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**Distribution of 5-OH Tryptamine (Serotonin)
 in Ulcerative Colitis**

Vasomotor and intestinal symptoms of both carcinoid and dumping syndromes have often been ascribed to the hypersecretion of 5-OH tryptamine (5-HT). Recent studies have, however, indicated that the pathogenic function of 5-HT in these conditions is limited to intestinal symptoms. Some vasoactive peptides, e.g. bradykinin and kallikrein, have possibly been involved in vasomotor symptomatology (Oates *et al.* 1964, Zeitlin & Smith 1966).

There are, however, sound arguments for believing that 5-HT plays an effective role in the pathogenesis of intestinal hypermotility and of diarrhoea characteristic of the carcinoid and dumping syndrome (Waldenström 1968, Luzietti *et al.* 1964); and also, since in normal physiology serotonin is implicated in the initiation of the peristaltic reflex (Bülbring & Crema 1959) and in the demonstration of mechanical effects following its administration (Misiewicz & Waller 1966, Ramorino *et al.* 1964), it appeared to us of considerable interest to see whether 5-HT was implicated in any way in the pathological changes accompanying ulcerative colitis.

Since excellent techniques for its visualization as a yellow fluorescence have recently become available, we decided to undertake a preliminary study of the enterochromaffin system in both normal subjects and ulcerative colitis patients.

As is well known, 5-HT is produced in the enterochromaffin cells present in the mucosa of the digestive tract from the gastro-oesophageal junction to the anus. There are many more such cells in the small intestine than in the large intestine, where they diminish along a gradient proceeding from left to right, opposite to that in the small intestine (Singh 1963, Pentilla & Lempinen 1968).

We studied 5 fragments of right colon and 5 fragments of the corresponding left colon, taken from healthy subjects using our method of intestinal biopsy by means of end-to-end intubation, as well as 6 fragments from the sigmoid taken by sigmoidoscopy. In addition, we studied 8 subjects with ulcerative colitis from whom we obtained 3 fragments of left colon taken at operation, 2 each of right and corresponding left colon taken by means of end-to-end intubation, and 3 fragments taken by sigmoidoscopy.

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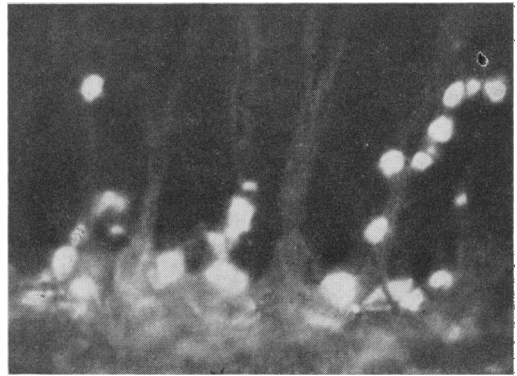


Fig 1 *Left colonic mucosa of healthy subject. Numerous deposits of 5-HT. × 150*

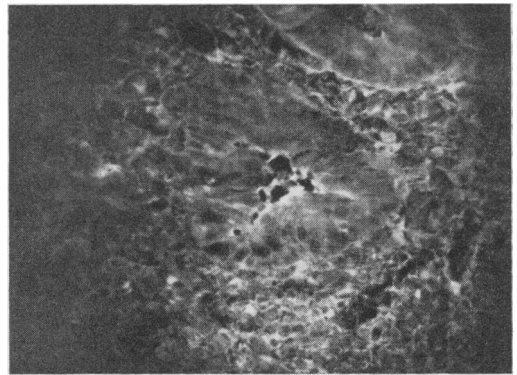


Fig 2 *Left colonic mucosa of patient with ulcerative colitis. Absence of 5-HT deposits. × 150*

To visualize 5-HT we used the method described by Falck (1962) in which freeze-dried specimens are exposed to formaldehyde vapour. This converts 5-HT into an intensely yellow fluorescing substance.

To summarize our results: we observed that in all normal cases the right colonic mucosa appeared to contain few cells in which there were observable quantities of 5-HT. In the left colonic mucosa, taken from the same subjects and in fragments taken by sigmoidoscopy, we observed a large number of fluorescent cells (Fig 1). The yellow fluorescent spots were situated in the glandular crypts, close to the basal membrane. In some cases, they were visible also in the interglandular spaces.

