Although an E.C.G. taken on June 27 showed no evidence of rotation in the standard or unipolar limb leads (except for a persistent Q₃) and the transition zone in the chest leads had moved back to V₄, it was assumed that further embolism had occurred. Intravenous heparin, 10,000 units, was given six-hourly instead of by the intramuscular route, and no further embolic episodes were observed.

On June 29 his blood pressure appeared to be stabilizing at about 160/80, and the strength of the infusion was gradually diminished, until it was stopped on July 3. A temporary fall in blood pressure to 85/50 necessitated restarting for about 24 hours, after which the infusion was permanently discontinued, and his blood pressure gradually became established at about 110/60.

The course of his illness was additionally complicated by moderately severe haemorrhage from the gastro-intestinal and urinary tracts (after the infusion had been stopped), due to temporary difficulties in adjusting his anticoagulant treatment, and by severe thrombophlebitis of the successive veins used for his infusion. Recovery from the acute cardiopathy was considered to have been reached by July 23, and he was discharged home on August 4.

Comment

Pulmonary embolism continues to remain the most sinister and justly dreaded of post-operative complications. It still robs surgeons of the fruits of careful and technically excellent operations, and it is a deadly interloper in many other spheres of medicine.

Apart from the supremely important problem of prophylaxis, any contribution to the treatment of a condition with a fatality rate of at least 33% is to be welcomed. The use of L-noradrenaline appears to be just such a contribution, and deserves to be widely appreciated. Although many readers are doubtless well aware of its value, the extreme paucity of references in the literature to its use in acute cor pulmonale would seem to justify presentation of a further case so treated.

There would appear to be a definite place for the use of L-noradrenaline in domiciliary practice. Hunter (1955) comments: "Those who have suffered a massive (pulmonary) embolism with shock and circulatory collapse are not fit to move. . . . Difficult though the treatment may be to carry out in the home, therapy . . . should be carried out there until the patient is sufficiently recovered to withstand the stress of the journey." In such cases, resuscitation with L-noradrenaline could be started in the home, until the blood pressure appeared sufficiently stabilized for the patient to be fit for transfer to hospital. The drip could be kept running in the ambulance, and transferred with the patient to the hospital bed. A service on the lines of the obstetric "flying squad" would be required, since Euler (1955) has recently pointed out that, if hypotension is prolonged, vascular responsiveness to noradrenaline is eventually lost, and so the time-factor in instituting treatment is extremely important.

The danger of circulatory overloading by intravenous drip therapy, which is fully recognized in the presence of acute myocardial infarction (Shirley Smith and Guz, 1953), exists *a fortiori* in acute cor pulmonale, where an already well-nigh intolerable burden is placed on the right ventricle, without additional iatrogenic strain. For this reason the maintenance of an effective L-noradrenaline concentration with minimal drip rates is of paramount importance in pulmonary embolism. A delivery rate of a litre of infusion fluid in 12 hours appears to be safe from this point of view.

For short periods, in order to deal with special emergencies producing superimposed hypotension (recurrent embolism, as in this case, or even haemorrhage inadvertently produced through anticoagulant therapy), the concentration may need to be increased by temporarily speeding up the drip rate, when a maximum concentration of the infusion itself is already in use. In this case a concentration of 150 µg. of L-noradrenaline a minute was required on two occasions over a period of about eight hours, by increasing

the drip rate to 2.5 ml. a minute, with an infusion strength of 64 ml. of levophed per litre in use. No circulatory overloading appeared to occur during these short periods, nor any evidence of toxicity, although the manufacturers of levophed do not appear to recommend a maximum strength exceeding one-seventh of the above.

In reporting the only previous case of acute cor pulmonale treated with L-noradrenaline, Wolff (1954) refers to an infusion of 16–20 µg. a minute for ten hours as "large doses." When the rate was increased to 24 µg. a minute toxic symptoms at once appeared. In the case herewith described, the patient had been receiving an infusion concentration of 110 µg. a minute for 30 hours, when recurrent embolism called for greatly increased concentration. Possibly by that time some degree of tolerance to the drug had been established, allowing for increase to 150 µg. without toxic effects.

