Epithelial Blood Group Antigens in Colon Polyps. I. Morphologic Distribution and Relationship to Differentiation 1,2

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SUMMARY—The distribution patterns of epithelial blood group AB antigens (BG) in colon polyps of varying degrees of differentiation were studied by the mixed cell agglutination reaction. BG appeared in colon polyps if a certain degree of dedifferentiation was present. Two different distribution patterns were recognized: 1) association of BG with the secretory part of goblet cells with slight-to-moderate atypia and 2) association of BG with the whole cells in cases of pronounced dedifferentiation and loss of secretory activity. The second type resembled the distribution pattern of BG found previously in colon carcinomas. With respect to BG, the mucosa of colon polyps behaved similarly to embryonal colon mucosa. The detection of BG represents a useful method to assess objectively the degree of dedifferentiation in most colon polyps.—J Natl Cancer Inst 54: 1313–1317, 1975.

EPITHELIAL BLOOD GROUP AB isoantigens (BG) appear in approximately 70% of carcinomas of the distal colon, regardless of their degree of differentiation [(1, 2); unpublished observation]. This finding contrasts with that in other carcinomas in which BG disappear or are greatly diminished (3, 4). Since BG are present in the epithelial lining cells of the whole large bowel in the embryo (either as cell-wall antigens or associated with secretions) but disappear soon after birth (5), the reappearance in the tumor cells reflects their regression to the embryonal stage. The anatomic precursor of colon cancer and the exact relationship of colon polyps to cancer are still somewhat controversial, though to date most authors consider not only villous papillomas but also adenomatous polyps as precancerous lesions (6–14).

Some well-differentiated colon polyps were included as nonmalignant control tissues in an earlier study on BG in colon cancers. Negative results were obtained in these instances (2). A more thorough investigation was initiated when BG-positive mucosal cells were found in some polyps.

In the present paper, we evaluate the significance of BG in neoplastic colon polyps showing different degrees of dedifferentiation and cell atypia to answer the question of whether tissue-bound BG may be used as a criterion to predict malignant potential. We report the appearance of BG in colon polyps and show that the presence of BG is related to the degree of cell differentiation.

MATERIALS AND METHODS

Of 120 surgically removed polyps derived from the descending colon, the sigmoid colon, and the rectum studied for BG, 92 were from patients with erythrocyte blood group A, 23 from those with blood group B, and 5 from patients with blood group AB. Samples from patients with blood group O were excluded, since in those the detection of tissue-bound BG in tissue sections gave inconclusive results (1). The specimens were divided into three main groups according to histology: 9 adenomatous polyps with pronounced proliferation leading to papilloma-like appearance, 79 adenomatous polyps without pronounced proliferation, and 26 villous papillomas. Six specimens of "hyperplastic" (non-neoplastic) polyps were included for comparison (table 1). Normal colon mucosa adjacent to the polyp served as control in each instance. The tissues were fixed in neutral 10% formalin and processed routinely for paraffin sections.

Differentiation was assessed morphologically, depending on the dissimilarity of the polyp from the normal colon mucosa, exemplified by altered glandular structures and changes in size, shape, position, and secretory activity of the cells (12, 15). The method designed by Davidsohn (3) and Kovarik et al. (16) for the detection of BG in formalin-fixed paraffin sections was used with minor modifications (1). Reagent controls were as previously described (1).

RESULTS

Table 1 shows the BG content of adenomatous polyps with and without pronounced proliferation, of villous papillomas, and of hyperplastic polyps. BG were more frequent in villous papillomas, and the number of BG-positive mucosal cells was usually higher. Hyperplastic polyps were consistently BG negative.

The appearance of BG in the mucosal cells of colon polyps was clearly related to the histologic type of the polyp. Table 1 shows the BG content of adenomatous polyps and hyperplastic polyps. BG were more frequent in villous papillomas, and the number of BG-positive mucosal cells was usually higher. Hyperplastic polyps were consistently BG negative.

<table>
<thead>
<tr>
<th>Histologic type</th>
<th>Number of specimens</th>
<th>Total</th>
<th>With BG</th>
<th>Without BG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomatous polyps</td>
<td>79(9)</td>
<td>35(8)</td>
<td>44(1)</td>
<td></td>
</tr>
<tr>
<td>Villous papillomas</td>
<td>26</td>
<td>22</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Hyperplastic polyps</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

* Numbers in parentheses indicate adenomatous polyps with pronounced proliferation leading to papilloma-like appearance.

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degree of differentiation. However, in individual patients, a similar histology was not always strictly associated with an identical distribution pattern of BG.

