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## Microcolpohysteroscopic Features of Cervical Condylomatosis and their Accuracy in Detecting Subclinical Papillomavirus Infection

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### Abstract

Hundrednine patients affected by cervical condylomatosis were investigated with the Hamou's microcolpohysteroscope. Five different types of abnormalities are described: superficial koilocytosis, cervical intraepithelial neoplasia (CIN) plus koilocytosis, "vortex" cellular arrangement, superficial keratosis and microcondylomata acuminata. The characteristic koilocytes, either alone or in association with dysplastic elements allowed the immediate diagnosis in 82 (75%) cases. A high percentage of cervical smears – however – were diagnosed as false negative. The Authors emphasize the sensitivity of the microcolpohysteroscopy, compared with the traditional colposcopy and the cervical smear, in the morphologic and topographic study of human papillomavirus lesions of the uterine cervix.

### Key Words

cervical intraepithelial neoplasia (CIN), condylomata, koilocytosis, microcolpohysteroscopy (MCH), (human) papillomavirus (HPV).

### Introduction

Human papillomavirus (HPV) infection of the uterine cervix is usually revealed by viral cytopathic effects (VCE) on the squamous epithelium (1) (2) (3). The coexistence of VCE and cervical intraepithelial neoplasia (CIN) (4) (5), and the lower mean age of the patients affected with VCE plus CIN com-

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pared to those suffering from CIN alone (6), stresses the importance to accurately detect this viral pathology and to investigate its relation with the CIN.

At least in this specific perspective of research, Hamou's microcolpohysteroscopy (MCH) seems to be able to improve the diagnostic possibilities not only of the traditional colposcopy, but also of the exfoliative cytology (7) (8).

The aim of this study is twofold: 1) to describe MCH cervical patterns in patients affected by subclinical cervical condylomata; 2) to evaluate the accuracy of the MCH scanning compared with the exfoliative cytology.

## Subjects Material and Methods

From July, 1981 to July, 1986, women referring to our private office for common screening programmes, and those with previously colposcopically and/or cytologically detected cervical HPV infection or CIN plus VCE, underwent contact microcolpohysteroscopy (MCH). A cervical smear was taken immediately before the MCH investigation; a MCH was performed and pathological areas consistent with cervical condylomatosis and/or CIN plus VCE were submitted to direct biopsies.

The characteristics of the instrument (Karl Storz GmbH & Co. Tuttlingen, West Germany), and the technique have been previously described (9) (10). Pictures, here presented, have been obtained with an Olympus OM1 35 mm. camera connected to the direct eye-piece of the microcolpohysteroscope with the Karl Storz zoom lens 593. A converter lens 2X was added to obtain a fully impressed photogram. Film used was Kodak Ektachrome 400 ASA daylight. An electronic flash generator (550 BK) and a flash tube (555 B) with connection for examination light was preferred.

Cervical smears were stained according to the common Papanicolaou's technique. Biopsies were taken on ectocervical areas on the guidance of the MCH scanning; samples, after alcohol or formalin fixation, were embedded in paraffin, sectioned and stained with H & E, as usual. In our Department, "CIN" instead of "dysplasia" is currently used by the Cytologists, the correspondance between cytological and histological diagnosis being near 100%, in their experience.

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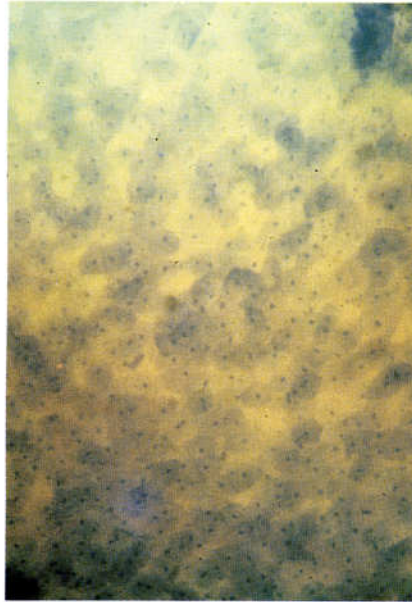
*Fig. 1 - Normal cervical epithelium: note the regular pattern of the cells (microcolpohysteroscopy, X = 150; waterman blue ink stain).*

