from opening up new possibilities in steroid chemistry and therapeutics. As the new hormones have such profound and fundamental effects upon the metabolism of the human body, it behoves us to scrutinize most carefully the indications for the use of this potent therapeutic agent, and to adopt means to ensure that the incredible power now placed in the hands of the medical profession should not be abused by the ignorant and the reckless.

**MESENTERIC VENOUS THROMBOSIS**

**CAUSATION OF ASSOCIATED HAEMATEMESIS**

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**CASE REPORT**

Sixpence M., a 35-year-old Mashangaan farm labourer, came to the Medical Out-Patients' Department on 3 April 1951 complaining of a bloody diarrhoea of 1 day's duration. One week before admission he felt ill and feverish, with occasional headaches. He took his meals regularly and his bowels acted normally. Three days before, he had experienced cramp-like pains over the whole abdomen; the pain was constant and severe, and maximal in the left lower quadrant of the abdomen; he did not vomit. On the day prior to admission he developed diarrhoea, passing frequent bloody and mucoid stools without formed faeces; he had no further complaints, and the previous and family history was non-contributory.

**Examination.** The patient looked ill and he appeared anaemic. There was no cyanosis or jaundice.

- **Pulse.** 130 per min.
- **Temperature.** 97.4°F.
- **Respiration.** 22 per min.
- **Blood pressure.** 135/100 mm. Hg.

The heart, lungs and central nervous system were normal.

**Abdomen.** Moved on respiration; moderate distention, no visible peristalsis; the hernial orifices were normal. There was guarding over the whole abdomen, but no pronounced rigidity. The spleen was enlarged, about three fingers' breadth below the costal margin. Shifting dullness was present in the flanks; no peristalsis on auscultation. Per rectum there was no palpable abnormality, but fresh blood was present on the examining finger.

The diagnosis of typhoid fever, mesenteric thrombosis, and dysentery, in this order, was provisionally made by the physician.

**Laboratory Investigations: Blood Count.** Haemoglobin, 90%; white blood count, 13,100 per c.mm.; polymorphs, 86%; lymphocytes, 3%; monocytes, 16%; others, 1%.

There was a shift to the left.

**Urine Analysis (Catheter Specimen):** Specific gravity, 1025; albumen, plus; no sugar; trace of acetone. Microscopic examination of the urine revealed casts, and a few white and red blood corpuscles.

**Plain X-ray Photograph of the Abdomen:** Erect: No gas under the diaphragm; some gas in the small bowel not considered of pathological significance.

**Differential Diagnosis.** It was obvious that the patient was suffering from an abdominal catastrophe. Typhoid Fever with perforation, sub-acute intestinal obstruction becoming acute, intussusception, and mesenteric vascular occlusion were considered, but no definite pre-operative diagnosis was made. The pulse was recorded hourly. Two hours after admission the pulse had increased to 140 per minute, and the blood pressure had decreased to 115/80 mm. Hg., and on consultation laparotomy was decided upon. Pre-operatively a Ryle's tube was introduced into the stomach, and 250 c.c. of dark brown fluid was aspirated. A benzidine test gave a strongly positive reaction for blood.

**Operation:** Anaesthetic. Intra-tracheal gas, oxygen and ether.

A long left paramedian incision was made. On opening the peritoneum, roughly about 1 litre of bloody fluid escaped. The descending colon was black.

The infarct commenced with a sharp line of demarcation in the middle of the transverse colon, extending the entire length of the descending colon.

Distally, about 2 inches of the intra-peritoneal portion of the recto-sigmoid was unaffected, the line of demarcation again being quite abrupt. The veins of mesentery of the sigmoid were palpably and visibly thrombosed.

The liver showed no gross signs of cirrhosis, but the spleen was enlarged to about twice its normal size and congested, and the splenic vein was thrombosed as well as the inferior mesenteric vein; the portal vein was not visibly or palpably affected: unfortunately the short gastric vessels were not inspected.

The patient's condition had deteriorated in spite of blood transfusion. The descending colon, together with half of the transverse colon, was quickly removed, the line of section being through normal tissue, but no primary anastomosis was attempted. Sufficient, viable large bowel remained distally to exteriorize the distal segment. Proximally the transverse colon was exteriorized as a terminal transverse colostomy, and the abdomen was closed with drainage.

Post-operatively heparin was introduced into the vial of dextrose and saline, and penicillin and streptomycin were also given.

Fluid intake and output were regulated. The patient's condition improved rapidly; on the third post-operative day the clamp on the transverse colon was removed, the colostomy functioning immediately.

