PATTERNS OF INTESTINAL ISCHAEMIA

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by

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I. INTRODUCTION

OF THE VARIOUS compartments of the circulation which supply organs essential to life, and which regulate themselves to the extent that flow through them is independent of central arterial pressure, the mesenteric circulation has received the least attention from surgeons and physiologists. The behaviour of the cerebral, coronary and renal circulations, if not understood, has at least been extensively studied and considered as a surgically accessible problem. The intestinal circulation receives a bigger share of the cardiac output than any of these, and although the intestine is not an essential organ in the immediate and dramatic sense of the myocardium, occlusion of its main artery leads to death more certainly, and often more quickly, than does occlusion of a main coronary vessel.

This unique importance of the superior mesenteric artery (S.M.A.) is difficult to explain, and our ideas of the working of the mesenteric circulation are primitive and inaccurate, because its behaviour varies so much with species that little can be learned from the experimental animal. Certain facts, however, are known.

1. The pressure at the origin of the S.M.A. is virtually identical to that within the aorta. If the pressure at this point falls to 25 per cent of the normal level, infarction of the entire small bowel results (Welch, 1920). The pressure in the portal vein is about one-tenth of that in the S.M.A. so that the resistance of the splanchnic vascular bed must be considerable (Texter, 1963).

2. Although flow through it remains constant within a broad range of inflow pressure (Johnson, 1960), the mesenteric circulation appears to be devoid of baroceptors which can influence arterial pressure elsewhere in the body (Boyer and Scher, 1960).

3. The volume of the splanchnic bed is difficult to measure and varies with circumstances, but massive pooling of blood in the portal system, which occurs in some species as a stress response, has never been shown to take place in man (Moore, 1957).

4. The intestinal vessels, like those of the skin, are extremely sensitive to the effects of catecholamines. Small amounts of adrenaline or noradrenaline will induce profound vasoconstriction throughout the entire system.

5. The intestine differs from every other organ in the body in that it is, in the normal state, populated by bacteria, of which the most important are the bacillus coli, various types of clostridia and, nowadays, with increasing frequency, the staphylococcus. We are accustomed to viewing these micro-organisms as harmless symbiotes, and indeed, during health, they probably are. But the last two produce exotoxins, and the first, the coliform bacillus, when its body disintegrates, liberates an endotoxin which is so powerfully vasoactive that it has been incriminated by some as the deciding factor in human shock (Fine *et al.*, 1959).

Anatomy of the intestinal circulation

The S.M.A., which supplies the whole of the small intestine apart from the first part of the duodenum and also the near half of the colon, arises from the front of the aorta about one centimetre below the coeliac axis. At its origin this artery is on an average 1.25 cm. in diameter, and at its termination it is still 8 mm. broad. As the S.M.A. passes downwards, it describes a curve, and from the left, convex, side of this curve 12 to 15 intestinal arteries arise to supply the small intestine. These vessels communicate with each other in a series of arcades, whose pattern becomes progressively more complicated as the terminal ileum is reached. From the arcades a number of short vasa recta run to the bowel and penetrate alternate aspects of its circumference to enter a subserosal network of vessels; from this network small arteries pass through the submucosa into the tips of the villi. Arterio-venous shunts exist at all levels of the human intestine, although they appear to be more common in the stomach and the colon than in the small bowel, and they occur in the mucosal layer, so that when they are open the submucosal circulation is by-passed (Boulter and Parks, 1960).

From the right side of the S.M.A. spring the three main vessels to the colon, the middle, right, and ileo-colic arteries, and this last anastomoses with the ending of its parent trunk. Just above the middle colic arises the inferior pancreato-duodenal branch, which is a small vessel but an important one, because it represents the only collateral blood supply to the small intestine from above. The lower route of anastomotic supply occurs at the point where the left branch of the middle colic artery connects with the marginal artery of the colon, but functionally the S.M.A. is the end-artery to the entire splanchnic bed.

The venous drainage of the intestine follows roughly the same course, the veins draining into the superior mesenteric vein which lies just to the right of the artery. However, as is well known from the study of patients with portal hypertension, collateral routes of venous drainage are prolific, and the portal and systemic circulations connect at several constant positions.

Two features of this familiar anatomy are important in the present study: in the first place the origin of the S.M.A. is variable—in 1 per cent of cases it arises from a common coeliaco-mesenteric trunk, and it may even arise from the hepatic artery. Secondly, the part of the bowel most distant from the origin of its blood supply, both embryologically and in the adult, is the ileocaecal region, so that in occlusive disease of the S.M.A. it is here that the damage is greatest.

Our estimation of the importance of the mesenteric vasculature in man depends on the study of its misbehaviour.

Certain patterns of events seem to recur fairly frequently in clinical work, and it is four of these patterns of intestinal ischaemia that I wish to describe to-day. First, I will discuss what happens when the whole bowel is acutely deprived of its blood supply by an embolus, a thrombosis or an experimentally applied ligature. Secondly, I shall be concerned with the effects of occlusion of the smaller peripheral vessels to a loop of intestine, and, thirdly, with chronic stenosis of the visceral arteries. Lastly, I shall speculate on the syndrome of " intestinal failure " and on the role of the intestinal circulation in shock.

II. ACUTE OCCLUSION OF THE SUPERIOR MESENTERIC ARTERY

In 1952, when I was Mr. Eric Crook's house surgeon at Putney Hospital, I admitted a woman of 67 as an emergency with a 16-hour history of abdominal pain. She had been under treatment for hypertensive left ventricular failure for three years. The onset of this pain had been sudden and agonizing under the right costal margin and around the umbilicus. She felt nauseated. On arrival in hospital she was in great distress, pale and dyspnoeic. She was fibrillating at 140–150 and the blood pressure was 190/110. There was obvious left ventricular enlargement and the jugular venous pressure was raised. The abdomen was distended, silent and exquisitely tender above the right inguinal ligament. There were no other signs of note and a straight X-ray was normal. Mesenteric embolus was diagnosed and laparotomy performed immediately by Mr. A. G. Parks. At operation, the whole of the ileum was congested and distended. Three feet of bowel which were clearly gangrenous were resected. During the next 24 hours she received intravenous saline and blood, and her pulse rate was controlled with digoxin. However, on the second post-operative day she began to vomit dark blood and died two days later. At post-mortem, the whole bowel, from the second part of the duodenum to the hepatic flexure, showed mucosal necrosis, but the outer layers were intact. There was an organized thrombus in the left atrium and a large embolus at the origin of the S.M.A. Microscopy of the bowel confirmed necrosis of the mucosa and in some places the submucosa and showed empty arteries and thrombosed veins.

Now, that is a perfectly typical case of mesenteric embolism and you may wonder why I chose to describe it. I did so for two reasons. Firstly, it was the first such case that I ever saw and was the beginning of my interest in the subject; secondly, there are two features which later experience has shown to be important. Although this patient's small intestine had been completely deprived of blood for three days, it was not necrotic except perhaps for the terminal ileum which had been resected. Necrosis had only spread as far as the mucosa at the time of death, and *the arteries of the specimen were empty and the veins were thrombosed.*

Acute occlusion of the S.M.A. is not an uncommon lesion; for instance, it accounts for two out of every thousand general surgical admissions to United States hospitals (Laufman and Scheinberg, 1942; Carter, 1952). The mortality is still tremendous, being in the neighbourhood of 90 per cent from all reported series (Bowen and Felger, 1942; de Muth *et al.*, 1959; Marrash *et al.*, 1962; Jackson, 1963). Earlier information suggested that embolism was commoner than thrombosis as a cause of bowel infarction (Cokkinis, 1926), but the opposite is now the case, perhaps due to the decline in rheumatic heart disease and the increase of atherosclerosis in our population. As in the brain or in the leg it is the *large* vessels which are involved, whether by emboli or atheroma; diseases of the smaller vessels, with the exception of polyarteritis nodosa, rarely affect the mesenteric system.

