A morphological and embryological study has been carried out on the enterochromaffin cells of the gastrointestinal tract of human foetuses and adults. Subsidiary observations have also been made on animal tissues. The results are summarised, section wise, below.

A. PRENATAL DEVELOPMENT:

1. The development of the enterochromaffin cells of the human gastrointestinal tract has been studied in a closely graded series of embryos and foetuses.
2. Enterochromaffin cells differentiate in situ in the epithelium and do not migrate into the epithelium from either the submucosa or the nerve plexuses.
3. Bodian positive argyrophile cells are first seen in the epithelium of the cardiac end of the stomach, the duodenum, and the proximal part of the jejunum at the 26 mm C.R. stage; at the pyloric end of the stomach and the distal part of the jejunum at the 32.5 mm stage; in the terminal ileum at the 35 mm stage; in the rectum at the 39 mm stage; and in the colon and appendix at the 65 mm stage.
4. True argentaffin cells are first seen in the duodenum and proximal part of the jejunum in a 59 mm embryo; in the stomach, distal part of the jejunum and rectum in a 45 mm embryo; in the terminal ileum in a 55 mm foetus, and in the colon and appendix in a 65 mm foetus.

5. There is a distinct interval between the appearance of Bodian positive argyrophile cells and that of true enterochromaffin cells in all parts of the gastrointestinal tract, suggesting that the argyrophile cells are pre-enterochromaffin.

6. There is a cranio-caudal gradient in the differentiation of the enterochromaffin cells of the small gut, and a caudo-cranial gradient of differentiation in the large intestine.

7. Following their first appearance the density of the enterochromaffin cells in the epithelium rapidly increases to a peak level at about the 120 to 140 mm stage and thereafter decreases.

B. DISTRIBUTION:

1. Enterochromaffin cells are present in all parts of the gastrointestinal tract from the lower end of the oesophagus to the rectum.

2. In the stomach they decrease in number from cardiac to the pyloric end.

3. In the small intestine an initial cranio-caudal gradient of distribution is later modified so that the density of the cells decreases cranio-caudally in the proximal part of the small
4. At the 65 mm stage enterochromaffin cells in the large intestine are least numerous in the caecum and sharply increase in density in a cranio-caudal direction. At the 75 mm stage they are abundant in the caecum; on proceeding towards the rectum they show an initial decrease in number followed by a progressive increase. By the 140 mm stage the gradient seen at the 65 mm stage is reversed and the cells now show a uniform cranio-caudal fall in density. At the 220 mm stage the cells are maximal in the caecum, but the rest of the large intestine shows no definite cranio-caudal gradient. At full term the pattern is again the same as at the 75 mm and 97 mm stages.

5. Relative to the rest of the gastrointestinal tract, the total enterochromaffin cell population of the appendix is small and shows no correlation with the high incidence of appendicular carcinoids.

C. RELATIONSHIP BETWEEN ARGYROPHILE AND ARGENTAFFIN CELLS:

1. The identity of 'argentaffin' cells with a variable proportion of 'argyrophile' cells is conclusively established by a comparison of cells in individual sections stained successively by argentaffin and argyrophile methods.

2. The presence of cells that are argyrophile but not argentaffin is confirmed by the same method.

3. All argentaffin cells are also argyrophile and there is no
evidence to support the claim of Kellweg (1952) and of Hamperl (1952) regarding the presence of non-argyrophile argentaffin cells.

4. The so called argentaffin cells can be divided into
   (a) those in which all granules are apparently argentaffin,
   and (b) those in which some granules are argentaffin while others are purely argyrophile. Thus a distinction can be made on the basis of argyrophilia and argentaffinity not only between individual enterochromaffin cells, but also between individual granules in a cell.

5. The proportion of argentaffin and argyrophile cells to one another is highly variable. Argyrophile cells predominate in the stomach. Beginning from the duodenum the relative proportion of argentaffin cells falls in the proximal part of the small intestine and thereafter shows a dramatic increase towards the ileo-caecal region. Almost all argyrophile cells of the terminal ileum and appendix are argentaffin. The argyrophile argentaffin ratio is variable at various levels of the large intestine but no definite gradient is obvious.

6. The non-argentaffin argyrophile cell is to be considered as an argentaffin cell depleted of its 5-HT content. It is thus an integral part of the enterochromaffin cell system. This applies also to purely-argyrophile granules within argentaffin cells.
D. POST-MORTEM DEGENERATION:

In tissues undergoing post-mortem degeneration the enterochromaffin cells lose the property of argentaffinity (and other specific reactions) earlier than that of argyrophilia. The time that elapses between death and the loss of stainability of cells varies considerably from animal to animal.

E. STAINING METHODS:

1. A modification of the Bodian silver-impregnation method, suitable for selective impregnation of enterochromaffin cells is described.

2. A modification of the Masson-Hamperl method is described. The modification has the advantage of being rapid to perform and of not being affected by room temperature.

3. A new argyrophile method for staining enterochromaffin cells in paraffin sections is described. Beginning with paraffin sections mounted on slides, the preparations are ready for examination in under 3 hours. The results compare favourably with those obtained with the Bodian method.

4. A technique for the staining of sections first by an argentaffin method and subsequently by an argyrophile method is described.

5. The use of tetrazotised benzidine for demonstration of enterochromaffin cells is described.
F. FUNCTION:

The possible functions of the enterochromaffin cells are
(a) local, in relation to intestinal movement, by stimulation
of mucosal nerve endings by 5-HT, or
(b) systemic as a central locus of production of 5-HT or 5-HTP
or (c) a combination of both these functions.

G. CARCINOIDS:

There is no correlation between enterochromaffin cell density
and carcinoid incidence in various parts of the gastro-intestinal
tract. However, areas showing a high carcinoid incidence show a
strikingly high argentaffin:argyrophile ratio. The significance
of argyrophile, and of the so-called 5-HTP producing carcinoids is
discussed in the light of the findings of the present investigation.

H. TERMINOLOGY:

A new terminology of the cells of the enterochromaffin system
is presented.