INFARCTION OF THE COLON

By C. I. COOLING, F.R.C.S.

and R. H. B. PROTHEROE, M.D.

Westminster Hospital Teaching Group, London, S.W.1

Introduction

Vascular lesions of the lower gastro-intestinal tract have recently been receiving some attention, both as a source of unexplained bleeding, and also in relation to fulminating ulcerative colitis, periarteritis nodosa and lupus erythematosus. Massive infarction of the colon is, however, rare and carries a high mortality. Dzialoswinski (1925) reported what he believed to be the first case of recovery from resection of the entire gangrenous transverse colon. A case of infarction of the transverse colon due to occlusion of the middle colic arteries is described, which was successfully treated surgically. The changes in the mucous membrane will be discussed in relation to ulcerative colitis and periarteritis nodosa and systemic lupus erythematosus (S.L.E.).

Case Report

Mrs. M. F., aged 69 years, was admitted to the Gordon Hospital on May 13, 1956, complaining of sudden onset of abdominal pain at 8.30 a.m. The pain was generalized and continuous. She had vomited on four occasions; the bowels had acted three times, the stools being loose and containing blood. Normally the bowels acted once daily apart from recent constipation. Four days previously she had been discharged from another hospital where treatment for bronchitis had been given.

On examination the temperature was 99.6° F., the pulse rate 120 per minute and respiration rate normal. The patient was in obvious distress, the tongue coated, and coarse rales were present in all lung areas. The heart was within normal limits but the blood pressure was 170/90 mm. Hg.

Examination of the abdomen revealed generalized tenderness and guarding with very infrequent bowel sounds. Rectal examination confirmed the presence of bright red blood, but the rectal mucosa appeared normal. The diagnosis was considered to be mesenteric thrombosis, or possibly an intussusception.

Laparotomy was performed under spinal and

general anaesthesia 12 hours after the onset of symptoms. The wall of the transverse colon was thickened and dark red in colour and its mesentery was congested and oedematous. Resection of the affected bowel was performed, continuity restored and a portion of caecum exteriorized in case of need.

Progress. Recovery from the operation was satisfactory, but the exteriorized caecum was opened on the fourth day due to abdominal distension and failure of the bowel to evacuate. The caecostomy acted freely and normal bowel actions commenced on the eleventh post-operative day. On the sixteenth day evidence of deep vein thrombosis appeared in the left leg and a course of anticoagulants was commenced using heparin in the first instance followed by Dindevan. By the eighteenth day the prothrombin time had risen alarmingly to 80 seconds, the normal value being 14 seconds. Further treatment was stopped but on the twentieth day she collapsed, became very shocked and complained of abdominal pain. Examination revealed a mass 6 inches in diameter deep to the wound. This was explored under local anaesthesia and large blood clots evacuated and the cavity drained.

Further progress was satisfactory and the caecostomy was formally closed. The patient is now in robust health.

The specimen consisted of 33 cm. of transverse colon, 4 cm. in diameter. There was intense mucosal congestion of the specimen over almost its entire length and also linear ulceration, the ulcers being parallel to the taenia coli (see Fig. 1). The peritoneal coat was also congested and no obvious thrombosed vessels could be seen. There was no dilatation of the colon. Microscopy showed numerous thrombosed arterioles in the submucosa of the colon with haemorrhagic infarction of the mucous membrane (see Fig. 2). There was loss of the normal architecture with intense haemorrhage into the lamina propria and necrosis of the cells of the crypts of Lieberkühn (see Fig. 2), together with linea frank ulcers lined by fibrin

FIG. 1.—Resected transverse colon showing throughout almost its length mucosal congestion and linear ulceration due to infarction of its wall.

FIG. 2.—Numerous thrombosed arterioles in the submucosa with infarction of the mucous membrane and necrosis of the cells of the crypts of Lieberkühn. Haematoxylin and eosin $\times 80$.

and an acute inflammatory exudate. The submucosa was thickened due to vascular congestion and also extravasation of blood into the tissues. The muscle coats were intact except for areas of vascular congestion and infarction due to scattered thrombosis of arterioles. The peritoneal coat was thickened and congested.

