the stress of adolescence or early adult life lacked the stamina to make a good adjustment after operation.

Another conclusion is that neurotic patients do not necessarily show the so-called post-leucotomy syndrome. Some are more lively, others more apathetic; some more careful, others careless; some irritable, others calmer. Moreover, these varying traits occur in patients with both good and poor results, and can be evaluated only against the past and present personality and social background. It is possible that the serious personality defects described following operation will be separable into those due to persistence of previous personality defects or disease symptoms, and those due to the cut being made too far posteriorly or in other anatomically undesirable areas.

Summary

A follow-up was made of 30 neurotic patients who had been treated by prefrontal leucotomy. Two-thirds were found socially well adjusted or with minor defects only. The factors on which the result depends are assessed and discussed.

REFERENCES

Board of Control (1946). *Pre-Frontal Leucotomy in 1,000 Cases.* H.M.S.O.

Fleming, G. W. T. H., and McKissock, W. (1943). *Lancet*, 1, 361.

Partridge, M. (1950). *Prefrontal Leucotomy.* Blackwell, Oxford.

Ström-Olsen, R., and Tow, P. M. (1949). *Lancet*, 1, 87.

Watts, J. W., and Freeman, W. (1944). *J. Neurosurg.*, 1, 291.

SIMPLE GASTRIC ULCER AND CARCINOMA

BY

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The possibility that a chronic gastric ulcer may become malignant has excited controversy for more than a century. In the early years of gastric surgery it was commonly believed that a large proportion of gastric carcinomata had their origin in chronic simple ulcers. For example, Wilson and MacCarty (1909) concluded that 71% arose in this manner, and, in this country, Moynihan (1906) stated that about 60% of cases of gastric carcinoma gave a history suggesting previous simple ulcer.

A more moderate school still holds the view that malignant transformation of simple ulcer may occur, but far less commonly. Ewing (1918) concluded that not more than 5% of simple ulcers undergo malignant change, and similar views have been put forward by Dible (1924), Cabot and Adie (1925), Stewart (1929, 1931), and Newcomb (1932). This school bases its opinion largely on the results of pathological studies of post-mortem material and specimens removed at operation.

By contrast, Brown (1930) studied the fate of 1,130 patients in whom there was good evidence of chronic gastric or duodenal ulcer and who were treated medically. In the 77 cases of chronic gastric ulcer only one subsequently developed a gastric carcinoma, and that at a different site from the ulcer. Of the remaining 1,053 patients with duodenal or combined duodenal and gastric ulcer, nine subsequently developed gastric carcinoma. He therefore concluded that chronic gastric ulcer is not a predisposing cause of carcinoma.

The problem is of considerable practical importance because the treatment of gastric ulcer must depend upon which view is held. In making a survey of 375 patients treated in the Radcliffe Infirmary for gastric carcinoma, we were interested to find 26 patients in whom there was some evidence that the neoplasm might have originated in a chronic gastric ulcer. It is our purpose to present the evidence derived from these cases and to discuss it.

Results

In Table III we have set out the salient features of all the cases in which there was evidence that the carcinoma might have arisen from a chronic gastric ulcer. In the final column we summarize the evidence which seems to support this view.

All the cases except two had pathological evidence in favour of their being "ulcer-cancers." We are not competent to judge whether the criteria adopted by the pathologists were adequate to permit of such a diagnosis. The fact that well-trained pathologists came to this conclusion indicates to our satisfaction that the lesions presented the characteristics of peptic ulceration in almost all cases.

If we consider other features of the group of cases, some interesting facts emerge. Only 13 of the patients had clinical histories which we can accept as probably indicating the presence of a chronic ulcer. The site of the carcinoma is also of interest. Of the 26 cases no fewer than 18 were pre-pyloric, the remaining 8 being in the body of the stomach (Table I). This distribution corresponds with what we have found for the site of carcinoma in the whole series of 375 patients, of whom the present group is a sample. It contrasts sharply with the well-known predilection for the body of the stomach shown by chronic gastric ulcer.