A typical case of mesenteric embolus presents as a fulminating abdominal catastrophe with severe pain, vomiting, fever, a distended silent abdomen and the passage of dark blood *per rectum*, though it is important to realize that many patients run a more chronic course (Mavor, 1963). Obvious associated cardio-vascular disease makes the diagnosis easier, but is not always present, and unless a high index of suspicion is kept it may only become apparent at laparotomy that the surgeon is faced with a patient who is insufficiently prepared to undergo correct operative treatment of this difficult lesion. Laboratory and X-ray tests have proved surprisingly unhelpful (Morris *et al.*, 1962). A straight film of the abdomen in the early stages is almost always normal; later dilated loops of oedematous bowel and gas bubbles in the portal vein may be seen (Stewart, 1963). No specific biochemical pointer has been found. The serum electrolytes simply reflect the degree of intestinal obstruction, and of the various enzymes that have been estimated only the lactic dehydrogenase shows a consistent rise. Leucocytosis, however, is almost invariable very early in the course of the illness, so that a patient with severe abdominal pain and few physical signs who is found to have 20,000 or more white cells in the peripheral blood must be considered to have a mesenteric infarction until this has been excluded.

Treatment has been exceedingly disappointing. Conservative treatment involves the use of naso-gastric decompression, intravenous fluids, antibiotics and heparin. Recent experimental evidence suggests that low

molecular-weight dextran may also be useful (D'Angelo *et al.*, 1963), but from all reported series inaction in this emergency carries an even higher mortality than does operation. It approaches 100 per cent. My own view is that laparotomy should be withheld only where there is strong evidence that a portal or superior mesenteric vein thrombosis has occurred, because venous lesions, though clinically similar, are usually secondary and are not reconstructable. If the artery is blocked then operation must be undertaken forthwith. In most centres, the operation still consists in resection of as much intestine as seems to be infarcted and, as we all know, it is most unusual to obtain a survival, partly because it is difficult to judge the vascularity of the remaining bowel, so that the anastomosis frequently breaks down, and also because unrelieved obstruction of the S.M.A. results in post-operative extension of thrombus to the peripheral vessels. Resection, therefore, is a second best and its unsatisfactory results prompted Klass (1951) to perform the first recorded embolectomy. His patient, who had severe mitral stenosis, died from cardiac failure four days following the operation, but at post mortem the reconstructed artery was patent and the entire bowel viable. The first successful embolectomy was performed in the same year, and reported in 1960 (Stewart *et al.*, 1960). Since then I have been able to find 22 reported survivors of this operation, and there surely must be many more (Shaw and Rutledge, 1957; Kleitsch *et al.*, 1957; Miller and di Mare, 1958; Shaw and Maynard, 1958; Saris and Uricchio, 1960; Atwell, 1961; Zuidema, 1961; Dumont *et al.*, 1961; Chalnot *et al.*, 1962; Brittain and Earley, 1963; Hardy, 1963; Jackson, 1963). On theoretical grounds a vascular reconstruction would appear to be the treatment of choice. However, the position is not so simple, because although viability may be restored to the bowel, death frequently occurs in the immediate post-operative period from apparently unrelated causes, such as cardiac failure, renal failure or an obscure toxaemia.

Two points, I think, deserve emphasis. Firstly, a vascular, rather than an intestinal, operation is usually possible from the technical point of view. Glotzer and Shaw (1959), in a retrospective study of all patients dying in the Massachusetts General Hospital from acute S.M.A. occlusion, found that of 20 fresh occlusions, 13 would have been amenable to direct attack on the blocked vessel, four would probably have survived following resection alone, and only three were irrecoverable. Secondly, it is very difficult at the time of the emergency operation to estimate the state of the bowel. Segments which appear hopelessly infarcted may recover when their arterial supply is restored, and others which appear comparatively normal may become gangrenous in the post-operative period. For this reason, it has been suggested by Shaw that the abdomen should be loosely closed and re-explored on the following day, regardless of the state of the patient, at which time any residual gangrenous areas can be dealt with.

The experimental background

For reasons of convenience, most experimental work on S.M.A. occlusion has been performed in the dog. In this animal, as in man, the S.M.A. is an end-artery, and constriction of the whole vascular pedicle produces a comparable situation from the anatomical point of view. However, the distal small bowel vasculature is quite different, and experiments involving short loops of intestine do not have this validity, as will appear later.

The first studies in experimental S.M.A. ligation were made by Litten in 1875, who found that ligation of the artery caused death within 12 to 48 hours, accompanied by vomiting, bloody diarrhoea and fever. At autopsy, the bowel was without sheen and soaked in bloody oedema, the serosal coat was raised in blebs, haemorrhage had occurred into the muscle and the mucosa was blown-up with sero-sanguinous fluid. The veins were engorged with blood but not thrombosed. (These appearances are identical to those described in human subjects following a mesenteric embolus [Hertzler, 1935; Boyd, 1947].)

The immediate effects of tying the artery were as follows: all pulsations disappeared, the bowel became blue-white and spastic with collapsed arteries and prominent veins. Contractions initially increased, but eventually disappeared and after some hours the loops became relaxed and distended. Microscopically, there was a backward-running venous stream and gradual filling of the veins, with outward necrosis of all layers of the bowel, which were oedematous and haemorrhagic.

Litten's observations have been repeatedly confirmed and are no longer in dispute. It is agreed that the result of acute occlusion of the S.M.A. is a haemorrhagic infarct of the intestine. What is not so apparent is the origin of the haemorrhage. Litten clearly believed that it originated from the veins. Later authors (Welch, 1920) disputed this and suggested that bleeding occurred from the arterial collateral entering the bowel from either end. Whatever the cause, it is clear that one of the effects of acutely occluding this artery is loss of fluid into the intestine. Fluid loss in intestinal obstruction, of which S.M.A. occlusion may be considered a variety, is hardly a novel concept, and was quantitated by Sir David Wilkie (1913) at Edinburgh, and later by Scott and Wangensteen (1932) in the United States and by the late Professor Ian Aird (1938) of this College. But the classical work was concerned with localized strangulation-obstruction of short intestinal loops as seen clinically in a strangulated hernia, rather than with total ischaemia of the midgut, where the veins and lumen remain open. It has always been assumed, and repeated in many surgical textbooks, that strangulation or venous thrombosis leads to massive exudation into the bowel, but occlusion of the arterial supply alone does not, because the intestine is no longer perfused with

blood, although Litten's original experiment in 1875 suggested that such was not the case. Ligation of the S.M.A. is followed by a steep rise in haematocrit, suggesting that plasma may be disappearing somewhere (Lillehei *et al.*, 1957; Shapiro *et al.*, 1958), but on reading the experimental literature I was struck by the fact that no-one had attempted to investigate the route, nature and quantity of body-fluid loss during the period that the S.M.A. was acutely occluded.

When the S.M.A. has been closed for more than a few hours it is dangerous to release it (Nelson and Kremen, 1950). The maximum tolerable occlusion period varies with species but, paradoxically, once the time limit has been reached an animal will die more quickly if the ligature is released than if it is left in place (Shapiro *et al.*, 1958). Release is followed by haemorrhage into the bowel, a fall in plasma volume and a rise in haematocrit and plasma haemoglobin, which may help to explain why removal of a mesenteric embolus is so often fatal. Nonetheless, the intestinal villi can renew themselves in a remarkable way after even a very deep ischaemic injury, though this may take several months. Indeed, the mucosa may never return entirely to normal, but may become flattened, as in coeliac disease or sprue (Glotzer *et al.*, 1962), and during the renewal process a prolonged period of exudation and malabsorption occurs (Joske *et al.*, 1958; Zuidema *et al.*, 1962).

Ischaemic destruction of the intestine results not only in loss of fluid into the lumen, but absorption of substances from it. It is reasonable to suppose that these substances are harmful, because they consist of catabolites and also of endotoxins derived from the bacteria which, as soon as the intestine is damaged, proliferate and invade its wall. During the last year, two groups of workers (Mavor, 1963; Kobold and Thal, 1963) have studied the chemical composition of blood issuing from the portal vein when the S.M.A. is occluded. They have shown that during a period of intestinal ischaemia there is a steep rise in the portal concentration of histamine, serotonin, catecholamines and free potassium ion, and a vasoactive polypeptide can be isolated, which is probably of bacterial origin. The blood from the bowel contains a mixture of vasoconstrictor and vasodilator substances whose total pharmacological effect is incalculable. Rather unexpectedly, concentration of these substances, with the exception of the free potassium ion, is not increased by releasing the ligature on the artery.

From what has been said up to now, it seems to me that two important concepts emerge.

1. Acute occlusion of the S.M.A. is almost always fatal. We do not know why this should be so. Death occurs at a time when the bowel may be still recoverable and is accompanied and perhaps caused by loss

of body fluid and absorption of poisonous material. Which of these two factors is more important is still unknown, and there are undoubtedly others.