One month after admission, after preliminary sulfasuccidine therapy, the continuity of the bowel was restored, by open anastomosis of the transverse colon to the rectum. At this operation the spleen appeared normal.
Control barium enema 3 weeks later showed no constriction at the anastomosis. The patient was discharged fit, 2 months after the first admission.

GENERAL CONSIDERATIONS

History. In 1876 Hilton Fagge published a report of a case of mesenteric venous occlusion. Prior to this, Tiedemann in 1843, and Virchow in 1847, published cases of mesenteric arterial occlusion. Pfiellet is reported by Elliot as being the first to perform a successful resection for venous occlusion in 1890. In 1898 Koster in his inaugural address at Gothenburg reviewed the literature, and described three further cases of mesenteric venous occlusion. Since then many successfully treated cases have been described.

Anatomy. The arterial and venous vascular patterns are now well known. With very minor alterations the venous drainage of the large and small bowel is patterned on that of the arterial supply, except that the venous collateral circulation is much richer than the arterial collateral circulation.

Etiology. Often there is no adequate cause discoverable (Eliot). This is the so-called primary group of cases. There are two main factors responsible for secondary mesenteric thrombosis. They are:

1. Portal obstruction, and
2. Peripheral Sepsis.

Rarer causes are due to conditions predisposing to thrombosis, such as blood diseases (polycythaemia vera), and post-operative stasis, as first described by Maylard; Bauer has reported its occurrence after paravertebral block of the sympathetic ganglia.

It has been reported following trauma, and after ingestion of phenolphthalein (Held and Goldbloom).

PATHOLOGY

1. Relative Incidence of Mesenteric Venous Occlusion. Venous and arterial occlusion probably occur with about equal frequency, though Boyd; Donaldson and Stout; and Eisenberg and Schlink, feel that venous is more common than arterial occlusion, while Milch and Masotti feel that arterial occlusion is the more common.

At laparotomy the macroscopic diagnosis of venous occlusion is more difficult to make than arterial. The patient is usually very ill, and the surgeon, pressed for time, proceeds with resection of the gangrenous bowel without differentiating between the venous and arterial varieties.

Hence in many cases no final decision is made as to whether the occlusion is venous or arterial.

2. Site of Occlusion has an important bearing on the clinical signs (see later). At operation these patients are usually very ill, and to spend valuable time on exact location of the occlusion is not justifiable. In many case reports, the site of occlusion is omitted, or merely stated as, 'the veins corresponding to the infarcted area'.

Occlusion of the inferior mesenteric vessels is a rare occurrence. Milch and Masotti state that the superior mesenteric artery is involved forty times more often than the inferior mesenteric artery.

Thrombosis of the inferior mesenteric vein is very rare; Jackson, Porter and Quinby state that of cases with venous mesenteric occlusion alone, 99% occur in the superior mesenteric vein.

Infarction following thrombosis in superior mesenteric veins occurred in only 91 of 137 cases referred to by Eisenberg and Schlink. As the venous collateral circulation of the inferior mesenteric vein is more elaborate than that of the superior mesenteric vein (Milch and Masotti), thrombosis of the inferior mesenteric vein, followed by infarction of the descending colon, is exceedingly rare. Milch and Masotti, Eisenberg and Schlink, and Brady refer to cases of inferior mesenteric venous occlusion without infarction.

Whittaker and Pemberton, Laufman and Scheinberg describe cases of inferior mesenteric venous thrombosis, without stating whether infarction occurred or not. Koster in 1898 described a case of inferior mesenteric venous occlusion followed by infarction of the large bowel, a case very similar to the one presented, and reference to a case, possibly with infarction, was made in the American literature (Warren and Eberhard).

In the operation of total pancreatectomy, Ian Aird states that the inferior mesenteric vein can be ligatured with impunity, and in certain operations for portal hypertension, this is also a recognized procedure.

It seems, however, that interruption of the inferior mesenteric vein is not absolutely devoid of danger.

3. Results of Mesenteric Occlusion. Occlusion of either type need not necessarily lead to infarction of the bowel. Cases of both arterial and venous occlusion are described in which the collateral circulation was sufficient to prevent infarction. The infarction caused by both venous and arterial occlusion is haemorrhagic.

In experimental animals, Scott and Wangenstein found that venous occlusion was more rapidly fatal than the arterial variety, but in human beings, Warren and Eberhard, Brown and others, have shown that venous occlusion is a relatively slower process and consequently less rapidly fatal.

