STRESS ULCERS IN THE STOMACH

BY

I. M. BRECKENRIDGE, M.B., Ch.B.

E. W. WALTON, M.D.

AND

W. F. WALKER, Ch.M., F.R.C.S.

Departments of Surgery and Pathology, University of St. Andrews, Queen's College, Dundee

[WITH SPECIAL PLATE]

Acute peptic ulceration resulting from a period of intense stress was probably first noted by Curling, who in 1842 described acute ulceration of the duodenum occurring after burns. The same alarming sequence has since then been reported after injury to the abdomen (Gray, 1945), nervous system (Opper and Zimmerman, 1938 ; Globus and Ralston, 1951), and bones (Merendino *et al.*, 1945 ; Wangensteen *et al.*, 1945), as well as after surgical operations (McDonnell and McCloskey, 1953 ; Lane Roberts, 1954), particularly those on the heart (Berkowitz *et al.*, 1957).

In this paper are presented six examples of acute gastric erosions developing after exposure to various forms of stress in previously eupeptic patients, none of whom had been receiving salicylate treatment. All were fatal, five with haemorrhage, and in all cases post-mortem examination seemed satisfactorily to exclude pre-existing peptic ulceration. Four of the cases were encountered within the past year. Our purpose here is to recall attention to the stress ulcer, to the fact that it can cause unheralded and massive gastric haemorrhage, and to suggest that prophylaxis is justified despite the apparent rarity of the condition.

Case Reports

Case 1.—A 78-year-old retired labourer was admitted with a fractured left femoral neck after a drunken fall. This was treated by the insertion of a nail-plate. He developed apparent bronchopneumonia, and then on the eleventh post-operative day he passed a melaena stool. His haemoglobin was 5.6 g. per 100 ml., and he was forthwith given 3 pints (1.7 l.) of packed cells. Three days later he passed another melaena stool, soon after which he became severely shocked ; 4 pints (2.3 l.) of blood was transfused and an emergency laparotomy performed. At operation the gut was found to be full of blood ; the duodenum was opened in preparation for a Polya-type partial gastrectomy, and an acute ulcer was seen on the posterior wall of the first part. After the gastrectomy his pulmonary condition became worse, and he died three weeks later.

At necropsy pulmonary embolism secondary to thrombosis of the femoral veins was found to be the principal cause of death ; there was no sign of peptic ulceration or fibrosis in the residual stomach. Examination of the resected sleeve of stomach revealed about ten shallow ulcers in the pyloric antrum, the largest being 0.5 cm. in diameter. Each was acute and confined to the mucosa ; little cellular infiltration was present and there was no evidence of healing (Special Plate, Fig. 1). The ulcers can thus be regarded as being somewhere between 70 and 100 hours old. There was no sign of long-standing ulceration.

Case 2.—An 80-year-old man, also alcoholic, was admitted after falling downstairs. Although not unconscious, he was disorientated ; neurological examination was negative apart from bilateral extensor plantar responses. There was no radiological evidence of skull fracture. Hypostatic pneumonia developed and he died four days later.

Necropsy showed an old right-sided pontine haemorrhage, and a recent massive left-sided cerebral haemorrhage which had ruptured into the lateral ventricle and subarachnoid space. The stomach contained a small quantity of altered blood, and there was a small acute ulcer situated low on the lesser curvature. No evidence of chronic peptic ulceration could be found. Unfortunately, the ulcer was not examined histologically.

Case 3.—A 54-year-old housewife, the mother of three children, had suffered from intermittent vaginal bleeding for two years before admission to hospital. She had never complained of dyspeptic symptoms. As uterine curettage disclosed a carcinoma of the body of the uterus, a pan-hysterectomy was performed. Post-operatively she required transfusion with 1 pint (0.6 l.) of plasma and whole blood. Four days after operation she vomited about 800 ml. of blood, and gastric aspiration continued to yield blood over the next three days ; during this time the haemoglobin concentration fell from its pre-operative level of 13 g. to less than 7 g. per 100 ml. On the seventh post-operative day she became acutely shocked, with a blood-pressure of 80/40 mm. Hg, and despite rapid transfusion of 2 pints (1.1 l.) of blood she died.

Necropsy revealed pelvic suppuration and generalized peritonitis. The stomach was distended with blood-clot, and there were numerous acute erosions on the mucosa of the anterior wall near the lesser curvature. The largest erosion, which measured 4 cm. in diameter, had extended to the serous coat and was clearly the source of the bleeding. Again there was no sign of chronic peptic ulceration. Microscopy was unsatisfactory because of post-mortem autolysis, but it was possible to recognize an acute erosion of uncertain age with little cellular reaction.