*Fig. 2 - Superficial koilocytosis (microcolpohysteroscopy, X = 150). Fig. 2A - Schematic representation of superficial koilocytosis: vertical section (at left) and superficial appearance (at right); empty circles represent koilocytes.*

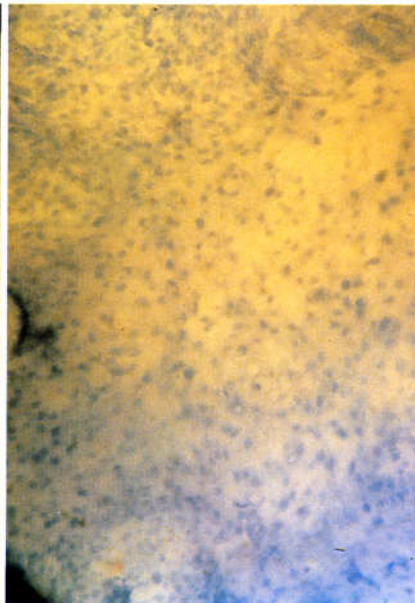
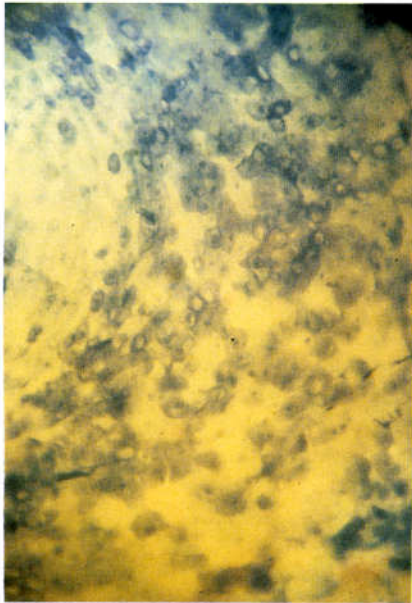
*Fig. 3 - Cervical biopsy: note the koilocytes in the intermediate and superficial layers (H & E stain, X = 150).*

*Fig. 4 - Cervical intraepithelial neoplasia plus koilocytosis: note the increase in the nucleo-cytoplasmic ratio, the cellular crowding and rare superficial koilocytes (microcolpohysteroscopy, X = 150). Fig. 4A - Schematic representation of cervical intraepithelial neoplasia plus koilocytosis (see above). Marked circles represent dysplastic cells.*

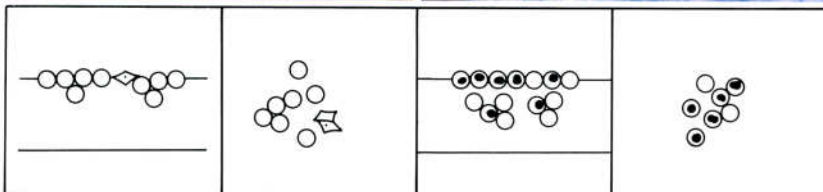
1-3



2-4



2A-4A



## Results

During the five years time interval, 109 women were enrolled in the study. In 60 of these, diagnosis of HPV infection a/o CIN was already suspected by colposcopy a/o cytology before the MCH investigation. In the others 49 patients, the presence of the above mentioned diseases was firstly suspected at the MCH examination, that recognized the following pathological patterns (at side of each of these, the percentage related to the total 109 cases is indicated).

*Microcolpohysteroscopic features.* The healthy squamous epithelia (either the native or the metaplastic one) viewed of polygonal, light blue stained cells, with a well visualized dark blue pyknotic nucleus; the monomorphism of the superficial layer and the regular pattern of the component cells were also evident (Fig. 1). Pathological areas, that could be referred to the HPV infection, were classified into 5 distinct types of abnormalities, as follows.

*Type 1: Superficial koilocytosis* (50 cases, 45.8%). It is characterized by round or polygonal cells on the epithelial surface, with a "hole" in the pale blue cutoplasm, and a large blue nucleus, often displaced toward the periphery (Figs. 2-2A). The histologic specimens displayed koilocytes in the superficial and intermediate epithelial layers (Fig. 3).

