

Case 4

Menopause and HPV

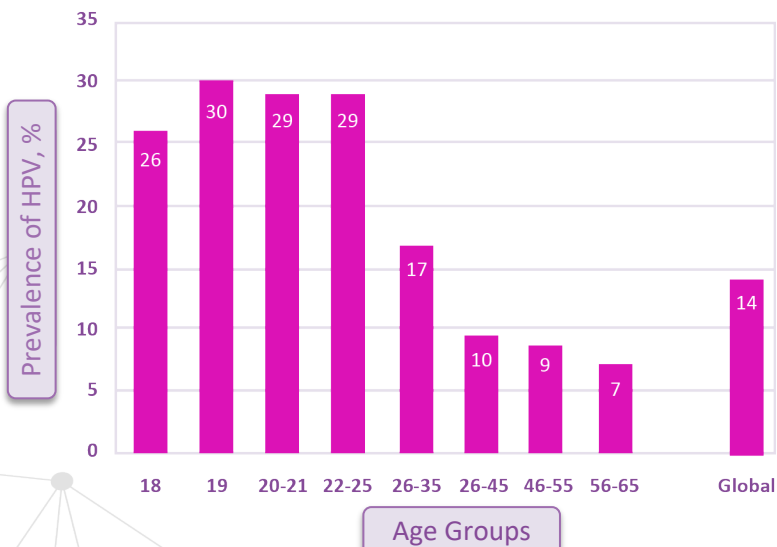
Dr. Santiago Palacios

- The maximum prevalence of HPV occurs in women between 18 and 25 years of age.
- However, we sometimes forget that women in peri and post-menopause can also have HPV. In addition, their ability to produce antibodies is lower than in young women and therefore, HPV infection could be higher risk.
- The CLEOPATRE study conducted in Spain found an HPV prevalence of 9% in women age 45-55 and 7% in women age 56-65¹.
- In fact, the majority of cervical cancers in Spain are detected in women over 50 years of age and, specifically, 27% of cancers are diagnosed in women over age 65².
- Therefore, the detection and management of HPV in women in peri- and post-menopause is critical for the prevention and early detection of cervical cancer.

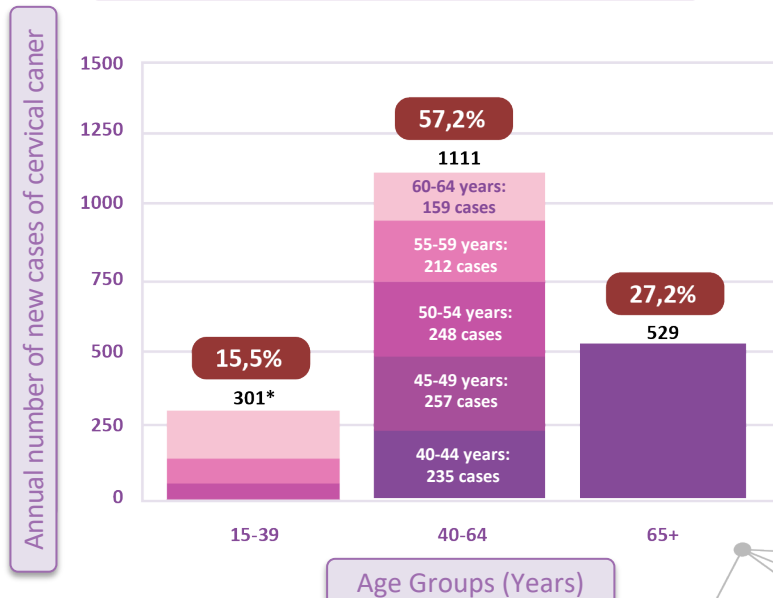
1. Castellsagué X, et al . The CLEOPATRE study. J Med Virol. 2012 Jun

2. Bruni L, et al. Human Papillomavirus and Related Diseases in Spain. Summary Report 10 December 2018

Prevalence of HPV in Spain¹



Cervical cancer in Spain²



1. Castellsagué X, et al. The CLEOPATRE study. J Med Virol. 2012 Jun

2. Bruni L, et al. Human Papillomavirus and Related Diseases in Spain. Summary Report 10 December 2018

In post-menopause, a woman with HPV:

- 1. Has no risk of developing a cervical lesion**
- 2. Has greater ease in developing antibodies than younger women**
- 3. Has a lower capacity for immune response than younger women**

- 61 year-old patient who consults in December 2018 for the first time to our clinic. She wants to have cytology and HPV determination performed. She says she is worried because she has started to have intercourse with a new partner and tells us that at 52 years of age, she was diagnosed with ASC-US positive for HPV 16, with the cytology normalizing and then being negative for HPV determination a year later.