Case 4.—An 82-year-old retired factory worker was brought into hospital after being found unconscious with dried blood about his face. He had Cheyne–Stokes respiration and a blood-pressure of 130/80 mm. Hg. Apart from bilateral extensor plantar responses there were no abnormal neurological findings. He failed to regain consciousness, and died three days after admission.

At necropsy the stomach was full of altered blood, and the mucosa showed several acute erosions, with submucous congestion and haemorrhage. Once again no evidence of previous ulceration could be found. On sectioning the brain the anterior part of the right thalamus was seen to contain a small recent haemorrhage which had ruptured into the ventricular system. An older left-sided pontine haemorrhage was also noted. The ulcer was not examined histologically.

Case 5.—A 65-year-old woman with a carcinoma of the urinary bladder had received radiotherapy, but haematuria continued. This worsened, and on admission her haemoglobin level was 8 g. per 100 ml. After transfusion of 3 pints (1.7 l.) of blood a total cystectomy was performed, with implantation of the ureters into the pelvic colon. On the fifth post-operative day she vomited altered blood and collapsed suddenly with signs of shock. Despite attempts at resuscitation she died a few hours later.

The resected urinary bladder was contracted and contained a sessile neoplasm on the left lateral wall. Histologically, this was a transitional-cell carcinoma which had extended through the muscularis. At necropsy the stomach was dilated by more than 1 litre of altered blood. Six mucosal erosions were present in the antrum, but there was no sign of chronic ulceration. A few small metastases were present in the liver. Histological examination of two of the gastric lesions showed that each was about 0.2 cm. diameter, confined to the mucosa and lamina propria, and sharply demarcated. There was no cellular reaction or evidence of healing, and the lesions were of about 24 hours' duration (Special Plate, Fig. 2).

Case 6.—A 24-year-old woman was five months pregnant when diplopia due to a right sixth-nerve paralysis developed. She had previously been well with no dyspeptic symptoms. Her illness progressed gradually, with the development of paraesthesiae in all limbs and upper motor neurone lesions

involving the legs, then the arms. There was also intellectual impairment. Lumbar puncture revealed a slightly raised cerebrospinal-fluid protein content and a lymphocytic pleocytosis. She was delivered of a healthy child at term, but there was no remission in her disease, which was regarded as a diffuse encephalomyelitis of unknown type. One month later, and four months before her death, she was treated with corticotrophin (A.C.T.H.), 20 units intramuscularly daily for six days. No steroids were given. Three days before death she became anorexic and febrile, vomited partly digested food, but did not complain of abdominal pain. She passed into coma and died, a year after the onset of her illness.

Necropsy revealed a massive perforation of the fundus of the stomach some 15 cm. in diameter. This had ruptured through the left dome of the diaphragm, so that both peritoneal and left pleural cavities contained reddish-brown gastric contents. The remainder of the stomach and the duodenum were healthy, without sign of chronic ulceration. Multiple small foci of demyelinization were scattered throughout the white matter of the brain and spinal cord. Histological examination confirmed the presence of focal demyelination in the cerebrum and spinal cord. There was an early peritonitis and pleurisy. The gastric mucosa was partly autolysed, but the appearances within the wall of the perforated ulcer could be taken as indicating a duration of three to seven days.

Discussion

In the six cases described acute gastric ulceration followed cerebral haemorrhage in two, diffuse encephalomyelitis in one, fracture of a long bone in another, and operation for carcinoma in two cases. Peptic ulcer is a common disease; McDonnell and McCloskey (1953) found ulcers in 3.2% of a series of 243 patients who came to necropsy after general surgical procedures, and Mears (1953) reported a similar incidence in medical cases. Stewart (1923) found active or healed gastric ulcer in 4.7% of a consecutive series of 1,500 necropsies on adults. In our six cases, however, there is nothing to suggest that the ulcers were not new, and necropsy disclosed no evidence of chronic ulceration.