*Type 2: CIN plus koilocytosis* (32 cases, 29.3%). At 60 X, the superficial epithelium exhibited a great degree of cellular crowding. At 150 X, contact scanning revealed a marked anisokariosis and an increase in the nucleo-cytoplasmic ratio. Binucleated cells were also identified (Figs. 4-4A). CIN plus VCE was suspected when rare superficial koilocytes could be observed in the affected area or in the contiguous zone. Histology confirmed the presence of CIN grade 1 or 2 with evident mitoses in the intermediate layers, and associated with the presence of classical koilocytes (fig. 5).

*Type 3: "Vortex" cellular arrangement* (25 cases, 22.9%). In these 25 cases this feature appeared alone; in others, however, it was coexistent with the above mentioned described patterns. The cells displayed a whirling trend; furthermore, when the tip of the instrument was pressed upon the stroma, they looked like a "beehive", and the borders of cytoplasmic membranes (deformed by reciprocal pressure) were easily seen, contrasting with the cellular clearing due to vacuolization (Figs. 6-6A). Rarely cervical scraping disclosed clusters of superficial cells in similar arrangement (Fig. 7). Histology showed the same whirling trend also in the intermediate layers (Fig. 8).

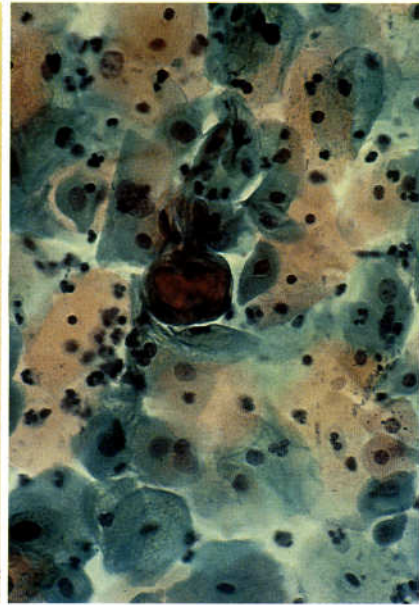
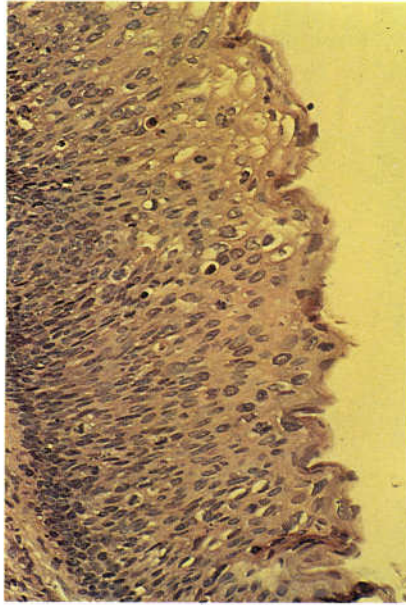
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Fig. 5 - Cervical intraepithelial neoplasia grade 2 plus koilocytosis: presence of mitoses in the intermediate layers (H & E stain, X = 250).

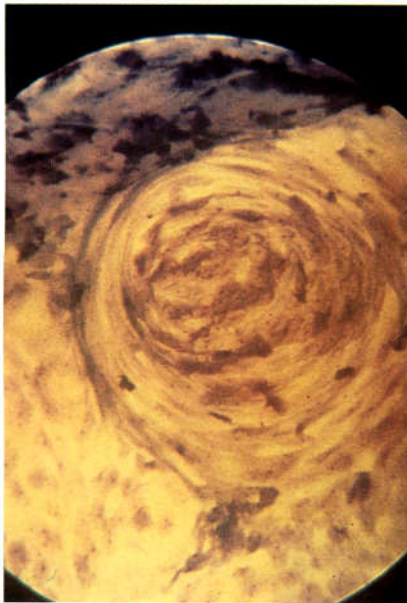
Fig. 6 - "Vortex cellular arrangement". The cellular clearing contrasts with the marked cytoplasmic membrane (microcolpohysteroscopy, X = 150). Fig. 6A - Schematic representation of the "vortex cellular arrangement": polygonal elements represent squamous superficial cells.

Fig. 7 - Cervical smear: whirling trend in scraped cells (Pap stain X = 250).

