Incidence and significance of argentaffin and Paneth cells in some tumours of the large intestine

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SYNOPSIS  The incidence of argentaffin and Paneth cells in epithelial tumours of the large intestine was investigated. Argentaffin cells were found in adenomatous polyps, villus adenomas, polyposis coli, Peutz-Jehgers' polyps, juvenile polyposis, and adenocarcinomas. Paneth cells were not found in metaplastic or juvenile polyps.

The crypt unit was destroyed in neoplasia and argentaffin and Paneth cells occurred either as a result of sequestration or were taking part in the neoplastic process.

The crypt unit was retained in the disorders of epithelial growth. The identification of argentaffin and Paneth cells enabled the crypt to be defined and thus provided a useful, practical aid in the differentiation between neoplasms and disorders of epithelial growth.

Argentaffin cells are normally found at the base of the glands throughout the entire large intestine. Paneth cells are scanty in the normal large bowel but may be found in the vicinity of benign and malignant tumours (Schmidt, 1905; Eklöf, 1914; Watson and Roy, 1960). They are also present in greatly increased numbers in some chronic inflammatory conditions, particularly ulcerative colitis (Paterson and Watson, 1961).

Feyrter (1931) found argentaffin cells in polyps of the large intestine but they were rather scarce. Hamperl (1927) examined 51 carcinomas of the intestinal tract and found argentaffin cells in three cases, but did not specify the site of these tumours. Paneth cells have been described in occasional adenomatous polyps (Schmidt, 1905; Kerr and Lendrum, 1936; Watson and Roy, 1960; Holmes, 1965) but Feyrter (1931) found that they were often present. Paneth cells have been reported only once in a case of colonic adenocarcinoma (Holmes, 1965).

There is no published study in the literature of argentaffin and Paneth cells in tumours of the large intestine. The object of this research is to investigate the incidence and significance of both types of cell in a large series of tumours from the large intestine representative of the histological varieties. Morson (1962) discussed the classification of mucosal polyps and for the purposes of this investigation the histological criteria described are followed, particularly in relation to juvenile, metaplastic, and Peutz-Jehgers' varieties.

MATERIAL  The following tumours were investigated: adenomatous polyp, papillary adenoma, polyposis coli, adenocarcinoma, metaplastic polyp, Peutz-Jehgers' polyp, juvenile polyp, and juvenile polyposis. The material was obtained from the Department of Pathology, St. Mark's Hospital, London, and the Area Laboratory, Guildford and Godalming Group Hospitals. Carcinoid tumours were excluded as they have been previously considered (Gibbs, 1963).

The tissues were fixed immediately in 10% formal saline. A single block was selected which included the centre of each tumour, and the tissue was processed and embedded in paraffin wax. Matching sections were cut at 5μ and stained routinely by Ehrlich's acid haematoxylin counterstained with eosin. Special stains included phosphotungstic acid haematoxylin (Mallory) and Gram stain (Weigert's modification) for Paneth cells; Fontana's silver impregnation, Schmorl's reaction, and the diazo method for enterochromaffin granules; and Perl's reaction for haemosiderin.

The following guide to the incidence of these cells in the tumours was used. The number of glands in each 5μ section which contained argentaffin and Paneth cells was

Received for publication 20 March 1967.
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located in Argentaffin cells adenomas examined of Paneth cells. Identification methods was in granules Paneth stained diffuse smoky granules Paneth Phosphotungstic acid haematoxylin (Mallory) and Gram stain (modified Weigert) proved most reliable. However, occasionally the staining reactions were a little inconsistent and variable so that in practice matching sections were stained by each technique and compared. It was found that the granules of both argentaffin and Paneth cells stained a deep red with phloxine tartrazine although the characteristic size and position of the granules within the cells usually precluded any confusion. Phosphotungstic acid haematoxylin stained Paneth granules a deep blue and argentaffin granules a diffuse smoky bluish-grey. The Gram (modified Weigert) stained Paneth cells a deep violet colour, while argentaffin granules generally were not visible. For the purpose of this investigation characteristic staining by each of these methods was considered necessary for the positive identification of Paneth cells.