2. Restoring circulation to a severely ischaemic intestine is dangerous and the reasons for this are equally obscure.

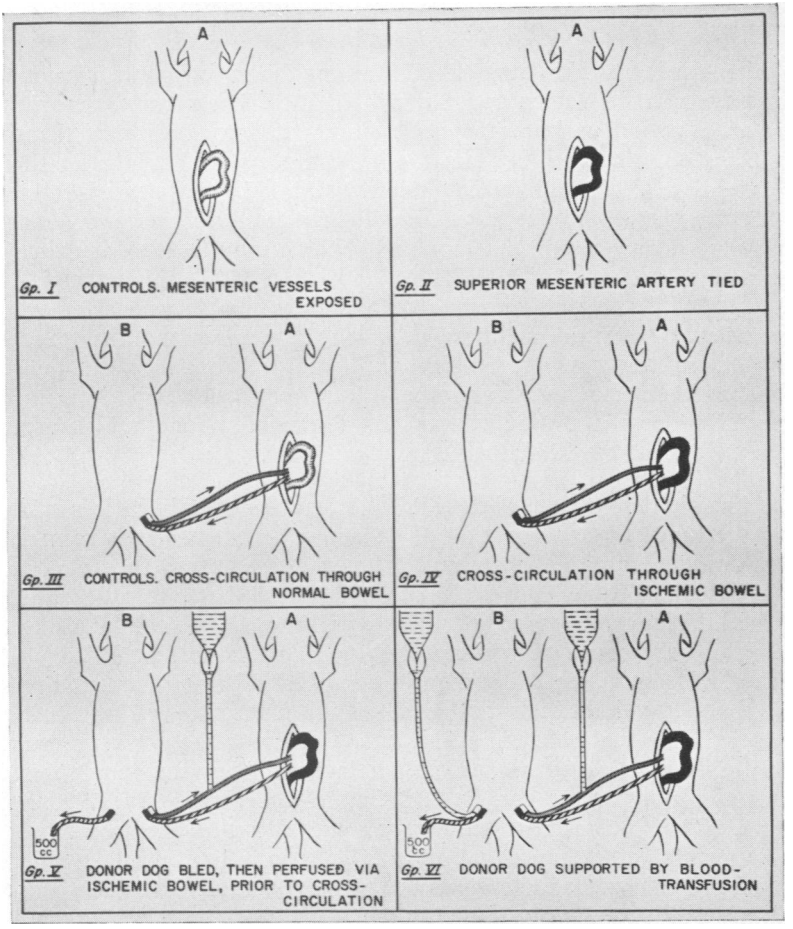


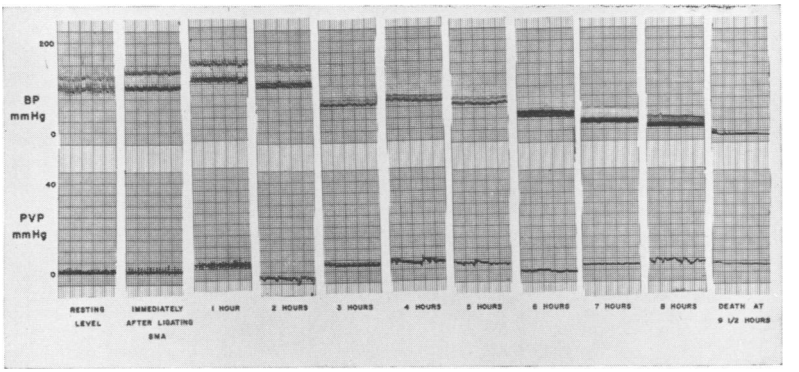
Fig. 1. Acute occlusion of the S.M.A. The experimental groups.

AN EXPERIMENTAL STUDY OF ACUTE S.M.A. OCCLUSION

I would now like to describe to you a series of experiments which were designed to shed some light on this problem. These experiments were performed on dogs, and about a hundred dogs in all were studied (Fig. 1).

Group I. Control experiments

Clinical evidence suggests that acute occlusion of the S.M.A. is very painful and we did not consider it a justifiable lesion to inflict on a conscious animal. For this reason, all experiments were performed under anaesthesia, and our first task was to establish some baseline responses. These dogs were treated as follows. They were anaesthetized with intravenous pentobarbitone (5 mg./Kg./hr.). Small cannulae were placed in both femoral veins for sampling and administration of drugs and the aortic bifurcation pressure was recorded via the right femoral artery. The blood volume was then estimated with a Volemetron, which measures the dilution of a predetermined dose of radio-iodinated serum albumen (R.I.S.A.), and the haematocrit recorded. A midline laparotomy was



EXPERIMENT 44
Group II
Following ligation of the S.M.A. there is a progressive decline in arterial blood pressure and death occurs at 9½ hours. The portal venous pressure remains stable throughout.

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Fig. 2. Experimental Record. Group II.

performed and the origin of the S.M.A. encircled with a snare tourniquet. A small polythene cannula was introduced into a tributary of the splenic vein to record the portal pressure. The arterial collaterals above and below were divided so as to produce a standard preparation in which the S.M.A. was the only blood-supply to the bowel. The blood pressure and portal pressure were recorded continuously for a period of 10 hours, at the end of which time the blood volume and haematocrit were again measured. The changes in blood volume, red cell mass and plasma volume were calculated and expressed as a percentage of the pre-operative level. At the end of the experiment the snare on the S.M.A., which had been left loose throughout, was removed.

Five out of the six dogs in this group survived in good health, the sixth died from pneumonia a few hours after the end of the experiment. The arterial and portal pressures remained steady throughout the period

of observation. The blood volume, however, contracted by about 10.5 per cent (approximately 1 per cent per hour), and the coincident rise in haematocrit showed that the loss was mainly of plasma. Operative haemorrhage never amounted to more than a few millilitres. This diminution in blood volume under prolonged anaesthesia was not altogether surprising and has in fact been noted before (Seavers and Price, 1949).

Group II. S.M.A. occlusion

In this group the procedural details were exactly the same except that the snare was tightened to occlude the S.M.A. The effects on the bowel, both gross and microscopic, were exactly those observed by Litten nearly a hundred years ago, that is to say transitory spasm, followed by cyanosis,

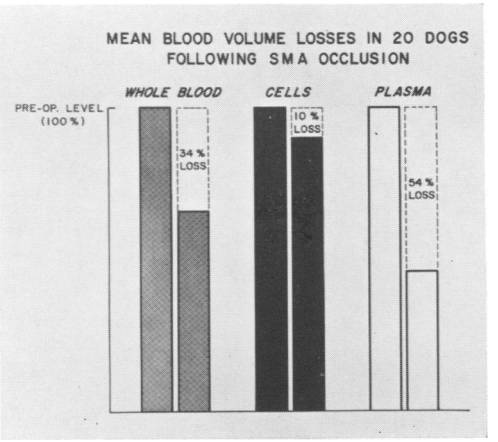

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Fig. 3. Blood volume losses following S.M.A. occlusion.

flaccidity, oedema and eventually haemorrhage. In no case was there frank perforation, although a few millilitres of turbid fluid accumulated in the peritoneum. Peristalsis could be evoked until quite late in the experiment and sometimes in a dog that had already died. One interesting finding was that the mesenteric veins were frequently distended with bubbles of gas, as has been noticed in patients with mesenteric emboli (Stewart, 1963), which must have originated from the bowel lumen, or from organisms invading the wall, as the venous system was never opened. Death occurred between 8 and 16 hours, with a progressive decline in arterial pressure, though the portal pressure, which is normally about 12 mm. Hg in the dog, remained fairly constant throughout (Fig. 2).

Figure 3 shows what happened to the blood volume: a striking contraction took place, of the order of 35 to 40 per cent, between the time of

arterial occlusion and death, or about 5 per cent per hour, while at the same time the haematocrit rose steeply, showing that the loss was almost entirely of plasma.

