Lymphoid tissue and lymphoid-glandular complexes of the colon: relation to diverticulosis

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SYNOPSIS The lymphoid tissue of the normal colon is compared with that of colons with diverticular disease. Colons with diverticular disease show a significant increase in the number of lymphoid nodules in areas not containing diverticula. Lymphoid-glandular complexes of the colon were studied in relation to diverticular disease.

It is suggested that the lymphoid nodules and the lymphoid-glandular complexes of the colon constitute weak points in the bowel wall and may play a part in the pathogenesis of diverticula.

Colonic lymphoid-glandular (L-G) complexes are, in all probability, normal structures (Kealy, 1976). However, Clark (1969) and Dyson (1975) raise the possibility that they may be the forerunners of diverticulosis. The relationship of lymphoid-glandular complexes and the lymphoid tissue of the colon to the development of diverticulosis has been studied.

Material and Methods

MACROSCOPIC

At necropsy colons were taken from subjects over 40 years of age. Colons from subjects in whom there was a possibility of alteration of the lymphoid tissue (e.g., due to drugs, lymphoma or primary colonic disease apart from diverticular disease) were excluded. Each colon included the terminal few centimetres of ileum and was cut opposite the third sacral vertebra. They were washed through with normal saline, distended with 10% formol saline to a pressure of about 30 cm of water, and fixed for at least three days. They were then opened along their mesenteric borders and examined. Altogether 100 colons were collected, 50 with diverticular disease and 50 with no evidence of disease. The number and site of the diverticula were noted together with the age and sex of the patient. Necropsy specimens of colon from three Nigerian subjects resident in Nigeria were also similarly examined and these showed no abnormality.

Received for publication 1 September 1975

Lymphoid Nodule Count

Samples about 10 cm² were taken from the midpoints of the ascending, transverse, descending, and sigmoid parts of each colon. The caecum and areas of colon containing diverticula were excluded. Each specimen was then treated according to a method based on that described by Dukes and Bussey (1926). Adventitial fat was removed from each piece, and the taenia were stripped off or divided at close intervals in some, in order that the mucosa should lie flat. The mucosa was removed from the surface of each specimen by light scraping with a scalpel under a gentle stream of cold water (fig 1), leaving the muscularis mucosae virtually intact. Each piece was blotted dry and placed in a dish containing 1% alcoholic methylene blue for three to five minutes. Differentiation was carried out in warm running water until the lymphoid nodules appeared as dark blue dots of variable size on a light blue background (fig 2). A small sheet of plate glass on which was etched an area 6 × 6 cm divided into square centimetres was placed on the surface of the specimen, and the number of lymphoid nodules in that area was counted under bright incident illumination.

MICROSCOPIC

It was originally intended to examine sections of standard blocks taken from each area of the colon but, because of the autolysis, surgical material was resorted to. Sections from surgical partial and total colectomy and proctocolectomy specimens at King's College Hospital and Kingston Hospital were...
examine for the years 1965-74 and 1958-74 respectively.

Results

NECROPSY SPECIMENS
Colons from subjects with diverticular disease showed an average age of 71-2 years, range 44-92, sex ratio 27 M:23 F. Diverticula were present mainly in the descending and sigmoid parts of the colon. In four specimens they were present throughout, and in one, they were limited to the ascending colon. Colons with no evidence of disease had an average age of 67-5 years, range 40-93, sex ratio 26 M:24 F. The Nigerian specimens were from two women aged 55 and 42 years and from one man aged 38 years.

LYMPHOID NODULES
The number of lymphoid nodules counted in each area was expressed as the average per square centimetre. In colons with diverticula the number of lymphoid nodules per square centimetre, expressed as an average for the colon as a whole, ranged from 2.4 to 9.5; in those without evidence of disease from 1.5 to 7.3; and in the Nigerian specimens from 3.2 to 3.9.

The average numbers of lymphoid nodules per square centimetre for all areas of colon are shown in the table.

<table>
<thead>
<tr>
<th>Colon</th>
<th>Ascending</th>
<th>Transverse</th>
<th>Descending</th>
<th>Sigmoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticular disease</td>
<td>4.2</td>
<td>4.9</td>
<td>5.2</td>
<td>5.8</td>
</tr>
<tr>
<td>Normal colon</td>
<td>3.4</td>
<td>3.6</td>
<td>3.5</td>
<td>3.8</td>
</tr>
<tr>
<td>Increase per cent</td>
<td>23.5</td>
<td>36.1</td>
<td>46.6</td>
<td>52.7</td>
</tr>
<tr>
<td>Nigerian specimens</td>
<td>3.6</td>
<td>3.4</td>
<td>3.4</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Table Average number of lymphoid nodules per square centimetre in all areas of colon and percentage increase in diverticular disease

No correlation was demonstrated between the number of diverticula and the number of lymphoid nodules, nor was any increase in the number of nodules noted with increasing age.

