and his co-workers, while emphasizing defects of treatment with these antiseptics, nevertheless stated that "pus was generally very small in amount, and even where it had been present it usually rapidly diminished in quantity. . . . Any spreading infection that already existed generally subsided quickly. . . . The patient is apparently protected in some way from the absorption of toxic products"—surely no mean achievement. Recently in the Middle East Mitchell and Buttle have dealt with "wounded men who, either in spite of chemotherapy or more probably owing to its inadequate application, arrive at the base with their wounds in a grossly infected and purulent condition. In these cases the sulphanilamide drugs can do no more than prevent the spread of infection and they have comparatively little influence on the course of the local suppuration." The wounds were commonly deep or extensive, often involving bones or joints. The novel procedure of applying proflavine in dry powder form was adopted, it being spread over the whole surface of extensive wounds or cavities—never exceeding 2 g. in any case, and usually only about 0.5 g. or less, depending on the size of the lesion. It was never employed on more than two or three consecutive occasions, at intervals of 4 to 28 days. Most patients found the dressing painless. Improvement followed proflavine irrespective of the type of infective organism; and good results might be attained in cases which had failed to respond to one of the sulphonamide series. No other drug was as effective as proflavine in controlling or eliminating staphylococcal infection. Oily preparations of proflavine oleate, originally used by Berkeley and Bonney for dressing large raw surfaces, are also valuable—e.g., on septic sites preparatory to radium therapy (Charteris, 1937).

Influence on Healing

After 4 to 7 days' treatment a yellowish fibrinous membrane often covered the wounds (Carslaw; Drummond and McNee; Colledge *et al.*). At this stage the flavines had fulfilled their therapeutic purpose in preventing or overcoming sepsis, and a change of treatment was indicated—e.g., on using eusol the pellicle disappeared, while granulation and growth of epithelium proceeded (Carslaw). Bashford and his collaborators, working at the Surgical Observation Hut organized by Surg. Gen. Sir George Makins, picked for trial with the flavines 50 patients of whom they said "almost all had been treated previously at the front by the Carrel-Dakin method within 24 hours of being wounded, and, in the majority of instances, very efficiently." The reason for this selection of cases already effectively treated by another method is hard to explain. However, despite the beneficial effects mentioned above, they chiefly dwelt on the delay in all the processes of repair; later, this work was quoted extensively by Makins (1922) in the *Official History of the War*. Pilcher and Hull, writing at the time from their own experience of over 5,000 cases in military hospitals, made the following comment: "For ease of preparation and application, rapidity when dealing with large numbers of cases, complete absence of surgical fidget, early cleaning of the wounds, and abatement of constitutional reaction to absorption, flavine is an admirable application under all circumstances, but especially where surgeons are few, time is short, and wounds are many." The factors in treatment which may retard healing have not yet been fully defined. Bennett did not experience it in over 600 cases. In tissues from this series Blacklock found mitoses of various cell types at levels of 1/50 to 1/5 mm. below the actual growing surface. The margin between the optimum and too high a concentration of the drug due to frequent renewal or evaporation may be narrow. A modified treatment consisting of less frequent applications and weaker solutions—1 : 5000 or under—in later stages has not been widely enough tried. Mitchell and Buttle attributed possible interference with healing to proflavine powder only once in 80 cases.

Conclusions

1. Aminoacridine ("flavine") compounds were introduced as surface chemotherapeutic agents for wounds because they combined outstanding antiseptic properties with relatively low toxicity, as demonstrated by simple methods *in vivo* and *in vitro*. Later tests *in vitro* have yielded discordant results *inter se*, which throw doubt on their value as a practical means of selecting drugs for such purposes.

2. Proflavine is the precursor of acriflavine, and so cheaper. Also, while equally antiseptic, proflavine is the less toxic generally, and especially is very little harmful to brain tissue. Recently introduced members of the series may prove even more suitable for therapy.

3. It has been shown under experimental conditions that the flavines when applied to the tissues at the site of inoculation are highly effective in preventing the development of infection with various organisms, including streptococci and certain gas-gangrene anaerobes.

4. Also, there is good clinical evidence that they can control established suppuration in wounds. This may occur where drugs of the sulphonamide group have failed.

5. Retardation of granulation and healing tends to follow continued use of the flavines, so that it may be advantageous to resort to other treatment later. But the point important practically is the capacity of the flavines to prevent or control infection. This so-called "pickling" or "cold-storage" effect has enabled wounded men to be transported without re-dressing, in the fair likelihood that their wounds would remain *in statu quo ante* as regards infection.

