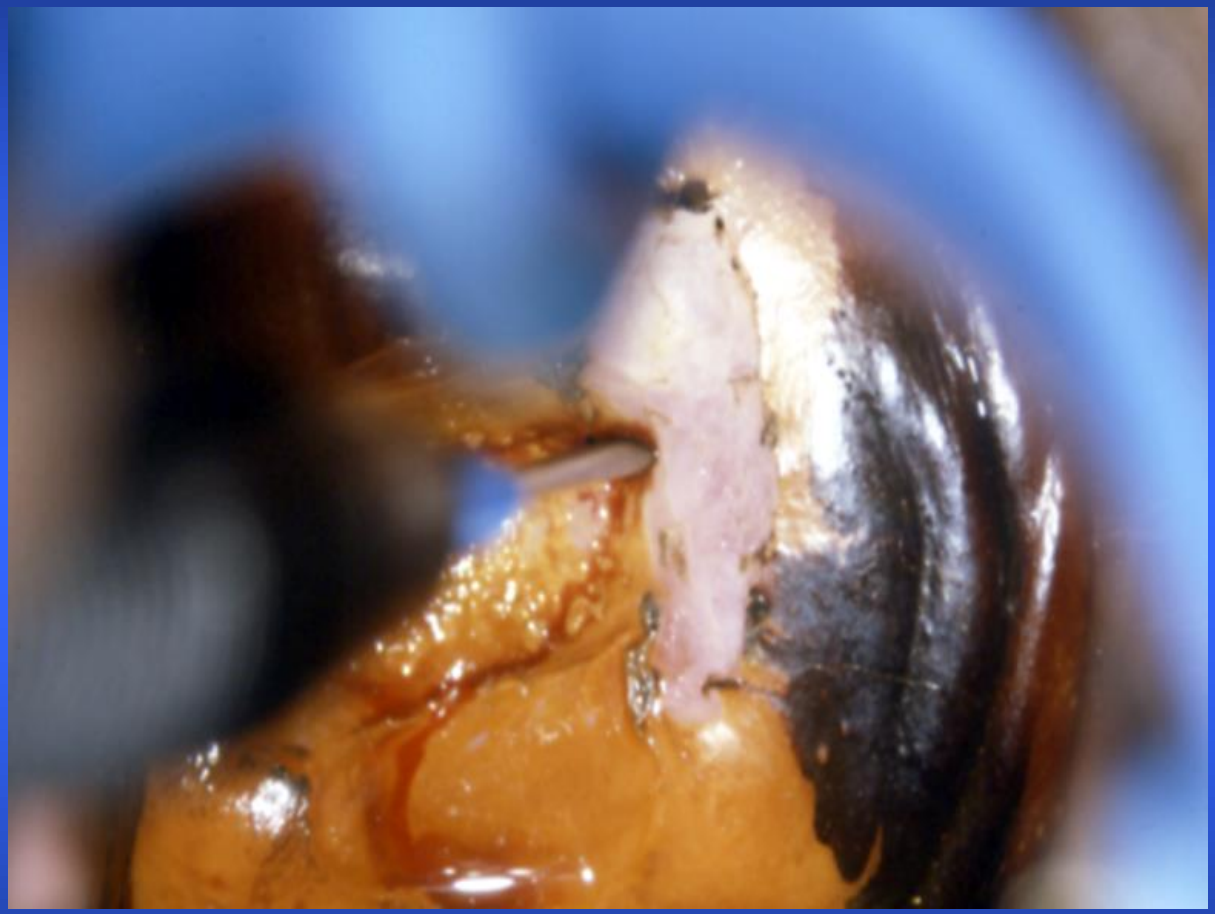


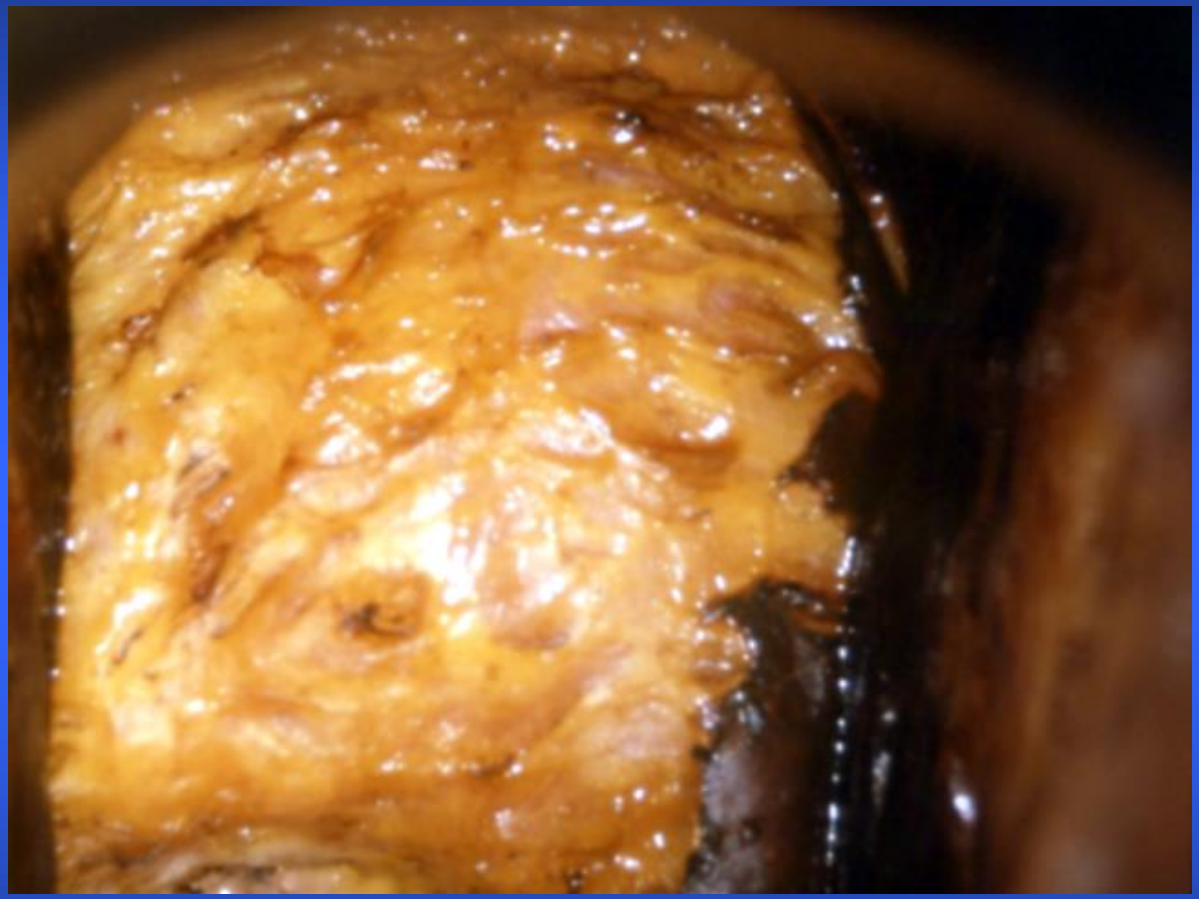












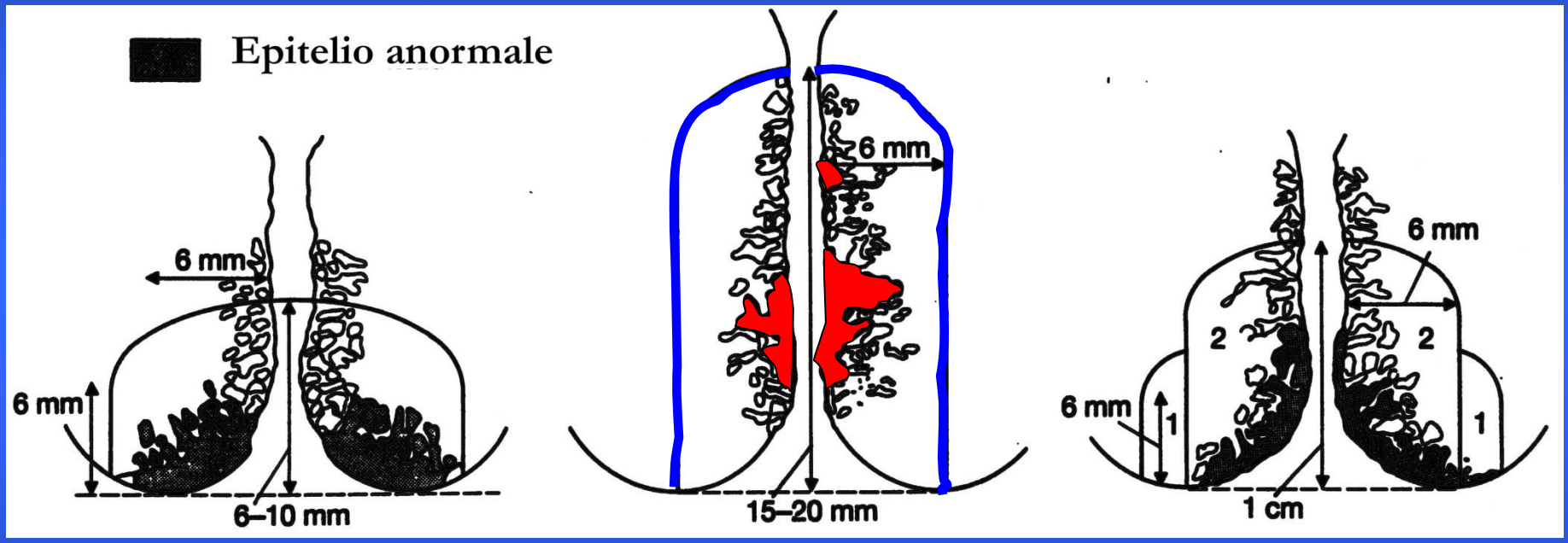




ENDOCERVICOSCOPIA



VARIABILITA'



Modificata da:
Singer A & Monaghan JM "Lower genital tract precancer. Colposcopy, pathology and treatment

