The Distribution of Argentaffin Cells in the Gastrointestinal Tract of the Sulfamerazine Treated Rat

Argentaffin (AG) cells are present throughout the gastrointestinal tract[1-3], and are known to produce serotonin[4,5]. The concentration of serotonin has been reported to parallel the AG cell distribution in guinea-pig duodenum[4], in human ileum and colon[6], and in the immunosympathectomized mouse[7]. However, MURRAY and WYLLIE[8] found no correlation between serotonin levels and the AG cell distribution reported for human stomachs.

In a previous publication we reported increased serotonin levels in some areas of rat gastrointestinal mucosa following treatment with sulfamerazine[9]. These increased serotonin levels might be due to either an increased AG cell population, or, more serotonin/cell. Reported here is the distribution of AG cells in the gastrointestinal mucosa of the normal and sulfamerazine treated rat, and its close correlation with the tissue serotonin levels.

Male Charles River rats weighing between 200–250 g were maintained in colony cages and fed commercial powdered Purina rat chow with a tryptophan content of 0.22%. The rats were randomly divided into 2 groups, 1 of which received 5 mg of sulfamerazine/20 g chow for 2–3 weeks. To avoid the problem of any circadian differences in bowel serotonin levels or AG cell granulation, rats were always killed between 08.00 and 09.00 on the day of study. The rats were decapitated by a small animal decapitator and the following tissues were rapidly excised: stomach fundus, body, and pyloric antrum, upper and lower duodenum, mid-jejunum, terminal ileum, appendix, cecum, ascending, transverse and descending colon, and rectum. After removal from the rat, the bowel segments were either opened longitudinally, cleaned, blotted dry, and the mucosa separated by scraping[10], or a small circular section of full thickness tissue was placed in 10% formalin for AG cell histology.

All the rats were used for the analysis of serotonin, which was measured spectrophotofluorometrically[11], whereas only tissues from 4 rats/group were taken for AG cell counts. After 36 h in 10% formalin the tissue segments were blocked in paraffin, and sections cut at 5 μ. All sections were stained by the GOMORI methenamine silver technique[12,13].

The number of cells in each tissue was expressed as cells/100 intestinal crypts (or in the case of the stomach, as cells/100 gastric pits). It was considered more accurate to express cell counts in this way, rather than as cells/high power field, because cell counting was facilitated, and in spite of the uncontrolable obliquity of some sections, remarkably constant results were obtained in preliminary counts in both rat and human intestinal mucosa. Although no crypts of Lieberkühn are present in the large bowel, the colonic mucosa is folded into crypts, and in the absence of edema or tissue reaction, these crypts have been shown to be adequate markers[6]. It was rare that less than 80 crypts/slide were present for counting, usually 300 crypts or more being available. The total section was scanned with a 43 mm objective using a binocular microscope and only typical AG cells were counted, extreme care being taken to identify and exclude the numerous mast cells also present.

The serotonin levels in the 13 bowel areas of normal untreated, and sulfamerazine pretreated rats are indicated in Figure 1; these are similar to data already published[9]. The AG cell counts/100 crypts, or gastric pits in the 2 rat

Mean argentaffin cell counts/100 intestinal crypts or gastric pits (see text) in normal, and sulfamerazine treated rats

Bowel tissue	Rat groups	
	No. treatment	Sulfamerazine treatment
Stomach fundus	4 (2–6)	4 (1–10)
Stomach body	6 (5–8)	3 (2–4)
Pyloric antrum	57 (50–62)	69 (55–80)
Upper duodenum	62 (48–70)	68 (63–72)
Lower duodenum	31 (29–40)	36 (34–39)
Mid jejunum	28 (26–31)	35 (27–43)
Terminal ileum	24 (17–29)	30 (24–41)
Appendix	51 (40–67)	69 (59–81)
Cecum	50 (46–52)	67 (60–74)
Ascending colon	83 (62–99)	79 (43–88)
Transverse colon	29 (22–41)	31 (29–36)
Descending colon	11 (10–13)	5 (4–6)
Rectum	18 (17–22)	10 (6–12)

The range is indicated in brackets.

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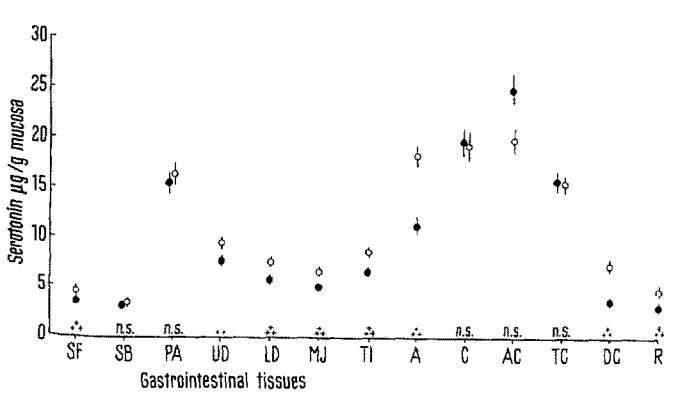

Fig. 1. Serotonin in the stomach fundus (SF), stomach body (SB), and pyloric antrum (PA), upper and lower duodenum (UD, LD,) mid-jejunum (MJ), terminal ileum (TI), appendix (A), cecum (C), ascending, transverse, and descending colon (AC, TC, DC), and rectum (R), of untreated and sulfamerazine pretreated rats. Data are expressed as means $\pm$ 1 S.E. Each group contains between 10–18 rats. $\overset{+}{++}$, $P < 0.001$; ++, $P < 0.01$; n.s., non-significant; •, normal male rats; o, sulfamerazine treated male rats.