TABLE I.—*Site of Carcinoma in Relation to Clinical History of Chronic Gastric Ulcer*

Clinical History of Chronic Gastric Ulcer	Site of Carcinoma		
	Pre-pyloric	Body Other Than Lesser Curve	Lesser Curve
Positive	7*	3	3
Negative	11†	0	2
Total	18	3	5

* Two had separate gastric ulcers on lesser curve.
† One had separate gastric ulcer on lesser curve.

Among the 18 patients with pre-pyloric carcinomata 3 had chronic gastric ulcers on the lesser curve which were separate from them.

It is also of interest to observe the results of the fractional test meal in the 21 patients of this group in whom it was carried out and to compare the results with

TABLE II.—*Fractional Test Meal Findings*

	No. of Patients	Normal or Hyperacid	%
Present group	21	12	57·1
Remainder of parent series	162	36	22·2

remaining cases of the parent series (Table II). The present groups showed a much higher proportion of patients with normal or increased free hydrochloric acid.

TABLE III.—*Evidence in 26 Cases in which there was some Evidence of "Ulcer-Cancer"*

Case No.	Age and Sex	Date of Admission	Clinical History	*X*-ray Findings	Operation	Morbid Anatomy and Histology	Diagnostic Criteria
1	46 M.	16/10/47	15 years' epigastric pain, unrelated to meals but relieved by alkalis. Remissions of 6–12 months. 1 year's alteration in character of pain	Large ulcer crater on lesser curve, with rigidity above and below—probably neoplasm	Large shallow ulcer of lesser curve with marked induration	Adenocarcinoma arising in chronic ulcer	History. *X*-ray. Histology
2	61 M.	24/9/48	20 years' indigestion 3–4 hours after meals. 1937: gastro-enterostomy. 1944: barium meal showed G.U. low down on lesser curve. Good response to medical treatment. Intermittent dyspepsia, but 3 months before admission the character of dyspepsia changed	1944: gastric ulcer low down on lesser curve 1948: fairly large ulcer crater low down on lesser curve	Large chronic gastric ulcer on lesser curve	Adenocarcinoma arising in a chronic ulcer. Lymph nodes not involved	History. *X*-ray. Histology
3	66 F.	30/9/46	1934: onset of intermittent dyspepsia 1–2 hours after meals and relieved by alkalis. 1943: anorexia. 1944: admitted because of loss of weight and lassitude. Gastroscopy: small ulcer on posterior wall, well above pyloric region; no evidence of malignancy. Improved with medical treatment. 1946: admitted with 7 weeks' history of anorexia, epigastric pain, and vomiting	1944: Large ulcer crater on posterior wall. Repeat examination in 1944: ulcer smaller on medical treatment		Macroscopic: carcinomatous ulcer arising from the edge of an old scar. Secondaries in the liver. Histology: adenocarcinoma	History. *X*-ray. Histology
4	42 F.	8/7/47	1943: central abdominal pain and vomiting in afternoon for 3 months. 1945: return of pain 3–4 hours after meals; improved with dieting and had periods of freedom up to 2 months. At time of admission no recent change apart from a haematemesis	1945: large G.U. on posterior wall at angulus. 1947: large ulcer at angulus probably fixed	Very large indurated ulcer at incisura, fixed to pancreas	Chronic G.U. with carcinomatous change	History. *X*-ray. Histology
5	55 M.	23/4/40	12 years' epigastric pain with remissions. April, 1939: perforation of gastric ulcer, treated surgically by closure of perforation. Thereafter free of symptoms. Recurrence of pain with radiation to back and bulky vomits for 4 months before admission	April, 1940: pyloric stenosis, probably due to carcinoma	Large ulcer on lesser curve near pylorus. One or two nodules in peritoneum. Very suggestive of neoplasm. Local enlarged glands	Pre pyloric ulcer. Naked eye suggests chronic peptic ulcer, but histological appearances do not entirely confirm this. Lymph nodes involved	History. Histology