In five of our cases the lesions were multiple, situated in the pyloric antrum near the lesser curvature, superficial, less than 1 cm. in diameter, and showing no sign of an eroded artery. The exception was Case 6 with its 15-cm. perforation involving the body and fundus of the stomach. In the four cases examined microscopically the ulcers showed similar histological features (Special Plate, Figs. 1 and 2). All were sharply demarcated, presenting an area of necrosis with little or no cellular reaction and no evidence of healing; there was little or no fibrin in the ulcer area and none in the near-by vessels. All the ulcers were regarded as acute and between one and seven days old. No histological features are known to us that distinguish the stress ulcer and the acute ulcer of, say, uraemia, or the haemorrhagic erosion of uncertain aetiology. These are quite different from the subacute and chronic peptic ulcers, which are deep and indurated, based on fibrous tissue, and show cellular infiltration, fibrinous exudation, and endarteritis of adjacent vessels.

Acute gastric erosions after injury to the central nervous system were described by Cushing (1932), who thought the diencephalon was the site of importance; but more recently Globus and Ralston (1951) have shown that all parts of the nervous system are equipotential in ulcer production. Indeed, they believe that diffuse cerebral damage is a more potent cause than is a focal lesion. In our cases of this type the cerebral damage was extensive rather than localized, and in those with haemorrhage there was rupture into the ventricular system.

The connexion between fracture of a long bone and gastric ulceration is perhaps more difficult to understand, but Baronofsky and Wangensteen (1945) and Wangensteen *et al.* (1945) have shown that fat embolism and mucosal ischaemia are important factors; they were able to produce such ischaemic areas in the gastric mucosa of experimental animals by the injection of fat particles. In a series of six guinea-pigs and 52 dogs subjected to fractures of long bones, gastro-duodenal ulceration developed in 53% (Merendino *et al.*, 1945). Wangensteen and his co-workers were unable to demonstrate any increase in gastric acidity after fractures either in these animals or in patients. In our patient we noted neither clinical nor post-mortem evidence of fat embolism. Other types of embolism—such as tumour cells or septic material—may have similar effects, and either could have happened in Case 3, where fatal haematemesis followed a panhysterectomy complicated by pelvic sepsis; there was, however, no obvious evidence to suggest this. In reviewing the association between sepsis and peptic ulcers Guthrie (1942) observed that suppurative meningitis in children was particularly liable to give rise to such ulcers.

Apart from vascular obstruction by embolism, ischaemia of the gastric mucosa can be produced by prolonged hypotension, passive venous congestion, or a combination of both. This might explain the high incidence of acute gastro-duodenal ulceration following cardiac surgery noted by Berkowitz (1957), who found such ulceration in 15% of necropsies on patients dying after heart operations.

The occurrence of gastric erosions after such diverse forms of stress recalls the association between peptic ulceration and adrenocortical hormones suggested by Selye in 1936, and to-day the development or exacerbation of ulcers during steroid therapy is well recognized. Although there is disagreement among experimental workers whether or not corticotrophin and steroids produce increased gastric acidity (Gray *et al.*, 1951; Moore, 1953; Shay, 1954; Hirschowitz *et al.*, 1955; Drye and Schoen, 1958; Zawoiski *et al.*, 1958), there can be little doubt that a more than casual relationship exists between adrenocortical activity and the production of ulcers in the upper alimentary tract, though the precise mechanism remains unexplained. Certainly the results of experimental work and observations in patients similar to those described in this paper do point to a connexion between the neuro-endocrine system of the body and the secretory activity of the stomach.

Recently Drye and Schoen (1958) in their studies on cortisone and gastric secretion pointed out that, though there is an increased gastric secretion of hydrochloric acid and pepsin after trauma, it is not accompanied by increased blood levels of adrenocortical hormones. On the basis of these observations they conclude that the action of cortisone in "cortisone ulcers" is one of depression of normal healing of the tiny erosions to which all people are subject, rather than of increased production of hydrochloric acid. They suggest that the victims of stress are usually unable to buffer their gastric acid by food or drink, and that this relative increase in acidity may contribute to the formation of ulcers. It would, therefore, seem a wise precaution to administer antacid therapy in cases of the type

described, and fully as justified as in those patients with known hyperacidity who run the risk of post-operative erosion of the oesophagus (Lodge, 1955).

Summary

The occurrence of acute peptic ulceration in six previously eupeptic patients is described. The gastric lesion followed cerebral haemorrhage in two cases, diffuse encephalomyelitis in one, fractured neck of femur in one, and operation for carcinoma in two others. Post-mortem examination showed no evidence of previous ulceration, and the acute erosions have therefore been accepted as examples of the so-called stress ulcer. Though there is ample evidence to connect the neuro-endocrine system of the body with the development of stress ulcer, the exact mode of production is unknown. It is suggested that antacid therapy merits consideration in cases where trauma, operation, or cerebral lesions may initiate this dangerous sequence.

