so well to expectation would also correspond so closely to a natural rhythm, or would show so wide a range of variation.

On average the ethyl biscoumacetate group showed a wider variation of prothrombin over the 24 hours than the phenindione group, four patients treated with ethyl biscoumacetate having a range of variation greater than 20%, whilst the greatest range among patients on phenindione was 19%. The variability of the two groups is compared in Fig. 2, where the standard deviation of the readings obtained at each interval of two hours is plotted against time. As in Fig. 1, the ethyl biscoumacetate figures are drawn both including and excluding one case with an unusually low prothrombin level. The only noticeable difference between

FIG. 2.—Standard deviation. Abscissa: hours after administration of anticoagulant. Ordinate: per cent. normal prothrombin.

phenindione and ethyl biscoumacetate is a vertical shift of the curve; the general shape remains unchanged, and each patient shows broadly the pattern of response exhibited in the mean curves of Fig. 1. The ethyl biscoumacetate group does not differ greatly when the aberrant case is excluded.

When allowances are made for differences between individuals and differences in times of day, the residual variation—attributable to uncontrolled factors and errors of determination—is small, amounting to a standard deviation of just over 3% in the phenindione group and about 5½% in the ethyl biscoumacetate group.

Conclusions

An experiment of this kind is laborious and involves considerable inconvenience to the patient. The number of observations has therefore been limited, but the following conclusions may be drawn.

1. Anticoagulants of the ethyl biscoumacetate and phenindione type are effective when given in a single daily dose as soon as the patient is considered to be stabilized.
2. The prothrombin concentration remains at a relatively high level for 8 to 10 hours after administration of the anticoagulant, and falls progressively to its lowest level after about 18 hours.
3. Blood for prothrombin estimations should be withdrawn from any individual patient at approximately the same time of day.
4. Although our investigation has shown a difference in response to the two anticoagulants, our observations are not sufficient to allow an appraisal of their relative merits.

A CASE OF ACUTE PHLEGMONOUS CAECITIS WITH PERFORATION

BY

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Acute phlegmonous caecitis is still regarded as a rare disease, and the condition is not described in standard textbooks. Only approximately 40 cases have so far been reported in the medical press, and most reports originate from practitioners in the U.S.A. The first case of phlegmon of the large intestine was reported by Goldschmidt (1887). Later on Hallopeau and Monod (1919) described the condition under the heading, "Gangrène massive du Caecum." Hagler (1920) reported a case of a dissecting interstitial abscess of the caecal wall. A case of ruptured gangrenous caecum in a child of 8 was reported by Rose (1932). Cox (1944) published two cases of acute gangrene of the caecum. Spivack and Busch (1943) reported two further cases of phlegmonous caecitis. A case of the same condition in a man aged 35 is described by Meyer and Disch (1945); further cases have been reported by McHardy and Browne (1946), Bulmer (1947), Riker, Gilchrist, and David (1949), and Nardell (1949); and Tagart (1953) surveys 21 cases reported during the last 25 years with three further cases.

Pathology

Two types of phlegmonous caecitis have been described by most authors, circumscribed and diffuse. A normal appendix is found in all cases, except when the appendix has become inflamed by contiguity. There are, however, distinct signs of an inflammatory lesion in the right iliac fossa, and, according to the type of the disease, there may be a well-defined thickening of the caecal wall or diffuse induration of the entire caecum. The affected area shows signs of acute inflammation, and ulcers penetrating as far as the serous coat have also been described. Gangrene with perforation and general peritonitis occurred in the case to be reported. On many occasions the lesion has been mistaken for carcinoma. The microscopical picture consists of infiltration by polymorphonuclear leucocytes in the submucosa and to a less extent in the subserosa, muscularis, and mucosa. According to Spivack and Busch the lesion is said to begin as a cellulitis of the submucosa. Streptococci and staphylococci, but also *Bact. coli* and pneumococci, have been isolated, and most authors agree that bacterial invasion of the submucosa following trauma by hard faeces, foreign bodies, fruit stones, or parasites is the most likely cause of phlegmonous caecitis. As additional causes anatomical abnormalities such as a mobile caecum with stasis have been suggested. The possibility of a haematogenous portal of entry has been stressed by Spivack and Busch.

