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Meisels A & Fortin R. Condylomatous lesions of the cervix and vagina. 1. Cytologic patterns. *Acta Cytol.* 20:505-9, 1976; and **Meisels A, Fortin R & Roy M.** Condylomatous lesions of the cervix. 2. Cytologic, colposcopic and histopathologic study. *Acta Cytol.* 21:379-90, 1977.
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These papers first described the morphologic characteristics of human papillomavirus (HPV)-induced changes on Papanicolaou smears, histologic sections, and colposcopic patterns of patients with subclinical infections of the cervix and vagina. These changes had previously been considered typical of "mild dysplasia," a lesion that was known to progress to carcinoma in a small percentage of cases. A relationship of HPV with cancer of the cervix was therefore suggested. [The *SCI*® indicates that these papers have been cited in more than 275 and 295 publications, respectively, making them the two most-cited papers published in this journal.]

Human Papillomaviruses and Carcinoma of the Cervix

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My own interest in human papillomavirus (HPV) infection of the cervix and vagina began in 1974 when I noticed the similarity of cells in histologic sections of condylomata acuminata of the vulva with cells that I had previously observed on Papanicolaou smears. These "koilocytes"[1] had been described by several authors, although without reference to their viral origin.[2] They represented a sign of HPV infection of the cervix. However, this cellular pattern had previously been interpreted as corresponding to a mild dysplasia—the earliest part of a continuum that could eventually lead to invasive carcinoma of the cervix. The possibility that HPV played a role in the etiology of this cancer had to be considered. Around that time, H. zur Hausen had begun his research into the relationship of HPV to human tumors.[3,4]

My colleagues (Roger Fortin, who is a staff pathologist at Saint-Sacrement Hospital, and Michel Roy, currently head of the Department of Obstetrics and Gynecology of Laval University) and I discussed the implications for many months because the concept of early squamous lesions of the cervix would be drastically modified by the finding that HPV could induce changes that had earlier been identified as precursors of carcinoma. One of our problems related to the name to be given to this lesion. Because the cellular changes mimicked those of condylomata acuminata, but the lesions were usually flat, we opted for the term "flat condyloma."

I had observed frequently an abnormal keratinization (dyskeratosis) in cases with HPV infection, in addition to koilocytosis. These two signs are now considered the classical cellular manifestations of HPV infection. At first, these findings were not well received—some said I had "condylomania." At that time, the herpes simplex virus (HSV) was considered the most probable agent causing cancer of the cervix, and I often found myself in a minority of one, upholding the role of HPV against the many defenders of HSV. With the identification of HPV within the affected cells by electron microscopy, immunoperoxidase, and molecular hybridization, techniques established in our laboratory by my collaborator C. Morin, the controversy finally ended and there is now a general acceptance for the role of HPV in the development of carcinoma of the cervix.[5,6]

Papillomavirus DNAs have now been detected in the whole continuum of cervical lesions, including low-grade and high-grade squamous and glandular intraepithelial lesions of the cervix (according to the newly proposed Bethesda System), as well as in invasive carcinomas. Research is now under way to define the role of cofactors (tobacco, dietary factors, etc.) and to accurately measure the incidence of HPV infections in asymptomatic women in various geographic areas, using the newly developed polymerase chain reaction.

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2. **Meisels A.** The story of a cell. The George N. Papanicolaou Award lecture. *Acta Cytol.* 27:584-96, 1983.
3. **zur Hausen H.** Attempts to detect virus specific DNA sequences in human tumors: I. Nucleic acid hybridizations with complementary RNA of human wart virus. *Int. J. Cancer* 13:650-6, 1974.
4. - - - - - - - - - . Condylomata acuminata and human genital cancer. *Cancer Res.* 36:794, 1976.
5. **Brisson J, Roy M, Fortier M, Bouchard C & Meisels A.** Condyloma and intraepithelial neoplasia of the uterine cervix: a case-control study. *Amer. J. Epidemiol.* 128:337-42, 1988.
6. **Morin C, Bouchard C, Fortier M, Levesque R & Meisels A.** A colposcopical lesion of the uterine cervix frequently associated with papillomavirus type 16 as detected by in situ and Southern blot hybridization: a cytohistological study. *Int. J. Cancer* 41:531-6, 1988.

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