These fairly simple experiments convinced us that large and hitherto unrecognized plasma losses did occur in acute ischaemia of the small intestine, and the oedema of the bowel-wall and the profuse quantities of muco-sanguinous fluid in the lumen suggested that plasma was escaping across the damaged intestinal capillary. If this were true, how did the fluid in fact arrive there, as the bowel was no longer being perfused via the S.M.A., and the collaterals at either end had been deliberately divided? The most likely path of plasma escape seemed to be from the valveless portal venous system. This was suggested by some further experiments, in which Indian ink was injected into the aorta at intervals following

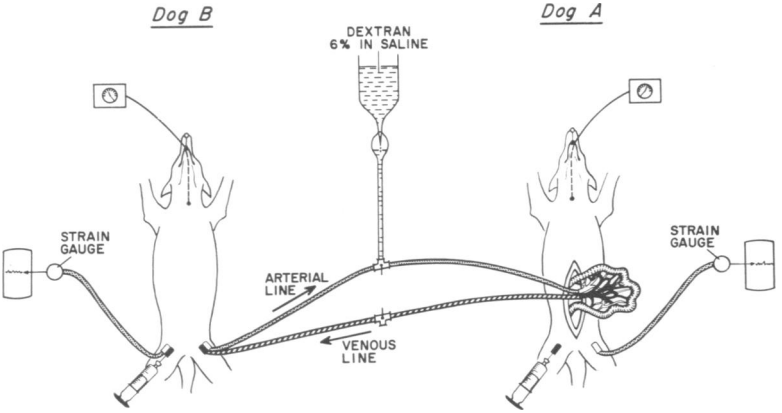

Fig. 4. Design of cross-circulation experiment.

ligation of the S.M.A. Particles of carbon could be seen in every tissue except the small intestine. When, however, the same injection of Indian ink was given into the portal vein, the carbon appeared in the vessels, the tissues and the lumen of the bowel.

Groups III–VI. Revascularization of the intestine

Having demonstrated that a factor in the causation of death following occlusion of the S.M.A. was plasma loss and haemoconcentration, the question arose as to how far the bowel was recoverable in an animal that had died from the effects of this lesion. The best fluid with which to " revivify " a damaged bowel was clearly arterial blood, and if this blood came from a normal donor who, in turn, received the portal effluent from the infarct, then something might be learned of the toxicity, or otherwise, of the products of intestinal necrosis. Accordingly, a cross-circulation set-up was devised which is shown in Figure 4. Dog A was treated as

already described in Group II and its S.M.A. occluded. Another normal dog, Dog B, of comparable weight, was then anaesthetized, its blood-volume and haematocrit measured, and its femoral vessels cannulated in such a way that they could be rapidly connected to the isolated mesenteric circulation of the other.

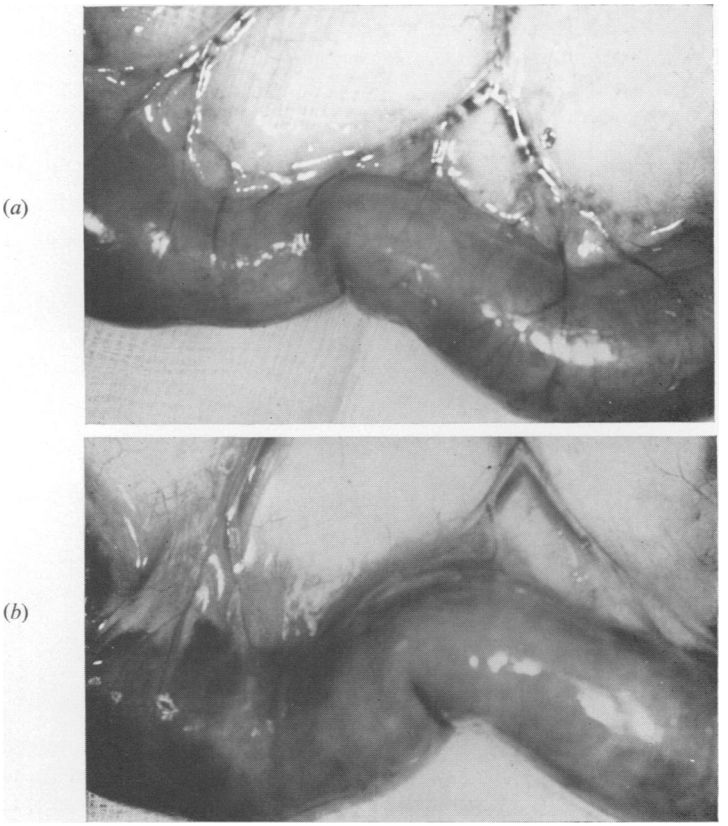

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Fig. 5. Loop of ileum (*a*) following twelve hours' S.M.A. occlusion and (*b*) two hours after revascularization; to show disappearance of gas from the mesenteric veins.

Group III

This was a control group of six dogs in whom cannulation was carried out immediately after ligation of the S.M.A. before ischaemia had had time to develop. Cross-perfusion was maintained for six hours. Five out of the six donor dogs survived, the sixth died on the day following the experiment. Blood volume estimations at the beginning and end of the experiment showed that no leakage was occurring through the perfused

bowel and that the cross-circulation model was balanced, i.e. one dog was not simply bleeding into the other.

Group IV

In this group, cross-circulation was not started until death of dog A appeared imminent and the bowel very severely ischaemic (Fig. 4). As soon as cross-circulation was started, dramatic improvement took place in the gross appearance of the bowel. In each case some three-quarters of its length appeared recoverable, in that it accepted circulation and became pink. Pulsations reappeared in the distal arcades and gas disappeared from the mesenteric veins (Fig. 5). After an hour's perfusion the colour changes became more pronounced and it was noticed that whereas the " better " segments of bowel continued to improve, the

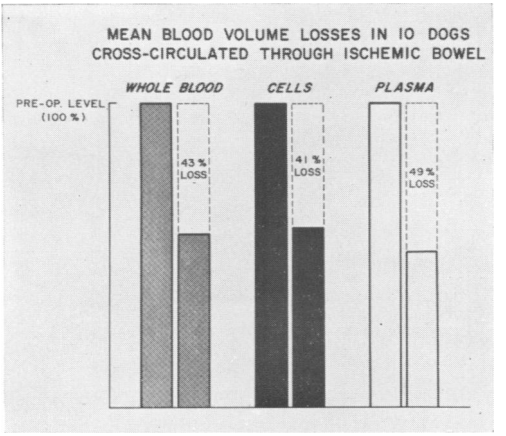

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Fig. 6. Changes in blood and plasma volume following cross-circulation.

" worse " areas (which were usually around the caecum) appeared more necrotic. At the same time, however, the revascularized bowel became engorged with blood, and serous fluid leaked from its peritoneal surface. Histological sections showed massive haemorrhage.

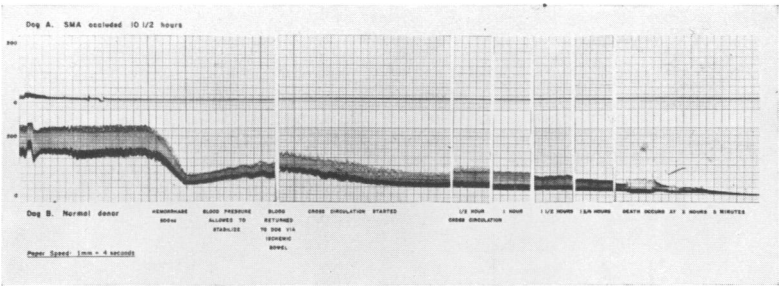
The changes in the donor dog B were equally striking. Immediately the arterial line was opened, its blood-pressure began to fall and death occurred in from two to four hours. This dog lost 40 per cent of its blood volume over the perfusion period, while at the same time the haematocrit rose only slightly, suggesting that cells and plasma were disappearing in roughly equal amounts (Fig. 6).

Group V

The reasons for the hypotension and rapid death of the dogs which were cross-circulated through ischaemic bowel were not immediately obvious.

Two possibilities suggested themselves. One was that this was a death from haemorrhage, the other that it was due to absorption of " toxins " via the portal venous line.

In Group V an attempt was made to differentiate between the effects of toxaemia and those of haemorrhage. In this experiment, immediately before cross-circulation was established, 500 ml., or about one-third of the blood volume, were removed rapidly from the donor dog into a Fenwal bag in order to sensitize it to endotoxin. Fine *et al.* (1959) have shown that whereas it is difficult to injure a normal animal by large doses of endotoxin, one that is reversibly shocked by pre-haemorrhage is extremely sensitive.



EXPERIMENT 33

Group V

When a transfusion of portal blood from a dog which has died of S.M.A. occlusion is given to a shocked test animal, the arterial B.P. rises. The test animal dies of heamorrhage when cross-circulation through the bowel is started.