BG were never found in well-differentiated polyp mucosa with regularly arranged goblet cells closely resembling normal colon mucosa. BG were noted in fairly well-differentiated polyps in association with goblet cells showing mild-to-moderate degrees of atypia (i.e., mucus localized in the apex rather than in the whole cell), proliferation, and pseudostratification. These features caused variations in gland size and shape. In these instances, BG were present in the secretory part of the goblet cells and in mucus secretions (fig. 1).

Cells with the histologic appearance of complete dedifferentiation with frequent mitotic figures and loss of secretory activity, at least to a degree where it was no longer evident by light microscopy, were often covered in toto by the indicator erythrocytes in a similar manner as carcinomas (1) (fig. 2). However, BG, again similar to carcinomas, were not always found in cells with histologic signs of complete dedifferentiation, and some polyps were devoid of BG reactivity, despite complete dedifferentiation of the cells.

A combination of both morphologic types was occasional: The basal layers of nonsecretory cells in areas with stratification were totally BG positive, and the superficial layers consisting of more or less atypical goblet cells contained BG associated with the secretory part of the cells. In other instances, despite identical histology, the superficial goblet cells were BG negative and only the basal cells expressed BG.

Occasionally, BG activity was restricted to the basal area (i.e., nuclear region) of cells with histologic evidence of mucus production, particularly in polyps with pseudostratification, whereas the secretory part was BG negative (fig. 3).

DISCUSSION

Colon polyps are usually regarded as precancerous lesions (8–14). The prediction of impending malignant transformation in a polyp, however, is hampered by the lack of unequivocal criteria. According to the studies of Potet and Soullard (12), the destiny of a polyp is largely determined by the degree of cell dedifferentiation; i.e., the more widespread the dedifferentiation the more likely the malignant transformation.

The present work adds another criterion which helps to define more accurately the degree of dedifferentiation by proving that colon polyp mucosa closely resembles its embryonal counterpart, at least in its ability to express BG. The lack of BG in some dedifferentiated polyps deserves further study. The fate of BG in the large bowel of embryos was studied by Szulman (5). In the early stages of embryo development, BG were present as alcohol-soluble, cell-wall antigens. Later these membrane-associated antigens rapidly faded, and mucus-associated BG appeared parallel to the onset of secretion. BG found in colon cancers were mostly alcohol soluble (1). Although neither alcohol nor water solubility has been tested during the present studies, it seems reasonable to assume that BG associated with secretions in rather well-differentiated polyps are water-soluble glycopeptides, whereas those in cells with a low degree of differentiation are alcohol-soluble glycolipids closely resembling the embryonal state. Limited to colon mucosa, BG associated with secretions (presumably water-soluble glycopeptides) behave similar to some other embryonic antigens (17–21).

In this context, the appearance of the carcinoembryonic antigen (CEA) of the digestive system (22) in benign colon polyps should be recalled (23, 24). The presence of CEA was most conspicuous in well-differentiated polyps with histologic evidence of secretory activity (23). Conversely, BG associated with the cell membranes (presumably alcohol-soluble glycolipids) may indicate altered membrane structure. Secreted fetal antigens and cell membrane changes are associated with the early phases of malignant transformation, as shown in experiments on chemical carcinogenesis (25–27). Analogous to the animal studies, particularly the experimental production of hepatomas (25, 26), the cell population of a colon polyp with its proliferation and cytologic alterations may result from an “initiating” process (26) (i.e., carcinogenic stimulus). The further evolution of cancer from these “initiated” cells is determined by the cell environment (25), which may account for the still-existing discrepancies between the incidence of polyps and the development of cancer in man. The sequence of events observed in experimentally induced cancer of the colon (28) further supports this assumption.

These results suggest that colon polyps are precancerous lesions in man. Studies are now in progress to determine the chemical nature of the BG found in colon polyps and to clarify the relationship of these isoantigens to malignancy.

REFERENCES

BLOOD GROUP ANTIGENS IN COLON PolyPS


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FIGURE 1.—Blood group substances associated with secretory part of goblet cells and with secretions in villous papilloma (blood group A), indicated by adhering erythrocytes. A. Positive reaction with BG-A antiserum and A-indicator erythrocytes. B. Negative control consisting of consecutive section treated with BG-B antiserum and B-indicator erythrocytes. Hematoxylin and eosin (H & E). × 400

FIGURE 2.—BG reactivity in adenomatous polyp with histologic signs of dedifferentiation. Cells are covered nearly in toto by indicator erythrocytes (BG-A). Well-differentiated glands (right bottom corner) are BG negative. A and B explanations are same as those given in figure 1. H & E. × 400
FIGURE 3.—BG activity restricted to basal area of goblet cells. Secretory part is BG negative (adenomatous polyp, BG-A).
H & E. × 400