# MICROSPECTROPHOTOMETRIC INVESTIGATION OF POLYMORPHIC GASTRIC CARCINOMAS

G. G. Avtandilov and V. S. Pashkova

UDC 616.33-006.6-074:543.42.062

A comparative microspectrophotometric investigation of the DNA content in the nuclei of ten polymorphic human gastric carcinomas showed that polyploidy and aneuploidy occur both in areas with a glandular structure and in parts of the tumor consisting of solid fields of cells. It is postulated that cells forming these parts of the polymorphic gastric carcinoma may differ in their karyotype.

The polymorphism of primary human tumors is associated with a varied degree of cataplasia of the tissue, the quantity and character of the secretion, the mosaic pattern of the sex chromatin, the level of enzyme activity, and many other factors [4, 7-9, 14]. The contradictory nature of views regarding carcinoma of the stomach as a whole justifies a quantitative study of the dynamics of nucleoproteins in the cell nuclei of polymorphic tumors.

This paper describes a comparative microspectrophotometric investigation of ten polymorphic human gastric carcinomas removed at operation (nine combining areas of glandular and solid structure, and one with glandular, solid, and scirrhus areas).

## EXPERIMENTAL METHOD

Sections of the tumor stained by Feulgen's method were examined on an integrating microspectrophotometer made by the Central Pathological Laboratory, Institute of Human Morphology, Academy of Medical Sciences of the USSR [1, 2]. To ensure reliability of the comparison, sections cut to a thickness of 5 $\mu$, in which different areas of the tumor parenchyma differed in structure, were used. The DNA content was determined under a magnification of 450 times in 50 nuclei of the tumor cells in the zone of the section studied (at a wavelength of 575 nm). The relative optical density (per $\mu^2$ of section) of the nucleus and its area (by gravimetric karyometry) were determined. The DNA content in the nuclei was expressed in conventional units (the product of the relative optical density and the area of section of the nucleus).

For comparison with the DNA content in a diploid set of chromosomes, the mean DNA content in the lymphocytes was measured in the same histological section. The results of these measurements were analyzed by statistical methods.

## EXPERIMENTAL RESULTS

The results agreed with data in the literature showing an increase in the DNA content in the cells of malignant tumors [3, 5, 11, 19, 24].

In the polymorphic gastric carcinomas the DNA content in the cell nuclei varied considerably, as the histograms in Fig. 1 show. In four tumors it varied from hypodiploid to polyploid, reaching values of 16 n

Central Pathological Laboratory, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. Department of Morbid Anatomy, Crimean Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 71, No. 4, pp. 82-85, April, 1971. Original article submitted September 15, 1970.

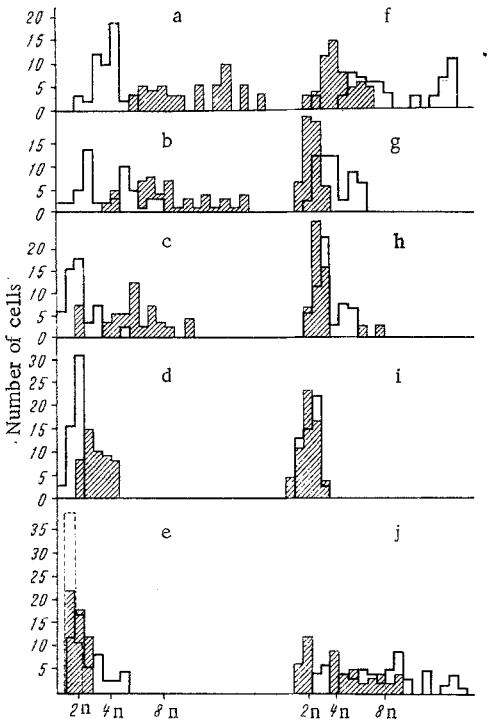


Fig. 1. Histograms of distribution of cell nuclei (based on DNA content) of polymorphic carcinomas (a-j). Unshaded columns represent glandular areas; shaded columns solid areas; broken line represents scirrhus areas.