Clinical Features

Most cases of acute phlegmonous caecitis have been diagnosed either as acute appendicitis or as appendix abscess. Most authors agree that a mass appearing in the right iliac fossa early, even in the first 48 hours, may be indicative of the condition. The disease has occurred in children and adults, and it is no more frequent in males than in females. The history is usually short. The diagnosis in the case reported below was made difficult by the fact that the patient was admitted in a diabetic coma. A precise history could not be obtained, and the symptoms of advanced peritonitis became obvious only when the patient started to regain consciousness. A mass could not be palpated.

In the differential diagnosis, in addition to acute appendicitis and appendix abscess, tuberculosis of the caecum, carcinoma, volvulus, and regional enteritis have to be considered.

Treatment and Prognosis

Because of the difficulty in arriving at a correct diagnosis laparotomy is essential at the earliest opportunity. The course of treatment to be taken will largely depend on the type and stage of the disease. Acute phlegmonous caecitis has a tendency to subside and to resolve, but, on the other hand, it may spread and progress to gangrene and perforation with peritonitis. It has been suggested that some cases of appendicitis or of appendix abscess, treated conservatively, may have been cases of phlegmonous caecitis which had resolved without leaving clinically or radiologically traceable sequelae. If a case of circumscribed phlegmonous caecitis without gangrene or perforation has been found at operation, removal of the lesion seems unjustifiable. Closure of the abdomen with or without drainage, followed by adequate chemotherapy, would appear to be the correct treatment for such cases. In the case of imminent perforation Taggart suggests excision of the diseased area and closure of the resulting defect in layers, or suture of the area to the anterior parietal peritoneum. Ileo-caecal resection is recommended by Spivack and Busch for the diffuse type of phlegmonous caecitis or if carcinoma cannot be ruled out. In the case reported below perforation of a circumscribed gangrenous portion of the caecal wall had occurred. The gangrenous area was excised and the resulting defect was used as a caecostomy. Because of general peritonitis the peritoneal cavity was drained.

The mortality in uncomplicated cases of acute phlegmonous caecitis is said to be in the region of 8% ; 45% if the lesion is not limited to the caecum.

Case Report

A married woman aged 23, a diabetic whose condition it had been difficult to control, was admitted to hospital on October 28, 1954. According to her doctor she had been in a coma for the last six hours, and, in view of her previous history, diabetic coma was diagnosed on admission. The usual regime for diabetic coma was begun immediately. It was also found on admission that she was bleeding from her vagina and was having an incomplete abortion. On October 30, two days after admission, she was still semi-conscious, but her general condition had somewhat improved. Her pulse, which had been imperceptible on admission, showed better volume and she appeared generally more responsive. On November 2 she seemed to complain of abdominal pain and she vomited large amounts of bile-stained fluid. She showed signs of an acute abdomen, and a surgical opinion was sought. The patient when seen by me appeared to be extremely ill ; her temperature was subnormal and the pulse rapid and of poor volume. She looked toxic, her tongue was dry, and she seemed to be dehydrated. Examination was very difficult because of her only partial response to questioning. The abdomen was distended and generally tender, and there was guarding and release tenderness in the entire lower abdomen. Bowel sounds were absent and there was no palpable mass. Rectal examination was inconclusive. A slight loss occurred vaginally, the external os admitted the finger-tip, and the internal os was closed. It was impossible to make out the size of the uterus because of her abdominal rigidity and distension. Blood sugar at the time of examination was 112 mg. per 100 ml. ; blood urea, 137 mg. per 100 ml. ; CO₂ combining power, 14.6 mEq/l. There was a trace of sugar in her urine, but no acetone.

Paralytic ileus due to general peritonitis, the cause of which was obscure, was diagnosed and laparotomy was decided upon.

First Operation.—Laparotomy was performed on November 2, under general anaesthesia (thiopentone ; pethidine, 30 mg. ; D-tubocurarine chloride, 10 mg. ; gas and oxygen). A right lower paramedian incision was made, and on opening

the peritoneal cavity a large quantity of thick yellow pus welled up. Advanced general peritonitis was found ; almost the entire small bowel was distended and caked together, with pockets of pus between the loops. It was impossible on first sight to detect the primary cause of the peritonitis. The appendix was found to be normal ; on closer inspection of the caecum a round patch of gangrene, 2 in. (5 cm.) in diameter, was discovered on the outer caecal wall. The affected part of the caecum was almost black, the tissues had begun to disintegrate, and there was a small perforation in the centre of the lesion through which the intestinal contents could be seen to ooze. The lesion was strictly circumscribed and there was no induration of the surrounding tissues. Apart from a few enlarged glands in the ileo-caecal angle and an enlarged uterus, no further abnormality was noticed. There was no sign of a foreign body near the lesion.

