

COMPARATIVE CHARACTERISTICS OF HISTOLOGICAL TYPES OF GASTRIC CANCER  
DEPENDING ON DNA CONTENT IN TUMOR CELL NUCLEI

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Lauren's classification of carcinoma of the stomach, according to which two main histological types are distinguished — intestinal and diffuse — has recently been widely acclaimed in practical oncology [7, 10]. The intestinal type has marked glandular structure, and the tumor cells have an enteroid brush border and no signs of secretion (Fig. 1a). Tumors of this type are distinguished by predominantly expansive growth with the formation of exophytic forms of cancer. The diffuse (muroid cell type) of cancer, on the other hand, is characterized by a diffuse, infiltrative type of growth, with the formation of endophytic anatomical types of tumor (Fig. 1b). The carcinoma usually does not form glands, but it forms scattered bands and collections of cells in whose cytoplasm muroid secretory granules can be detected. The two types of gastric cancer differ from each other in the nature of their metabolism, the size of their nuclei, and also the DNA content of their nuclei [2, 4]: An increase in DNA synthesis is an important indicator of proliferative activity and, consequently, of the aggressiveness of the tumor itself. However, the microscopic structure of gastric cancer is not limited to the two types specified above, each of which has structural variants.

The object of this investigation was to compare the main histological types of carcinoma of the stomach and their variants by analyzing the DNA content in the tumor cell nuclei in order to obtain an objective assessment of the proliferative activity and infiltrative power of its microscopic forms.

## EXPERIMENTAL METHOD

Material obtained at operations on 10 patients with early gastric carcinoma, aged from 40 to 60 years (seven men and three women) was studied histologically and microspectrophotometrically. Because the tumors were small they could be studied in their entirety by the use of staggered sections. The sections were stained with hematoxylin and eosin and by the Feulgen reaction. In five cases the gastric carcinoma was considered to be of the intestinal type and in another five cases the diffuse type. The DNA content in the nuclei of the tumor cells was assessed on the basis of their optical density, in conventional Feulgen-DNA units, as determined on the SIM-2 scanning integrating microspectrophotometer at a wavelength of 575 nm, in sections 5  $\mu$  thick, in a 5  $\times$  5  $\mu$  frame [1]. Up to 10 different areas were studied in each tumor, and in each histological preparation the DNA content was determined in 30 tumor cell nuclei. The optical density of 30 lymphocytes, whose modal class was accepted as 2c because of their diploid DNA content, was determined in these same sections. The results of the measurements were subjected to statistical analysis, with a 0.95 level of probability.

## EXPERIMENTAL RESULTS

The proliferative activity of the tumor, determined from the mean weighted DNA content per cell nucleus of the intestinal type of carcinoma (6.4c), was found to be considerably higher than that of the diffuse type (3.4c). These results are in agreement with the conclusions drawn by other workers [2-6], who used different terms to describe the basic types of gastric carcinoma ("adenocarcinoma" instead of "intestinal cell carcinoma" and "undifferentiated carcinoma" and "scirrhous" instead of "diffuse type"). These results contradict the well-known clinical fact that the prognosis is worse in the diffuse type of carcinoma, but

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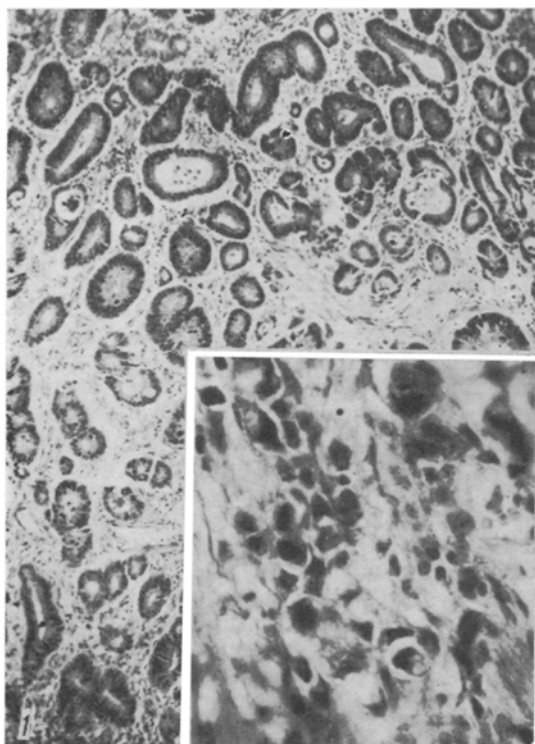