CLINICAL FEATURES

It is not within the scope of this paper to deal with these in detail. Only a few remarks about mesenteric venous thrombosis in general will be made.

Donaldson and Stout, Brown, Whittaker, and others, are of the opinion that venous mesenteric thrombosis is a definite clinical entity; there is a slower onset of symptoms which suddenly become acute and present as an 'acute abdomen' resembling intestinal obstruction. Pain, localized or general, is always present; cramplike before becoming continuous when peritonitis supervenes; constipation or diarrhoea may be present. Donaldson and Stout state that occult blood can always be found in the stools. Vomiting is not always present. When it occurs it contains blood in 16% of cases, according to Reich.

Moderate distention of the abdomen and rigidity (less than expected in relation to the pain) occurs. Sometimes thickened coils of intestine can be felt as an indefinite mass, with evidence of bowel obstruction. On rectal examination there may be blood on the examining finger, and occult blood is always found on examining the stool (Donaldson and Stout). In the later stages of the disease the picture is that of a neglected intestinal obstruction (Moore).
**Diagnosis.** Only in 4% of Trotter's series was the condition diagnosed pre-operatively.

The presence of occult blood or fresh blood in the stools after an enema is an important diagnostic point.

**Prognosis.** The mortality rate is very high, about 60%, but Murray, in a recent report on six cases, treated by resection and heparin subsequent to operation, lost only two patients from unrelated causes.

**TREATMENT**

The precise diagnosis is seldom made confidently pre-operatively, and as surgical treatment has been proved to be life-saving, this is the treatment of choice.

Luke, d'Abreu and Humble, Murray, and others, have stressed the use of heparin in conservative treatment, but Laufman is of the opinion that anti-coagulants must be reserved for cases following resection, the danger of increasing blood loss into the lumen of the bowel being too great in conservative treatment.

Anti-coagulants have a place in the post-operative therapy, notwithstanding the findings of Moses that administration of heparin and dicoumarol in adequate doses to delay coagulation, was not sufficient to prevent development of experimental intra-vascular thrombosis, in the presence of stasis of the venous circulation, as induced in mice experiments.

**DISCUSSION**

1. **Haematemesis.** Warren and Eberhard state that its occurrence is a highly valuable diagnostic point and of some prognostic value. It generally occurs rather late and is apt to indicate a lesion high up in the jejunum, large in extent and not amenable to treatment.

In the author's case no haematemesis occurred, but there was blood in the gastric contents, without any involvement of the jejunum. An alternative explanation to a lesion in the jejunum had to be found. It would seem that, due to the splenic vein thrombosis, there was a greater flow of blood through the short gastric veins, causing congestion of the mucosa and the appearance of blood in the stomach. Alternatively there was an extension of the thrombosis into the vasa brevia, with commencing infarction of the stomach wall.

A case described by Larson is interesting. This patient had a fatal haematemesis; at autopsy the superior mesenteric vein was normal, but there was an old thrombosis of the splenic vein with more recent thrombosis in the inferior mesenteric vein and the veins over the stomach wall.

A case of Geppert's, described by Warren and Eberhard, further illustrates this point. The patient had a haematemesis, the stomach mucosa was haemorrhagic, and there was thrombosis of the portal and splenic veins, with infarction of the jejunum. Cabot also demonstrated a somewhat similar case: Mallory, giving the autopsy findings, demonstrated venous thrombosis of about 2 weeks' standing in the portal and splenic veins. A compensatory circulation had developed between the spleen and the gastric plexus. This circulation had developed too slowly to prevent infarction of the spleen. He concluded by stating that if the patient had lived long enough he would have developed oesophageal varices. In this case there was no haematemesis.

On reviewing the literature on haematemesis in venous mesenteric occlusion, the following interesting facts come to light; Warren and Eberhard quote Reich as saying that haematemesis occurs in 16% of cases. Of their own 75 collected cases, haematemesis is stated to have occurred in only 3 cases. In 2 cases the splenic vein was thrombosed.

In Larson's 15 cases of venous occlusion, haematemesis occurred only twice and in both instances the splenic vein was thrombosed.

Of 30 other cases described in the literature, haematemesis occurred only in 2. In the cases of Fagge, and of Rolleston, the splenic vein was thrombosed in both instances.

In all cases with haematemesis, the splenic vein was thrombosed. On the other hand, splenic vein thrombosis is not necessarily followed by haematemesis, as shown by Cabot's cases.