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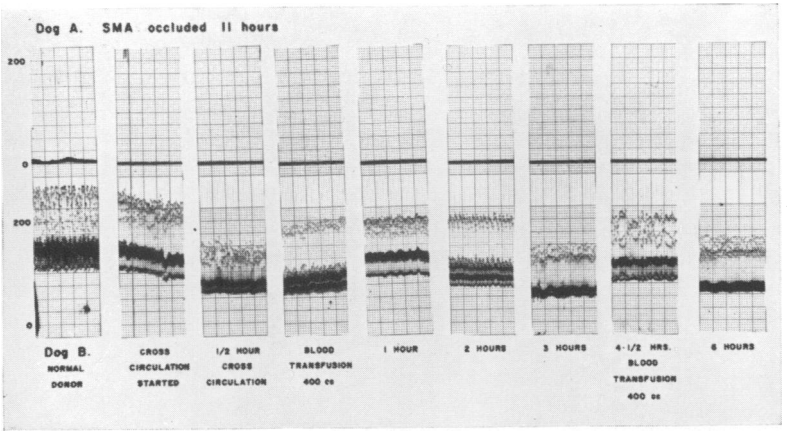
Fig. 7. Group V. Experimental record.

When the blood pressure appeared to be stabilized, the bag was connected to the centre of the arterial line and the blood returned to its owner via the ischaemic bowel of dog A. In this way, any toxic products present would be washed through into the donor. The effect on blood pressure was recorded. When the bag was empty, cross-circulation was started in the normal way by opening the stopcocks. The results of this experiment were quite unexpected. We had anticipated that the sudden introduction of a large quantity of active material from the ischaemic bowel into the circulation of a dog already suffering from the effects of haemorrhage would be to plunge it immediately into irreversible shock. In fact the opposite occurred. Figure 7 shows how a *rise* rather than a fall in blood pressure was observed during the period in which the shed blood was being returned. In other words, it seemed to act as a simple volume replacement. When the arterial stopcock was opened, the expected hypotension and death in shock occurred. This suggested that haemorrhage rather than toxaemia was the lethal factor.

Group VI

If in fact this was a haemorrhagic death it should be preventable by transfusion, whereas if it was due to endotoxaemia it would not.

In Group VI, therefore, the same experiment was carried out, but while cross-circulation was in progress, the donor dog A was transfused with previously collected pooled blood. By watching the arterial tracing it was possible to support dog A during the period of cross-circulation by altering the transfusion rate. The experiment was continued for a longer period than was found to be fatal in the preceding groups, and five out of six



EXPERIMENT 34
Group VI
The shock which occurs in a normal dog when it is cross-circulated through ischaemic bowel is preventable by replacement of blood.

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Fig. 8. Group VI. Experimental record.

of these donors survived. Figure 8 shows how the blood pressure of the donor could be maintained by blood transfusion, even though it was cross-circulated through nine feet of ischaemic intestine.

CONCLUSIONS

How can we explain these experimental results and what relevance have they to the clinical problem of a mesenteric embolus? Here is a hypothesis which, at any rate, fits the facts, although I am aware that it needs experimental testing at many points.

When the S.M.A. is suddenly occluded, necrosis of the small bowel at once begins, starting at the tips of the villi and extending outwards towards the serosa. The minute vessels of the intestinal mucosa rapidly suffer anoxic damage and lose their power to retain plasma. Although

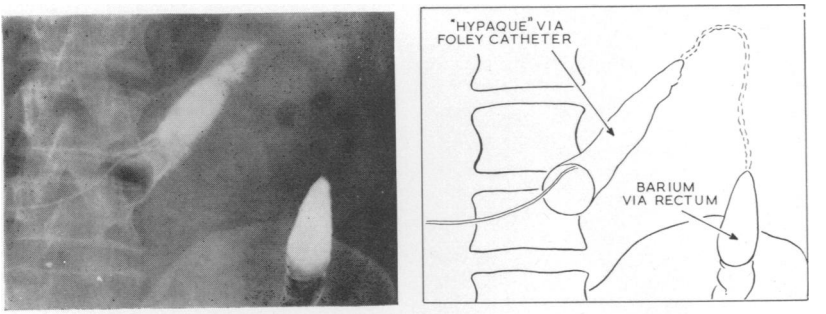
no blood is entering the arterial side, the portal system is still receiving an inflow from the coeliac and inferior mesenteric routes and also from its connections with the systemic veins. A fairly normal portal pressure is thus maintained, which, acting across the enormous area of the intestinal lining, causes an exudation of plasma into the wall and lumen of the bowel, with consequent contraction in blood volume and rise in haematocrit. The dog's intestinal mucosa measures approximately 1.6 square metres, an area about the same as its body surface, so that plasma loss will occur as in a total body surface burn. In the laboratory this loss is artificially magnified because the animal is anaesthetized and is receiving no additional fluid.

While all this is proceeding, toxic products are accumulating in the portal blood and, via the liver, reaching the general circulation. The combination of hypovolaemia, sludging in the peripheral vessels, reduced arterial flow to the brain, kidneys and heart, and reduced portal flow to the liver, together with absorption of vasoactive material, leads to a state of peripheral circulatory failure which kills the individual before complete necrosis of the intestine may have had time to develop. Of these various factors fluid-loss appears to be more important than toxaemia, though clearly it is not the *only* cause of death. To say this would be to say that a patient with an infarcted small bowel could be saved purely by transfusion, which is obviously not true. Nonetheless the importance of these fluid shifts has probably been underestimated, and the clinical lesson would seem to be that acute bowel ischaemia demands massive plasma replacement pre-operatively. Unfortunately, these cases, though common, are sporadic emergencies, and no one surgeon sees a great many of them, so that it is difficult to confirm such laboratory results in the human. This is under investigation. Other measures which would probably be valuable in improving our mortality figures would be the use of hypothermia to delay bowel necrosis, of intestinal antibiotics to prevent the accumulation of bacterial endotoxins, and of vasodilators to counteract their peripheral effects.

When blood-supply is re-established, the chief danger would seem to be haemorrhage. These experiments showed that the anoxic intestinal capillary subjected to a normal portal pressure exudes plasma, but that when this same vessel is exposed to the full arterial pressure, it ruptures and bleeds, and half a blood volume can then be rapidly lost. The bowel accommodates large volumes of blood quite inconspicuously, and I suspect that a proportion of patients who die following a technically successful reconstruction of the blocked S.M.A., apparently from renal failure or toxaemia, in fact die of haemorrhage, and that transfusions of whole blood are essential in this phase of treatment.

III. ACUTE OCCLUSION OF THE DISTAL INTESTINAL VESSELS

When the arterial supply to a loop of intestine is suddenly cut off, three things may happen. If the vessel is a small one, and provided that the origin of the S.M.A. is not narrowed and the haemoglobin level is normal, the collateral circulation from either end rapidly heals the injury. If circumstances are not so propitious, the loop will slough and the patient will die of overwhelming peritonitis. There is an intermediate state. If the collateral supply is adequate to prevent full thickness necrosis, but not enough to allow complete healing, a permanent abnormality of the segment results, which takes the form of a fibrous stricture. These lesions are quite common, and usually follow failure to resect a doubtfully viable piece of intestine which has been nipped by an external hernia (Raw,



(*a*) (*b*)

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Fig. 9. Barium enema appearances following occlusion of the middle colic artery.

1943), but it is not necessary, particularly in the arteriosclerotic subject, to have a strangulated hernia in order to develop an ischaemic stricture of the bowel. Here is a typical example (Marston, 1962*a*).