Discussion

Occlusion of the mesenteric vessels is not rare. The condition may occur at any age, but the ages of the majority are in the third to seventh decades. Cases in childhood are usually associated with intra-abdominal infection. The male sex predominates in the ratio 3 : 2. Trotter (1913) found in a series of 360 cases that 41 per cent. of cases of intestinal infarction were due to venous occlusion, 53 per cent. to arterial occlusions and 6 per cent. to simultaneous occlusions of both vessels. The vessels most commonly affected are branches of the superior mesenteric vessel supplying the small intestine. It is rare for the colon to be involved and the commonest site is the ascending colon which is involved twice as frequently as the transverse colon and this twice as frequently as the descending and sigmoid colon. The recto-sigmoid junction has been thought to have an inadequate collateral circulation (Sudeck, 1907). However, McGowan (1955) considers that intramural anastomotic channels are the means whereby the collateral circulation is maintained in this area following ligation or obstruction of the inferior mesenteric artery below its last sigmoid branch. It is of interest that although this portion of the large intestine has been thought to have the weakest collateral circulation, that infarction is least common in the distal colon (Thomson, 1948).

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FIG. 3.—Total colectomy specimen of fulminating ulcerative colitis with dilatation of the ascending colon and hepatic flexure.

The effects of mesenteric vascular occlusion depend on its site and extent. Trotter (1913) records a case of complete occlusion by an aneurysm of the superior mesenteric vessels, yet the bowel remained healthy as a sufficient collateral circulation had time to develop. Should the occlusion be sudden the result is infarction of a portion of the bowel since the superior mesenteric vessel is functionally an end artery under such conditions. Arterial occlusion may be due to an embolus from the heart or athero-sclerosis or even an aneurysm of the mesenteric vessels. In the case under discussion there was no clinical evidence of a cardiac lesion and the most likely cause was thought to be thrombosis of the middle colic artery due to athero-sclerosis with subsequent peripheral spread to involve the intramural arterioles of the colon. Venous occlusion may be a primary thrombosis from no apparent cause, or may be secondary to intra-abdominal sepsis such as a gangrenous appendicitis, or portal venous thrombosis and cirrhosis of the liver, or malignant infiltration of the mesenteric veins.

The prognosis in mesenteric infarction is poor.

In the series of 60 cases at the Mayo Clinic reviewed by Whittaker and Pemberton (1938) the mortality was 95 per cent. and of those treated surgically it was 84.2 per cent. Gordin and Laurent (1956) reviewed 47 cases, of which only three left hospital alive. This may be due to the fatal extent of intestinal damage, poor health from the causative disease in the heart, intra-abdominal sepsis, malignancy or spread of the thrombosis following treatment. Smith (1951) considered infarction of the large intestine to be particularly lethal. However, some cases probably recover without surgical treatment and remain undiagnosed. The introduction of anticoagulants held great promise and if the damage to the bowel is extensive, may offer the only hope. Its use after resections theoretically prevents further thrombosis and has been recommended by Murray (1939). Laufman (1949), in experimental work in animals, was unable to show any difference in the results after resection whether anticoagulants were used or not.

Recently a most interesting case was described by Lister and Jungmann (1956) in which infarction

of the transverse colon and splenic flexure occurred due to mesenteric thrombosis. Resection was not performed and barium enema studies revealed pictures analogous to those seen in chronic ulcerative colitis. Ultimately a faecal fistula developed and the infarcted bowel sloughed through the fistula.

Mucosal Infarction

Vascular lesions have been suggested as a cause of mucosal damage in ulcerative colitis by a number of authors (Proc. Int. Congress of Gastroenterology, 1956). It is of interest, therefore, to compare the changes due to colonic infarction with those of fulminating ulcerative colitis.

The macroscopic appearances of the mucous membrane in the two conditions are very similar, as mucosal ulceration and congestion are a feature of the two diseases. Also in ulcerative colitis the ulceration is frequently linear and related to the taenia coli (Lium, 1939) (see Fig. 3). However, in fulminating ulcerative colitis whilst the history may be short, two to three months on occasions, it is never as short as that in mesenteric infarction. Frequently there is an antecedent history of mild symptoms (Lumb, Protheroe and Ramsay, 1955) with evidence of recent mucosal spread to involve the majority of the colon. Also dilatation of the colon due to muscle damage is a common finding (see Fig. 4). This was not found in the case of infarction described by Lister and Jungmann (1956) or in the present case.

Vascular lesions of the intramural vessels have been suggested as the cause of the mucosal damage in ulcerative colitis. Gallart Mones (1954 and 1956) believes that submucosal thrombosis occurs with subsequent infarction and miliary abscess formation. Warren and Sommers (1949) felt that the changes in 19 of 180 specimens resulted from mucosal degeneration following an inadequate blood supply caused by necrosis and thrombosis of blood vessels in the submucosa and mesentery. Similar findings in a smaller series were reported by Ihre (1956).