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HERNIA THROUGH THE FORAMEN OF WINSLOW, EMERGING THROUGH THE GASTRO-HEPATIC OMENTUM

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Hernia through the foramen of Winslow into the lesser sac is one of the more uncommon abdominal surgical conditions, and the re-entry of the herniated bowel back into the general abdominal cavity through the lesser omentum appears to be still more rare. The transverse colon probably acts as a barrier to herniation. The anterior and posterior boundaries of the foramen during life are in direct contact, and the opening is a slit-like passage (Cunningham's *Anatomy*, 7th ed., p. 576).

Moynihan and Dobson (1906) state that herniation through this foramen requires one of the following conditions: (a) a common mesentery of the whole intestine; (b) absence of

secondary fusion of the ascending portion of the colon; (c) an abnormally large foramen; (d) abnormal length of mesentery and consequently marked mobility of the intestine. These writers call attention to the unlikelihood of a hernia into the lesser sac because of the normal anatomical conditions at the potential "foramen."

Since 1910 29 cases of internal herniae have been seen at the Mayo Clinic; of these one occurred into the lesser sac (Mayo *et al.*, 1940). Silverstone (1939) describes a case. He states that it is unlikely to occur in a normal abdomen. The condition is more common in men than in women—28 of the former to 11 of the latter. In his view there are two clinical groups: acute, with intestinal obstruction; chronic, with digestive symptoms for years. The small intestine is twice as often involved as the large bowel, and the site of strangulation appears to be at the margins of the foramen, which in Silverstone's case was enlarged and admitted the index and middle fingers at the time of operation. It was found possible to reduce the hernia, but the patient died a few hours later. In Mitchell's (1938) case the caecum, appendix, and 9 in. of the lower ileum had passed into the lesser sac in a male infant of 15 months. After reduction of the bowel at operation the foramen admitted the forefinger with difficulty. In Barrington-Ward's (1937) series, in the case reported by Haw the involved portion of bowel (lower part of ileum, caecum, and appendix) could not even be reduced at the necropsy till the gastro-hepatic omentum had been divided.

Cases in the Literature

Four cases occur in the literature which seem to resemble the one described below. The first is that reported by Treves (1888), in which a coil of colon had entered the foramen and forced its way through the lesser omentum so that the vermiform appendix was actually lying on the anterior aspect of the lesser curvature of the stomach, close to the oesophagus. In Copenhagen's (1923) case the caecum and ascending colon had a long free mesentery: after entering the lesser sac, rupture had occurred through the anterior leaf of the lesser omentum and they were hanging down in front of the stomach. It was found impossible to reduce the hernia, but later a fatal volvulus developed. In that of Rock Carling and Smith (1925) the patient had been perfectly well the previous day. The following morning he felt rather sick, and towards night there was severe pain. This pain was extreme, and sitting up in bed tended to give some slight relief. He was admitted to hospital on the third day, when a leaking gastric ulcer was diagnosed. The pulse was 68 and the temperature 97° F. There was some tenderness in the upper abdomen, but this was not pronounced. At operation a loop of small bowel was seen to have herniated through the foramen of Winslow and then re-entered the general abdominal cavity through a gap in the gastro-hepatic omentum. The gut was reduced and the rent in the omentum repaired. The bowel involved was the middle 20 in. of the ileum. The mesentery was unduly long. Post-operative recovery was complete. In Schmilinsky's (1919) case a similar condition was found, and this patient was operated on successfully. Some similar features were also observed by Blandin (1834), but in this case the gut after entering the lesser sac had left it and then re-entered the lesser sac through the transverse mesocolon.

This type of hernia is accompanied by a considerable mortality. In Rendle Short's (1924) series of retroperitoneal herniae 24 were through the foramen of Winslow; 6 men were not operated on, but died of strangulation; 11 died in spite of operation; and 7 survived. Souttar (1940) states that it is fortunate that internal herniae are rare, since if strangulation does occur the condition is almost invariably fatal.

A fifth case of this type of herniation is now placed on record.