ADENOMATOUS POLYP

Argentaffin cells were found in 19 (41%) of the 46 adenomas examined (Fig. 1 and Table). They were located in the basal part of the gland when present in small numbers. Sometimes argentaffin cells were numerous and were scattered throughout the tumour. Two tumours showed giant argentaffin cells (Fig. 2). Paneth cells were found in nine (19%) of the 46 adenomas examined (Fig. 3) and in seven argentaffin cells were present. (Fig. 1 and Table).

PAPILLARY OR VILLUS ADENOMA

Argentaffin cells were found in nine (39%) of the 23 tumours examined and they appeared normal. Paneth cells were present in eight tumours and in five they were very numerous (Figs. 1 and 4, and Table).

POLYPOSIS COLI

Twenty-three polyps from 11 cases of polyposis coli were examined and argentaffin and Paneth cells were found in eight adenomas (Fig. 1 and Table). Argentaffin and Paneth cells were not seen in four tumours which had undergone malignant transformation. One case was selected for detailed examination of adenomas from all parts of the large intestine but argentaffin and Paneth cells were found to be distributed fairly evenly in all parts of the bowel although the incidence was higher in the distal polyps which were, however, larger in size than the proximal polyps.

MALIGNANT TUMOURS OF THE LARGE INTESTINE

One hundred and fifty primary adenocarcinomas of the large bowel were examined. Argentaffin cells (Fig. 6) were found in three tumours (vermiform appendix, caecum, and rectum). Paneth cells were found in four tumours (Figs. 7a and 7b). In one case

FIG. 1. The incidence of argentaffin and Paneth cells in tumours of the large intestine.
FIG. 3. Adenoma of rectum showing giant argentaffin cells. (Diazo x 100.)

FIG. 4. Villus adenoma of rectum with Paneth cells. (Phloxine tartrazine x 80.)

FIG. 2. Adenoma of rectum with Paneth cells. (Phloxine tartrazine x 100.)
(adenocarcinoma of the caecum) they were scanty and situated near the growing edge, and in the remainder (caecum, transverse colon, and sigmoid colon) they were found in great numbers (Figs. 7a and 7b). One of these seven tumours (adenocarcinoma of caecum) contained both argentaffin and Paneth cells. All the positive tumours produced copious secretion of mucin.

### TABLE

<table>
<thead>
<tr>
<th>Cases</th>
<th>Argentaffin Cells</th>
<th>Paneth Cells</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Tumours</td>
<td>Cell Count</td>
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<tr>
<td>Adenomatous polyp</td>
<td>46</td>
<td>19</td>
</tr>
<tr>
<td>Papillary adenoma</td>
<td>23</td>
<td>9</td>
</tr>
<tr>
<td>Polyposis coli</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>23 polyps</td>
<td>6-5 cells in</td>
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<td>Adenocarcinomas</td>
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<td>3</td>
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<tr>
<td></td>
<td>34</td>
<td>Numerous</td>
</tr>
<tr>
<td>Metaplastic polyps</td>
<td>9</td>
<td>23-2 cells per tumour</td>
</tr>
<tr>
<td>Peutz-Jeghers' syndrome</td>
<td>15</td>
<td>In normal numbers</td>
</tr>
<tr>
<td>Juvenile polyps</td>
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<td>15</td>
</tr>
<tr>
<td>Juvenile polyposis</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

### METAPLASTIC POLYPS

Thirty-four metaplastic polyps were examined (Fig. 1 and Table) and argentaffin cells were seen in the gland bases in similar numbers to the adjacent normal mucosa. Most of the argentaffin cells appeared enlarged and the cytoplasm was eosinophilic. Paneth cells were absent.
PEUTZ-JEHGERS' SYNDROME

Nine polyps from nine cases of Peutz-Jehgers' syndrome were examined (Fig. 1 and Table). Argentaffin cells were found in the basal part of most glands and Paneth cells were also present in very large numbers in three polyps.

JUVENILE POLYPS

Fifteen polyps were examined and argentaffin cells were present in gland crypts in every case. The argentaffin cells appeared normal in size in spite of enlarged epithelial cells which formed the tumour. Paneth cells were not found.

JUVENILE POLYPOSIS

Polyps from three cases of juvenile polyposis (McColl, Bussey, Veale, and Morson, 1964) were examined. Argentaffin and Paneth cells were present in small numbers in the majority of polyps from each of the cases, and these cells were confined to the gland crypts (Fig. 5).