A man of 64 was admitted to hospital under the care of Mr. M. T. Pheils, having been awakened in the small hours of that morning by a sudden severe central and lower abdominal pain. The pain had gradually become worse and had spread upwards over the epigastrium causing difficulty in breathing. He felt nauseated but had not vomited, and shortly after the onset had developed bloody diarrhoea. His past history was unremarkable, but two years previously he had experienced a milder attack of the same pain which again had been accompanied by diarrhoea and rectal bleeding. On that occasion he had been treated at home as a case of gastro-enteritis and had got better within a few days. His bowel action thereafter had been perfectly normal and regular. On admission there were signs of a lower abdominal peritonitis. A provisional diagnosis of perforated sigmoid diverticulum was made. At laparotomy, the

whole of the transverse colon and the splenic flexure were engorged and thickened. The process appeared to be inflammatory, and was thought to represent an acute regional colitis. A colostomy was made proximal to the affected area, in fact just encroaching on it, and a piece of bowel from the distal edge of the colostomy opening sent for section. He made a smooth recovery from this operation, and, somewhat to our surprise, the colonic biopsy was reported on by the pathologist as an infarction. Three weeks later a barium enema was attempted but it was found that no medium could be induced to enter the lumen of the bowel from either end (Fig. 9). Retrograde aortography was then performed and revealed that the middle colic artery had thrombosed. Thirty-six days after the onset of the illness the abdomen was re-explored. The entire colon, from the hepatic flexure to the lower sigmoid, had contracted to a

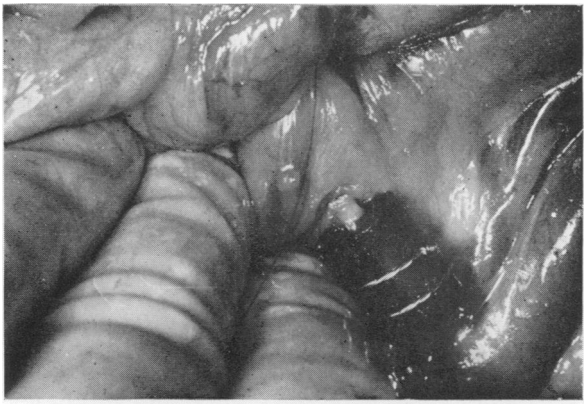

Fig. 10. Ameroid cylinder in position around the S.M.A.

thin, fibrous cylinder. No trace of the middle colic artery could be found. There was an obvious thrill at the origin of the S.M.A. indicating a stenosis. The diseased bowel was resected and the ascending colon anastomosed to the lower sigmoid.

Microscopy of the excised colon showed that the mucosa was missing and had been replaced by fibrous tissue, which also extended into the submucosa. The outer layers were somewhat thickened but otherwise fairly normal. Changes, in fact, were typical of those of an ischaemic episode in the bowel, all coats being affected, but the mucosa most conspicuously so. When seen a few weeks ago, that is three years after his original operation, he was well and having normal bowel actions.

The X-rays of three other patients all show on the barium enema changes very similar to the patient I have just described. I have no proof that these are in fact vascular lesions, because in no case has resection been necessary, and aortography has not been justified. On the radiological appearances

one might well suppose that they are cases of localized Crohn's disease or atypical ulcerative colitis, but certain clinical features are against this. Firstly, they are all elderly and all have evidence of athero-sclerosis elsewhere. They thus belong to an age group in which colitis is rare. Again, they all have a history of acute pain and rectal bleeding, which cleared up completely and permanently. Finally, the lesions have all occurred around the splenic flexure, where the vascular supply to the colon is somewhat insecure because it is the point of inosculation of the superior and inferior mesenteric systems, but is not a characteristic site for intestinal granulations. Such lesions, probably vascular, which can occur in both small bowel and colon have been known about for some time (Pope and O'Neal, 1956; Hawkins, 1957). Their great interest lies in their resemblance to regional enteritis in that they show ulceration of the mucosa, sub-mucosal thickening, fissures and even non-caseating giant-cell systems. I do not wish to imply that Crohn's disease is a simple matter of impaired arterial supply, but I do think that certain cases, particularly in the older age-groups, which are uncritically labelled as such, may in fact be infarcts. From a practical point of view their management should be somewhat different. Most of them clear up spontaneously. If resection becomes necessary, this may be expected to have a good result, unlike most cases of Crohn's disease, where management should be as conservative as possible. To this I would add one proviso. If there is serious atheromatous impairment of more than one of the three main visceral arteries, then serious thought should be given to a deliberate reconstruction of the origin of the S.M.A., because this lesion, as will be shown later, has a bad prognosis.

I have attempted to reproduce this condition in the laboratory, but without much success. The method chosen was the obvious one of occluding small intestinal vessels in the dog for varying periods of time and observing the effect on the bowel histology. To my embarrassment the appearances were absolutely normal. Later I learned the reasons for this. In the first place the vasa recta of the dog communicate freely, which is not the case in man, so that it is much more difficult to produce a standard ischaemic lesion. In the second place I had underestimated the capacity of intestinal mucosa to recover following ischaemic injury (Glotzer *et al.*, 1962). I should, however, mention one abnormality that was consistently found and whose significance at the time I missed. This was that the loops which had been damaged in this way were densely adherent to other areas of bowel and that the omentum was plastered firmly on to them. There is now experimental evidence to suggest that adhesions are, in fact, vascular grafts and form in response to ischaemia (Ellis, 1962).

IV. STENOSIS OF THE VISCERAL ARTERIES AND INTESTINAL ANGINA

That life may continue with obliteration of the S.M.A., provided that this occurs slowly, has been known since Chiene's (1868) description of a

body received for dissection at the Edinburgh Medical School of a 67-year-old woman who had died of " paralysis ". An aortic aneurysm was present, with complete obliteration of both the coeliac axis and the S.M.A. The bowel was principally nourished by the superior haemorrhoidal artery, which was enlarged to the size of the femoral. This state of affairs had clearly persisted for some time, and the patient had lived with no normal arterial supply to the mid-gut. Many other cases of stenosis or occlusion of the S.M.A. during life have since been reported (Mandell, 1957; Rob and Owen, 1956; Mavor and Michie, 1958; Keeley *et al.*, 1959). Autopsy studies have shown that the three visceral arteries are, in fact, among those most commonly affected by atheroma. From published series (Carucci, 1953; Derrick and Logan, 1958; Derrick *et al.*, 1959) it appears that about one-third of those over the age of 45 have some narrowing at the origin of the S.M.A., though disease of the distal intestinal vessels is rare.

Just as occlusive disease of the femoral artery can cause ischaemic muscle pain in the calf, so can stenosis of the visceral arteries give rise to an analogous type of pain in the intestine. This concept is not new. It was originally described by Schnitzler (1901) and has been revived sporadically since (Meyer, 1924; Mikkelsen and Zaro, 1959; Fry and Kraft, 1963). For one reason or another it has received more attention on the continent of Europe than in England or America. Mikkelsen (1957) proposed that this type of pain should be called " intestinal angina ", which avoids the use of such ambiguous words as " claudication ", and the general adoption of this name has been advocated. The clinical features of intestinal angina are now well known. The most prominent is severe pain occurring very shortly after meals, which may be of such severity that the patient becomes terrified of eating. (Intense food-fear in the elderly person is strongly suggestive of disease of the visceral arteries.) Weight-loss inevitably follows, there may be steatorrhoea with occult blood in the stool, and very occasionally a bruit can be heard over the origin of the S.M.A. Apart from this there are no physical signs whatever, and, as intestinal angina occurs in an age-group where other causes of abdominal pain and weight loss are common, the diagnosis is not easy. In the few patients who have been accurately studied no laboratory or radiological test has been found useful (Bentlif *et al.*, 1962). The only way in which the diagnosis can be made certain is by an aortogram taken in the lateral position, and this clearly is not a practical screening test. The discrepancy between the apparent clinical rarity of the condition and the frequency of the lesions found at post mortem may be because at least two out of the three main visceral arteries must be compromised for symptoms to develop (Fry and Kraft, 1963).

The following case will illustrate this. A man of 43 underwent placement of a prosthetic cusp for aortic incompetence in February 1962. His

initial post-operative course was smooth, but a week after operation he developed a sudden pain in the left arm and an embolus was removed from the brachial artery. Over the next few weeks he began to notice discomfort after meals, diarrhoea and loss of weight. He was readmitted to hospital five weeks post-operatively and was found to have a partial large bowel obstruction due to a fibrous stricture at the recto-sigmoid. A colostomy was constructed. Shortly after this he sustained a mild transitory cerebral vascular accident, presumably due to a further embolus. He continued to complain of pain and to lose weight, however, and the colostomy was overactive. The blood picture, small bowel meal and *d*-xylose absorption were normal. Re-examination of the abdomen now disclosed a loud bruit over the S.M.A. An aortogram in the lateral position showed poor filling of the mesenteric vessels, but the origin of the artery was not visualized. At laparotomy, the whole of the small intestine was collapsed and pale, but otherwise normal. The coeliac axis was pulsating normally. The S.M.A. had a pulse for the first 1.5 centimetres, but the next two centimetres felt solid. The inferior mesenteric artery was a thin, stenotic cord. The S.M.A. was opened and a large thrombus removed. When the arteriotomy was closed and the clamps removed, excellent distal flow was obtained and the bowel became pink and normal looking, although we could still feel no pulsation in the arcades. (In view of what was said earlier about revascularization of the intestine, it was interesting that there was a sharp drop in blood-pressure as soon as these clamps were released, which returned to normal when a litre of blood was rapidly infused.) This man made a good initial recovery from operation, but one week later died suddenly from an unrelated cause. At post mortem the bowel was normal. The S.M.A. was injected with barium suspension and patency of the distal vessels confirmed.

