Relation between the mucosal flora and Paneth cell population of human jejunum and ileum

MARGARET E ELMES,* MR STANTON,* CHL HOWELLS,† GH LOWE†

From the *Department of Pathology, and †Public Health Laboratory Service, University Hospital of Wales, Cardiff

SUMMARY The Paneth cell population in surgically resected human jejunum and ileum was estimated using image analysis of the granule area in patients who had not received antibiotics. The mucosa was cultured aerobically and anaerobically. In the jejunum 22 samples were sterile and five yielded bacteria; in the ileum four were sterile and three were non-sterile. The mean Paneth cell granule area in the sterile jejunum was 122.7 ± 37.2 μm² and in the non-sterile samples 67.2 ± 36.6 μm² (p < 0.006). The corresponding values for the ileum were 137.9 ± 109.8 and 100.5 ± 9.1 (NS). Thus an increase in the Paneth cell population may occur in response to changes in the intestinal luminal environment. Failure of this response and resultant Paneth cell deficiency may lead to bacterial overgrowth.

Using the Paneth cell granule area measured by image analysis as an indicator of the Paneth cell population in the human small intestine we have shown a significant increase in Paneth cells in the jejunum of patients requiring surgery who have had previous partial gastrectomy for peptic ulcer.1 We suggested that as Paneth cells may be concerned in the maintenance of a normal bacterial flora in the intestinal lumen,2 the proliferation may be an attempt to prevent bacterial overgrowth in an abnormal hypochlorhydric state. This may also occur in other conditions of abnormal gut motility. In a study of the bacterial flora of the small intestinal mucosa in patients requiring intestinal resection3 we compared the Paneth cell population of the jejunum and ileum as measured by image analysis in patients who had an intestinal mucosa which was sterile on culture with those whose mucosa yielded bacteria.

Material and methods

Patients requiring surgical resection of the small bowel who had not received preoperative antibiotics were studied; ethical approval for the collection of samples of mucosa was obtained. Twenty seven samples of jejunum and seven samples of ileum were examined. Jejunal samples were obtained from 14 men (mean age 63.6 ± 11.0 years), and 13 women (mean age 63.6 ± 12.8 years). The indica-
filter is placed in the incident light path of the microscope. This makes the Paneth cells appear black against a lighter mucosal background (Fig. 2a). After the cells have been identified the image is stored in a memory comprising $512 \times 512$ picture elements (pixels). Each element also has a digital “grey” value between 0 (black) and 255 (white). The areas occupied by the cell granules are then separated from the background by adjustment of the threshold control (Fig. 2b). These areas are then transferred from the memory which contains the original image to an adjacent memory, where they are measured.

Regions which share the same range of densities, such as entero-chromaffin cells, are selected as well as the Paneth cell granules and are edited out by means of an operator controlled digitiser tablet. The numerical value of the Paneth granule area is then displayed in units of square microns ($\mu m^2$). The image analyser is calibrated using a stage micrometer. An IBAS calibrator function is then used to calculate (and store) the relation between the television system and the micrometer.

All the above procedures are carried out by a computer program. Operator intervention occurs at three stages, which are: (a) selection of the appropriate region from the slide; (b) adjustment of the threshold (discrimination) level; (c) editing of any artefact.

**Results**

A Paneth cell granule area measurement was carried out on 35 suitable specimens: 27 jejunum and 8 ileum. In the jejunum a sterile mucosa was found in 22 of 27 samples, and five yielded bacteria on culture. The mean Paneth cell granule area in the sterile jejunum was $122.7 \pm 37.2 \mu m^2$, and in the non-sterile group the mean value was $67.2 \pm 36.6 \mu m^2 (p < 0.006)$ (Table 1). The organisms isolated are shown in Table 2.

In the ileum five specimens were sterile and three were non-sterile; the mean Paneth cell areas were $137.9 \pm 109.8$ and $100.5 \pm 91.1$, respectively (NS) (Table 3). It can be seen that the patients with sterile mucosae had a higher mean Paneth cell area than those with non-sterile mucosae, although the difference was not statistically significant.

**Discussion**

We have previously shown that patients with bacteria in the jejunal mucosa have fewer Paneth cells than those with mucosa which is sterile on culture. Most of the jejunal samples were sterile on culture. Those with bacteria were from patients with carcinoma of the stomach or duodenum or those who had had a previous partial gastrectomy with consequent hypochlorhydria and flow disruption. The
three patients with peptic ulcer had sterile mucosae. The Paneth cell population was considerably smaller in patients with non-sterile mucosae, which suggests that Paneth cell deficiency is associated with bacterial proliferation.

The number of ileal samples was small as few patients come to intestinal surgery without receiving some antibiotic, usually prophylactically, and even an antibiotic given with premedication was considered a contraindication to inclusion in the study. The proportions of sterile and non-sterile mucosae were roughly equal. The two patients with Crohn's disease and one with carcinoma of the caecum were non-sterile, and the remainder were sterile. The mean Paneth cell count in the sterile mucosa cases was higher than in the non-sterile cases, although the difference was not significant.

In our previous study we found pronounced Paneth cell proliferation in patients who had had a previous partial gastrectomy and postulated that this was a response to an altered pH and flow which could lead to bacterial overgrowth. The present work confirms that when Paneth cell proliferation does not occur bacteria may be isolated from the mucosa. The mechanism of this response or failure of response requires further investigation.

We thank Dr T Khosla for statistical advice, Dr JP

Table 2 Organisms isolated from patients with non-sterile mucosa

<table>
<thead>
<tr>
<th>Organism</th>
<th>α-haemolytic Streptococci</th>
<th>Streptococcus faecalis</th>
<th>Enterobacteriaceae</th>
<th>Anaerobes</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jejunum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenal ulcer (2nd operation)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma of the duodenum</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Gastric carcinoma</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Ileum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma of the caecum</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Relation between the mucosal flora and Paneth cell population of human jejunum and ileum

Table 3  Paneth cell area per crypt in the ileum (μm²)

<table>
<thead>
<tr>
<th>Sterile mucosa</th>
<th>Non-sterile mucosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>185.1</td>
<td>87.9</td>
</tr>
<tr>
<td>82.9</td>
<td>62.9</td>
</tr>
<tr>
<td>166.1</td>
<td>156.9</td>
</tr>
<tr>
<td>117.6</td>
<td>112.3</td>
</tr>
</tbody>
</table>

Overall mean 137.9 ± 109.8

Pooled t test: t = 0.49 (NS).

Clarkson for general assistance, and the surgeons of the University Hospital of Wales for their cooperation in obtaining samples of mucosa.

References


Requests for reprints to: Dr Margaret E Elmes, Department of Pathology, University Hospital of Wales, Cardiff, Wales.
Relation between the mucosal flora and Paneth cell population of human jejunum and ileum.

M E Elmes, M R Stanton, C H Howells and G H Lowe

*J Clin Pathol* 1984 37: 1268-1271
doi: 10.1136/jcp.37.11.1268

Updated information and services can be found at:
http://jcp.bmj.com/content/37/11/1268

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/