6	53 M.	29/6/43	1917: onset of epigastric pain after meals; relieved by vomiting and by alkalis. No recent change in symptoms	June, 1943: prepyloric deformity and deformed duodenal cap	Pre-pyloric carcinoma with many lymph nodes	Ulcer on lesser curve of pre-pyloric region, with thickened edges. Adenocarcinoma arising in a chronic ulcer. Lymph nodes *not* involved	History. Histology
7	51 M.	12/9/41	6 years' intermittent epigastric pain 2–3 hours after meals, relieved by food and vomiting. 5 weeks before admission the pain became continuous, with vomiting and anorexia	1939: barium meal normal. 1941: ulcer crater at angulus — nature unknown	Ulcerated mass on lesser curve	Irregular ulcer not suggestive of malignancy. Histologically an ulcer-cancer	History. Histology
8	62 F.	2/1/40	4 years' epigastric pain immediately after meals, at first with remissions, later continuous. Pain aggravated by food	Large pyloric neoplasm	Large growth adherent to pancreas	Pre-pyloric chronic gastric ulcer undergoing malignant change	History. Histology
9	62 F.	30/11/42	5 years' epigastric pain 2 hours after meals, relieved by food and alkalis, with remissions. Attacks of pain gradually became more severe	Large filling defect of body and stomach	Large mass on greater curvature	Carcinomatous ulcer with an area of scarring proximal to it. Microscopical appearances suggest an ulcer crater	History. Histology
10	50 F.	5/5/39	7 years' dull abdominal ache related to meals with complete remissions. Relief by vomiting and alkalis. Three months' bulky vomits; haematemesis led to admission	Pyloric stenosis, probably simple	Hard, nodular pyloric swelling, with local glands	Deep pre-pyloric ulcer. Carcinoma developing in the edges of a chronic ulcer. Lymph nodes involved	History. Histology
11	73 F.	5/2/48	1905: onset of intermittent dyspepsia. 1927: wedge-resection of G.U. 1929: gastro-enterostomy. Following this, intermittent dyspepsia, when the pain became more continuous and went through to the back	Extensive filling defect of lower third of stomach	Large growth of stomach distal to stoma of gastro-enterostomy. Secondaries in liver and local glands		History
12	41 M.	6/12/46	1943: dyspepsia 2 hours after meals relieved by alkalis and food with periods of freedom. Loss of weight	1944: G.U. low down on lesser curve	Mobile carcinoma of pylorus, with local glands	Ulcer on posterior surface on pre-pyloric region with raised edge. Probable ulcer-cancer. 2–4 lymph nodes involved	Histology
13	36 M.	20/9/40	2½ years previously: isolated vomiting attack. 6 months later epigastric pain 2½ hours after meals with occasional vomiting. 8 months before admission: increased severity of symptoms	Pre-pyloric ulcer and infiltration	Diffuse thickening on lesser curve near pylorus. Small local glands	Pre-pyloric peptic ulcer undergoing malignant change	Histology
14	80 M.	1/4/47	2 years' flatulence. 6 months' epigastric pain unrelated to meals, relieved by alkalis. March, 1947, admitted to R.I. Sent out. Readmitted 1/4/47 with increasing pain	March, 1947: huge ulcer crater on posterior wall near angulus	Posterior ulcer at pylorus— ? malignant	Died 26/5/47 of coronary thrombosis. Chronic G.U. with infiltrating anaplastic adenocarcinoma. Secondaries in glands and lungs	Histology
15	65 M.	2/4/48	2 weeks' epigastric pain 2 hours after meals. 1 week before admission: haematemesis	Gross deformity of lower half of stomach with large ulcer crater	Very large G.U. on lesser curve infiltrating pancreas. Pancreas nodular	Biopsy: no evidence of malignancy. Suggests base of chronic peptic ulcer. Died 19/12/48	Histology