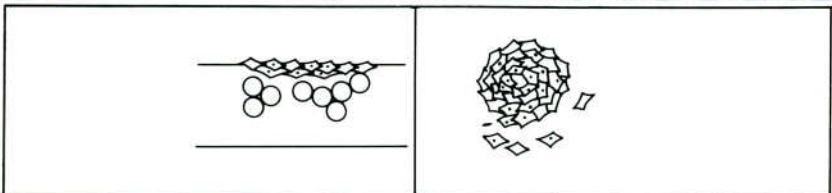
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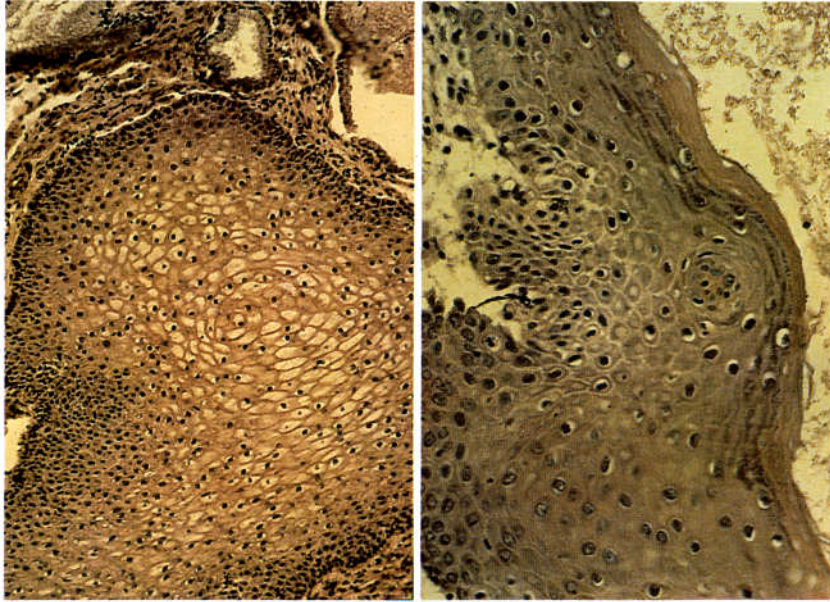


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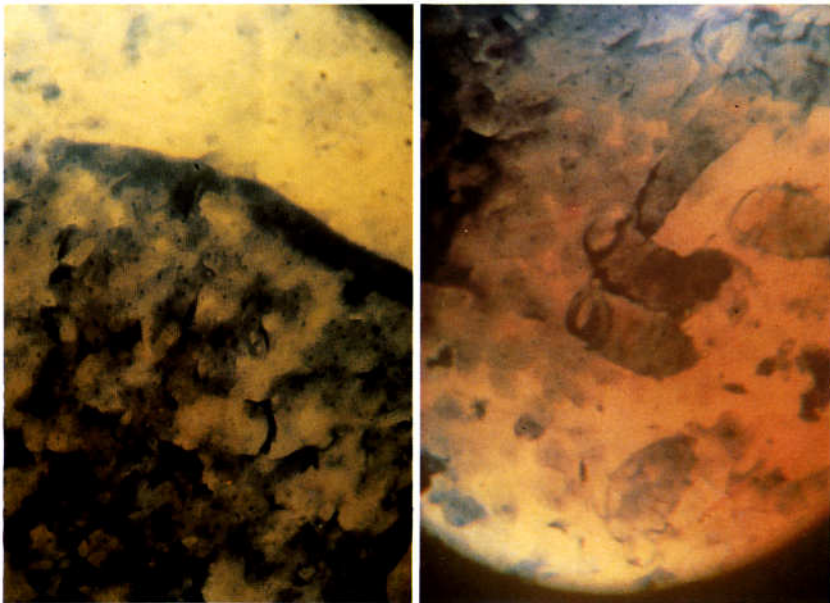