History of the Present Case

A young guardsman aged 26 was admitted to a Service hospital with a history of dull, aching, non-radiating pain in the upper abdomen of some eight hours' duration. About two hours after the onset he had vomited twice; this vomit consisted of food, and no blood had been seen. No constipation was present, his bowels having been opened the previous day. A few similar attacks had occurred in the past. On admission

the pulse was 64, temperature 98° F., and respirations 21; the blood pressure was 120/96. Abdominal examination revealed some tenderness and resistance in the upper part, but the respiratory excursions were maintained. Liver dullness appeared normal. The other systems showed no abnormality. A few hours later his general condition worsened: generalized abdominal rigidity and tenderness set in; the liver dullness disappeared; the pulse, after falling, increased considerably; and the systolic blood pressure dropped to 90. A transfusion with plasma was given, and laparotomy was performed under local anaesthesia followed by oxygen and ether. The abdomen contained much blood-stained fluid and, in the right upper quadrant below the liver, a large mass of engorged haemorrhagic small bowel. The bowel was seen to pass through the foramen of Winslow, which easily admitted one finger. The patient collapsed on the operating table, and attempts at resuscitation failed.

At the post-mortem examination the abdomen was found extremely distended. The heart was normal apart from some terminal dilatation, the mitral valve taking three fingers and the tricuspid four; the aortic and pulmonary valves were also normal. The lungs showed some congestion. An increased amount of thymus tissue was present. The abdominal cavity contained much blood-stained fluid, and lying under the liver were loops of strangulated small intestine which had passed through the foramen of Winslow and then re-entered the general abdominal cavity through an opening in the lesser omentum (see Fig.). The site of strangulation was seen to be

at the opening in the omentum and not at the margins of the foramen. The bowel involved in the strangulation was the lower ileum except the terminal 12 in., and it measured 6 ft. The proximal portion of the bowel was much distended and congested. The stomach was ballooned out, and contained 1½ pints of fluid and undigested food. Liver, spleen, kidney, suprarenals, urinary bladder, and prostate showed nothing of note, and the brain was normal.

The strangulated portion of bowel could only be reduced with difficulty, but it was not necessary to divide the lesser omentum. After reduction the mesentery was seen to be unduly long. The foramen of Winslow was dilated, taking two fingers easily; no rounded anterior margin was present, but there was a dense band of fibrous tissue stretching between the gall-bladder and the first part of the duodenum; this appeared to blend with the lesser omentum (see Fig.). The bile duct, portal vein, and hepatic artery were present in the lesser omentum, occupying a position midway between the free margin of the fibrous band and the right lateral wall of the artificial opening in the lesser omentum. The breadth of the band of fibrous tissue from the cystic duct to the free margin measured 4 cm. The further opening into the lesser sac was immediately beneath the opening in the lesser omentum. The artificial opening in the omentum measured 1.5 cm. in length by 1.25 cm. in breadth. No fluid, blood adhesion, or other abnormality was seen in the lesser sac.

Discussion

The slow pulse rate was rather unexpected. The condition of the patient on admission was undoubtedly serious, and yet the rate was only 64, with a further drop later. It did not increase till a few hours before death. A slow pulse rate was also present in Rendle Short's case. This degree of bradycardia may clinically be misleading, and is possibly due to the close association between the nerve supply of the site of the artificial opening in the lesser omentum and the innervation of the heart. The site of the strangulated coils in the present case varies slightly from that of the cases described by others. In our

case no coils were overlying the stomach, the amount of intestine was greater, and there was the extreme gastric distension which would push the strangulated bowel towards the right lobe of the liver.

The herniation itself presents interesting features which merit consideration—the opening in the lesser omentum and the accessory band of tissue between the gall-bladder and the duodenum. Prof. Blair has given us his opinion of these. The aperture in the lesser omentum is not likely to be congenital; it is more likely to be “acquired.” He has not seen such a congenital defect, nor does he know of any developmental reason why it should occur. In the dissecting-room the lesser omentum is of so delicate a nature that one can imagine it would be readily torn by any hernia spreading within that part of the lesser sac. Indeed, in the anatomy room the lesser omentum is often torn through at the first attempt to pull down the stomach a little in order to explore the region between it and the liver. The band of tissue between the gall-bladder and the duodenum was an unusually well-developed example of the hepato-duodenal fold, which is not infrequently present to a lesser degree and represents a thinned-out part of the lower free border of the ventral mesentery of the fore-gut, which amounts to a prolongation, rather further to the right than usual, of the lesser omentum. The presence of this cystico-duodenal fold of membrane would produce a funnel-shaped approach to the foramen of Winslow and considerably assist an unusually mobile loop of bowel towards the foramen and into the lesser sac. This appears to us a considered and well-founded explanation of the appearances found post mortem.