We have attempted to evaluate quantitatively these 5-HT-containing deposits in 100 glandular lumens, in both the left and the right colon. In the right colon we found 46 deposits per 100 lumens and, in the left colon 186; this difference was highly significant statistically.

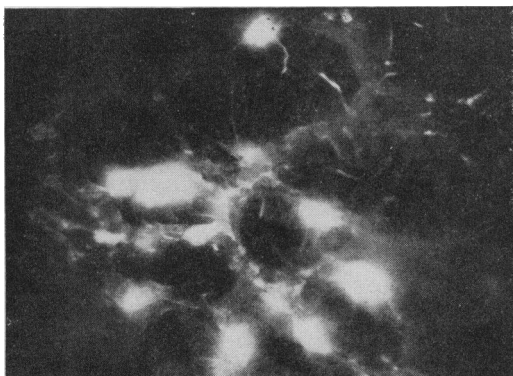


Fig 3 Left colonic mucosa of healthy subject. Adrenergic nerves in contact with 5-HT deposits. $\times 150$

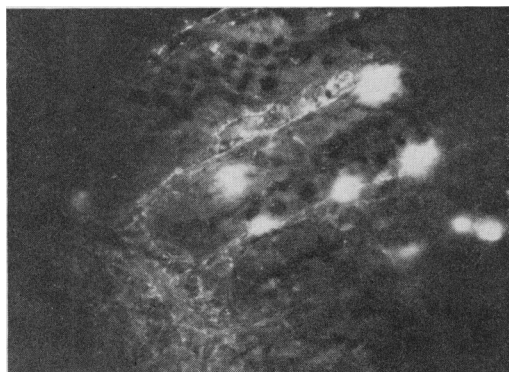


Fig 4 Left colonic mucosa of normal cat. Adrenergic fibres in contact with 5-HT deposits. $\times 150$

In all the fragments taken from ulcerative colitis patients it was not possible to visualize 5-HT fluorescent deposit in the right as well as in the left colonic mucosa (Fig 2). However, the mucosal structure was very distinct in 6 specimens: only in 2 severe cases was the mucosa quite destroyed.

During this work we were often struck by the observation that there was marked sympathetic innervation throughout the region between the glands. In some cases we found that adrenergic nerves actually entered some cells containing 5-HT (Fig 3). This was intriguing and we wondered whether it was significant. In fact, in the specimens from colitis patients we saw a complete absence not only of 5-HT, but also of adrenergic nerves.

To test this hypothesis of possible interaction between 5-HT and adrenergic nerves, we examined the effect on mucosal 5-HT in cats sympathectomized by removing the inferior mesenteric ganglion and then touching the inferior mesenteric artery with a cold probe at -90°C for three minutes. Some days later the cats were killed and speci-

mens of mucosa were taken from the right and left colon. Not only had all noradrenaline fluorescence disappeared from the tissues including the adrenergic fibres surrounding the crypts (Fig 4), but, in some cases, all the 5-HT in the crypts.

The significance of these observations is being further evaluated, particularly in relation to the physiological and pharmacological implications.

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Arterial Infusion Chemotherapy of Liver Metastases Arising from Rectal and Colonic Cancer

In 1960 we assembled a clinical and research team of physicians and surgeons for the study and use of chemotherapy in the treatment of patients with advanced cancer. A well-staffed research laboratory and adequate resources were available.

Table 1 presents a series of patients with colonic and rectal cancer treated at the Lahey Clinic Foundation between 1956 and 1961 inclusive. They were treated with surgical procedures alone. The five-year survival rate, and these are uncorrected figures, approximates to that from other institutions with a primary interest in this disease. It seems that we have probably reached the limit as far as survival rates are concerned following surgical intervention alone. Table 2 shows a breakdown of these end-results and relates them to the presence or absence of lymph node or blood vessel invasion. Again, these are uncorrected figures. We have never utilized the Dukes classification. Comparison of these two types of classification shows, however, that they are quite similar. The percentage of patients with nodal or vessel, or both nodal and vessel,

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