6A

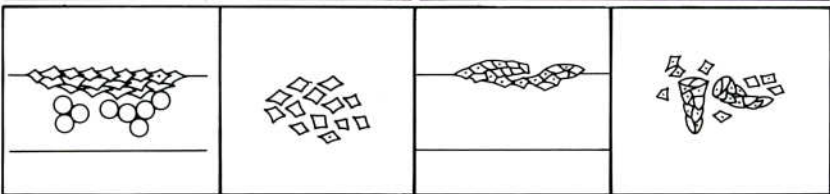




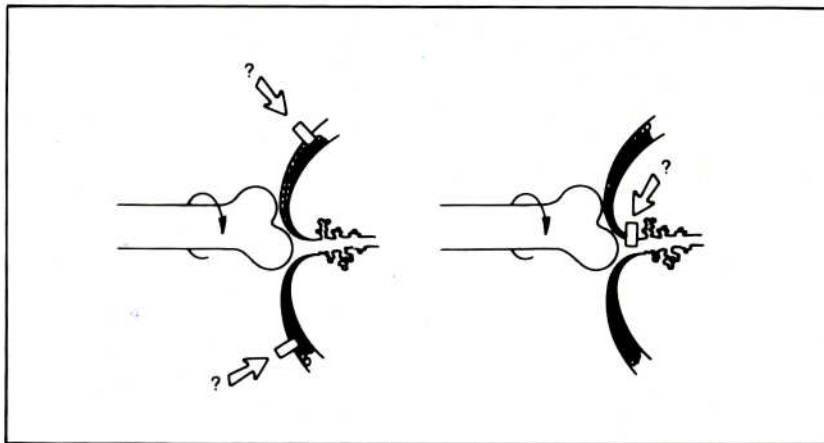
8-10



9-11



9A-11A



12

*Type 4: Superficial keratosis* (see Tab. I). All these cases were associated with one or other of the three types above described. The superficial epithelium barely takes up the Waterman blue ink; contact scanning allowed to observe an area often far from the squamo-columnar junction, quite different from the surrounding healthy epithelium, characterized by anucleate squamous cells among which it was possible to see rare koilocytes arising from the deeper layers (Figs. 9-9A). Biopsies clearly demonstrated superficial parakeratosis associated with the presence of scattered koilocytes (Fig. 10).

*Type 5: Microcondylomata acuminata* (2 cases, 1.8%). This feature was observed near the squamo-columnar junction in a young nullipara, and on the anterior lip in a pluripara with marked keratosis. It was characterized by some raised, cone-shaped, micropapillary formations. They were movable and at-

Fig. 8 - Cervical biopsy: the whorled pattern is also represented in the histologic section (H & E stain, X = 400).

Fig. 9 - Superficial keratosis: note the sharp boundary between the normal and the pathologic area (microcolpohysteroscopy, X = 150). Fig. 9A - Schematic representation of superficial keratosis: the polygonal elements without dots represent anucleate superficial cells; the empty circles represent the koilocytes.

Fig. 10 - Cervical biopsy: the thick superficial keratinized layer hides the koilocytes below (H & E stain, X = 250).

Fig. 11 - Microcondylomata acuminata: note the circular base made up of few squamous cells (microcolpohysteroscopy, X = 150). Fig. 11A - Schematic representation of microcondylomata acuminata.

Fig. 12 - Schematic representation of cervical scraping: the arrows indicate areas not usually sampled.

tached to the epithelium by a circular base, made up of three-four cells at the most, similar to the superficial cells described in the "vortex" cellular arrangements type (Figs. 11-11A). Cytology was not helpful, in one case, in establishing the diagnosis. Histology confirmed the well known feature.

*Correspondence between microcolpohysteroscopy and cytology.* Tab. I clearly shows that Pap smears were negative in about forty per cent of the type 1 cases. In the type 2 group, only few cases were cytologically negative. The "vortex" cellular arrangement group had the eighty percent of negative cytology.

**TABLE I. Microcolpohysteroscopy (MCH) / cytology correlation.**

MCH-features	Cytology					
	total	%	pos	%	neg	%
Type 1: superficial koilocytosis	50	45.8	31	62.0	19	38.0
Type 2: CIN + koilocytosis	32	29.3	30	93.7	2	6.2
Type 3: "vortex" cellular arrangement	25	22.9	5	20.0	20 (+)	80.0
Type 4: superficial keratosis (*)	(32)	(29.3)	(22)	(68.7)	(10)	(31.2)
Type 5: microcondylomata acuminata	2	1.8	1	50.0	1	50.0
All the features	109	100.0	67	100.0	42	100.0

(+) It is evident that this condylomatous feature is rarely disclosed by cervical scraping, giving the highest rate of false negative cytology (20 cases = 18.3% of total 109 cases).