ESCISSIONE CON AGO



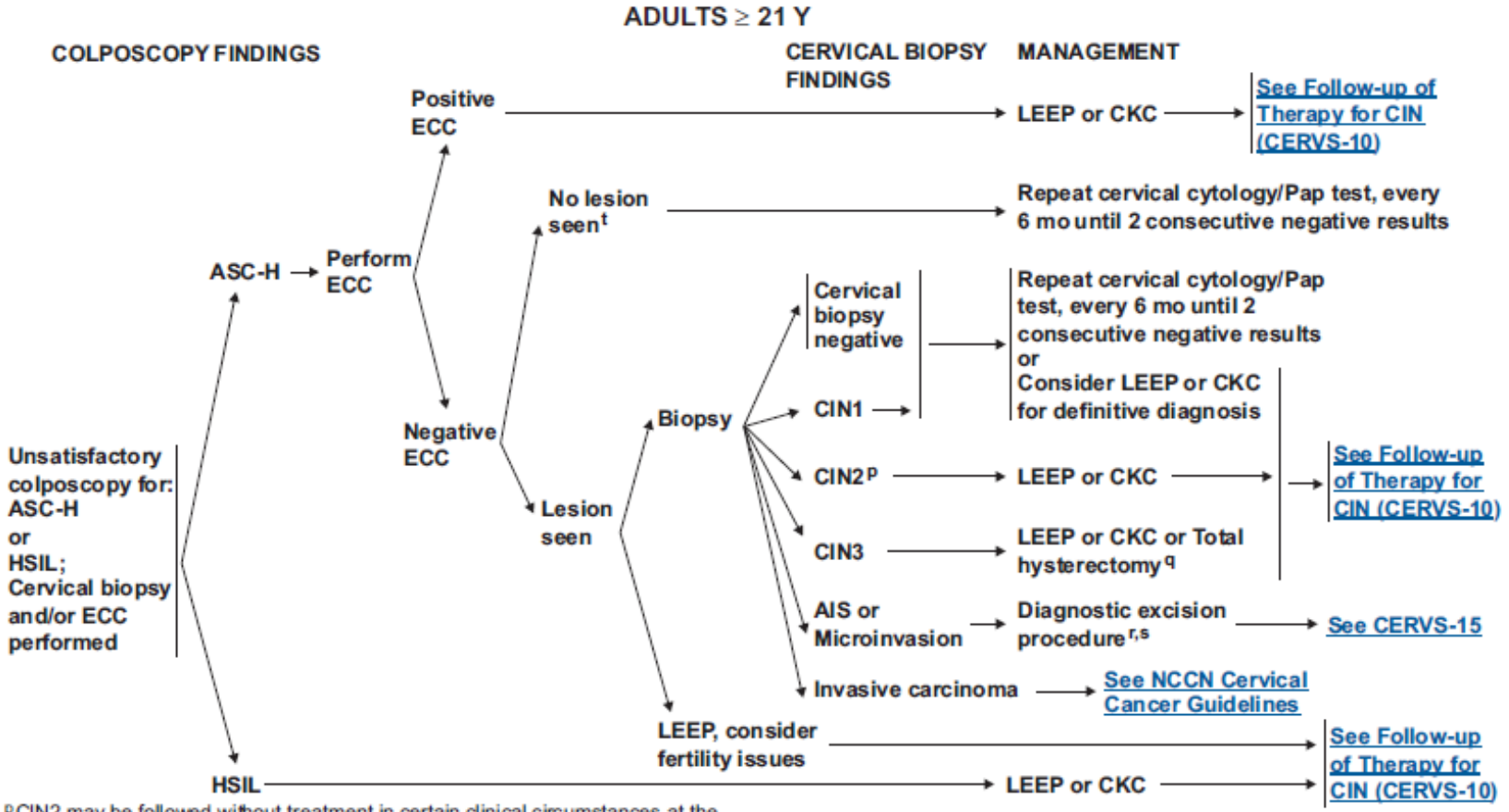
LINEE GUIDA SICPCV

HSIL → COLPOSCOPIA → BIOPSIA MIRATA

↓

TRATTAMENTO

NCCN Guidelines Version 2.2012
Cervical Cancer Screening



[p] CIN2 may be followed without treatment in certain clinical circumstances at the discretion of the physician.

[q] If appropriate for preexisting pathologic condition or quality of life.

[r] CKC is preferred. However, LEEP is acceptable provided attention is given to adequate margins.

[s] If results favor neoplasia, microinvasion, or adenocarcinoma in situ, follow CKC or LEEP with endometrial sampling if not yet done.

[t] Perform vaginal and vulvar colposcopy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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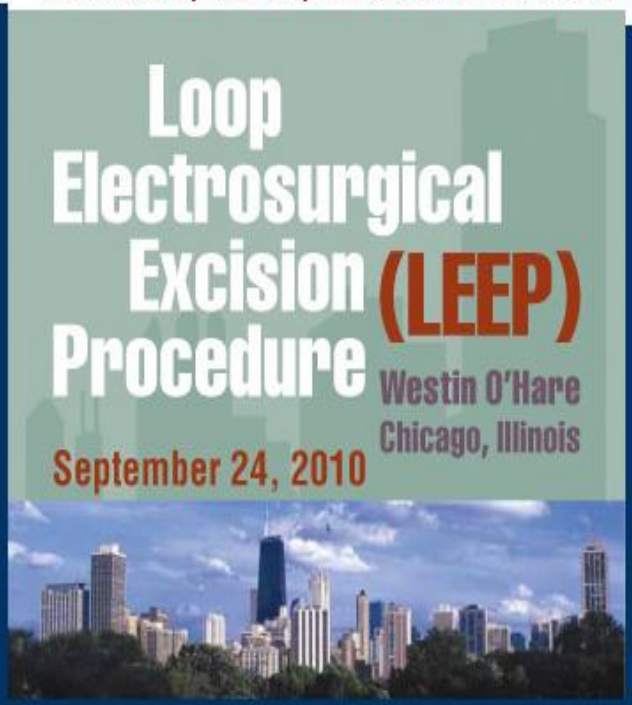
ASCCP

AMERICAN SOCIETY FOR COLPOSCOPY AND CERVICAL PATHOLOGY

The society for lower genital tract disease since 1964

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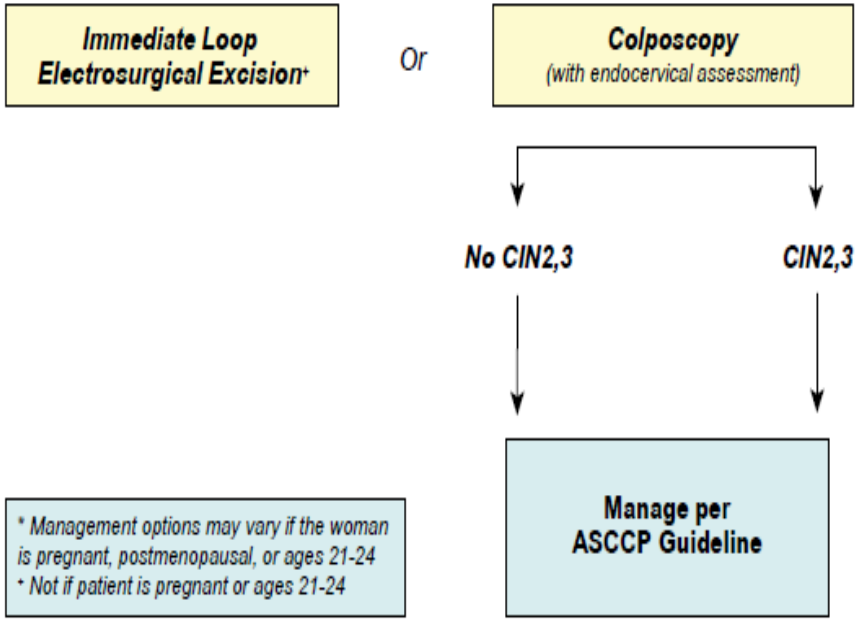
HON @ CODE CERTIFIED 04/2010

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Content last modified on January 11, 2010

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Management of Women with High-grade Squamous Intraepithelial Lesions (HSIL)*



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H-SIL: QUALE ISTOLOGIA ?

100 casi H-SIL

LLETZ



94% CIN 2 - 3
2% CIN 1
1% NO CIN
3% MICROINV

Dunn TS 2003

SEE AND TREAT

CITOLOGIA ANORMALE



COLPOSCOPIA



TRATTAMENTO

SEE AND TREAT

ASSENZA DI ANOMALIE ISTOLOGICHE	5 %	Luesley,	1990
	5 %	Bicrilg,	1990
	10 %	Howe,	1991
	14 %	Ferenczy,	1996

…. Loop electrosurgical excision procedure using the "see and treat" approach should be limited to cytologically and colposcopically unequivocal intraepithelial lesion….

…. Loop electroexcision represents an attractive means of diagnosing and treating cervical cancer precursors.

Conclusions

Implications for research

We would advocate a large multi-centre trial of sufficient power to evaluate the role of primary “see and treat” versus LLETZ or Laser Ablation after confirmation of disease by representative biopsy

”Evidence supporting see-and-treat management of cervical intraepithelial neoplasia: a systematic review and meta-analysis” RMF Ebisch at all, BJOG Jul 2015

3732 pubblicazioni → **13 studi**

4611 pazienti

OVERTREATMENT → **NO CIN- CIN1**

OVERTREATMENT

HSIL + COLP. G II → 11,6%

HSIL + COLP. G I → 29,3%

LSIL + COLP. G II → 46.4%

LSIL + COLP. G I → 72.9%

TWO STEP 11-35%

CONCLUSIONI

SEE AND TREAT → HSIL+ COLP. G II

In accordo con ASCCP

EFC

NHSCSP

RISULTATI DEL TRATTAMENTO

Grado CIN	N° casi	**Guarigione**	**Persistenza**	**Neoplasia**
I	702	660 (94%)	42 (6%)	1 Adenoca i.m.
II	778	735 (94,5%)	44 (5,5%)	1 Adenoca i.m
III	520	488 (94%)	31 (6%)	30 Microinv. 4 Adenoca i.m. 4 Adenoca inv.
TOTALE	**2000**	**1883 (94,3%)**	117 **(5,7%)**	**40**

Correlazione tra esame citologico ed **esame istologico da biopsia mirata:**

372 casi HSIL:

- 2.7% negativi (10 casi)
- 7.5% CIN 1 (28 casi)

POSSIBILE RUOLO DEL SEE AND TREAT

- Citologia H-SIL, Colposcopia G2
- Citologia H-SIL, Lesione endocervicale
- Nel follow-up di pazienti trattate per H-SIL, con colposcopia e citologia positiva
- Nel follow-up di pazienti trattate per ca invasivo, con colposcopia e citologia positiva
- Pazienti non affidabili
- Pazienti in situazioni ambientali e sociali disagiate

To Take Home: S & T

- ✓ The risk of OT rate is closely related to the quality of cervical smear and to the colposcopist's training and can be reduced with the use of appropriate criteria.
- ✓ The decrease of dropout rates exceeds the risk of OT rates mainly in low-income countries in which there is a failure to actively search for patients, including Brazilian health services.
- ✓ It is time-saving and cost-effective for health care services and patients compared with the two-step approach.