An alternative explanation of the haematemesis in venous mesenteric thrombosis thus presents itself, namely that it follows splenic vein thrombosis.

2. **Thrombosis of the Inferior Mesenteric Vein.** This condition rarely occurs. Milch and Masotti, Eisenberg and Schlink and Brady have described cases without infarction.

When thrombosis of the inferior mesenteric vein occurs it is rarely followed by infarction.

A case with infarction is described: one from literature recorded, and one which the author could not verify.

**SUMMARY**

A case of thrombosis of the inferior mesenteric vein followed by infarction of the colon descendens is described. The patient recovered after resection of the infarcted bowel.

An alternative explanation is submitted for the haematemesis which sometimes occurs.

My thanks are due to Prof. J. K. Bremer for drawing my attention to the exact diagnosis at laparotomy; and to Dr. W. Waks for permission to publish this case.

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Camoquin in Malaria

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Camoquin is chemically known as 4' (3'—diethylamino–methyl—4'—hydroxyanilino)—7—chloroquine.

It is supplied as the dihydrochloride dihydrate, a light-yellow crystalline powder which forms a 5% solution in water at room temperature. It was first reported by Burckhalter, et al., at the meeting of the American Chemical Society in 1946.

Dosage Schedule

For therapeutic purposes the dosage recommended is:

**Adults.** Three tablets (a total of 0.6 gm.) taken as a single dose. In regions or circumstances where an increased dose is deemed expedient, the recommended single adult dose is 3 to 5 tablets (0.2 gm. each) depending on the weight and condition of the patient.

**Children.** 10 mg. per kg. of body-weight, or at 1–2 years half a tablet; 3–5 years 1 tablet; 6–15 years 2 tablets; over 15 years adult dose.

As the result of field studies, it is universally accepted that the single dose produces more favourable results than the same or even larger amounts given in divided doses. The drug is claimed to be of low toxicity and the manufacturers state that it may be safely given to the normal adult in doses of 0.4 gm. 3 times a day for a period of 5 days should this be considered necessary.

**Suppressive Dose**

**Adults.** Three tablets (0.6 gm.) taken as a single dose every two weeks.

**Children.** According to age.

It is claimed that this dosage affords protection against an acute attack except in areas where malaria is highly endemic or during the period of high virulence that is associated with a malaria epidemic.

It is stated that the drug has proved successful in benign tertian, quartan and malignant tertian fevers. It is rapidly absorbed from the gastro-intestinal tract but is excreted slowly. It produces an effective blood-concentration within an hour of its oral administration.

**Results of Clinical Trials**

At the instigation of one of us (M.L.F.) supplies of camoquin were made available for a controlled series of trials at the Jubilee Hospital, Francistown, where the clinical investigation was carried out solely by the other author (W.E.L.). In this district malignant tertian malaria can be stated to be almost endemic, though subject to exacerbations during the rainy season.

All the patients were Africans and were treated in hospital. All had positive blood smears before treatment and were given 3 tablets of camoquin (0.6 gm.) on the day of admission, except cases 14 and 23, both children of 18 months who were given 1 tablet each. Blood smears in each case were repeated 24 hours and 72 hours after receiving the camoquin. There were no toxic symptoms attributable to the camoquin. No cases of cerebral malaria or of blackwater fever are included in this series.

Table I summarizes the results, all cases other than case 13 (which was benign tertian) being malignant tertian fever.

**Special Remarks about Cases**

**Case 3.** This patient had an acute exacerbation of chronic malaria, and responded poorly to camoquin. She was discharged at her own request after a week in hospital, and was given quinine on discharge. Five days after discharge she reported again and was subjectively and objectively well, except for slight anaemia.

**Case 13.** This patient had benign tertian malaria, rather a surprising finding. However, the response was prompt and good.

**Case 14.** A child aged 18 months. Malaria and bacterial pneumonia. Treatment for the pneumonia was by sulphadiazine and penicillin. Blood smears remained positive, and as the mother requested the discharge of the child, quinine was given as out-patient treatment. Three weeks after discharge the child reported again, and the mother stated that it had been healthy since discharge. This case has, therefore, been recorded as a cure.

**Case 17.** This man developed a typical rigor on the day after his first dose of camoquin. Therefore 2 tablets of camoquin were given the same evening, and produced a cure.

**Case 18.** This patient's second smear was negative, but the third was again positive. She was symptom free by the fourth day, but showed symptoms again on the fifth day. Thus camoquin, tablets 2, were given on the fifth day, with a good response and recovery.

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