(\*) Since superficial keratosis was observed in association with types 1, 2, 3 and 5 condylomatosis, values here reported between ( ) have not been summed in the total.

## Discussion

Hamou's microcolpohysteroscope allows identification of the cells modified by the action of the HPV. Furthermore, when it could be interesting, the "in vivo" cellular observation allows the evaluation of the site and the extent of the pathologic process, at least when it has reached the surface (11).

The particular "vortex" arrangement is characterized by cellular elements that in 25 cases (22.9%) were the only hint of cervical condylomatosis. This feature presumably corresponds to the first phase of the florid process, that can be arrested at this stage; whirling trend, in particular, could be the base of future papillary growth. Cervical scraping rarely disclosed superficial cells in similar arrangement, giving a high percentage of negative cytology



(18.3% of total 109 cases), mostly in patients in which this feature was the only element useful to the diagnosis.

Superficial keratosis was always observed in association with other MCH features. It was present in 32 cases, ten of which (9.1% of total) gave negative Pap smears. Keratosis must be considered as an aspecific cellular disorder, but more often it expresses the superficial suffering of an HPV affected epithelium. Since it can hide not only VCE, but even CIN grade 1 or 2 in the layers below, a well aimed biopsy is essential for the diagnosis.

Comparing MCH with cytology, it is evident that only CIN plus koilocytosis (type 2 abnormality) showed a low rate of negative cytology. Superficial koilocytosis, that is the most common and pathognomonic feature of HPV infection (12) (13) (14), enabled us to immediately diagnose viral infections in the 50 cases (45.8%) in which these cells were clearly visible on the surface, against the 62% positivity rate of cytology. Negative reports in cervical scrapings from cases with "vortex" cellular arrangement (type 3 abnormality) amounted to the 80% of the cases, a very high percentage. Superficial keratosis showed a third of cases, approximately, of negative cytology. Type 5 abnormality was minimally represented, with half of cases of negative smears.

The possible explanation of such discrepancies could be as follows: 1) the lack of obvious cellular changes compatible with the diagnosis of viral infection when the squamous epithelium was arranged exclusively in the "vortex" shape; 2) the underestimation, or the absence of cellular elements, such as dyskeratocytes, keratocytes etc., in the smears that were negative for CIN.

In conclusion, our data suggest that the use of MCH is helpful in cases of subclinical cervical condylomatosis, as it allows the operator to observe highly specific cellular pictures, with a sensitivity which is noticeably superior to the traditional colposcopy or cervical smear. This possibility could open a new perspective into the study of the development of viral processes.

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## Riassunto

### ACCURATEZZA DIAGNOSTICA E QUADRI MORFOLOGICI MICROCOLPOISTEROSCOPICI NELLA CONDILOMATOSI CERVICALE.

Dal luglio 1981 al luglio 1985 gli AA. hanno utilizzato il microcolpoisteroscopia di Hamou (MCH) per esaminare tutte le pazienti che afferivano al loro studio privato per i comuni programmi di screening. Tutti gli esami MCH sono stati fatti precedere da un prelievo citologico e – in caso di positività alla MCH – fatti seguire da un prelievo biptico mirato.

I quadri MCH osservati nelle 109 pazienti considerate sono stati suddivisi in cinque tipi, sulla base delle caratteristiche morfologiche presentate, e cioè: la "Coilocitosi Superficiale", il "CIN + Coilocitosi", la "Disposizione a Vortice", la "Cheratosi Superficiale" e i "Microcondilomi Acuminati". La citologia ha presentato una percentuale di falsi negativi estremamente bassa (6%) nei casi di VCE associato a CIN, ma variamente elevata in presenza di "Coilocitosi Superficiale" (38%) o nei casi in cui la diagnosi MCH si basava sulla presenza isolata di cellule con "Disposizione a Vortice" (80%). Circa un terzo dei casi con "Cheratosi Superficiale" (31.2%) e uno dei due soggetti con "Microcondilomi Acuminati" risultarono negativi al Pap-test. Gli Autori discutono sul significato di questi risultati e concludono sottolineando l'importanza della MCH nei casi di condilomatosi cervicale sub-clinica.