- **61 years of age. 4 pregnancies with normal deliveries.**
- **Smoker of 4 cigarettes per day.**
- **Divorced 22 years ago, then had several partners and has had a new partner for the last 4 months.**
- **Hypothyroidism taking Eutirox 50 mg/day. Arthritis of the right knee.**
- **Appendectomy and breast augmentation**
- **Menopause at 51 years of age, taking Hormone Replacement Therapy for 5 years.**
- **Not vaccinated against HPV.**

- The patient requests cytology and HPV determination.
- A gynecologic examination is performed, cytology, and a sample is obtained for HPV determination.

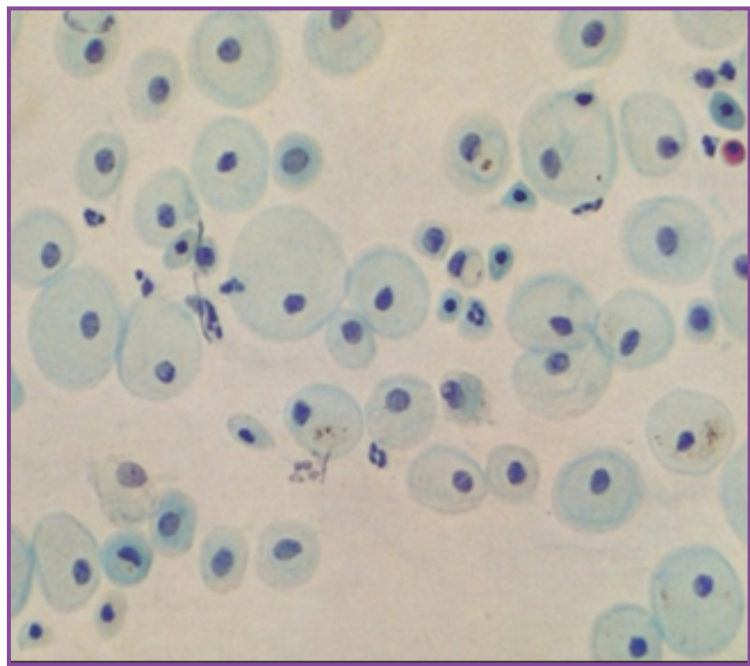
Results

- Gynecologic examination clinically compatible with post-menopausal woman. Vulvo-vaginal atrophy.
- Normal cytology with signs of atrophy.
- HPV determination. **Positive for 16.**

Examination



Cytology

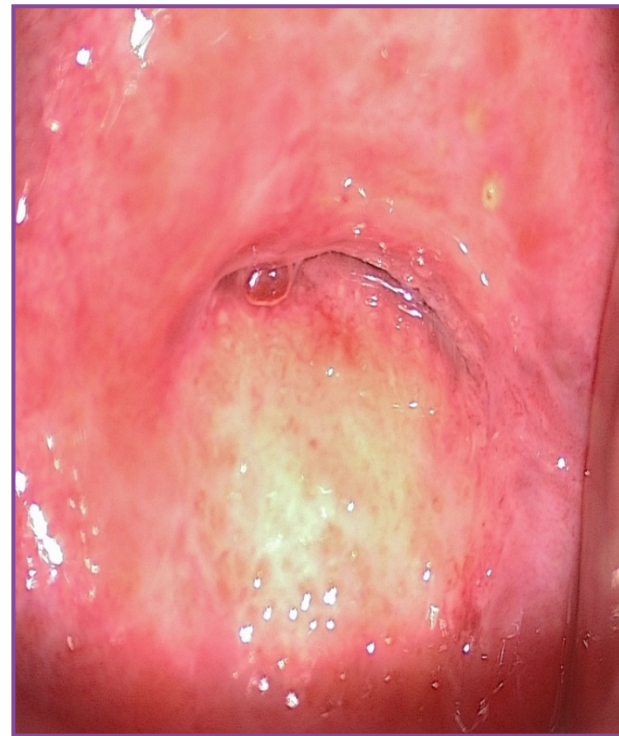
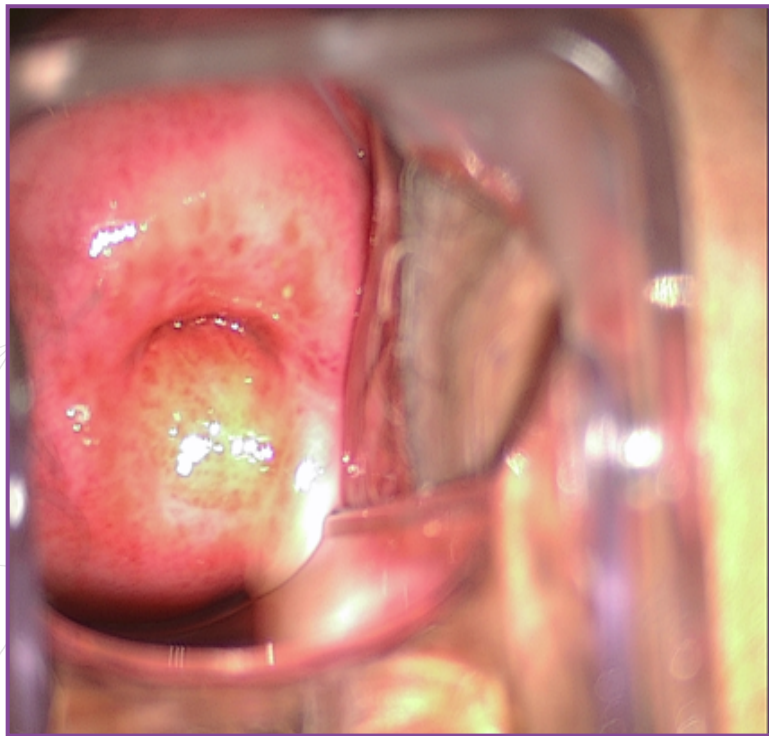