The appearance of the foramen at the necropsy led one to suspect that perhaps a loop of bowel had been herniated for some time. Such a condition has been described by Schwalbe (1904) in which strangulation did not occur.

In comparison with herniae into the lesser sac, herniation into paraduodenal fossae is relatively common and the literature on such is now quite voluminous.

Summary

A fifth case of this unusual type of herniation is now described. Three abnormal features were present in the abdominal cavity: (1) a well-developed hepato-duodenal fold which had produced a funnel-shaped approach to the lesser sac; (2) a dilated foramen of Winslow; (3) an undue length of mesentery of the small bowel.

We consider that the first and third factors, in association with the normal peristaltic movements, could produce a dilatation of the foramen and so give rise more readily to the herniation which had ruptured through the lesser omentum.

It is a pleasure to us to express our gratitude to Prof. D. Blair, Regius Professor of Anatomy, University of Glasgow, for his co-operation and help, and to Col. M. J. Williamson, M.C., late R.A.M.C., for permission to record this case.

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Hospitals in the Midlands (especially those in Birmingham), children in Yugoslavia and Greece, and youth organizations are among the beneficiaries under the will of Sir Charles Hyde. He has left £10,000 for the benefit of children in Yugoslavia and Greece, and £2,000 each to the Royal Cripples Hospital, Birmingham, and the Coventry and Warwickshire Hospital. A number of hospitals in Birmingham and Worcester will receive £1,000 each, and £3,000 is for the Ophthalmic Hospital at Jerusalem. The Senate of Birmingham University is to receive £20,000 for enlargement of the students' union, and Clifton College a similar sum for scholarships. The residue of the estate is to be divided equally between the University of Birmingham, Queen Elizabeth Hospital, Birmingham, King George's Jubilee Trust, and Dr. Barnardo's Homes.

USE OF METHEDRINE, A NEW BLOOD-PRESSURE-RAISING DRUG, IN SURGICAL OPERATIONS

REPORT OF A CLINICAL STUDY

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During the last ten years one of us (H.D.) has studied the use of pressor agents to counteract the serious falls of blood pressure unaccompanied by severe reduction of blood volume that often occur during major operations. The pressor effects of adrenaline, ephedrine, pholedrine (veritol), and neosynephrin have been recorded, but none of these drugs is effective for more than 30 to 45 minutes, and repeated injections are often necessary. S-methylisothiurea has recently been reported on (Smirk and McGeorge, 1942), but has the disadvantage that it must be injected intravenously. In a search for an effective pressor agent with a sustained action that could be administered by any route under average clinical conditions we examined methedrine.* This is a sympathomimetic drug, and was chosen because of its relation to pholedrine.

Conditions of Use

Blood pressures and pulse rates were recorded every three to five minutes in 130 operations, many of them major, and in 54 of these the systolic pressure or the pulse pressure dropped sufficiently for the patient to need a pressor agent. Methedrine was used solely in these cases—no other agents or stimulants were given—and was administered when the systolic pressure fell to and remained at 80 mm. or less, or when the pulse pressure was 10 mm. or less; 20 minutes was allowed first for natural recovery. According to Hewer (1943) the systolic pressure during operation should not be allowed to drop below 80 mm. for more than 20 minutes. Methedrine was administered only when the surgeon, anaesthetist, and recorder agreed that the patient's condition required it. If the systolic pressure fell to 60 mm. or less during the operation methedrine was usually given after a few minutes, as such low levels were considered inadequate for the vital processes to be sustained, and if prolonged might lead to surgical shock (McMichael, 1942). The low blood pressure often resulting from spinal anaesthesia is regarded by some as a type of secondary shock (Schuberth, 1936). We found that spontaneous recovery from blood pressures as low as 60 mm. did not occur within 1½ hours.

We wish to point out the necessity for the routine determination of blood pressures in all major operations, irrespective of risk, to anticipate and prevent surgical shock. The behaviour of the patient cannot be predicted. We have seen elderly poor-risk patients survive a splenectomy or a complicated gastric resection with hardly any fall in blood pressure, yet young and moderately fit patients have shown a pronounced fall in comparatively minor operations.

* “Methedrine” is the Burroughs Wellcome and Co. trade mark for N-methylamphetamine, the hydrochloride of which was used in this study. The Continental name is pervitin.