Argentaffin cells are present in the gland crypts throughout the large intestine and occasional Paneth cells are also found, particularly in the caecum. The gland crypt is the site of normal cell regeneration and in neoplasia the normal basiglandular cells of the crypt are replaced by tumour cells. This occurs as a primary process if the neoplasm is derived directly from basiglandular cells and as a secondary process if the neoplasm arises elsewhere in the gland whence the crypt cells are displaced by tumour cells.

The adenomatous polyps of polyposis coli were investigated by Lane and Lev (1963) who concluded that these neoplasms arose from the crypt cells, and by Cole and McKalen (1963) who found that they originated at the superficial part of the gland. This apparent contradiction may be resolved by the hypothesis that neoplasia may commence in both parts of the gland and that the tumours showing numerous argentaffin and/or Paneth cells are derived from the basiglandular cells of the crypt. It is not surprising that tumours arising from the basiglandular cells of the crypt produce argentaffin and Paneth...
cells by differentiation as these cells are present in
normal crypts. Neoplastic argentaffin and Paneth
cells may be expected to be scattered throughout
the tumour instead of being confined to the crypts.
The presence of occasional argentaffin and Paneth
cells in gland crypts occupied by neoplastic cells is
explained by the occasional survival of normal
basiglandular cells which are 'sequestrated' amidst
neoplastic cells. Sequestration accounts for the
presence of argentaffin cells in five of the 19 cases
(26%) of adenomatous polyps and eight of the nine
cases (89%) of villous adenomas. A similar explana-
tion accounts for the presence of Paneth cells in
three of the nine cases (33%) of adenomatous polyp
and one of the eight cases of villus adenoma (12%).
In others, argentaffin and Paneth cells are scattered
throughout the tumours, sometimes in great num-
bers, and it is concluded that these cells are part of
the neoplastic process. Mitoses in Paneth cells and
argentaffin cells are not seen, possibly because the
characteristic granules are not present in the di-
ving stage. However, neoplastic argentaffin and
Paneth cells show loss of orientation and bizarre
forms. The majority of the tumours with argentaffin
and Paneth cells showed prominent mucin secretion
in some parts illustrating their differentiation.
Neoplastic argentaffin cells were present less
commonly in the villous adenoma than in the adeno-
atous polyp, while the reverse was found in the
case of Paneth cells. These findings do not suggest
any difference between the malignant potential of
the two tumours. However, no clear differences were
present between the solitary adenomatous polyp and
the multiple adenomatous polyps of familial
polyposis.
In contrast to the tumours already described where
the cytology of the gland crypt is destroyed, the
remaining tumours are distinguished by the retention
of the basic gland crypt unit. Argentaffin and Paneth
cells are located in the crypt and their presence
provides a useful aid in the identification and the
assessment of the gland crypt. The gland crypts in
metaplastic polyp, Peutz-Jehgers' polyp, juvenile
polyp, and juvenile polyposis are easily recognized
by this method even though they may be greatly
distorted. This distortion is minimal in metaplastic
polyp, but very conspicuous in juvenile polyposis
(Fig. 5) where it is caused by abnormal and florid
development of the superficial part of the gland.
Paneth cells are present in juvenile polyposis but
absent in the solitary juvenile polyp suggesting a
difference in the growth processes, even though the
polyps have many similarities. The cytology of the
crypt in some Peutz-Jehgers' polyps and in juvenile
polyposis where Paneth cells are found suggests a
local variation in crypt metabolism. These findings
support the view that this group of tumours arises
as an anomaly of growth.

I wish to thank Dr. B. C. Morson for his advice and
encouragement and the consultant staff of the Royal
Surrey County Hospital and St. Marks’ Hospital for
permission to study their cases. For technical assis-
tance I am grateful to Mrs. R. M. Shrub, Mr. Lloyd Soodeen,
Mr. Norman Mackie, and Mr. L. W. French.

The expenses of this investigation were defrayed from
a research grant from the South West Metropolitan
Regional Hospital Board, and from a block grant to the
Research Department of St. Mark’s Hospital from the
British Empire Cancer Campaign.

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McColl, I., Bussey, H. J. R., Veale, A. M. O., and Morson, B. C.
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*J Clin Pathol* 1967 20: 826-831
doi: 10.1136/jcp.20.6.826

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