Vascular lesions of the colon are found in periarteritis nodosa. Gastro-intestinal symptoms and lesions are found in 62 per cent. of cases (Nizum and Nizum, 1954), but they are usually confined to the upper gastro-intestinal tract. However, the mesenteric arteries are involved in 25 per cent. of cases (Diaz Rivera and Miller, 1946), but thrombosis of the principal branches of the mesenteric arteries is rare (Felsen, 1941). It is usually the intramural branches which are involved and arborization is sufficient to prevent massive infarction.

The lesions in the colon, however, are usually

FIG. 4.—Vascular congestion of the ulcerated mucous membrane and destruction of muscle coats in fulminating ulcerative colitis. Haematoxylin and eosin $\times 96$.

overshadowed by others in more important organs. Lawrie (1955) described two cases with widespread small ulcers in the colon the result of small submucosal infarcts, and in one of the seven cases reported by Diaz Rivera and Miller (1946) there was widespread involvement of the colon with small ulcers separated by intact mucosa. According to Felsen (1941) the sigmoidoscopic appearances of periarteritis nodosa are very characteristic, and different from ulcerative colitis. Indeed, he considered that periarteritis nodosa could be diagnosed by sigmoidoscopic examination as horizontal linear dark red streaks in parallel lines can be seen beneath the intact mucosa of the rectum.

Interest has recently been revived in the gastro-intestinal manifestations of systemic lupus erythematosus (S.L.E.). Harvey *et al.* (1954) reviewed 138 patients with S.L.E. and found that 14 per cent. complained of nausea, 11 per cent. of vomiting, 8 per cent. of diarrhoea, 5 per cent. of gastro-intestinal haemorrhage, 10 per cent. of abdominal pain and 6 per cent. of dysphagia. They reported

FIG. 5.—Thrombosed submucosal arteriole in fulminating ulcerative colitis. Note absence of infarction. Haematoxylin and eosin $\times 30$.

involvement of the large bowel in five patients with S.L.E.; in four of whom there was an arteritis, with ulceration of the mucosa. They did not report whether the findings were similar to those seen in ulcerative colitis.

Brown *et al.* (1956b) reviewed the gastrointestinal manifestations in 87 patients having S.L.E. Seven had severe gastro-intestinal symptoms which constituted major problems in diagnosis and treatment. Two patients had S.L.E. and ulcerative colitis. One patient (Brown *et al.*, 1956a) had a long history of colitis and the entire colon was involved with superimposed rheumatoid arthritis and cardiac involvement. The second patient had atypical ulcerative colitis with hepatitis and lupus erythematosus. This association is uncommon and only three cases, including a case seen by Boone and McKee (1955) have been reported. The two conditions have much in common. The systemic complications of ulcerative colitis (arthritis, erythema nodosum, iritis, pyoderma gangrenosum, stomatitis, etc.) suggest that it might be a collagen disease similar to S.L.E. Some authors (Levine *et al.*, 1951, and Jacobson and Kirsner, 1956) have shown that there is a deficiency of 'ground glass substance' of the basement membrane of the mucosal cells in chronic ulcerative colitis. However, this has not been confirmed in the uninvolved mucous membrane (Lumb and Protheroe, 1957). The L.E. test will clearly be of use in differentiating the two conditions provided it is remembered that the L.E. test is not entirely specific for S.L.E. (Holman, 1951).

One of the authors has recently had the opportunity of examining 152 surgical specimens of ulcerative colitis (Lumb and Protheroe, 1958). In the fulminating cases of the disease, vascular

dilatation and congestion and haemorrhage into the inflamed tissues is a marked feature leading to intense mucosal reddening, and isolated thrombosed or thickened arterioles are seen due, we think, to spread of the inflammation to involve the walls of blood vessels (see Fig. 5). No case of colonic infarction or sloughing was seen, due probably to the abundant anastomoses and overlap between the small arterioles supplying the wall of the colon. Further study is needed to determine whether the earliest changes in this disease occur in the capillaries of the lamina propria of the mucous membrane, as suggested by Busson, Delarue and le Quintrec (1954), or in the basement membrane (Jacobson and Kirsner, 1956), or in the lining epithelium (Lumb and Protheroe, 1957). In the meantime it seems best to separate ulcerative colitis from the group of so-called collagen diseases.