The patient's condition had steadily deteriorated during the operation, her pulse had become imperceptible, and when the cause of the peritonitis had become obvious she was practically moribund. The gangrenous part of the caecal wall was quickly exteriorized, the gangrenous area was excised with diathermy, and the remaining opening was used as a caecostomy into which Paul's tube was tied. The peritoneal cavity was drained through the original incision.

Post-operative Course.—After her return to the ward the patient's condition seemed to have slightly improved. Intravenous 5% glucose in physiological saline, which had been started during the operation, was continued together with intravenous chlortetracycline, 250 mg. four-hourly, gastric suction was instituted, and the diabetes was supervised by the physicians. By November 5 her condition had much improved ; intravenous drip therapy and gastric suction were discontinued, and chlortetracycline, 250 mg. orally, was given. She was fully conscious from the second post-operative day, the caecostomy was acting satisfactorily, and by November 15 the paramedian wound was healed. From then her convalescence was quite uneventful ; her diabetes seemed fairly well controlled, the caecostomy was acting less every day, and she started to have normal bowel actions. Because of considerable skin irritation round the caecostomy, which by December 2 had become stationary, it was decided to close the opening by operation.

Second Operation.—Closure of the caecostomy was carried out on December 6. The caecum was dissected out with considerable difficulty because of dense adhesions, and closed in layers intraperitoneally. Her convalescence was again uneventful, and she was discharged healed on December 23. She has been seen fortnightly at the surgical and medical out-patient clinics since ; her diabetes is fairly well stabilized and her general condition is quite satisfactory.

The pathologist's report on a swab taken during laparotomy on November 2 stated : Cultures have yielded a growth of coagulase-positive *Staph. aureus*, sensitive to penicillin, streptomycin, chloramphenicol, and chlortetracycline.

Comments

The fact that the correct diagnosis could not be arrived at sooner was largely because the patient had been admitted in a diabetic coma, which was probably also responsible for the extent of the lesion found at operation. A precise history could not be obtained on admission, and perforation of the gangrenous part of the caecum had probably occurred while the patient was comatose. On reviewing the literature on acute phlegmonous caecitis I was unable to find a case that was complicated by diabetes mellitus. Lowered resistance to infection, so commonly found in this disease, was presumably responsible for the extent of the peritonitis.

Two types of phlegmonous caecitis are usually described, and the case reported was of the circumscribed variety progressing later to gangrene and subsequent perforation with general peritonitis. In spite of the very high mortality for cases of advanced acute phlegmonous caecitis (45%), the patient made a remarkable recovery.

Summary

A further case of acute phlegmonous caecitis is described. The condition is still relatively uncommon and a correct diagnosis is almost impossible. Some authors draw attention to the presence of a mass in the right iliac fossa in the early stages, appearing soon after the onset of symptoms. The case reported was complicated by diabetic coma, which added to the difficulties and probably delayed adequate treatment.

The two types of the disease, circumscribed and diffuse, are described and the respective treatment is discussed. In the case reported, exteriorization of the affected part of the caecum, utilizing the gangrenous part of the caecal wall for a caecostomy, was carried out successfully.

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Medical Memoranda

Dextrocardia, Situs Inversus, and Twinning

A possible relationship between dextrocardia, situs inversus, and twinning has received some attention from geneticists. Thus, Ruud and Spemann (1922) produced situs inversus by division of the amphibian egg, the twin derived from the right half frequently showing this abnormality. This mirror-image mechanism, while a most attractive hypothesis, obviously does not occur in humans, as otherwise the condition would be relatively common. Reports of the incidence of situs inversus vary considerably, LeWald (1925) giving an incidence as low as 1 in 1,400, while Tanner-Cain and Crump (1951) quote an incidence of 1 in 35,000 in the United States Army recruits in 1947. Cockayne (1938) gives a figure of 1 in 19,500, which is probably more accurate, and is in agreement with most figures reported in the literature.