We are grateful to Professor D. M. Douglas and Professor A. C. Lendrum for helpful advice and criticism; to Dr. G. D. Malcolm for permission to publish Case 6; to Dr. J. A. Kirkland and Dr. R. S. Davidson for necropsy reports; and to Mr. J. W. Corkhill for the illustrations.

REFERENCES

Baronofsky, I., and Wangensteen, O. H. (1945). *Bull. Amer. Coll. Surg.*, **30**, 59.
Berkowitz, D. Cited by Berkowitz *et al.* (1957).
—— Wagner, B. M., and Uricchio, J. F. (1957). *Ann. intern. Med.*, **46**, 1015.
Curling, T. B. (1842). *Med.-chir. Trans.*, **25**, 260.
Cushing, H. (1932). *Surg. Gynec. Obstet.*, **55**, 1.
Drye, J. C., and Schoen, A. M. (1958). *Ann. Surg.*, **147**, 738.
Globus, J. H., and Ralston, B. L. (1951). *J. Mt Sinai Hosp.*, **17**, 817.
Gray, I. (1945). *N.Y. St. J. Med.*, **45**, 887.
Gray, S. J., Benson, J. A., Reifenstein, R. W., and Spiro, H. M. (1951). *J. Amer. med. Ass.*, **147**, 1529.
Guthrie, K. J. (1942). *Arch. Dis. Childh.*, **17**, 82.
Hirschowitz, B. I., Streeten, D. H. P., Pollard, H. M., and Boldt, H. A. (1955). *J. Amer. med. Ass.*, **158**, 27.
Lodge, K. V. (1955). *J. Path. Bact.*, **69**, 17.
McDonnell, W. V., and McCloskey, J. F. (1953). *Ann. Surg.*, **137**, 67.
Mears, F. B. (1953). *Surgery*, **34**, 640.
Merendino, J. A., Litow, S. S., Armstrong, W. D., and Wangensteen, O. H. (1945). *Bull. Amer. Coll. Surg.*, **30**, 58.
Moore, F. D. (1953). *Ann. Surg.*, **137**, 289, 315.
Opper, L., and Zimmerman, H. M. (1938). *Yale J. Biol. Med.*, **11**, 49.
Roberts, P. A. Lane (1954). *Brit. med. J.*, **1**, 1295.
Selye, H. (1936). *Nature (Lond.)*, **138**, 32.
Shay, H. (1954). Cited in *Gastroenterology*, **26**, 316.
Stewart, M. J. (1923). *Brit. med. J.*, **2**, 1021.
Wangensteen, O. H., Merendino, J. A., and Litow, S. S. (1945). *Bull. Amer. Coll. Surg.*, **30**, 58.
Zawoiski, E. J., Braunschweig, L. W., and Beyer, K. H. (1958). *J. Pharmacol. exp. Ther.*, **122**, 512.

The Minister of Health and the Minister of Agriculture, Fisheries and Food have issued jointly two codes of practice on the hygienic handling of meat in the retail trade and in course of transport. The codes, which have no statutory force, have two broad aims: the meat should be handled and transported under the best possible conditions, and those handling it should never through familiarity treat it with less care than they would expect to have been given to meat which they eat themselves. In addition to re-emphasizing the obvious requirements of hygiene, the codes give much common-sense advice about the construction of premises and their working. If all the recommendations are followed at least two familiar, even traditional, features of butchers' shops will disappear: dogs and sawdust. (No. 1, *Hygiene in the Retail Meat Trade*; No. 2, *The Hygienic Transport and Handling of Meat.* H.M.S.O., price 9d. each.)

HOME ON THE SECOND DAY: THE BRADFORD EXPERIMENT

THE COMBINED MATERNITY SCHEME*

BY

G. W. THEOBALD, M.D., F.R.C.S.Ed., F.R.C.O.G.

St. Luke's Maternity Hospital, Bradford

The term "experiment" refers to the allocation of obstetric beds and not to any procedures carried out on patients. St. Luke's Maternity Hospital had 66 lying-in and 25 antenatal beds with which to serve a city of 300,000 and to provide specialized hospital care for double that population. The average number of confinements in hospital is approximately 2,800 per annum. From 1947 to 1951 inclusive there were 71 cases of eclampsia and a large number of cases of pre-eclampsia in the hospital, and it was realized that the antenatal care would have to be improved.