To Take Home: S & T

- ✓ Given the side effects of cervical surgery on pregnancy outcome, young women with a discrepancy between the cervical smear and colposcopic impression, a biopsy prior to treatment is advisable (OT rate is higher than 2-step procedure).

- ✓ In older women (> 40 yo or completed childbearing) the advantages of S & T improves patients' compliance by reducing emotional stress and time off from work, outweighing the possibility of OT rates.

NHS CERVICAL SCREENING PROGRAMME
Third Edition 14 March 2016

8.4.3 Depth of excision

TYPE I CERVICAL T.Z

- … remove to a depht/lenght of more than 7 mm (95%)…< 10mm in woman of reproductive age

TYPE II CERVICAL T.Z

- …depth/lenght of 10 mm/15 mm, depending of the position of SCJ in the endocervical canal

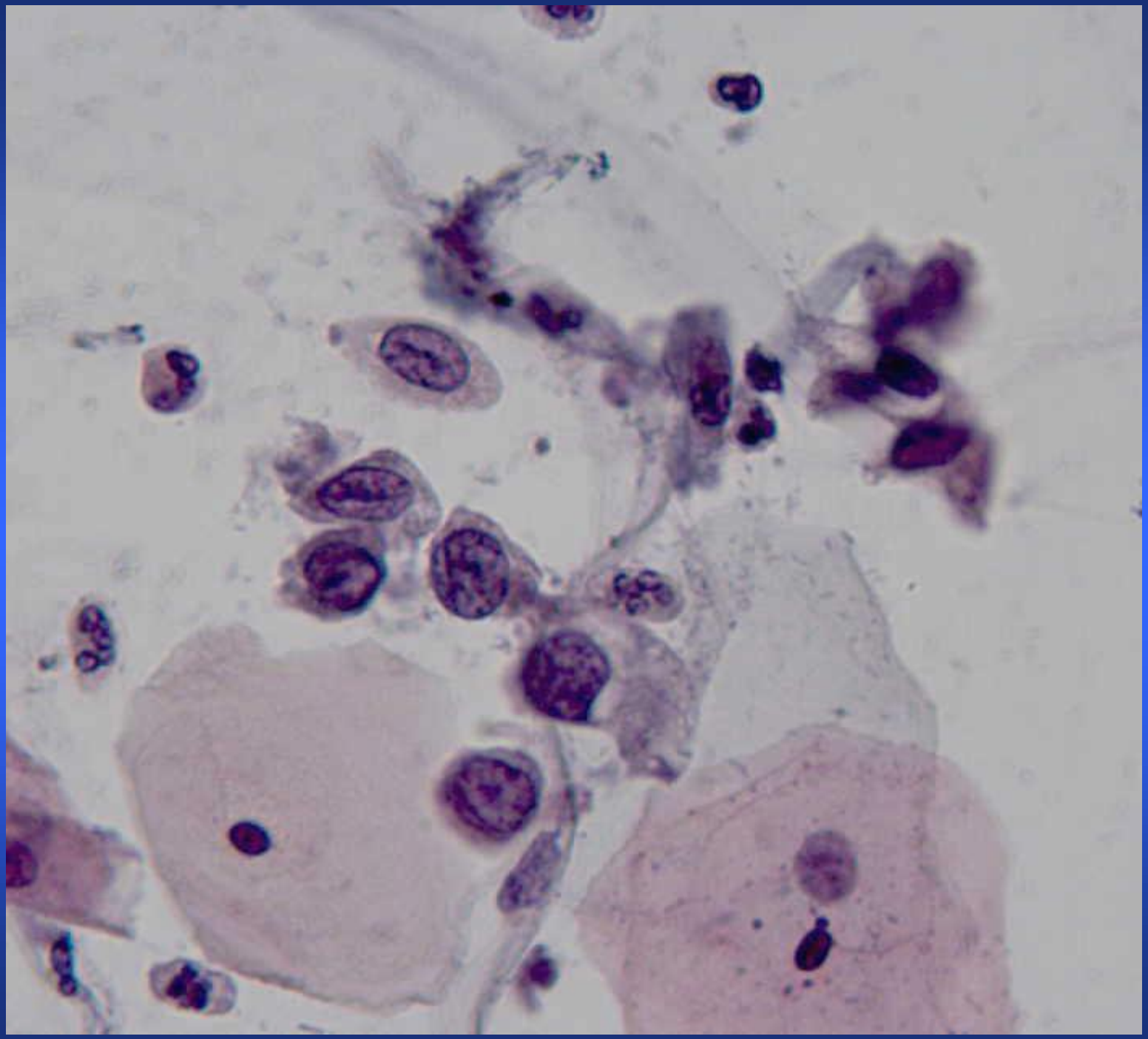
TYPE III CERVICAL T.Z

- … of 15 mm to 25 mm

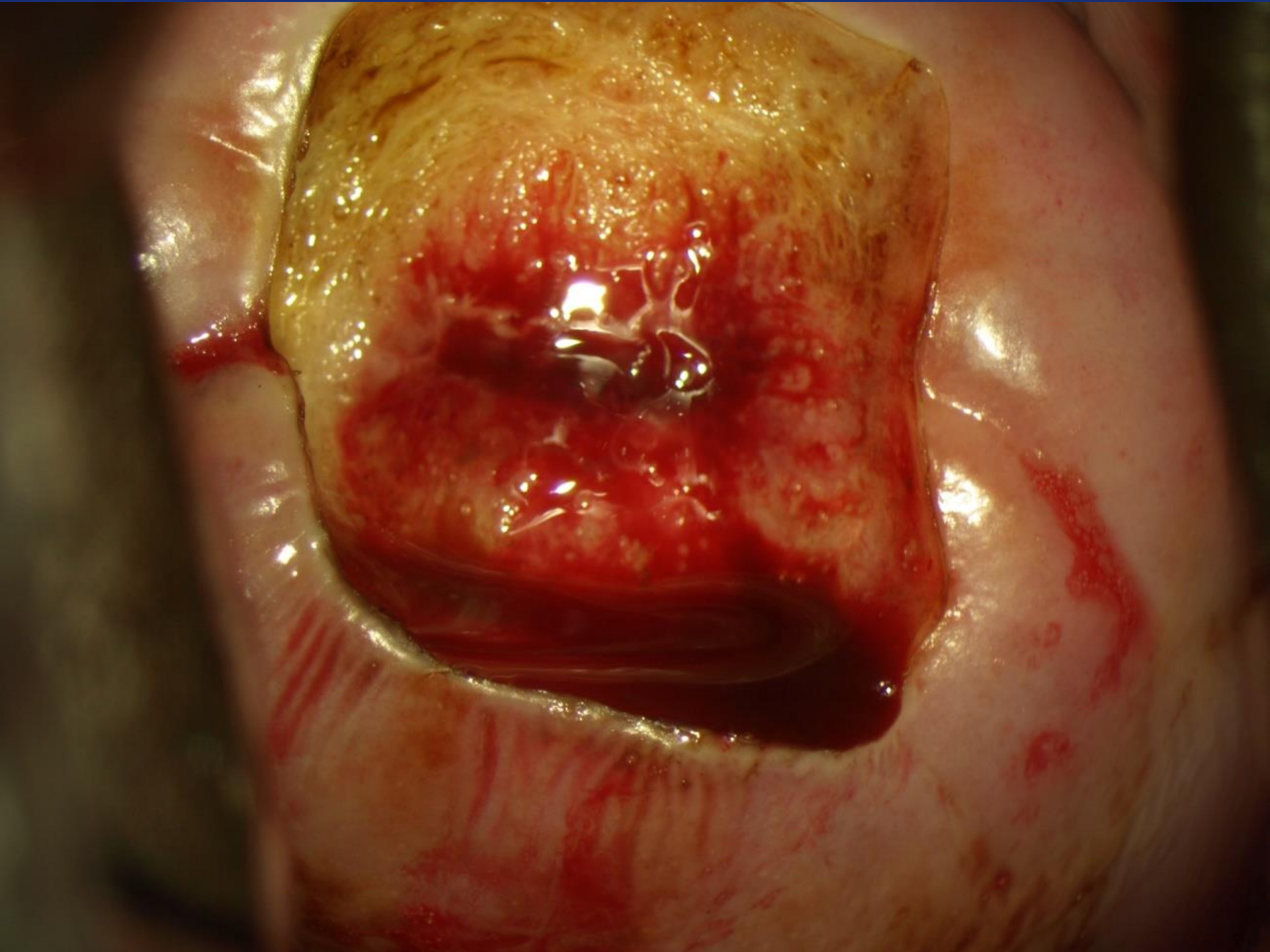
One prospective cohort and 19 retrospective studies