Microscopic
Altogether sections from 1924 partial and total colectomy specimens were examined. Diverticular disease was present in 351 cases, and L-G complexes were observed in 51 of these. The L-G complexes were always associated with a lymphoid nodule and protruded through a gap in the muscularis mucosae (fig 3). The extent of mucosal protrusion through the gaps in the muscularis mucosae was variable, as also were the sizes of the lymphoid nodules which were often hyperplastic with germinal centres. Lymphoid nodules were often observed at the advancing point of developing diverticula in the muscle coat situated inside a gap in the muscularis mucosae (fig 4). On the other hand, L-G complexes were seldom seen at the tip of advancing diverticula within the muscle coat but were occasionally present in diverticula which had penetrated the bowel wall to the serosa (fig 5).

Study of sections from the Nigerian specimens showed a distribution of lymphoid tissue similar to that already described for normal colons (Kealy, 1976). No L-G complexes were observed in any of these sections.

Discussion

The exact mechanism by which diverticula occur is still not understood (Raia et al, 1973) and no single factor explains their origin, but the process probably results from a summation of several factors (McGrath, 1912). It is accepted that acquired colonic diverticula are pulsion in type associated with increased intraluminal pressure (Edwards...
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Fig 2  Plan view of scraped surface of colon showing lymphoid nodules (black dots) (methylene blue × 1:5).

Fig 3  Colon showing L-G complex (H and E × 30).
Fig 4  Developing diverticulum with lymphoid nodule at advancing tip (H and E × 26).

Fig 5  Established diverticulum with L-G complex in its wall at the serosa, bottom left (H and E × 16).

1934; Almy, 1965) and a disorder of muscle function with increased tone causing shortening of the bowel with consequent muscle thickening (Williams, 1968; Morson, 1975).

The results show that in the colon as a whole there is a significant ($p < 0.001$) increase in the number of lymphoid nodules in colons with diverticular disease compared to those without disease. The increased number is present in those areas of colon which did not include any diverticula, and this increase becomes more pronounced from the ascending colon to the sigmoid. Because the lymphoid nodules are distributed in close apposition to the muscularis mucosae and are often situated between its fibres or in gaps in its substance, these foci could be considered as weak points in the bowel wall, and since an increase in size of the lymphoid nodules is paralleled by an increase in width of the gaps in the muscularis mucosae (Kealy, 1976), it is plausible to suggest that these points are made weaker by hyperplasia of the lymphoid nodules. In addition, it is possible that the increased number of lymphoid nodules in colons with diverticular disease may be partly explained by the presence of diverticula with the associated chronic inflammatory state, but this effect on the nodule count could be regarded as minimal since the pieces of colon examined did not include any diverticula and, in the case of the ascending and transverse colons, they were taken from areas of bowel far removed from the sites of diverticula which in most cases involved only the descending and sigmoid parts. Also it is conceivable that L-G complexes, which are present at the sites of gaps in the muscularis mucosae, may increase in size when factors such as lymphoid hyperplasia, increased intraluminal pressure, and muscle dysfunction are present together.

The incidence of diverticular disease in African countries is rare (Painter and Burkitt, 1971; Hunt, 1972) and the Nigerian specimens were included in this study to see if there existed any gross or microscopic differences between them and the other specimens. It is interesting to note that the number of lymphoid nodules in the Nigerian colons is very closely similar to that present in the colons showing
no disease. The number of Nigerian colons examined was small and because of postmortem autolysis a study of surgical colectomy specimens from Nigeria is now being undertaken.

It is concluded that the lymphoid nodules in apposition to the muscularis mucosae may constitute weak points in the bowel wall, that the increase in their number in diverticular disease may represent a pre-diverticular state, and that these and the L-G complexes may act as the 'thin edge of the wedge' in the development of diverticula.

I wish to thank Dr M. E. A. Powell, Kingston Hospital, for his criticism and advice; Professor E. A. Wright, King's College Hospital, and Dr J. H. Earle, Queen Mary's Hospital, Roehampton, for access to surgical sections; Dr Ed. 'B. Attah, University of Ibadan, Nigeria, for necropsy material; Mr J. Spicer, Kingston Hospital, for technical assistance; and Miss B. R. Hume for typing this paper. The work was supported by a grant from the South West Thames Regional Health Authority for the purchase of photomicrographic equipment.

This paper constitutes part of the work for an MD thesis to be submitted to the National University of Ireland.

References