The purpose of this paper is to report an apparent association between dextrocardia, situs inversus, and a family history of twinning in ascendants and collaterals. This occurred in four out of five cases seen in general practice and school medical inspection. The first patient volunteered such a history, and investigation of three other cases, seen over a period of years, tends to confirm this finding.

CASE HISTORIES

Case 1.—A man aged 44. On routine examination in general practice in Lancashire a previously unknown situs inversus was diagnosed. This finding was subsequently confirmed by chest x-ray examination, screening, and barium meal. The mother and father were each one of twins.

Case 2.—A woman aged 48. Situs inversus was found on routine examination in general practice in Lancashire. The existence of this condition had been diagnosed previously as a result of an abdominal operation. Confirmation was

obtained on x-ray and barium-meal examination. (a) The grandmother and grandfather were each one of twins. (b) A sister had twins. (c) An uncle had three sets of twins.

Case 3.—A girl aged 7. Previously unknown situs inversus was diagnosed at a routine school medical inspection in Lancashire. There was, in addition, a systolic murmur in the mitral area, suggestive of a small septal defect. This finding was confirmed by x-ray examination, screening, and electrocardiogram. It is of interest to record that her brother, aged 11, had a precisely similar systolic murmur in the mitral area, but no transposition of the viscera. (a) The father is a twin. (b) The paternal grandmother, twice married, had a set of twins by each husband.

Case 4.—A boy aged 6. Dextrocardia without reversal of viscera was diagnosed at a school medical inspection in Roscommon. There was, in addition, cyanosis of the lips and finger-tips, and a moderate degree of clubbing of the fingers and toes. A loud systolic murmur was audible at the base maximal to the right of the sternum, and a systolic thrill was also palpable. Pulmonary stenosis was the probable diagnosis. However, in view of the complicated necropsy findings in previously reported cases of isolated dextrocardia, it is possible that a more complex lesion may have been present. The diagnosis of dextrocardia was confirmed by x-ray examination and E.C.G. (a) The mother is a twin, probably monozygotic in type. (b) A full cousin, resident in America, has two sets of twins.

Case 5.—A girl aged 10. Previously unknown situs inversus was diagnosed at a routine school medical inspection in Lancashire. It was subsequently confirmed by x-ray examination and E.C.G. This was an adopted child, and it was not possible to investigate the family history.

DISCUSSION

The exact genetic mechanism of situs inversus is in doubt. An association with twinning is mentioned by Doolittle (1907), who observed dextrocardia in a man who had a twin sister; both of his parents were one of twins, and he produced opposite-sexed twins, the boy showing dextrocardia. Foerster (1861) observed that in the majority of conjoined twins, particularly thoracopagi and pygopagi, one had complete or partial transposition of the viscera, and he advanced the theory that in cases of transposition there has been monozygotic twinning, with the subsequent death and absorption of the normal twin. This finding was not confirmed in the conjoined twins of Kano (Aird, 1954). In this instance there was dextrorotation of the heart in the twin surviving separation, but the E.C.G. was not that of a case of situs inversus. It was concluded, therefore, that there was no true mirror-image of the twins. Aird, however, states that 73% of conjoined twins show the latter abnormality.

In an extensive review of the subject, Cockayne (1938) stated that situs inversus is transmitted as a recessive characteristic caused by a single autosomal gene. He cited as proof for this theory, "its familial incidence and general distribution within a family, its occurrence in both members of a pair of monozygotic twins, and the high percentage of first-cousin marriages that give rise to it. In addition, the ratio of affected to normal sibs in the fraternities agreed with that expected of a recessive character." Twinning has long been admitted by both the medical and the actuarial professions to be a hereditary character, and if this association with twinning is accepted it tends to confirm that theory. However, there is some difficulty in explaining the occurrence of situs inversus discordantly in monozygotic twins. This was first reported by Dubreuil-Chambardel (1927) and has since been reported on a number of occasions, the most recent being that of Helweg-Larson (1947) in a pair of male twins. The normal twin produced one child and a pair of twins that miscarried.

Torgersen (1950) published details of 270 cases of situs inversus, discovered by mass radiography in Norway. He collected data concerning the familial occurrence of twinning in 100 unselected cases. He concluded that it did not