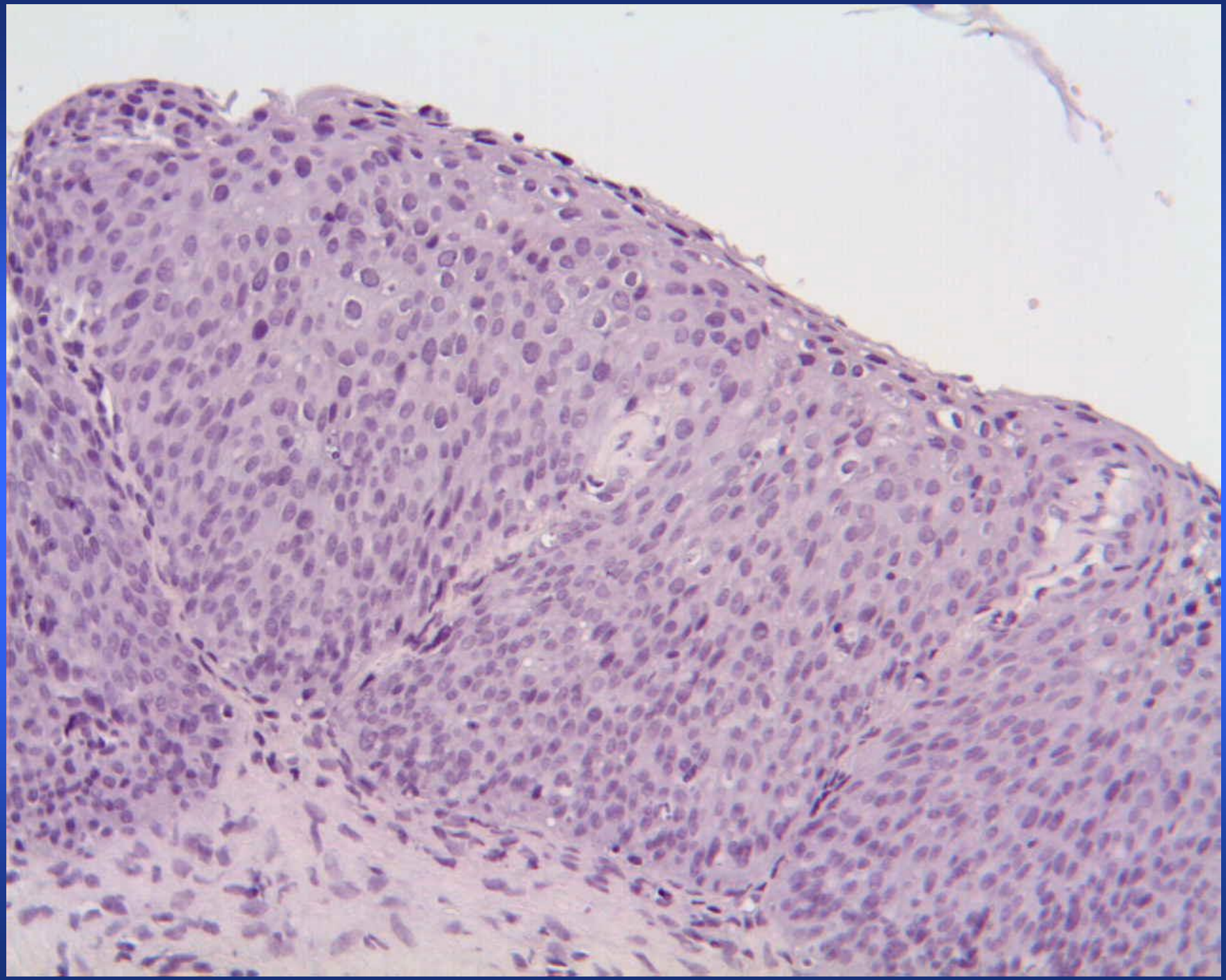
- **Cold knife conisation** was associated with a significantly increased risk of perinatal mortality (relative risk 2.87, 95% confidence interval 1.42 to 5.81) and a significantly higher risk of severe preterm delivery (2.78, 1.72 to 4.51), extreme preterm delivery (5.33, 1.63 to 17.40), and low birth weight of <2000 g (2.86, 1.37 to 5.97).
- **Laser conisation**, was followed by a significantly increased chance of low birth weight of <2000g and <1500 g.
- **Large loop excision** of the transformation zone and ablative treatment with cryotherapy or laser were not associated with a significantly increased risk of serious adverse pregnancy outcomes.
- **Ablation** by radical **diathermy** was associated with a significantly higher frequency of perinatal mortality, severe and extreme preterm delivery, and low birth weight below 2000 g or 1500 g.