TABLE III.—(*Continued*)

Case No.	Age and Sex	Date of Admission	Clinical History	*X*-ray Findings	Operation	Morbid Anatomy and Histology	Diagnostic Criteria
16	56 M.	10/1/49	8 months before admission: pain under left costal margin every day, unrelated to meals	Large ulcerating filling defect near incisura	Carcinomatous ulcer straddling lesser curve in pre-pyloric region	Large pre-pyloric ulcer with raised edges and thick fibrotic base. Histology: ulcer-cancer	Histology
17	59 M.	25/2/49	1 year's history of pain 1½ hours after food and at night, sometimes relieved by alkaline powder. Recent change to constant pain	Large nodular mass in region of pyloric canal	Large pre-pyloric neoplasm invading pancreas and omentum	Large simple pre-pyloric ulcer with anaplastic adenocarcinomatous changes in the edges (ulcer-cancer)	Histology
18	49 M.	9/10/47	Pernicious anaemia, under treatment since 1932. 7 weeks' dyspepsia	Pyloric obstruction	Large pre-pyloric neoplasm, involving one side of a possibly benign ulcer	Adenocarcinoma, Broders 1. Appearances consistent with its origin in a benign ulcer	Histology
19	44 M.	19/1/46	2½ years' vague indigestion. 1½ years' stabbing epigastric pain 2 hours after meals, relieved by alkalis. 7 months previously: haematemesis and melaena, relief of symptoms with rest in bed	Pre-pyloric ulcer—nature uncertain	Pre-pyloric ulcer	Naked eye: chronic gastric ulcer. Histology: ulcer-cancer	Histology
20	74 M.	25/11/38	Admitted with perforation. No previous history of indigestion		Closure of perforation in pre-pyloric region just proximal to a carcinomatous mass	Macroscopic: appearances suggest an ulcer. Histology: evidence of carcinoma arising at the site of a simple ulcer	Histology
21	68 F.	18/3/42	3 months before admission: epigastric pain after meals, worse at night. Frequent small vomits and steady loss of weight	Filling defect of pyloric antrum with gastric stasis	Pre-pyloric ulcer with thickened edges	Pre-pyloric ulcer with rolled edges. Anaplastic signet-celled carcinoma arising in the margins of a chronic ulcer	Histology
22	66 F.	14/5/40	1 year previously: flatulence and indigestion	Pre-pyloric obstruction due to a mass	Pyloric stenosis and ulcer on lesser curve causing hour-glass stomach	Hour-glass stricture upper part of body, with a proximal chronic ulcer. Adjacent to this is an adenocarcinoma. Macroscopic stricture of pylorus without pathological changes at microscopy	Histology
23	62 F.	25/3/47	30 years previously: perforated gastric ulcer. 7 months previously: pain left side unrelated to meals but relieved by alkalis. Later developed constitutional symptoms	Constant filling defect pyloric antrum	Stony-hard mobile mass just above pylorus	Chronic gastric ulcer with carcinoma infiltrating base. Lymph nodes involved	Histology
24	47 M.	7/3/42	20 years' dyspeptic history with remissions. 12 years previously: perforation; surgical closure. Continued to have dyspepsia. 10 weeks before admission: alteration in character of dyspepsia	Large G.U. adhesions to pancreas and gross deformity of pylorus (two examinations)	Biopsy of gland in neck	Anaplastic carcinoma	History
25	73 F.	21/9/46	Pain after meals for nearly all her life. 6 years previously: increasing severity of pain with many remissions. 4 months previously: frequent vomiting	Ulcer crater on middle third of lesser curve and pyloric stenosis	Polypoid pre-pyloric carcinoma. Ulcer on lesser curve	Adenocarcinoma pyloric region and simple gastric ulcer on lesser curve	History. Histology
26	73 F.	17/7/40	No details—patient admitted moribund			Old G.U. scar halfway along lesser curve. Pyloric carcinoma extending up to lower edge of scar	Histology