It is decided to perform a colposcopy

RESULTS

- No atypical vessels, no aceto-white lesions, no transformation zone.
- Cervix appears atrophied.
- No biopsies taken.

Colposcopy



We pose three questions

- 1. For a patient who previously had HPV 16 and has it again with apparently normal cytology and colposcopy. Do we do nothing and wait a year, or...**
- 2. This is a post-menopausal patient with atrophy. Should we prescribe local estrogens?**
- 3. She has never been vaccinated. Should we recommend it?**

**For a patient who previously had HPV 16 and has it again with apparently normal cytology and colposcopy.
Do we do nothing and wait or...**

- We talk to the patient and effectively decide to perform viral messenger RNA determination of the E6/E7 oncogenes.
- The E6/E7 oncogenes are recognized as responsible for initiation and progression of invasive tumors. For their detection, there are a series of commercial techniques that differ substantially insofar as the HPV genotypes evaluated (5 or 14) and the analytic method (quantitative or qualitative). DNA tests locate certain HPV genes, but do not allow the differentiation between the mere presence of the virus and active infection. On the contrary, mRNA tests detect an active HPV infection that is susceptible to give rise to pre-cancerous lesions.

Viral mRNA for E6/E7 oncogenes: **NEGATIVE**

- Aptima HPV assay³
- We tell the patient she can relax because she does not have an active infection



Viral mRNA determination of E6/E7 oncogenes

1. Is used to determine the type of papillomavirus.
2. Indicates an active HPV infection.
3. Does not detect HPV.

**This is a post-menopausal patient with atrophy.
Should we prescribe local estrogens?**

- There are data to suggest that the use of local estrogens can improve the transformation zone, making a biopsy more feasible⁴.
- Moreover, this is a post-menopausal woman with clear vulvo-vaginal atrophy and who is sexually active.
- We discuss with the patient and decide to prescribe treatment with vaginal estriol suppositories (2 times per week).

For these two questions

- If I already have an HPV positive determination, can I be vaccinated?

Answer: Yes

- If I am post-menopausal, can I be vaccinated?

Answer: Yes

We recommend
Vaccination with Gardasil 9®

- **Women with infection by one of the types protected against obtain high levels of protection against the other types covered by the vaccine.**
- **Vaccination against HPV of women previously infected with HPV has a favorable safety profile and generates a high level of immune response.**
- **In productive infections, HPV vaccination may reduce:**
 - 1. Dissemination of virions towards the transformation zone.**
 - 2. Transmission of virions to their partner.**

In post-menopause, a woman:

- 1. Does not benefit from being prescribed the vaccine.**
- 2. The vaccine only works if she has not had HPV before.**
- 3. The vaccine has a good response and a favorable safety profile.**

Do not forget that women in peri- and post-menopause have:

- **A lower capacity for immune response to HPV.**
- **A greater probability of persistent infections, especially of the most oncogenic types.**
- **A greater potential risk of developing premalignant lesions or cancer over time.**