Arbyn M. et al. BMJ 2008;337:a1284











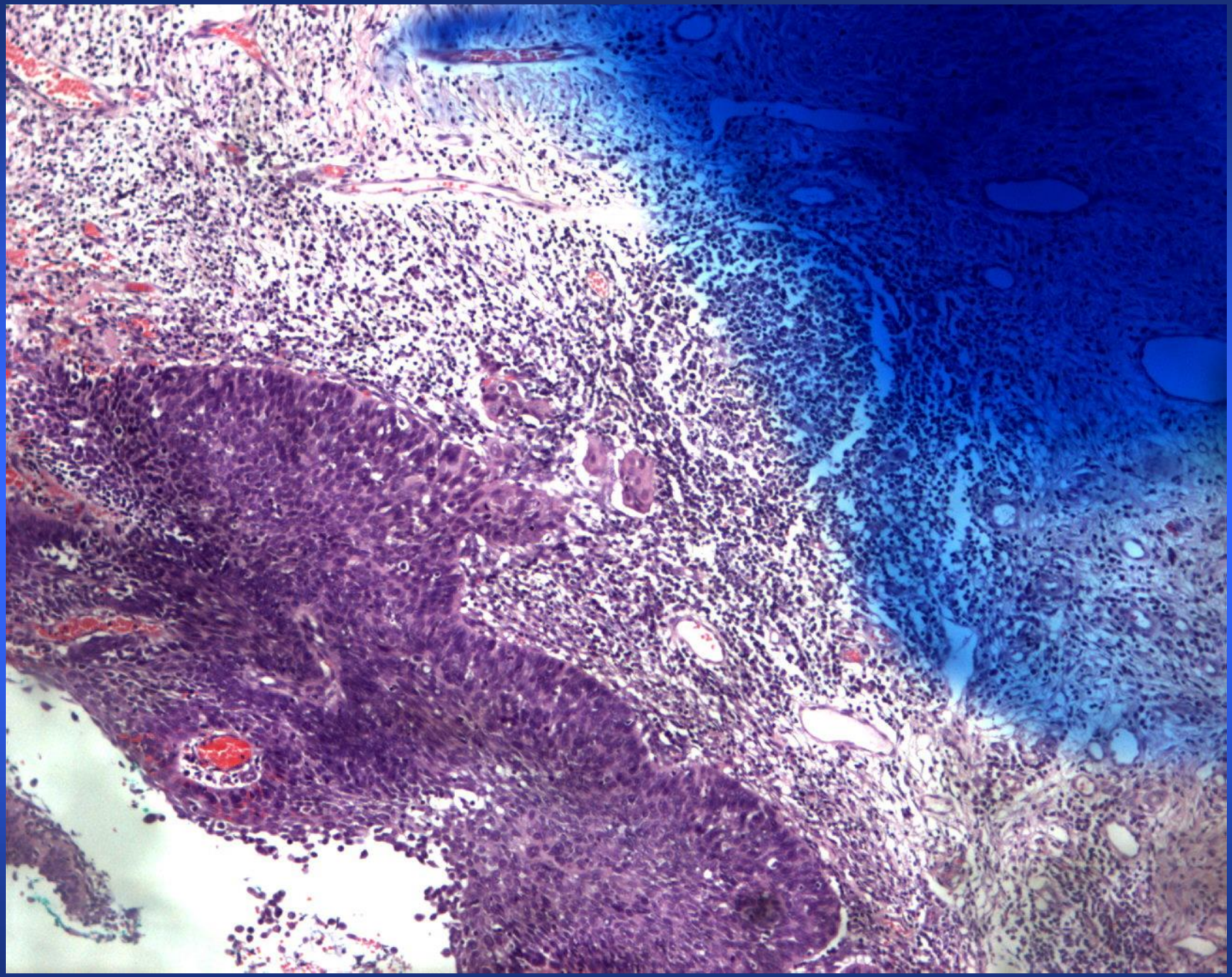
CASO CLINICO

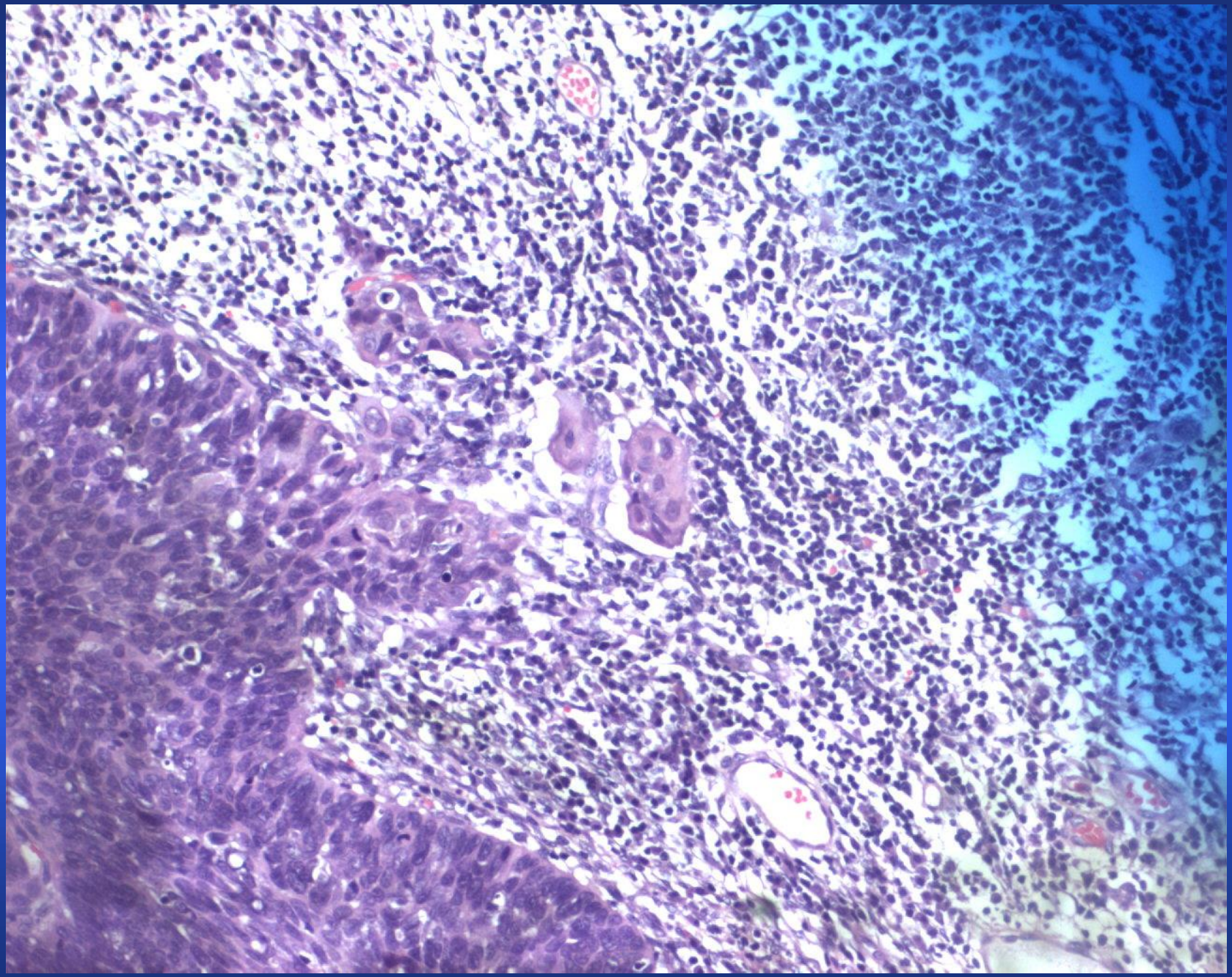
J.N. 21/06/1964

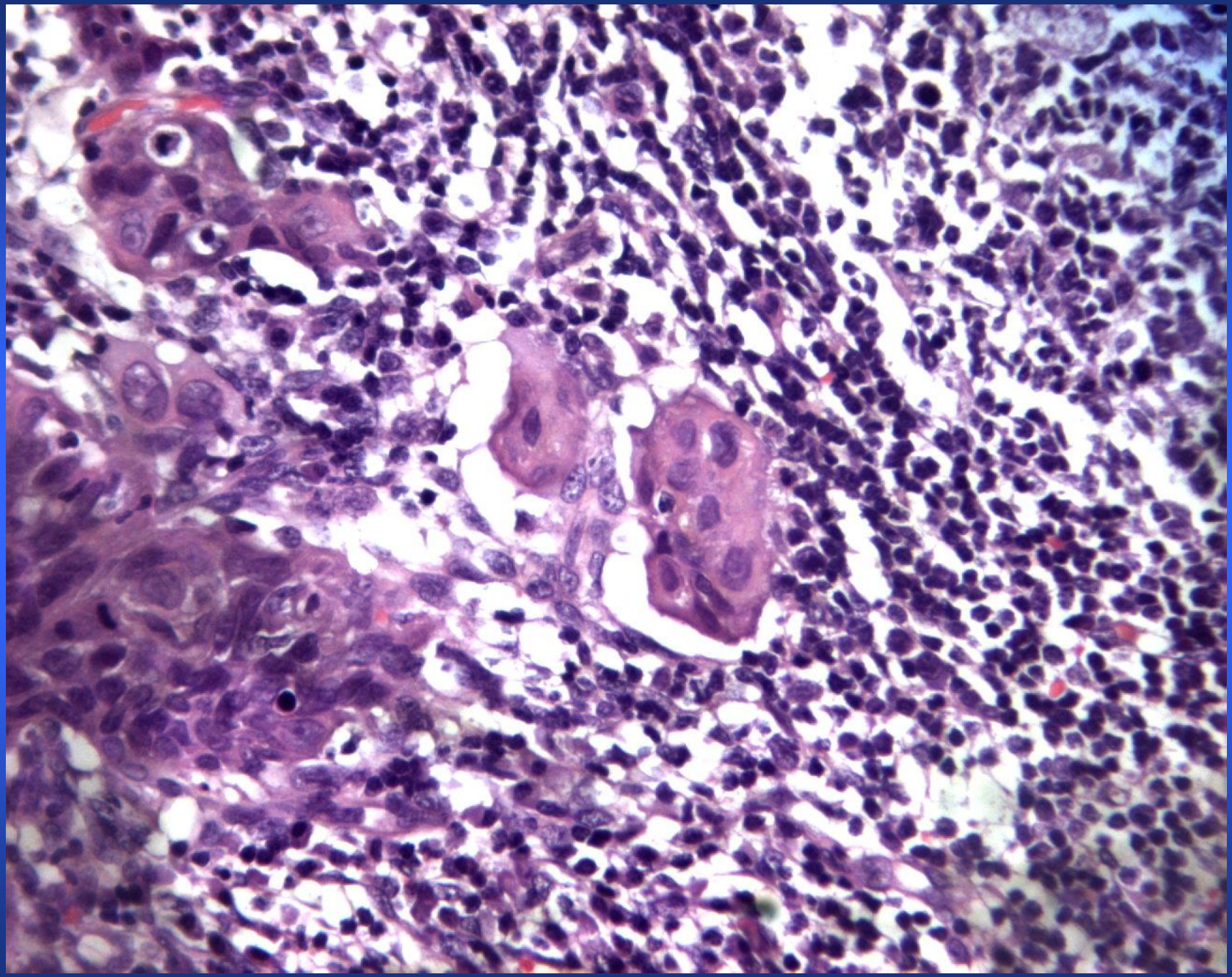
Nel 2000 36 anni Ansa a RF PER CIN III
altezza 1,8 cm

Nel 2012 47 anni Ansa a RF PER CIN III
altezza 2 cm

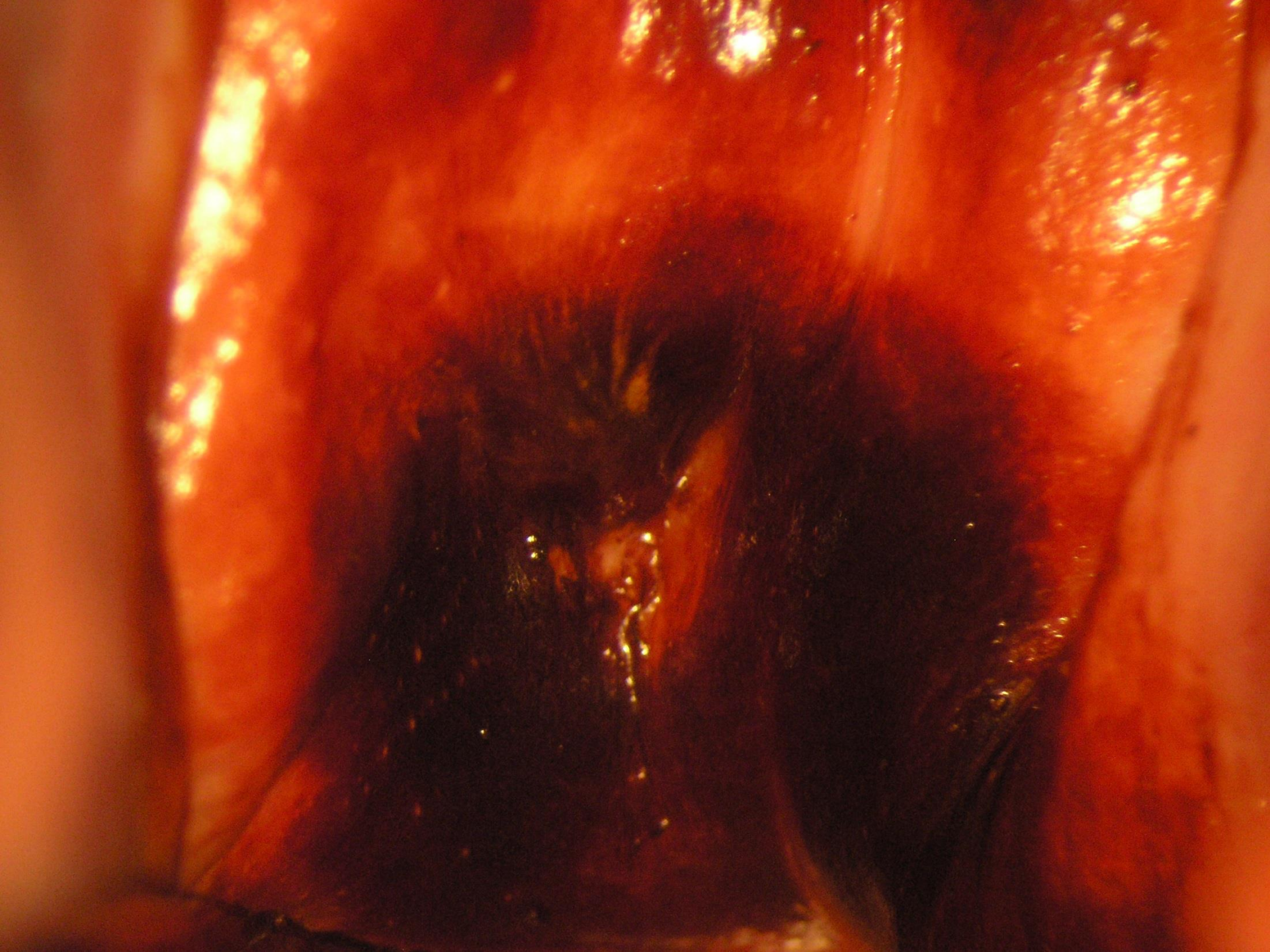
Nel 2013 49 anni Ansa a RF per CA microinvasivo (<1mm)
altezza 2,2 cm











