Progression and Regression of Carcinoma in Situ of the Uterine Cervix

The international symposia by mail introduced by the founder and editor, George L. Wied, in the inaugural volume of Acta Cytologica, in 1957, continued in volume 6. The topic for discussion, progression and regression of carcinoma in situ of the uterine cervix, selected by the editors, was not only timely in 1962 but it is still fascinating 40 years later, though not debated anymore.

In 1962, the first time, several hundred pages of Acta Cytologica were devoted to publication of peer-reviewed articles on a wide range of topics in cytology. It was also the first time that the honorary editor, George N. Papanicolaou, had an asterisk after his name, indicating that he was deceased. He had died of a heart attack on February 19, 1962, at age 79, shortly after he assumed the directorship of the Papanicolaou Cancer Research Institute in Miami, Florida. It is noteworthy that the editorial board and the editorial advisory board were heavily international.

A. PROGRESSION OF CARCINOMA IN SITU

H.K. Fidler, D.A. Boyes, Vancouver, British Columbia, Canada:

Theoretically, all carcinomas must commence as intra-epithelial lesions. In studying the relationships between intra-epithelial carcinoma and invasive carcinoma certain progressive phases are apparent and are characterized by first,
surface carcinoma which spreads laterally and gradually extends into and fills mucous glands then, second, small discrete scattered microinvasive foci penetrate the stroma beyond the basement membrane but during this phase the lesion appears to be held in biologic restraint until, third, a stage is reached in which restraint is lost, invasive foci become confluent and frank invasion seen although at first constituting a small occult lesion which however develops with relative rapidity to be recognized finally in the fourth stage, that of clinically invasive carcinoma. During a ten-year period the mean ages in these four groups have been as follows:

1. Carcinoma in situ - 41.7 years (473 cases)
2. Carcinoma with discrete microinvasive foci - 46.0 years (31 cases)
3. Occult invasive carcinoma with confluent invasive foci - 51.0 years (20 cases)
4. Clinical invasive carcinoma - 52.4 years (512 cases)

All cases were associated with carcinoma in situ. It is our feeling that the great majority of clinical carcinomas are preceded by carcinoma in situ of such significant extent and duration that annual cervical screenings will detect most cases before invasion has occurred.

H.G. Hillemanns, Freiburg i. Br., Germany:

We could not find an unequivocal squamous cell carcinoma of the cervix without intra-epithelial preinvasive stage and latent period. Therefore, we have to answer the important question of whether every squamous carcinoma is passing through the stage of carcinoma in situ or not, “probably with yes.”

Leopold G. Koss, New York, New York, USA:

It is very likely that 100 per cent of invasive cervix cancer passes through the stage of in situ carcinoma. The author has always found an in situ carcinoma either adjacent to or contiguous with invasive cancer. The in situ carcinoma may be extremely well differentiated to the point of imitating normal epithelium to the uninitiated. To quote Fred W. Stewart (Chairman of Pathology at the Memorial Hospital for Cancer and Allied Diseases, in New York City) who said at the Third National Cancer Conference of the American Cancer Society in Philadelphia in 1957: that “every infiltrative cervix cancer must come from in situ cancer, there being no other thing it can come from.”

John J. Sullivan, Auckland, New Zealand:

We are in complete agreement that the majority, if not all, invasive cervical carcinomas are preceded by a pre-invasive stage. This clear morphological association, and the established ability of the preinvasive stage of this disease to progress to invasive carcinoma leave little doubt that carcinoma in situ is one step in the genesis of all invasive cervical carcinomas.

Leopold G. Koss, New York, New York, USA:

A certain percentage of cervical carcinoma in situ is not visible to the naked eye of expert examiners. Hinselmann, of course, knew that over a quarter of a century ago and helped his eye with a colposcope. With few exceptions, in situ carcinoma is an asymptomatic and therefore clinically latent disease until invasion; thus the period of latency may vary tremendously from two years anywhere to 20 years or more. The important matter appears to be: what precedes in situ carcinoma and for how long. It appears that some patients may develop carcinoma in situ rapidly without any obvious intermediate stages and some go through a variety of intermediate stages.

Michael J. Jordan, Genevieve M. Bader and Emerson Day, New York, New York, USA:

In a great number of cases carcinoma in situ has a long latent period up to ten years and it may even be that some in situ lesions remain static for the lifetime of the patient.

Werner Schreiner and Hans-Iselin Wyss, Zürich, Switzerland:

The latent period of invasive cervical carcinoma is at least 5.5 years on the average.

B. REGRESSION OF CARCINOMA IN SITU

Jules-André Bret, Fernand Coupez, Paris, France:

If we admit, that the invasive cancer my have been preceded by a histological state called irregular
dysplasia, we no longer believe that a term as imprecise as that of carcinoma in situ is necessary. The stage of carcinoma in situ is only a particular pattern in the imprecise definition of irregular dysplasias. The factors which develop such lesions may, if they disappear, let the lesions regress. Their persistence causes the lesions to remain. Invasion is probably due less to an aggravation of the epithelial atypia than to a breakdown of the underlying defenses.

Leopold G. Koss, New York, New York, USA:

One should clearly differentiate between spontaneous regression of the lesion and a regression following a trauma or a procedure, however, insignificant. This writer has never seen a carcinoma in situ, diagnosed and followed cytologically without any additional procedures, that would regress spontaneously. On the other hand, approximately 15 to 20 per cent of cervical carcinoma in situ cannot be traced following biopsies, superficial cautery, topical antibiotics, and, in the rare instances, the trauma of childbirth.

Hans Limburg, Homburg, Saar, Germany:

I have never seen a spontaneous regression of a carcinoma in situ. The malignant epithelium may persist for years in a latent stage before the development of a true carcinoma.

Alexander Meisels, México, D.F., México:

Of our cases, only a very few regressed, always after ample biopsies. No case was observed to regress spontaneously.

Violette M. Nuovo, Paris, France:

I believe that few have ever seen a regression of a carcinoma in situ which was diagnosed and followed only cytologically without any additional diagnostic procedure.

Edited by Steven I. Hajdu, M.D., F.I.A.C.

Financial Disclosure: The editor has no connection to any companies or products mentioned in this article.

Keywords: cervical cancer, carcinoma in situ, Acta Cytologica. (Acta Cytol 2002;46:1158–1160)