Summary

A case of massive infarction of the transverse colon due to thrombosis of the middle colic artery is described.

The case was successfully treated surgically.

The aetiology of massive colonic infarction is discussed.

Colonic infarction is discussed in relation to periarteritis nodosa, systemic lupus erythematosus and ulcerative colitis. Notwithstanding the frequency of thrombosis of submucosal vessels in these conditions, massive infarction is rare presumably due to abundant intramural anastomoses.

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BIBLIOGRAPHY

- BOONE, J., and MCKEE, J. A. (1955), 'Hospital for Sick Children, Toronto, Ontario, Canada.' Unpublished communication.
 BROWN, C. H., HASERICK, J. R., and SHIREY, E. K. (1956a), *Cleveland Clin. Quart.*, **23**, 43.
 BROWN, C. H., SHIREY, E. K., and HASERICK, J. R. (1956b), *Gastroenterology*, **31**, 649.
 BUSSON, A., DELARUE, J., and LE QUINTREC, Y. (1954), *Arch. Mal. Appar. dig.*, **43**, 1154.
 BUSSON, A., and DELARUE, J. (1956), 'Proc. Int. Cong. Gastroenterology,' London, June 1956. *Gastroenterologia*, **86**, 656.
 DIAZ-RIVERA, R. S., and MILLER, A. J. (1946), *Ann. intern. Med.*, **24**, 420.
 DZIALOSWYNSKI, H. (1925), *Zbl. Chir.*, **52**, 2120.
 FELSEN, J. (1941), *Ann. intern. Med.*, **15**, 251.
 GALLART MONÉS, F. (1954), *Minerva chir. (Torino)*, **9**, 477.
 GALLART MONÉS, F. (1956), 'Proc. Int. Cong. Gastroenterology,' London, June 1956. *Gastroenterologia*, **86**, 632.
 GORDIN, R., and LAURENT, L. E. (1956), *Acta med. scand.*, **154**, 267.
 HARVEY, A. M., SHULMAN, L. E., TUMULTY, P. A., CONLEY, C. L., and SCHOENRICH, E. H. (1954), *Medicine*, **33**, 291.
 HOLMAN, S. (1951), *J. clin. Path.*, **4**, 290.
 IHRE, B. J. E. (1956), 'Proc. Int. Cong. Gastroenterology,' London, June 1956. *Gastroenterologia*, **86**, 666.

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Bibliography continued from preceding page—C. I. Cooling, F.R.C.S., and R. H. B. Protheroe, M.D.

- JACOBSON, M. A., and KIRSNER, J. B. (1956), *Gastroenterology*, **30**, 279.
 LAUFMANN, H. (1942), *Surg. Gynec. Obstet.*, **74**, 479.
 LAWRIE, T. D. (1955), *Glasg. med. J.*, **36**, 220.
 LEVINE, M. D., KIRSNER, J. B., and KLOTZ, A. P. (1951), *Science*, **114**, 552.
 LISTER, E. F., and JUNGSMANN, H. (1956), *Brit. J. Radiol.*, **29**, 341.
 LIUM, R. (1939), *Arch. intern. Med.*, **63**, 210.
 LUMB, G. D., PROTHEROE, R. H. B., and RAMSAY, G. S. (1955), *Brit. J. Surg.*, **43**, 182.
 LUMB, G. D., and PROTHEROE, R. H. B. (1958), *Gastroenterology*, in press.
 LUMB, G. D., and PROTHEROE, R. H. B. (1957), *Gastroenterology*, **33**, 457.

- McGOWAN, J. R. (1955), *Arch. Surg. (Chicago)*, **71**, 531.
 MURRAY, G. D. W. (1939-40), *Brit. J. Surg.*, **27**, 567.
 NUZUM, J. W. (Jnr.), and NUZUM, J. W. (Snr.) (1954), *Arch. intern. Med.*, **84**, 942.
 SMITH, R. (1951), *Postgrad. med. J.*, **27**, 502.
 SUDECK, P. (1907), *Munch. med. Wschr.*, **54**, 1314.
 THOMSON, F. B. (1949), *Canad. med. Ass. J.*, **58**, 183.
 TROTTER, L. B. C. (1913), 'Embolism and Thrombosis of the Mesenteric Vessels,' Cambridge University Press.
 WARREN, S., and SOMMERS, S. C. (1949), *Amer. J. Path.*, **25**, 657.
 WHITTAKER, L. D., and PEMBERTON, J. J. (1938), *J. Amer. med. Ass.*, **111**, 21.