CASO CLINICO

A.D. 29/04/1972

Nel 2013 41 anni - gennaio/luglio 2 Coniz. per CIN 3

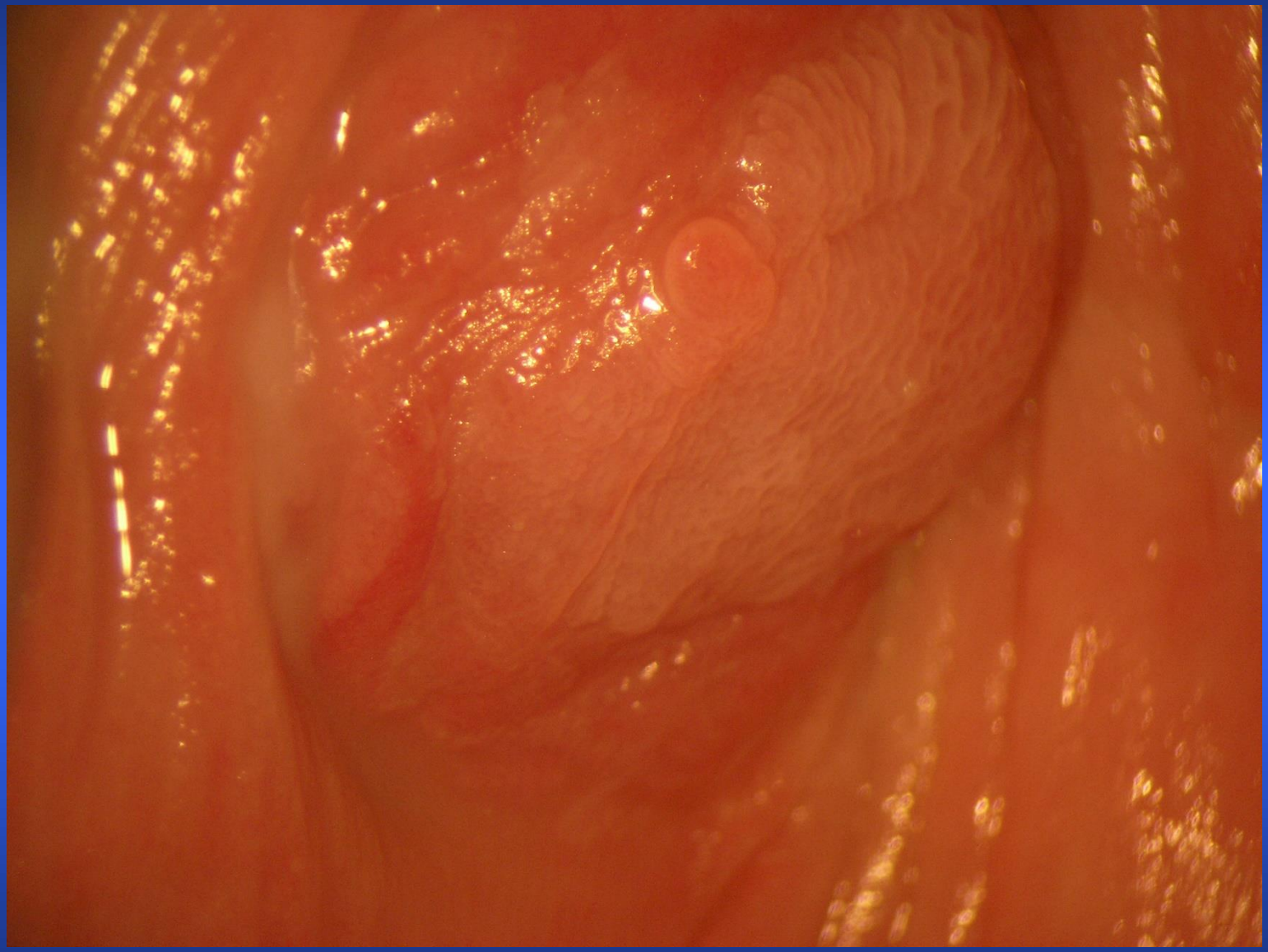
Nel 2013 – ottobre – H-SIL/CIN 3

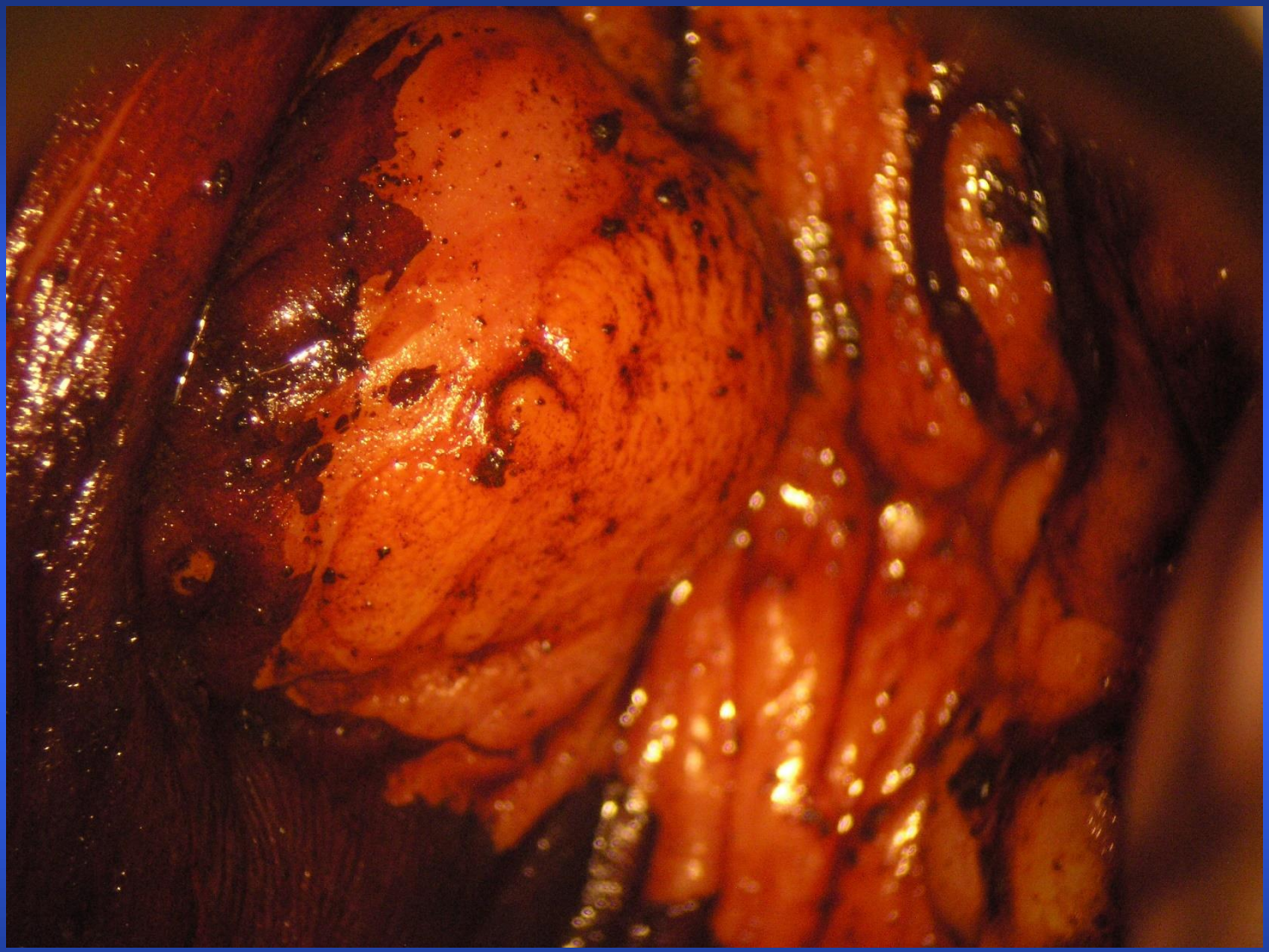
Nel 2013 – dicembre - isterectomia laparoscopica
E.I.: CIN 3 sul margine esocervicale

