In spite of the considerable attention that enterochromaffin cells have attracted over the last century their precise function still remains obscure. Kultschitzky (1897) thinks that they are concerned with absorption of proteins, the granules representing protein derivatives in passage through the cell. They are considered to be externally secreting by Cordier (1923) and internally secreting by Kull (1925), Parat (1924) and most subsequent workers. Masson (1923) calls them 'sympathotropen' or 'neurocrine' in function and states that their secretion, which is directly poured on mucosal nerve endings, stimulates the musculature.

A relationship of the number of cells to feeding is suggested by Kultschitzky (1897) and by Törö (1931), but is denied by Kull (1913), Suda (1918) and Jacobson (1939). No clear relation to the type of diet has been demonstrated (Jacobson, 1939).

Jacobson's (1939) interesting hypothesis suggesting that argentaffin cells play a part in normal erythropoesis is rejected by Gillman (1942).

Schofield (1951, 1952, 1953) suggests that while enterochromaffin cells of the small intestine represent a stage in the maturation of mucous cells those of the large intestine represent neuro-endodermal receptors. Popoff (1939) on the other hand regards the argentaffin
cells of the human large intestine as an intermediate stage in the dedifferentiation of functionally exhausted mucous cells.

With regard to the non-argentaffin argyrophile cells they are believed to represent pre-enterochromaffin cells (Hamperl, 1952; Clara, 1957; Monesi, 1960). Clara (1957) emphasises that only a proportion of non-argentaffin argyrophile cells can be considered pre-enterochromaffin, while Falck, Hillarp and Torp (1959) suggest that dopamine containing cells may also be present. The fact that all non-argentaffin argyrophile cells may not be related to the enterochromaffin system is suggested by the considerable variation in argentaffin:argyrophile ratio in various parts of the gastrointestinal tract and by the fact that argyrophile cells do not develop into argentaffin ones in certain situations (Pages 56, 57). On analogy with the α cells of the pancreas it has been suggested that argyrophile cells may produce glucagon (Campbell, 1959; Hamperl, 1952; Helander, 1961).

The nature of the specific chemical substance present in enterochromaffin cells is closely related to the question of their function. The specific substance is considered to be an ortho-diphenol (catechol) having a short side chain in the para position (Cordier and Lison, 1930; Lison, 1953); a metadiphenol (resorcinol) (Gomori, 1948; Lillie, Burtner and Greco-Denson, 1953); and a pterine (Jacobson, 1939; Jacobson and Simpson, 1945). However, following the work of Erspamer and his associates (Erspamer, 1946, 1948; Erspamer and Boretti, 1950; Erspamer and Vialli, 1951;...
Erspamer and Asero, 1952) and that of Barter and Pearse (Barter and Pearse, 1953, 1955; Pearse, 1956) it is now generally accepted that the active substance in unfixed enterochromaffin cells is most probably 5-hydroxytryptamine or a closely related precursor like 5-hydroxytryptophan. However, most of the usual histochemical tests employed in demonstrating the enterochromaffin granules are positive only after fixation in formalin; the granules as usually studied are therefore to be regarded as a formalin artifact (Shepherd, West and Erspamer, 1953; Barter and Pearse, 1953, 1955). Barter and Pearse suggest that the compound actually present is a β-carboline derivative formed by condensation of 5-HT and formaldehyde. Gomori's (1954) contention that with the histochemical tests at present available it cannot be determined whether the reactions of human enterochromaffin cells are due to a derivative of resorcinol or 5-HT is refuted by Pearse (1956) who using the alkaline thioindoxyl reaction clearly demonstrates that resorcinol and its derivatives cannot be considered the active substance in enterochromaffin cells.

Indirect evidence of the presence of 5-HT in enterochromaffin cells is afforded by the fact that this substance can be recovered in considerable amounts from carcinoids (Lembeck, 1953; Batzenhofer and Lembeck, 1954), by the consistent correlation between enterochromaffin cell population and 5-HT content of various parts of the intestine and of other organs of various species (Erspamer, 1954b; Faustini, 1955), and by the fact that the first appearance of enterochromaffin cells during prenatal development coincides with the
appearance of the first traces of 5-HT in extracts of intestinal tissue (Faustini, 1955). The results of reserpine administration on 5-HT content of tissues (Pletscher, Shore and Brodie, 1955), and on enterochromaffin cells (Vialli and Quaroni, 1956; Zbinden, Pletscher and Studer, 1957; Benditt and Wong, 1957; Won, 1964) also point to the same conclusion.

In spite of the recognition of the association of enterochromaffin cells and 5-HT the precise function of these cells remains obscure. Their function may either be local in relation to intestinal movement; systemic as sites of production of 5-HT or 5-HTP; or a combination of both.

The location of these cells in the gastrointestinal tract in itself suggests a local function. As early as 1923 Masson suggested that these cells produce a secretion that stimulates the mucosal nerve endings and influences intestinal movement. Bülbbring (cited by Bell, Davidson and Scarborough, 1961) has shown that 5-HT is released when the intraluminal pressure is raised and she believes peristalsis that it facilitates by stimulating the mucosal endings.

The major objection to the acceptance of this local function is the great variation in the distribution of these cells within the gastrointestinal tract, as is also the variation in argyrophile-argentaffin cell ratio. There is no obvious correlation between the distribution of these cells and intestinal peristalsis. However, the presence of a cranio-caudal gradient in enterochromaffin cell distribution in the small intestine of certain laboratory animals
fits in perfectly with the findings of Alvarez and his pupils (cited by Thomas, 1961) who describe a cranio-caudal gradient in various properties of the intestine, the activity being highest at the duodenal end and lowest at the ileal end. Among the properties for which this gradient has been established are rhythmicity, irritability, shortness of latent period and susceptibility to drugs. The frequency of rhythmic contractions of small intestine is maximum in the duodenum, least in the lower ileum, and intermediate between these extremes elsewhere. This strongly suggests a correlation between enterochromaffin cell density and rate of rhythmic contractions and it will be of interest to see if rhythmic contractility in the human small intestine shows the same departure from the pattern in laboratory animals as does the enterochromaffin cell distribution.

A systemic function for enterochromaffin cells has been suggested by Dalgleish and Dutton (1957). According to these authors the 5-HT present in various tissues of the body is formed by local conversion of 5-HTP which is formed at some central locus; the central locus is very probably the enterochromaffin cell. If this is indeed the sole function of the enterochromaffin cells it is necessary to enquire why they are located in the gut, and in what way their variation in distribution may be explained.

The available evidence for and against a local versus a systemic function is inconclusive either way, but a combination of both a local and systemic endocrine function may well prove to be the real role of the enterochromaffin cells.