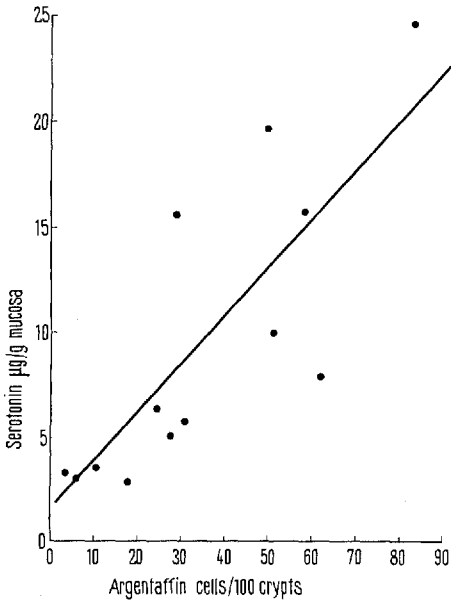

Fig. 2. Regression line demonstrating the relationship between the mean serotonin concentration (μg/g mucosa), and the number of argentaffin cells throughout the gastrointestinal tract of the normal rat. t, 4.446; $P < 0.001$; r, + 0.80.

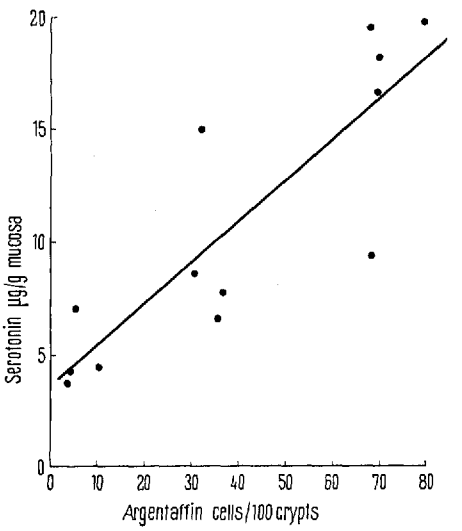

Fig. 3. Regression line demonstrating the relationship between the mean serotonin concentration (μg/g mucosa), and the number of argentaffin cells throughout the gastrointestinal tract of the sulfamerazine pretreated rat. t, 5.335; $P < 0.001$; r, + 0.85.

groups are indicated in the Table. Mean values and the range are presented because of the small number of rats in each group.

The relationships between the mean AG cell counts, and the fluorometrically determined serotonin values for each of the tissues are indicated in Figures 2 and 3 for the untreated, and the sulfamerazine pretreated rats respectively. For the untreated control rats the plot has a correlation coefficient $r = +0.80$, which is statistically significant ($t = 4.466$, d.f. II, $P < 0.001$), and in the sulfamerazine treated rats the curve has a correlation coefficient $r = +0.85$, which is statistically significant ($t = 5.335$, d.f. II, $P < 0.001$). These data are in keeping with the suggestion that serotonin is the material stored within the AG cell granules. In comparing the slopes of the 2 lines, there was no significant difference between them.

From this report there is some suggestive evidence that the increased serotonin concentrations reported in some intestinal areas following sulfamerazine[9] could be due to a higher level of serotonin/cell, and a larger population of visable AG cells[14].

Zusammenfassung. Eine direkte Korrelation zwischen Serotoninspiegel und der Zahl der argentaffinen Zellen im gastro-intestinalen Trakt normaler Ratten und solcher, die nach Sulfamerazinbehandlung einen höheren Serotoninspiegel aufweisen, wird festgestellt.

J. H. THOMPSON and L. B. CAMPBELL

Department of Pharmacology, University of California School of Medicine, Center for Health Sciences, Los Angeles (California 90024, USA), 24th April 1967.

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The Effect of Reserpine upon Gastrointestinal Serotonin in the Sprague-Dawley Rat

It is well known that reserpine causes a release of serotonin from the gastrointestinal tract[1–4], however, there are certain discrepancies in the literature concerning its degree. In the present study, the effects of reserpine were observed on 14 areas of the rat gastrointestinal tract to determine the degree of response to reserpine from one anatomical area to another.

Male and female Sprague-Dawley rats from the Charles River Laboratories (breeding shed 1), ranging in weight from 200–300 g were maintained on normal Purina rat chow, with a tryptophan content of 0.22%. The rats were housed in colony cages and exposed to a regular 24 h light/dark cycle (light: 05.00–19.00). In order to avoid any possible circadian influences on bowel serotonin, the rats were always killed between 08.00 and 09.00 on the day of assay by decapitation. The tissues sampled are indicated in Figure 3. In the experiments on the dose and time response to reserpine, only upper jejunal samples were taken. Upper jejunum was selected because of the ease of removal, the availability of duplicate samples,

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