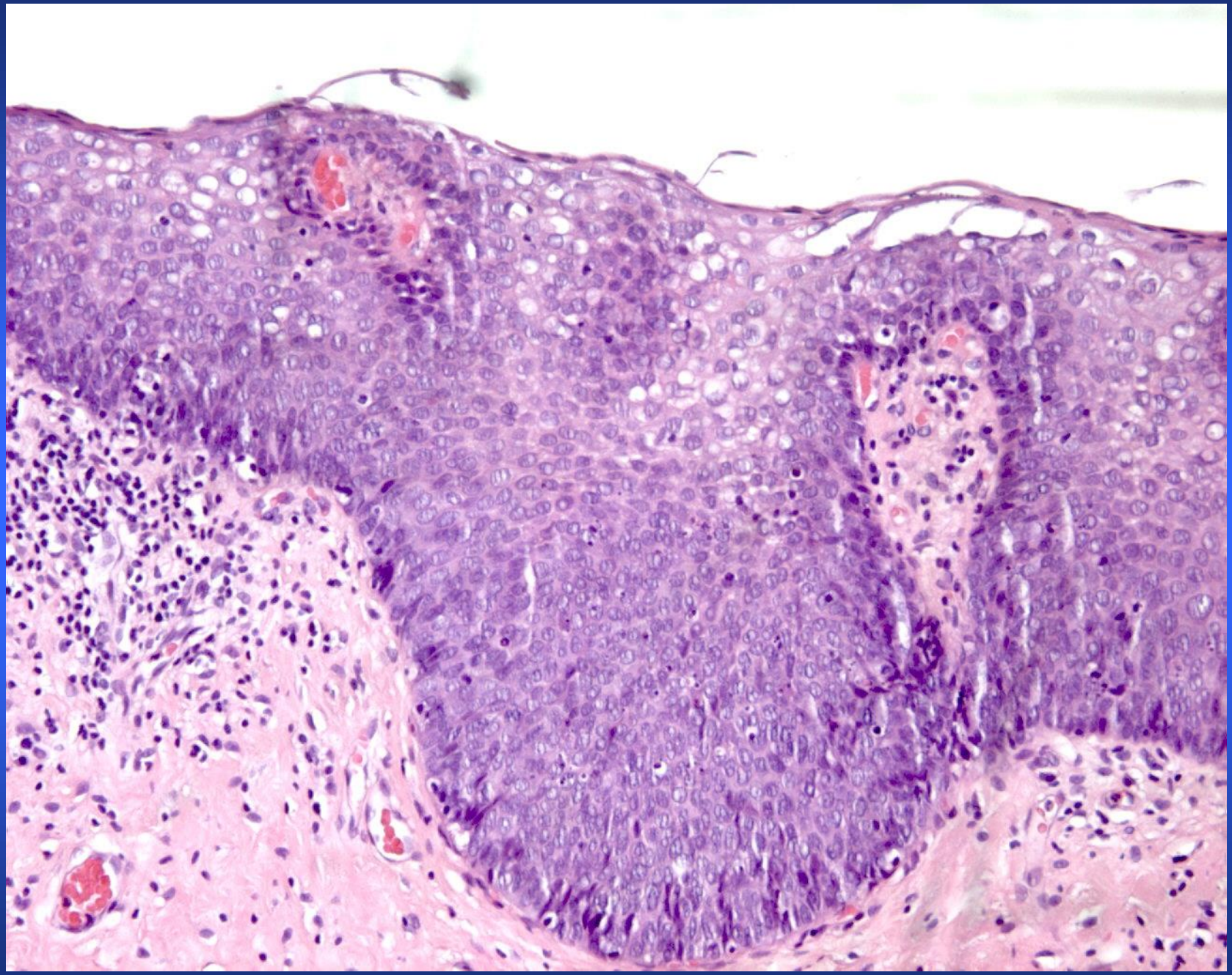
Nel 2014 – marzo- HSIL/VaIN 3

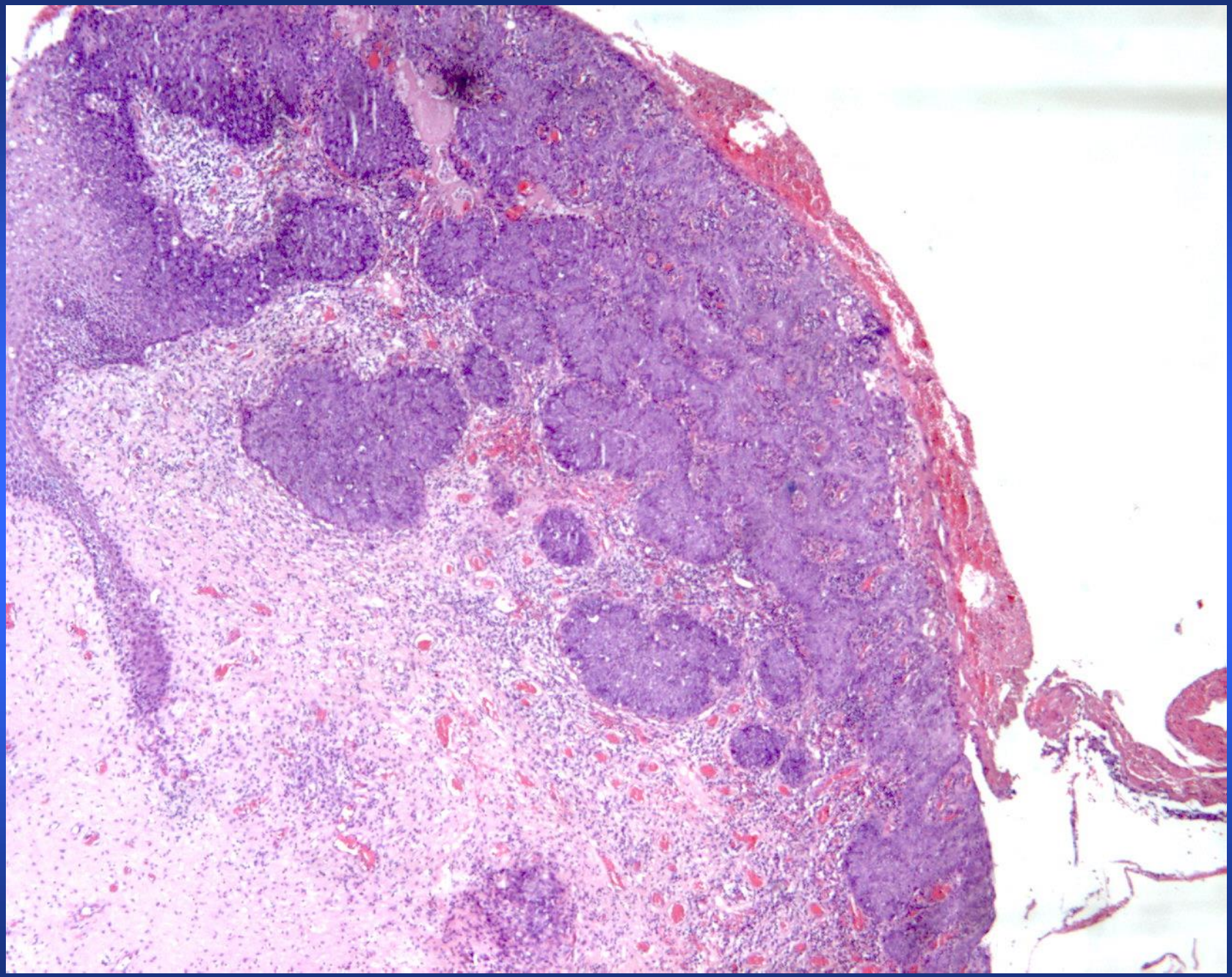
Nel 2014 – settembre – Escissione cupola vaginale con ago a RF