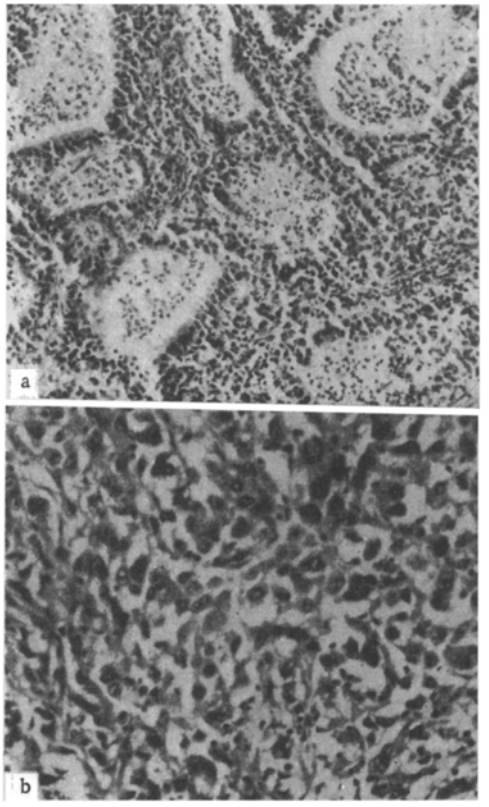


Fig. 2. Area of adenocarcinoma of the stomach. Hematoxylin-eosin: a) 120 ×; b) 250 ×.

(Fig. 1: a, b, f, j), in four tumors 8 n and above (Fig. 1: c, e, g, h), and in two tumors to the tetraploid level (Fig. 1: d, i). The histograms show varied degrees of aneuploidy in the tumors also.

Differences in DNA content and in the size of the nuclei also were found in parts of the same malignant focus differing in their degree of morphological cataplasia. In 5 cases larger nuclei were found in the cells of the solid* components of the tumor, while in others they were found in the glandular areas. Parallel with a change in size of the nucleus, its optical density also changed: in 8 cases, a higher relative optical density was found in the larger nuclei, indicating high concentrations of DNA. Only in two tumors was an increase in size of the nuclei associated with a small decrease in DNA concentration, not statistically significant.

Histograms of distribution of the DNA content in the cell nuclei in glandular and solid areas of the same tumor differed substantially. Sometimes these differences were so marked that the histograms hardly overlapped at all. Cell nuclei of an adenocarcinoma contained DNA in amounts varying from 2 to 4 n or more, while in a solid area they contained DNA in amounts varying from 4 to 16 n (Fig. 1: a, b). In other cases (Fig. 1: c, d) these differences were less marked, although still statistically significant.

The results of the investigation were not sufficiently clear to detect a parallel trend between the DNA content and the degree of polyploidy, on the one hand, and the degree of cataplasia of the gastric carcinoma (the presence or absence of glandular structures) on the other hand. In some tumors, cells from areas of glandular structure (Fig. 2a) contained DNA in amounts of about 2 n (Fig. 1d) and 4 n, while cells from areas of solid structure (Fig. 2b) contained 4 or 8 n or even more (Fig. 1: a, b, c). In other cases, on the contrary, areas of solid structure had nearer 2 n (Fig. 1e) or 2 and 4 n (Fig. 1: f, g, h, i), while areas of adenocarcinoma contained from 2 to 8 n or more (Fig. 1: e, f) or from 2 to 4 n and more (Fig. 1: g, h, i) of DNA. The distribution of nuclei with an identical DNA content in the glandular and solid parts

*This term is used to describe continuous fields of polymorphic cells.

of the tumor was roughly identical (Fig. 1: i, j), although it must be emphasized that the DNA content in the cell nuclei of the glandular areas was higher than in the areas of solid structure (the difference is statistically significant).

Sometimes the areas of adenocarcinoma and at other times the solid areas were thus closer to the normal prototype in DNA content in gastric carcinomas. Inui and Oota [17] likewise found no direct relationship between the mean DNA content in the nuclei of tumor cells and the histological features reflecting the degree of malignancy of gastric carcinoma. A higher or lower DNA content in the nuclei of cancer cells is evidently an important characteristic of malignant growth, but not the only one. From this point of view, the qualitative differences between the nucleotide composition of DNA from tumor tissue and from normal tissue, observed by a number of investigators [5], may be of prime importance. The more marked changes in the DNA content observed in the present investigation in the nuclei of gastric carcinoma cells than those described previously [17] were evidently attributable to specific features of tumors of polymorphic structure.

Taking into account the correlations between the DNA content and size of the chromosomes [6, 10, 22, 23, 25], it can be assumed that the pattern of DNA content discovered in areas of the same tumor with different morphological structure indicates differences in the karyotypes of the cells forming these areas. Makino et al. [20] found variations in the karyotype of cells in 30 gastric carcinomas and concluded that neoplasms of the same genesis may differ in the composition of the chromosomes of the stem lines. Variations in karyotype have been demonstrated in carcinomas of the mammary gland [12, 15], in carcinomas of the uterus [18, 26], in carcinoma of the large intestine [13], and in malignant tumors in other situations [21]. Assuming that variation of the karyotype is accompanied by changes in the properties of the tumor [16], a connection can evidently be established between the polymorphism of different parts of gastric carcinomas and differences in the karyotypes of the cells forming them.

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