In 1951 a pilot scheme was started at which most booked hypertensive patients were seen weekly from the 24th week of pregnancy until delivery. This proved so convincingly successful that towards the end of 1954 the hospital staff decided that all primigravidae, and those multigravidae who had shown any abnormality in previous pregnancies, and in particular either hypertension (H) or hypertension associated with proteinuria (HP), should be given such antenatal care. The faith and co-operation of Sister D. M. Holden made a start possible.

The underlying philosophy of this step was that whereas it is impossible to affect the number of patients with H (two readings of 140/90 mm. Hg or above before the onset of labour), it is possible to delay its onset, to lessen its severity, and to prevent it developing into HP or HP+. The most important time to detect these changes and to prevent them from becoming irreversible is between the 24th and the 34th week of pregnancy, for after that period adverse changes are less likely to occur, and, in any case, the infant will be viable. The means at our disposal to achieve the above ends are (1) to control weight-gain; (2) to detect early evidence of the onset of H, HP, and HP+; and (3) to encourage mothers with twin pregnancies to enter the antenatal ward for prolonged rest, to detect and treat the anaemias of pregnancy (physiological anaemia is not recognized), and to offer as much rest as possible for pregnant women with heart lesions. The logical developments in this trend of antenatal care would be to offer advice to potential mothers before they became pregnant and to establish the fact that antenatal rest is far more important than postnatal rest.

The indications laid down for immediate admission to the antenatal ward were: (*a*) blood-pressure of 140/90 mm. Hg, or a sudden rise in blood-pressure—for example, from 110/70 to 135/85 mm. Hg in one week; (*b*) proteinuria; (*c*) bleeding per vaginam; (*d*) the sudden onset of oedema either up to the knees

*Those mainly concerned with starting the above scheme.—*Local Health Authority:* Dr. J. Douglas (medical officer of health), Dr. W. Edgar (deputy medical officer of health), Dr. K. Horne (senior medical officer for maternity and child welfare), Dr. M. U. Rhodes (assistant medical officer for maternity and child welfare). *Hospital staff:* Mr. G. W. Theobald, Mr. G. A. Craig, Mr. A. C. Muir, Miss J. M. B. Muirhead (senior registrar), Dr. M. W. Arthurton (paediatrician). *General Practitioners:* Dr. R. H. Sunderland (chairman, obstetric committee), Dr. J. E. Allan, Dr. H. R. Sparrow, Dr. J. Wright.

B. MALAMOS *ET AL.*: LYMPHADENOGRAPHY IN HAEMATOLOGY

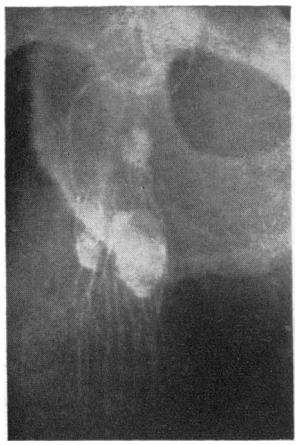

FIG. 1. — Normal inguinal glands.

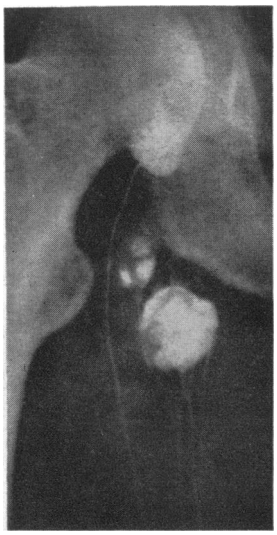

FIG. 2.—Inguinal glands in chronic lymphocytic leukaemia.

FIG. 3.—Inguinal glands in chronic myeloid leukaemia.

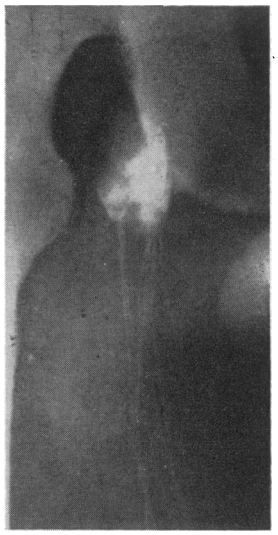

FIG. 4.—Inguinal glands in acute leukaemia.

