Hamartomas in the alimentary tract

Liddell and Scott’s Greek lexicon defines the word αμαρτάω as ‘to fail of one’s purpose or go wrong’ and Eugen Albrecht¹ used the derivative ‘hamartome’ to describe a group of tumour-like malformations or inborn errors of tissue development in which tissues indigenous to the part or organ ‘went wrong’, in that they were abnormally intermixed, usually with a preponderance of one or more than one type of tissue. Such malformations are not primarily neoplastic though some, particularly neurofibromatoses, may later become so. Willis² strictly limits the term hamartoma to lesions ‘for which there is clear evidence of an underlying developmental abnormality’ whether the hamartoma is present at birth or develops later as a disproportionate growth in tissue elements as they mature. Others, including myself, feel that while this is probably true of all predominantly epithelial hamartomas it is not necessarily so for those in which connective tissues predominate. Mature connective tissue has such great potentiality for reverting to a more embryonic pattern under diverse stimuli that malformations indistinguishable from hamartomas may arise from it. It is thus only that Peutz-Jeghers polyps and other hamartomas first appearing in late childhood or adolescence can be explained.

A number of hamartomas are genetically transmitted and a careful family history is always essential in their investigation. A number, too, show more than one pattern of malformation in different tissues, as in tuberose sclerosis. It is interesting to speculate whether the different patterns are the result of a single pleiotropic gene affecting a number of tissues, or of the action of linked abnormal genes, or whether, once a single tissue abnormality is established, it can secondarily give rise to others.

Hamartomas are not uncommon in the gastrointestinal tract; the preponderant tissues in them are connective tissue derivatives including lamina propria, smooth muscle, vasformative tissue, and nerve elements, though epithelial tissues also occur. It is important to differentiate them from ectopic or heterotopic tissue deposits such as pancreatic rests, where the tissues predominating in the abnormality are not indigenous to the part. The mouth, tongue, oesophagus, and anus are barren fields, though ectopic pancreatic acinar elements intermixed with smooth muscle and incorrectly designated as hamartomas have been found in them. Predominantly epithelial hamartomas appear to be confined to the stomach and duodenum. They are described under various terms, including myoepithelial hamartomas and adenomyomas, and are usually symptomless so that one does not know at what age they first developed. Usually lying in the wall of the organ they occasionally become pedunculated; they consist of whorls, bundles, and bands of smooth muscle surrounding gland elements whose epithelium histologically and histochemically may resemble that of Brunner’s glands or pancreatic acini.³,⁴,⁵,⁶ While many represent ectopic pancreas,⁷,⁸ others are genuine.

The predominantly connective tissue hamartomas are divisible according to the type of connective tissue whose overgrowth predominates. They are found throughout the gastrointestinal tract and are often multiple in more than one site.
Maldevelopment with unusual preponderance of lamina propria results in the juvenile (retention) type of large intestinal polyp, wrongly called congenital polyps or juvenile adenomas since they are often not present at birth and are certainly not neoplastic. Common in early childhood they are also seen in adolescents and young adults; they have a marked tendency to bleed and may give rise to a secondary anaemia, and they may prolapse or undergo autoamputation. There is not, in the vast majority, any evidence of genetic inheritance but there are isolated examples with familial incidence where multiple polyps have been present throughout the tract. Macroscopically they are small oval or disc-shaped polyps, pedunculated from the start, more commonly single than multiple and usually present in the distal rather than the proximal large bowel. They are readily recognized by the naked eye by their narrow pedicle, smooth unlobulated outer surface, and by the presence of dilated mucin-filled spaces clearly visible on the cut surface. Ulceration and haemorrhage are common. Microscopically the bulk of the polyp consists of connective tissue identical to that of the lamina propria in which are embedded gland elements, some of which are distended by mucin. There is none of the nuclear hyperchromatism or glandular irregularity that are associated with neoplasia. Probably allied to this group, because the intestinal polyps are similar in structure, are cases of Cronkite-Canada syndrome in which there is extensive gastrointestinal polyposis combined with ectodermal changes including alopecia, hyperpigmentation of the skin, and atrophy of the nails.