Discussion

It is clearly impossible to say that in any of the present group the carcinoma did not originate in a chronic peptic ulcer. However, so far as the site is concerned, the distribution is that of carcinoma. This suggests that a large number of the cases may have been carcinoma unrelated to preceding peptic ulcer. There are two pieces of evidence to support this possibility. The first is that half of the patients had clinical histories compatible with the diagnosis of carcinoma of the stomach arising *de novo*. Secondly, three of the patients had chronic peptic ulcers which were distinct from their carcinoma. A further small additional point is that one case had suffered from pernicious anaemia for many years, and it has been clearly demonstrated that chronic peptic ulcer does not occur in that disease.

The results of the fractional test meal show that this group of patients contained a large proportion (57%) with normal or high levels of acid. By some workers the finding of free acid has been thought to favour the diagnosis of "ulcer-cancer," but an alternative possibility exists—namely, that the presence of normal acidity greatly increases the chance of peptic ulceration of gastric carcinoma. It is true that some pathologists have claimed that they can distinguish such an event from the appearance of a true "ulcer-cancer," but Palmer and Humphreys (1944) claim that all diagnostic features of an "ulcer-cancer" can occur in ulcerating carcinoma.

It is reasonably certain that the data can be explained only in terms of one of the following possibilities: (*a*) that chronic peptic ulcers of the pre-pyloric region are extremely liable to become malignant; or (*b*) that

pre-pyloric carcinomata frequently undergo peptic ulceration and may then present with the histological features of so-called "ulcer-cancer."

We believe that the second possibility is inherently more likely. But, in any event, from a practical standpoint the main conclusion is unaffected by one's choice between these two possibilities. It is that pre-pyloric ulcers are commonly malignant and should be resected.

Summary

Among 375 patients with gastric carcinoma treated in the Radcliffe Infirmary there were 26 with some evidence that the neoplasm might have arisen in a simple ulcer.

There was good clinical evidence of chronic simple ulcer in only half the patients.

The site of the neoplasm for the group of 26 patients conformed with the distribution of carcinoma of the stomach and not with that of simple gastric ulcer.

In three cases the carcinoma had apparently arisen at a site different from that of a pre-existing simple ulcer.

We believe that most of these cases were examples of ulcerating carcinoma. In any event, the majority were pre-pyloric, and it is evident that pre-pyloric ulcers should be deemed malignant and treated by surgical resection.

We wish to thank the physicians and surgeons of the Radcliffe Infirmary for permission to make the study out of which the present article arises.

REFERENCES

Brown, R. C. (1930). *J. Amer. med. Ass.*, **95**, 1144.
Cabot, H., and Adie, G. C. (1925). *Ann. Surg.*, **82**, 86.
Dible, J. H. (1924). *Brit. J. Surg.*, **12**, 666.
Ewing, J. (1918). *Ann. Surg.*, **67**, 715.
Moynihan, B. G. A. (1906). *British Medical Journal*, **1**, 370.
Newcomb, W. D. (1932). *Brit. J. Surg.*, **20**, 279.
Palmer, W. L., and Humphreys, E. M. (1944). *Gastroenterology*, **3**, 257.
Stewart, M. J. (1929). In Hurst and Stewart's *Gastric and Duodenal Ulcer*. Oxford Univ. Press, London.
—— (1931). *Lancet*, **2**, 565, 617, and 669.
Wilson, L. B., and MacCarty, W. C. (1909). *Amer. J. med. Sci.*, **138**, 846.

THE USE OF ORAL CORTISONE IN PAEDIATRICS

BY

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Since the preliminary report describing the effects of cortisone on 14 adult patients with rheumatoid arthritis was made by Hench, Kendall, Slocumb, and Polley in April, 1949, much work recording the action of the drug in this and numerous other diseases has been reported. However, the use of a microcrystalline suspension of cortisone acetate to be administered intramuscularly either once or twice daily presented an obvious disadvantage for prolonged therapy, especially in children, so that when limited supplies of cortisone became available in tablet form the opportunity arose to test its therapeutic efficiency by mouth.