Fig. 1

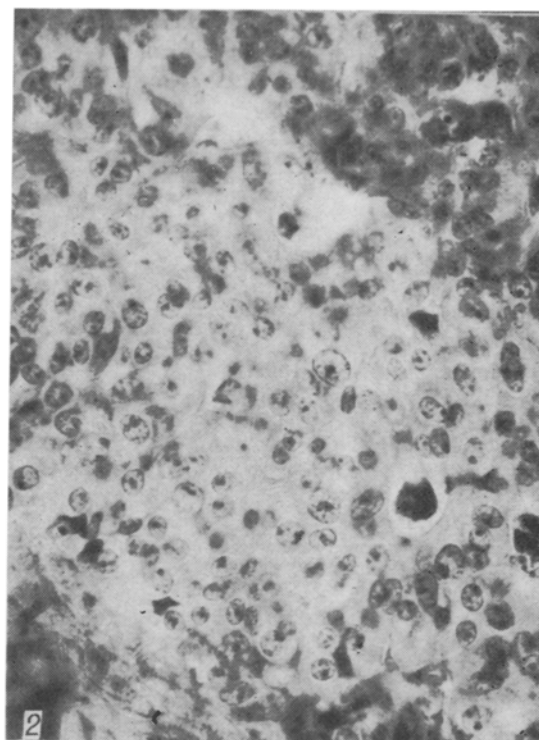


Fig. 2

Fig. 1. Principal histological types of gastric cancer: a) intestinal type — differentiated adenocarcinoma, 80  $\times$ ; b) diffuse type — bands of tumor cells, 400  $\times$ .

Fig. 2. Solidizing adenocarcinoma, a variant of the intestinal type with high proliferative activity, 400  $\times$ .

there is no doubt about their reliability. The length of survival of patients with cancer is evidently the result of integration of several of the biological properties of the tumor, including its proliferative activity, which is only one of several components. An important role in the prognosis of the disease may be played, for example, by the intensity of the stromal, cellular, and immune reactions in the tissues of the neoplasm.

In the intestinal type of gastric cancer areas of solidizing adenocarcinoma, with large nuclei, are readily distinguishable, usually "along the front" of the tumor (Fig. 2). The DNA content in the cells of these areas reaches 11.4c, whereas the mean DNA content per nucleus in the intestinal type of cancer was 6.4c. The presence of these structures in the tumor may be evidence of its aggressiveness [6].

In the diffuse type of cancer collections of large mucus-containing signet ring cells with deformed, pycnotic nuclei, displaced toward the peripheral parts of the cell, were noted more often in the central, "dorsal" regions of the tumor (Fig. 3). The DNA content in these nuclei was low, not more than 2.0c. It can accordingly be concluded that the signet ring cells of the carcinoma are dying cells, ending their life cycle. This is confirmed by the results of an enzyme histochemical study [9].

The DNA content in the nuclei of gastric tumor tissue is an important indicator of the state of that tissue. An increase in the content of nuclear DNA in tumor cells is a characteristic feature of solidizing adenocarcinoma of the stomach and it reflects its aggressiveness. A decrease in the DNA content in the nuclei of the signet ring cells of the tumor is evidence of their trophic disturbances and their approaching death. The study of the peripheral regions of the cancer, i.e., its zones of growth, deserves particular attention [3, 8]. The high proliferative activity of the carcinoma in these areas is an unfavorable factor in its prognosis.

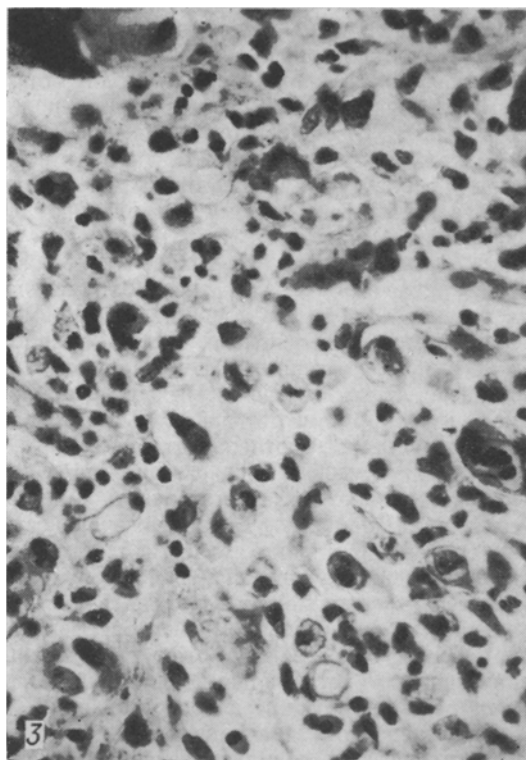


Fig. 3. Signet ring cells in diffuse type of carcinoma: displacement of pycnotic nuclei toward tumor cell membrane, 400  $\times$ .

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