The prognosis of intestinal angina is almost certainly bad. Dunphy in 1936 demonstrated that most patients who die from mesenteric thrombosis give a prodromal history of intestinal angina which is usually brief. Other authors have found that their patients seldom had this pain for more than a year or two before it was cut short by operation, by death or by both (Berman and Russo, 1950).

Although it is true that people who suffer a fatal S.M.A. occlusion have a prodromal period of angina, it is not certain that those who have angina will necessarily die from infarction of the bowel. The natural history of the symptom is still unknown. Clearly what is needed is an accurate diagnostic test to help us select these patients in an early stage.

Several workers have tried to produce such a lesion in the laboratory. The first, and in some ways the most successful, attempt to do so was made by Blalock and Levy (1939), who, while investigating the effect on the arterial blood-pressure of constricting various vessels, produced seven healthy dogs whose intestinal arteries were completely closed. (Their

blood-pressures incidentally were normal.) The bowel itself was not investigated.

In two later studies (Laufman, 1942; Spencer and Derrick, 1962) a state of chronic ill-health was produced following gradual occlusion of the S.M.A., but again no biochemical, radiological or histological investigations were done. Because of the great need for a diagnostic test for intestinal angina, I decided to make a further attempt to produce this situation in the laboratory and to study it in detail.

Experimental study of chronic intestinal ischaemia

Fourteen dogs were used in these experiments, of whom eight are excluded for technical reasons. The remaining six form the basis of the study.

As the first step the dog was weighed, and the haematocrit recorded. A xylose absorption test was then performed. Estimation of excreted *d*-xylose has been found in clinical practice to provide a good general index of small bowel absorptive function (Benson, 1957; Fordtran *et al.*, 1962), but I could find no reference to this test having been used in the dog, and had to invent a method *de novo*. Following a 24-hour fast the dog was induced to urinate, and was then given to drink 10 gm. xylose in 50 ml. water, that is to say a little over a third of the dose used clinically. Anaesthesia was induced and a Foley catheter passed into the bladder and clamped off. At the end of five hours all the urine was collected and frozen, and its xylose content estimated by the method of Roe and Rice (1948).

One week later the dog was re-anaesthetized, the origin of the S.M.A. exposed, and the collateral vessels at either end of the intestine divided. A cylinder of Ameroid was then slipped over the origin of the artery (Fig. 10). (Ameroid is a plastic which has the property of expanding at a constant rate when it is wet, so that, if outward expansion is prevented, any structure enclosed in it will be predictably compressed.) We were able to calculate that obliteration of the lumen would be complete in about three weeks and this proved to be the case.

At weekly intervals after the Ameroid had been positioned the dog was re-anaesthetized, and the weight, haematocrit and *d*-xylose absorption again measured. In some of the dogs aortography was performed in order to confirm obliteration of the S.M.A. and to demonstrate the pattern of collaterals. Later, at a further laparotomy, obliteration of the S.M.A. was confirmed, and the bowel biopsied. We also investigated the electrophoretic pattern, and serum vitamin B_{12} and folate levels in these dogs.

One would have thought that such a lesion would have created an obvious illness in the animals and that this would be accompanied by major structural and biochemical abnormalities. In fact, the changes

produced were slight and transient. The dogs appeared recovered from the operation within a few hours and ate, drank and exercised normally. Some four to seven days later, a period of listlessness, anorexia, weight loss and diarrhoea set in. Blood occasionally appeared in the stools at this time, and the stools of all six dogs gave a positive reaction to hematest tablets for a period of one to three weeks. The situation then began to improve and by six weeks all the dogs had come near to their pre-operative weight and appeared normal in every way.

At laparotomy, the bowel appeared pale but otherwise normal, and no pulsations could be detected in the arcades. A pressure gradient of 100 mm. Hg was found across the occluded segment of artery. Vascular adhesions had formed around the Ameroid, the loops of bowel, and the

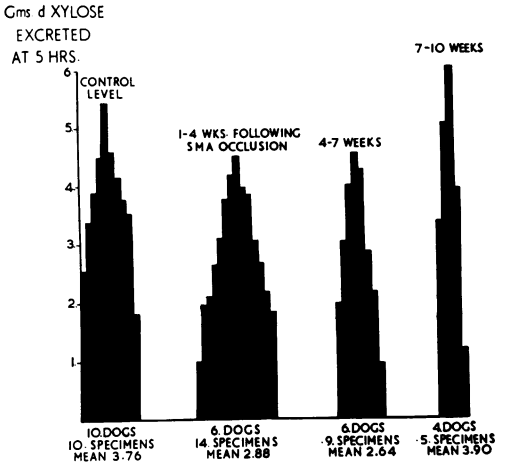

Fig. 11. Changes in *d*-xylose absorption following chronic occlusion of the S.M.A.

abdominal incision. The coeliac axis and the inferior mesenteric artery did not appear enlarged, neither did the lumbar and lower intercostal arteries, as seen from within the abdomen. Aortography showed that the bowel was nourished by a network of fine collaterals originating from extra-coelomic vessels.

The haematocrit tended to fall during the first few weeks while blood was being lost in the stool. Later this was partially restored, but did not quite reach pre-operative levels. The film showed hypochromasia and anisocytosis. Serum folate and B_{12} levels did not differ significantly from control levels and serum electrophoresis six weeks after insertion of the Ameroid showed a normal strip.

The xylose absorption studies were not conclusive and probably reflected the inaccuracy of the method. Overall, absorption tended to

decrease over the first six weeks and then gradually to revert to normal (Fig. 11). There was little correlation between xylose excretion, haematocrit and body-weight, which often tended to shift independently.

Biopsies of the lower ileum were obtained either by laparotomy or at post mortem at 3, 4, 6, 12 and 13 weeks post-operatively, and the histology of the small bowel in each specimen examined was quite normal. In particular there was no mucosal flattening.

To sum up, the abnormalities produced in these experiments were slight in nature, non-specific and, in fact, occurred while the bowel circulation was inadequate and the collateral was establishing itself, but apparently before the S.M.A. was completely closed. I report these experiments mainly to emphasize how very difficult it is to produce a structural or biochemical lesion by interfering with the arterial supply to the gut. Dr. Joske of the University of Western Australia, who has great experience in this field, tells me that he too has had a similar lack of success. We have thus got no further, except in a negative way, towards a reliable test for intestinal ischaemia which might be of use in human beings. These studies are now being repeated using a rather more refined technique and taking more especial care to eliminate routes of collateral supply to the bowel.

V. INTESTINAL FAILURE—THE ROLE OF THE BOWEL IN HUMAN SHOCK

It not infrequently happens that a patient dies from total or partial intestinal necrosis, and yet at post mortem no embolus and no thrombosis can be discovered in the S.M.A. although its origin may be narrowed (Berger and Byrne, 1961; Jackson, 1963).

A few weeks ago we had a patient at St. Thomas's Hospital who underwent a straightforward operation which did not involve his abdominal cavity. He was mildly atherosclerotic and during the operation underwent a period of hypotension. Over the next two weeks he became increasingly ill, with silent abdominal distension, and was considered to have developed a reflex ileus. In spite of all normal resuscitative measures he died in profound toxaemia and electrolyte imbalance. At post mortem he was found to have patchy necrosis of the whole gastrointestinal tract. His peripheral intestinal vessels were normal but the origin of the S.M.A. was reduced to a quarter by an atheromatous plaque.

Now I want to digress for a few minutes to discuss the role of the intestine in the development of irreversible shock. Even if time allowed, I would not be capable of covering the enormous field of shock physiology, and I am forced to dogmatize and to oversimplify. By shock I mean a clinical state which indicates too little blood in the arterial circulation,

By irreversible shock I mean shock resistant to transfusion. Shock becomes irreversible when treatment is applied too late: but it is not clear why. Sometimes the reason is obvious, for instance if there is a large wound of the aorta the heart will stop because there is no pressure to fill the coronary arteries, and any treatment except prompt closure of the wound will be " too late ". But in prolonged shock there is time for all manner of lethal abnormalities to pile up, any one of which may become irreversible. Metabolic acidosis, hyponatraemia (Brooks *et al.*, 1963) and microemboli due to sludging of blood in peripheral vessels (Hardaway *et al.*, 1962) are the current scapegoats, and are beyond doubt important. In the laboratory, as is usual, and perhaps in this case unfortunate, the dog has been the animal most often studied. Fine *et al.* (1959) have developed a standard model for the investigation of irreversible shock in the dog. In his preparation bleeding occurs into a receiver, so arranged that haemorrhage stops when the arterial pressure falls to the lowest level the animal can tolerate, that is 30 to 35 mm. Hg. After an hour or so blood begins to run back from the receiver into the artery, the phenomenon of " taking up ". If at the end of $1\frac{1}{2}$ to 2 hours all the shed blood is returned, the animal recovers, but at four hours, if the blood which has not been " taken up " is re-infused or even if more blood is given than has been lost, the arterial pressure fails to rise, and death ensues. During the third and fourth hours something has happened which has caused the shock to become irreversible. The arrival of irreversibility is signalled by congestion and haemorrhagic necrosis of the bowel, much as is found following acute occlusion of the S.M.A. Pathological changes in the brain, heart, lungs, liver and kidneys are milder, variable and not directly related to mortality, suggesting that a crucial factor in the causation of irreversible shock is intestinal damage.