Abnormal overgrowth of the muscularis mucosa also results in polyp formation. There is usually associated mucocutaneous melanin pigmentation as macules around the lips, nose, and eyes, and as more diffuse pigmentation of the lips and buccal mucosa, which, with transmission as a Mendelian dominant, comprises the well known Peutz-Jeghers syndrome. Polyps occur most commonly in the upper small bowel, commonly in the stomach, more rarely in the large bowel, appearing in childhood and often in successive crops and very often producing intussusceptions. Other members of an affected family may show formes frustes, such as polyps without pigmentation or pigmentation without polyps. Macroscopically the striking feature is a tree-like branching of the muscularis, the branches becoming secondarily clothed in mucosa with lamina propria which is essentially normal and reproduces the mucosal pattern from which the polyp arose. Although there are some who still classify these polyps as neoplasms, and though occasional examples of genuine neoplastic change do occur, it is clear that many workers have been misled by pools of mucin which become trapped between mucosal folds in the polyp and cause misplacement of epithelium with the production of curious histological changes which can be misinterpreted as carcinoma. Special care is needed in interpreting the solitary polyp in the large bowel, for unless the normal appearance with lack of nuclear hyperchromatism in gland elements is recognized a malignant adenoma may be wrongly diagnosed.

Abnormal proliferation of vasoformative tissue gives rise to a range of vascular hamartomas in the gastrointestinal tract, rare in incidence and variable in appearance. There are many workers who regard such proliferations as neoplastic and describe 'metastases' to account for the multiple nature of many of the lesions; since many are found incidentally and their regularity of structure does not suggest malignancy it is more correct to
consider them as multiple hamartomas. Classifying them is difficult since no one sees more than a few in his working life, but when collected series are studied individual cases fall broadly into one of three groups: those which are solitary; those which are multiple but confined to the bowel; and those in which the bowel lesion is only one manifestation of a more generalized haemangiomatosis. Within each group the haemangiomas may be predominantly cavernous, when they lie in the submucosa and may project inwards from it; simple capillary in the same site; or multiple phlepectasias directly connected with veins and sometimes calcified. They occur at all ages, may be single or multiple, and, as might be expected, usually present with massive, often symptomless, haemorrhage. Whenever a patient presents with melaena and anaemia and clinical and radiological examinations are negative, their possible presence should be remembered and a search for other haemangiomas elsewhere should be undertaken.

That abnormal proliferation of neural connective tissue leading to generalized neurofibromatosis occurs, no one doubts, nor is there argument that sometimes sarcomatous change supervenes. Nevertheless Willis advances convincing reasons for regarding such proliferations as initially hamartomatous. The question is here an academic one, for although gastrointestinal involvement is described in generalized neurofibromatosis and as an isolated lesion, it is so rare as to be an alimentary curiosity.

There remain for discussion one or two conditions whose hamartomatous nature is genuinely in doubt. In Gardner's syndrome, familial adenomatosis occurs in association with osteomatosi, epidermoid cysts, and ill-defined connective tissue masses. The large bowel adenomas are genuinely neoplastic, but the connective tissue manifestations are probably hamartomas; the condition is inherited as a Mendelian dominant and may represent the combined effect of two linked abnormal genes or of a single pleiotropic gene. Since the large intestinal lesion is not hamartomatous it is probably better for gastroenterologists to regard the syndrome as a variant of familial adenomatosis. Most workers regard the eosinophil fibrous polyps, which occur in the stomach and small bowel as either of neurogenic origin or as inflammatory, but a hamartomatous origin has been suggested. Three personally studied cases have not suggested to me any definite overgrowth of indigenous tissue and they should not be regarded as hamartomas without further proof.

It is a maxim of British law that a man is innocent until proved guilty. Hamartomas are, with rare exceptions, innocent and should not be convicted of malignancy without very exacting microscopic proof of cancerous change. It is, after all, the patient who may receive the unwarranted punishment of a guarded prognosis and an unnecessary resection. The very derivation of the word hamartoma should encourage us, in adjudging them, not to go wrong.

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REFERENCES

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20— (1962). Follow-up study of family group exhibiting dominant inheritance for syndrome including intestinal polyps, osteomas, fibromas and epidermal cysts. Ibid. 14, 376-390.