Three children with rheumatoid arthritis, one child with acute rheumatic pericarditis, and one child with nephrosis were given 25-mg. tablets of cortisone acetate ("cortone"—Merck and Co.) once, twice, or three times daily as required. The tablets are slightly bitter if dissolved in the mouth, but were easily swallowed whole by the older children. They were given crushed in milk to the two younger children. No gastric intolerance was noted.

Case 1

A 12-year-old girl was admitted to hospital on January 27, 1951, because of swelling, deformity, and restricted movement of her wrists, elbows, fingers, knees, and ankles. She had been ill since July, 1949, when vague pains occurred in several of her joints. Swelling of the knees, associated with pyrexia, was first noted in January, 1950. A diagnosis of acute rheumatic fever was made and she was admitted to another hospital. Although her fever subsided with salicylate therapy, her knees remained swollen and her ankles also became similarly affected. During the summer months her general condition improved. She was allowed to go home, but was unable to walk about very much because of the swelling of knees and ankles. In October, 1950, her wrists and fingers also became swollen and were restricted in movement. She was readmitted to hospital, where a diagnosis of rheumatoid arthritis was made and gold therapy was begun. She was reported to be worse after the second injection, and so treatment was discontinued. She was transferred to the Royal Manchester Children's Hospital for cortisone therapy.

On admission (January 27, 1951) she was a poorly nourished, chronically ill-looking child with dryness and desquamation of the skin of the arms and legs and temperature of 99° F. (37.2° C.). The heart was normal. There was no lymphadenopathy or enlargement of the spleen. There were full movements of the neck and, so far as could be ascertained, full movements of the spine. The elbows and wrists were swollen and all movements were severely limited. The shoulder-joint movements were also restricted. All fingers showed fusiform swelling. The hips and knees were fixed in flexion; the latter were grossly swollen, were incapable of extension, and had no more than 2½ in. (6.3 cm.) separation. The ankles were also swollen, with marked foot-drop and hardly any dorsiflexion. There was slight pitting oedema of the dorsum of each foot.

Her blood pressure was 105/75 and the sedimentation rate 45 mm. in one hour. The haemoglobin was 54% (Haldane), with 4,490,000 red blood cells and 10,400 leucocytes per c.mm. The eosinophils were fewer than 5 per c.mm. Radiographs showed soft-tissue swelling around the joints, no narrowing or alteration of joint spaces, and severe rarefaction of all the long bones. Electrocardiograms were normal.

On February 10 cortisone was started. She was given 300 mg. by mouth in the form of four 25-mg. tablets three times a day. This was continued for four days. She was then given 150 mg. daily for three days and 100 mg. daily for seven days, so that she received 2.35 g. by mouth in 14 days.

Within 24 hours of the beginning of treatment her temperature became normal and remained between 97 and 98° F. (36.1 and 36.7° C.) throughout the course. Within 48 hours pain in the affected joints was much less. Whereas, before treatment, passive movements had made her wince with pain, the joints, although restricted in mobility, could now be moved without hurting her. On February 13, after 72 hours' treatment, all joints except the right ankle and left elbow measured less in circumference and the range of movement had definitely increased. She seemed much brighter mentally and began to take an intelligent interest in her progress and to co-operate with the physiotherapist. On February 16, after one week's treatment, she could separate her knees by 3½ in. (8.9 cm.) and the swelling of the joints was decreasing. There was an almost complete range of movement in the wrists, although some swelling was still present. The fingers had very slight fusiform swelling and the elbows seemed normal in shape and mobility. The skin was much improved in texture. For the first time she began to knit and could comb her hair, and she could sit on the side of her bed or in a chair. At the end of the two weeks' therapy her upper limbs seemed to be perfectly normal in all respects, apart from a weakness of the handgrip due to wasting of the small muscles of the hand. Her