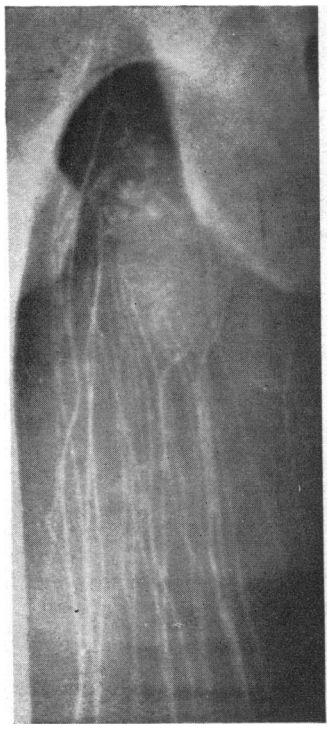

FIG. 5.—Inguinal glands in lymphosarcomatosis.

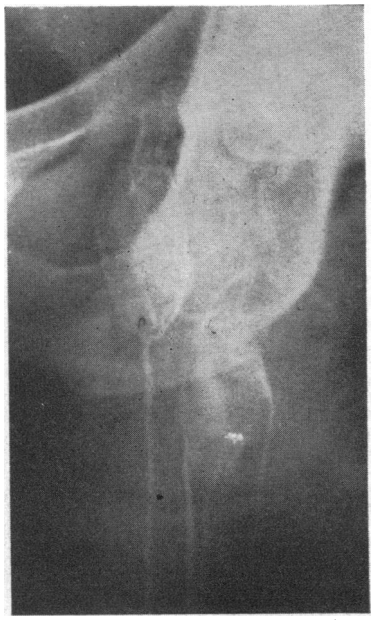

FIG. 6.—Inguinal glands in lymphogranuloma (Hodgkin's disease).

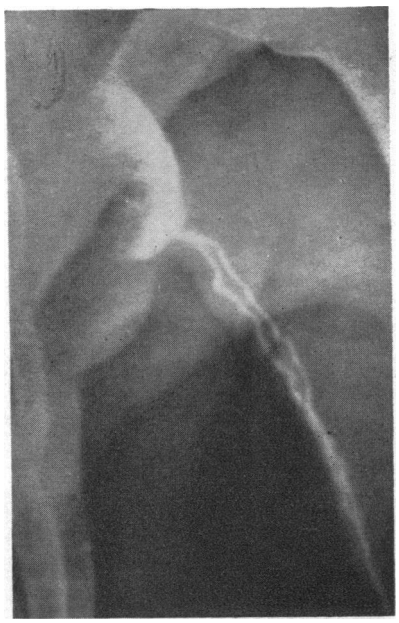

FIG. 7.—Axillary glands in lymphogranuloma (Hodgkin's disease).

I. M. BRECKENRIDGE *ET AL.*: STRESS ULCERS IN STOMACH

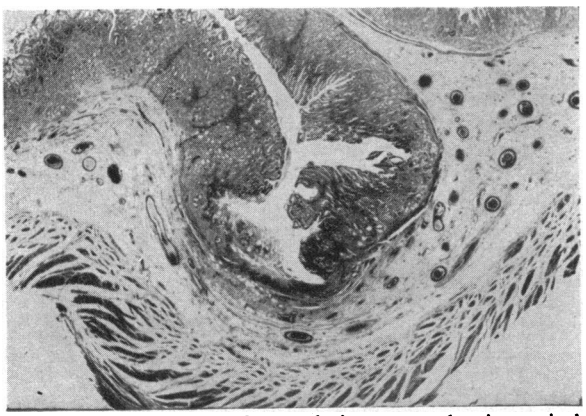

FIG. 1.—Case 1. Section from pyloric antrum, showing typical acute ulcer confined to mucosa. (H. and E. ×7.5.)

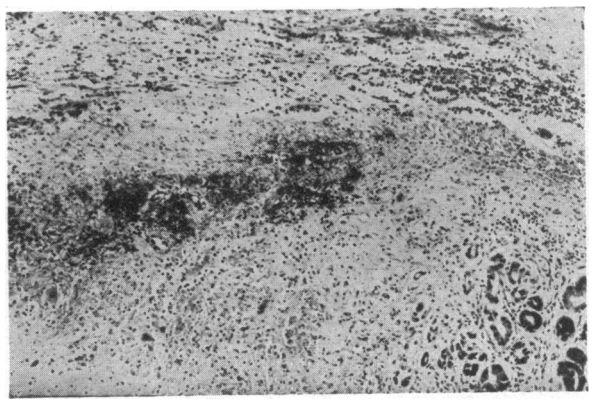

FIG. 2.—Case 5. Edge of acute ulcer in pyloric antrum, showing recent necrosis and almost complete absence of cellular infiltration. (H. and E. ×60.)