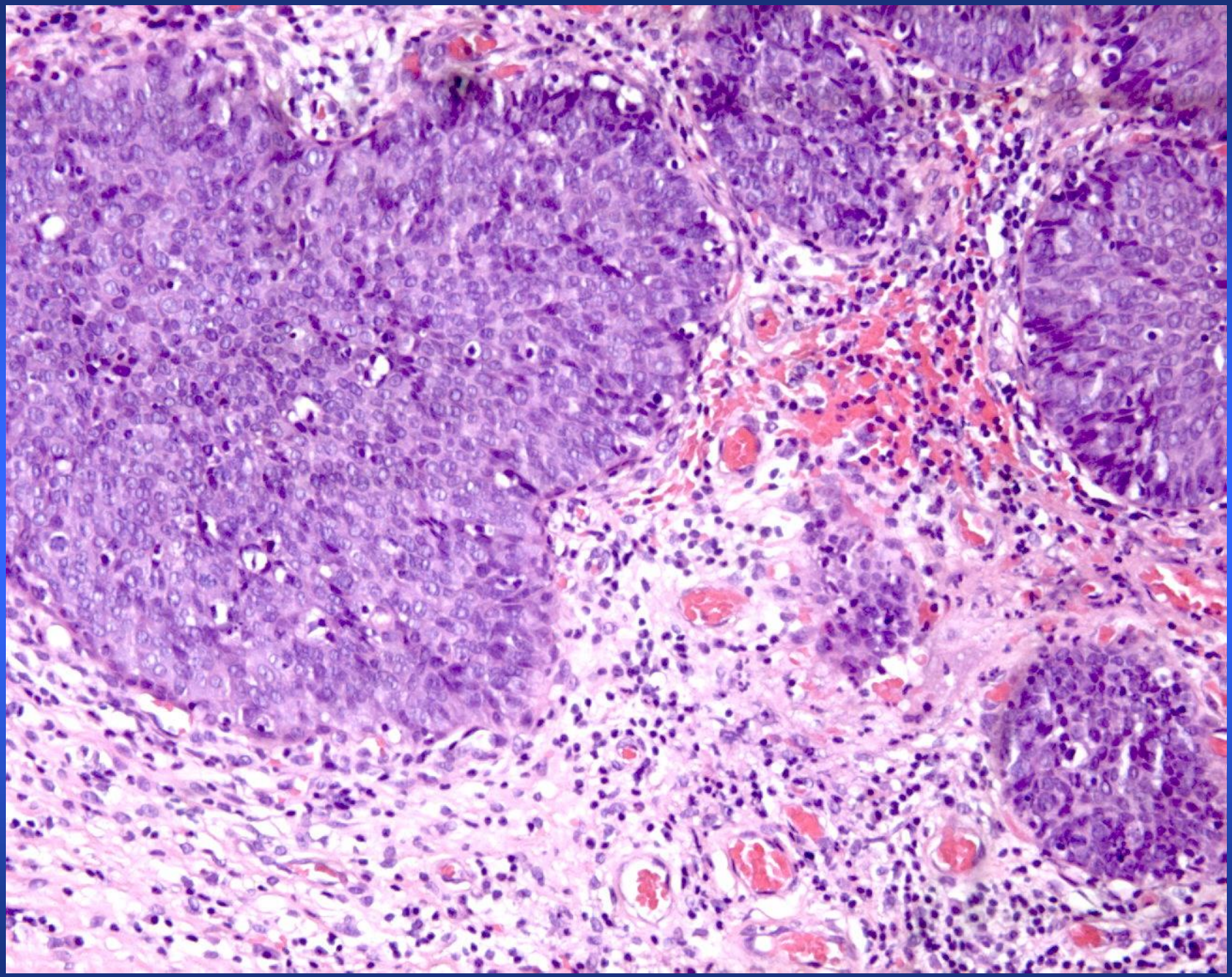


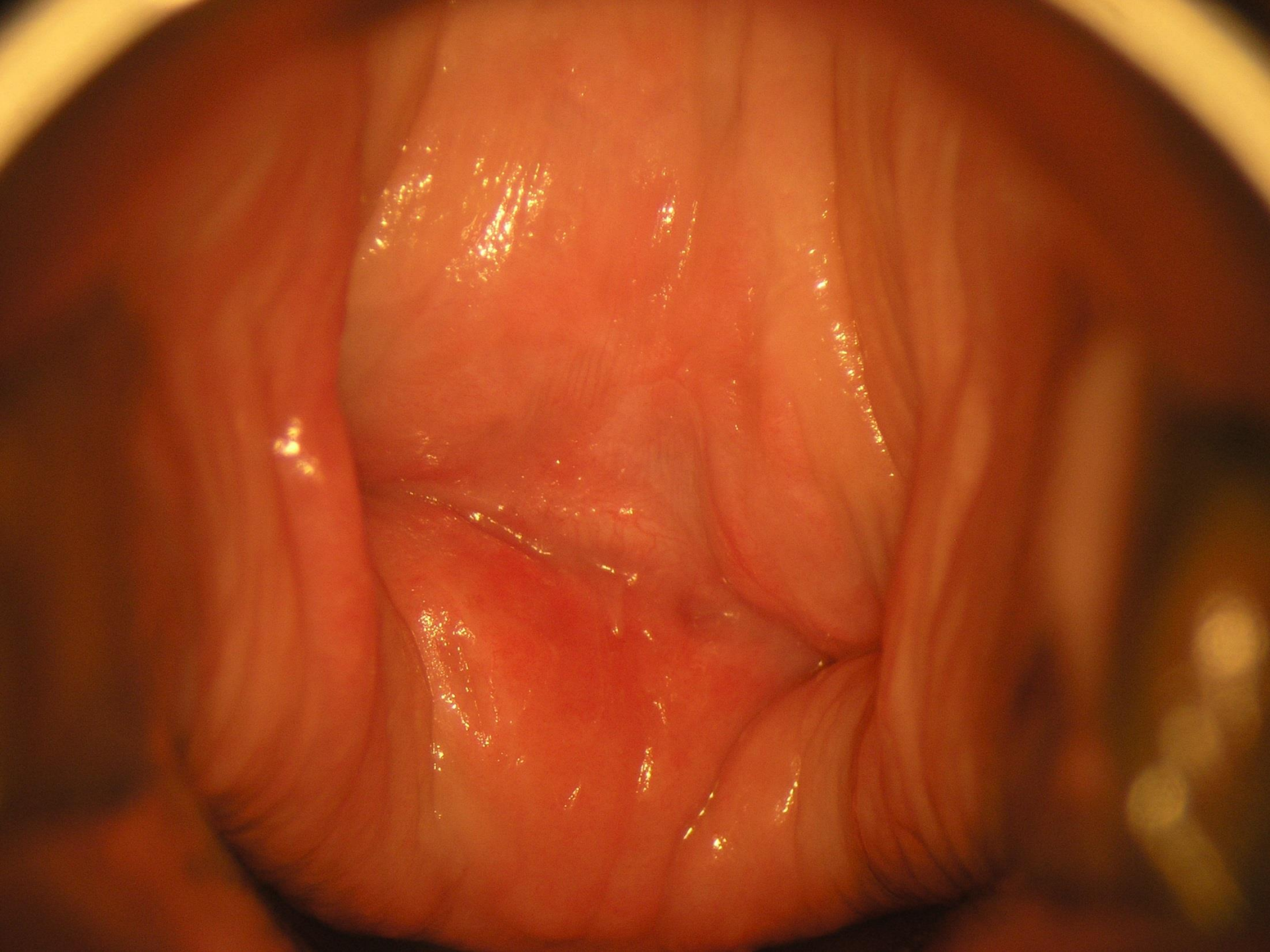


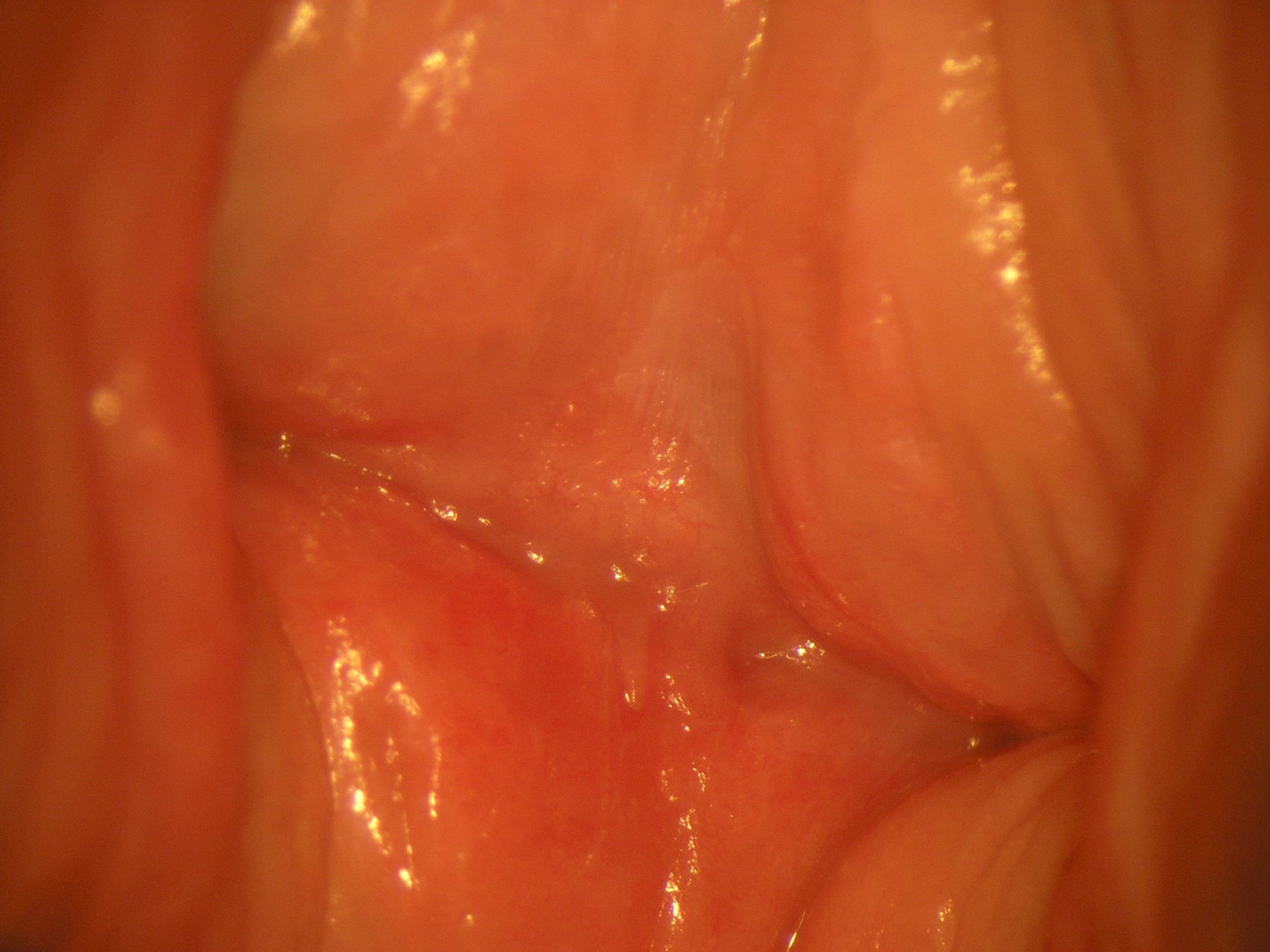




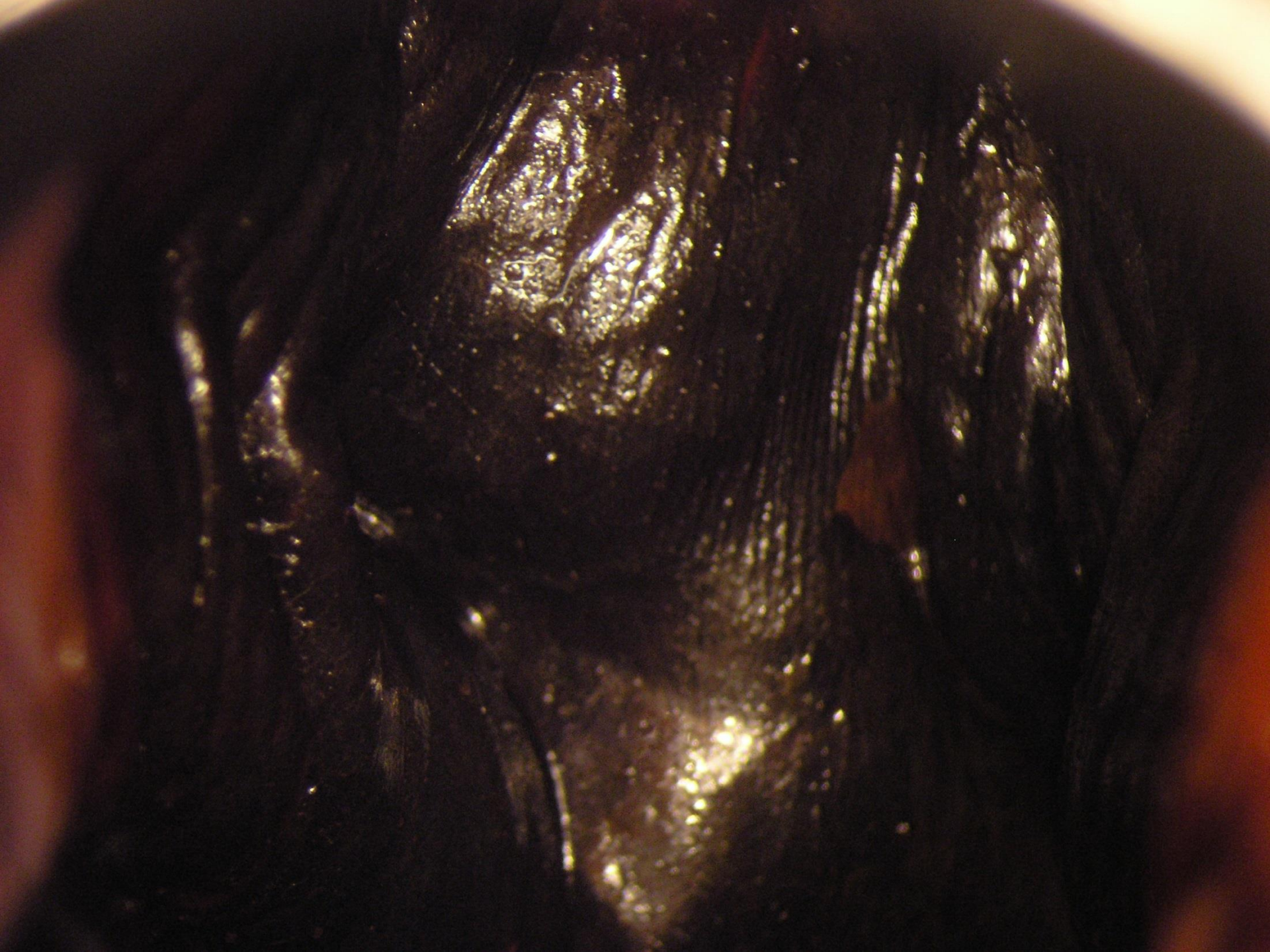














PUNTI FERMI

- Importanza dell'età
- Importanza del follow-up
- Importanza trattamento escissionale
- Biopsia mirata non sempre necessaria
- Ruolo fondamentale della Colposcopia
- Controindicata l'Isterectomia