THE PROBLEM OF EARLY DIAGNOSIS OF CANCER OF THE UTERINE CERVIX

by N. V. Fedorova

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FOREWORD

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- USSR -

Following is a translation of an article by N. V. Fedorova in the Russian-language periodical Laborator-
nye Delo (Laboratory Work), Moscow, Vol. 6, No. 3, May-June 1960, pages 4-6.

The development of malignant neoplasms is preceded by a pro-
longed period in which no expressed clinical manifestations are
noted. Many authors (1 and others) think that the earliest cli-
nical manifestations of cancer essentially appear in the latest stages
of the disease.

Franke, in 1907, was the first to turn his attention to the
atypical changes in the epithelium. For a long time, however, this
atypia was explained as an inflammatory and other processes in the
tissues. A diagnosis of cancer was made by histologists only in
those cases in which the changed epithelium began to penetrate into
the surrounding tissues.

Experimental research work has shown that a period of modi-
fication in the epithelium precedes invasive cancer, and that on
the basis of these modifications it is possible to identify a mali-
gnant neoplasm. This made it possible to introduce a new stage, a
zero stage into the International classification of cancer of the
uterine cervix. The duration of this stage differs; in some cases
a number of years lapse before the penetration of the epithelium
into the tissues occurs. The early discovery and therapy of pre-
invasive cancer of the uterine cervix provides cure in 100 percent
of the cases (1).

The complex examination of the patients is required for the
early diagnosis of cancer of the cervix of the uterus. The histolo-
gical method of the investigation of a piece of tissue from the
affected section of the uterine cervix is the leading method of
microscopic examination. The cytological method of investigation
is used along with that of the histological method. It does not
replace biopsy, but makes possible a dynamic observation, and in
the case of invasive cancer provides a high percentage of coinci-
dence with the histological conclusions.

Cytological diagnostics are based on the study of the mor-
phological indices of the cell and groups of cells. In cases of
preinvasive cancer, histological examinations disclose in addition
to the disordered disposition of the cells in the epithelium layer,
their polymorphism, the increase in the size of the nuclei, the increase in the number of mitoses, that is, modifications which concern the morphology of the cells.

We carried out cytological examinations of a group of patients who arrived at the dispensary with precancerous diseases (erosion, ectropion, polyp). The material was gathered by means of scraping, and smears were immediately prepared. Fixation was accomplished by the use of the Nikiforov mixture, and the smear was stained by azure-eosin of Philipson's modification. Our conclusions were compared with those of the histological conclusions. Three hundred-twenty patients were examined in all, and the results are presented in the following table.

<table>
<thead>
<tr>
<th>Histological Investigations</th>
<th>Number of cases</th>
<th>Cytological Investigations</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erosion of the uterine cervix (mainly Glandular erosion)</td>
<td>276</td>
<td>Normal epithelium</td>
<td>265</td>
</tr>
<tr>
<td>Erosion of uterine cervix with spreading epithelium</td>
<td>13</td>
<td>Epithelium, Cells of epithelium</td>
<td>2</td>
</tr>
<tr>
<td>Erosion of uterine cervix with spreading epithelium with atypia</td>
<td>4</td>
<td>with some Atypia</td>
<td>1</td>
</tr>
<tr>
<td>Erosion of uterine cervix with cystic spreading of glands</td>
<td>5</td>
<td>Malignant Neoplasms</td>
<td>3</td>
</tr>
<tr>
<td>Erosion of uterine cervix with glandular hyperplasia</td>
<td>10</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>Hyperkeratosis</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Inflammatory process</td>
<td>7</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>Glandular polyp</td>
<td>4</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>320</td>
<td>264</td>
<td>33</td>
</tr>
</tbody>
</table>

Quantities of leukocytes, single cells of squamous epithelium, groups of cells, and disconnected cells of cylindrical epithelium were usually found among the erythrocytes in the scrapings taken from the uterine cervix afflicted with erosion. Cytological investigations revealed normal epithelium in 264 of the 320 patients suffering from different processes in the area of the uterine cervix, including patients afflicted with inflammatory processes and polyps of the uterine cervix.

Deviations from the normal were found in the smears of the epithelium taken from the other 36 patients. The very early changes were marked by an enlargement of the cells of the cylindrical epithelium and their nuclei. Single enlarged nucleoli appeared in the
nuclei. The protoplasm became basophilic, frequently alveolar. In other preparations, normal epithelium was either absent or present in insignificant quantities; cells of predominantly rounded or polygonal forms were found, but with still larger nuclei which occupied almost the entire cell and with one or two enlarged nucleoli and basophilic protoplasm.

In the beginning of the investigations, we classified the latter cells as being clearly malignant. Thus, in two cases, we expressed our suspicion of a malignant process after a clinical and histological diagnosis of the erosion of the uterine cervix was made. Following electrocoagulation, an examination of the patients found the uterine cervix to be clean, and the patients felt improved.

Further, we turned our attention to the fact that epithelium with some atypia is found in those cases in which histological investigations disclose not only erosion, but erosion with a spreading epithelium, sometimes with cystic expansion and hyperplasia of the glands, etc.

Cytological examinations made of 33 patients revealed epithelium with atypia in 24, while in one patient newly formed malignant cells with atypia were clearly identified. Histological investigations of material obtained following a biopsy which was carried on the patient revealed glandular erosion with growing atypical epithelium. Among the erythrocytes of the scrapings were found many cells with epithelium free nuclei or groups of cells with large nuclei containing several nucleoli, with basophilic protoplasm, that is, those cells which we usually find in malignant neoplasms. A diagnosis of "suspicion of cancer of the uterine cervix" was made, and recommendations were made that the patient be kept under observation.

Some difference in the data obtained from histological and cytological investigations may be due to the fact that a biopsy is limited to a smaller section of the affection than is the scraping. Therefore, there are better chances for the discovery of atypia in the latter than in the former.

Thus, the cytological method of investigation makes it possible to determine early deviations from normal in the epithelium and to identify the early symptoms of atypia. This should warn the physicians that these patients should be kept under observation, and that a biopsy should be performed at an early time. Even if the histological examination provides a negative result, the physician should carry out the necessary therapy until complete recovery takes place.
Bibliography