There exist two opposite schools of thought on this subject. The proponents of the " endotoxin " theory of irreversible shock, of which Fine is a notable representative, argue somewhat as follows: irreversibility is due primarily to the presence of Gram-negative bacteria in the intestine which produce endotoxin. Under normal circumstances small amounts of this are absorbed, which can be demonstrated immunologically and do no harm. However, prolonged hypotension, from any cause, results in deficient blood flow through the intestinal wall and liver, causing increased absorption of endotoxin and, at the same time, weakening the reticuloendothelial defences, so that the organism is unable to detoxify it, and dies. Transfusion is of no avail and death may occur with a normal blood volume. A toxic factor similar in all respects to endotoxin is demonstrable in the plasma of animals that have died from haemorrhagic shock.

Although there is a mass of experimental evidence in its favour, this view is still not widely accepted. I will not try to cover the whole of the dispute, but one piece of evidence which the proponents of the toxin

theory have found very difficult to explain away is that Zweifach *et al.* (1958) have succeeded in producing irreversible shock, intestinal lesion and all, in germ-free animals.

Quite apart from the possible presence and activity of endotoxins in this situation there is another way in which intestinal necrosis could cause death. We have seen that the mesenteric circulation is of large volume and is very sensitive to the effects of catecholamines. The levels of these substances rise as much as one hundred-fold in prolonged haemorrhagic shock (Greever and Watts, 1959). It is possible, therefore, that the basic factor in irreversibility is vaso-constriction in the mesenteric bed, with resulting damage to the intestinal mucosa which leaks plasma and, to a lesser extent, red cells into the lumen. Death eventually occurs from simple hypovolaemia. If this is true then preservation of normal flow through the S.M.A. should confer some immunity. Lillehei (1957) has shown that this is in fact the case. His method was to lower the systemic blood pressure of the animal by haemorrhage, but at the same time to maintain normal flow through various regions of the body by the use of a pump. He found that maintaining the S.M.A. flow in this way prevented irreversibility in 90 per cent of his animals, whereas perfusion of other essential vessels conferred no such protection, the animals dying with the usual bowel lesion.

Most laboratory work on irreversible shock has been performed, not only on artificial experimental models, but also on an animal whose intestine is peculiarly vulnerable. The intestinal lesion of shock is certainly a fact in the dog, but it does not occur in either the rabbit or the monkey. Nonetheless, that such a mechanism exists at all is clearly important and it is essential for us as human beings to know whether we behave like dogs or like rabbits when faced with prolonged hypotension. I have already mentioned that intestinal necrosis can occur in man in the absence of a complete block of the S.M.A. and have described an illustrative case. On going back through the literature over the last 10 years or so I discovered that sudden, unexplained necrosis of the intestine is, in fact, quite common, and I had no difficulty in collecting case reports of 425 such patients, many of whom had been described by the authors as suffering from completely new syndromes, such as " intestinal apoplexy ", " necrotizing jejunitis ", " acute haemorrhagic necrosis ". (For references see original paper [Marston, 1962*b*].) Among them are several patients who had " pseudomembranous enterocolitis ", and it may be objected that this is a perfectly respectable disease on its own and I had no right to include it. In fact, however, all the clinical and laboratory evidence suggests that " pseudomembranous enterocolitis " is nothing more than ischaemic necrosis, and that it has no connection with antibiotics or the staphylococcus (Penner and Bernheim, 1939; Kleckner *et al.*, 1952; Carter and Ashley, 1960; Dearing *et al.*, 1960).

From this series of patients who developed necrosis of the intestine with no vascular block certain rather striking features emerge.

1. There are twice as many men as women and all but seven of the 134 women had passed the menopause.

2. The mean age for the series is 55 years.

3. This syndrome usually follows an episode of hypotension and peripheral vasoconstriction, such as a myocardial infarct, an operation or a major fracture.

4. The overall mortality is 70 per cent.

Now, of course, there is no proof that all these variously named conditions have a common vascular basis, but I think it is fair to say this. The pattern of age and sex incidence in this series strongly hints that many

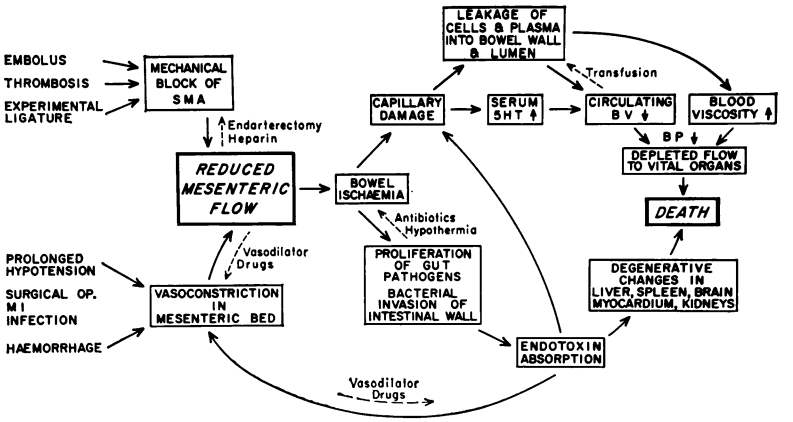

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Fig. 12. Mechanisms of death in intestinal ischaemia.

of these patients were atheromatous and we know that stenosis of the origin of the S.M.A. is common in such people. Again, these patients developed their intestinal lesions following an episode of hypotension and we know that a reduction in pressure at the mouth of the S.M.A. will result in widespread peripheral shutdown and patchy necrosis of the mucosa (Fig. 12). Although there is no evidence that this mechanism operates in the young and fit (and most studies of shock involve battle casualties) it is possible that an *atheromatous* patient whose blood-pressure is sharply reduced from any cause may die from " intestinal failure " in exactly the same way as does the irreversibly shocked dog. At post mortem such necrosis may be missed altogether or it may be dismissed as acute terminal erosions. In any case the bowel mucosa autolyses so rapidly following death that after a few hours very little useful histology remains. From this hypothesis three points follow:

1. We should pay more attention both at laparotomy and at post mortem to the diameter of the S.M.A., which may be as important as a coronary or renal artery in the preservation of life. By correlating lesions of this artery with the clinical history of the patient we shall find out whether or not this is true.

2. Any shocked elderly patient with peritoneal signs should be suspected of having a mesenteric infarction until proved otherwise and, if there is no obvious contra-indication, should be treated by plasma replacement, sterilization of the bowel and vaso-dilator drugs.

3. We should be less hesitant to reconstruct chronically stenosed visceral arteries.

CONCLUSION

In this lecture I have tried to give some idea of the various ways in which the intestine can behave when its blood supply goes wrong, and to suggest that this may happen more frequently than has been suspected in the past. From a number of clinical and experimental observations I have drawn the following conclusions.

Acute occlusion of the superior mesenteric artery is still usually fatal and one factor in the causation of death may be plasma loss. The treatment of choice is reconstruction of the blocked artery, but this carries a danger of severe haemorrhage into the bowel.

Acute occlusion of distal intestinal vessels occurs quite commonly and produces a picture which may be confused with Crohn's disease or segmental forms of ulcerative colitis.

Chronic occlusion of the superior mesenteric artery gives rise to intestinal angina, which is an important symptom to recognize because it carries a bad prognosis. A reliable diagnostic test is needed, but it has proved extremely difficult to produce such a test in the laboratory.

Finally I have introduced the concept of " intestinal failure " and suggested that we may underestimate the role of the intestine as a limiting organ in human shock.

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