Summary

In spite of the fact that massive pulmonary embolism, with its attendant state of hypotensive shock, is a common and often fatal emergency, only one reported case of the use of L-noradrenaline in treatment appears to have been published at the time of writing. A second case is reported, illustrating the value of this drug in treatment of the established state and two recurrences, in which a maximum concentration of 150 µg. of L-noradrenaline a minute was required over two periods of eight hours, and in which a total of 798 ml. of levophed was given in eleven days. Profuse sweating was the only evidence of any toxic effect, and recovery ensued. Wide recognition of this form of treatment is urged, including its use in domiciliary practice.

ADDENDUM.—Since this paper was submitted for publication Sibthorpe (1955) has mentioned the use of noradrenaline in a case of antenatal pulmonary embolism.

I would like to acknowledge the unremitting care and tireless attention in supervision of the infusion that was exercised by my house-physicians, Dr. B. Gupta and Dr. M. D. Enoch, and without which the patient's survival would have been most unlikely.

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Medical Memoranda

A Case of Vestigial Gall-Bladder

Apparent absence of the gall-bladder is such a rarity as to warrant its being recorded. In the present case a small nodule in relation to the common bile duct proved to be a vestigial gall-bladder.

CASE REPORT

A retired man of 79 was admitted to hospital on July 25, 1953. He had been well until eight weeks before admission, when he had begun to vomit an hour after his meals. In addition he had continuous nausea and a vague aching epigastric pain. At the same time he had noticed that his stools were pale and that his urine was dark. This was followed by jaundice which progressively increased. These symptoms persisted, and resulted in a considerable loss of weight. One month before admission he noticed generalized pruritus. There was no history of past attacks of jaundice or colic.

Examination showed him to be a thin elderly man, obviously jaundiced, but alert and cheerful. His tongue

was furred, the heart and lungs were normal, and the blood pressure was 150/80. There was no lymphadenopathy. The abdomen was slightly distended, and the liver tender and enlarged three fingerbreadths below the right costal margin. Rectal examination was normal, but the stools were clay-coloured. The urine contained a large quantity of bile. The haemoglobin was 13.9 g.%; white blood count, 9,500, with a normal differential count; blood group, O Rh positive; serum bilirubin, 2.9 mg. per 100 ml.; serum alkaline phosphatase, 30 K-A units; thymol turbidity, 1 unit; zinc sulphate turbidity, 6 units; blood urea, 38 mg. per 100 ml. The pre-operative diagnosis was in favour of an obstructing neoplasm.

Operation.—An exploratory laparotomy was performed by Mr. J. B. Hume through a right paramedian incision on August 6. The liver was enlarged, but no gall-bladder could be seen. The common bile duct, when dissected, was found to be dilated into a tube 2 cm. across, and impacted within it was a single stone. On the right side of the duct at the porta hepatis there was a small body 1 cm. in diameter, which was removed for section. There was no connexion between this mass and the bile duct. The common duct was explored, but no further stones were found; a T-tube was left in the duct.

The patient's post-operative course was uneventful. The jaundice rapidly faded, and the stools and urine returned to normal. Ten days after operation a cholangiogram showed a normal biliary tract, but no trace of a cystic duct or an intrahepatic gall-bladder. When last seen (October 29, 1953) he was well.

Histology.—Section of the mass removed showed it to be a small nodule with a hollowed centre; there was a fibromuscular coat and a mucous membrane having the histological characteristics of gall-bladder mucosa. There was excessive underlying fibrosis.

COMMENT

Anomalies of the biliary tract are common, occurring in about 10% of necropsies, but absence of the gall-bladder is exceedingly rare. Latimer, Mendez, and Hage (1947) collected only 71 cases from the literature; to these they were able to add three of their own. According to Gross (1936) the probable cause is a failure of the caudal portion of the embryological hepatic diverticulum to become tubular.

In our case the bud had become completely separated from its parent stem. In the previously reported 31 cases found at operation, 11, like ours, had an enlarged and dilated common bile duct containing stones. The discovery of this rarity was a welcome finding, and reversed a gloomy prognosis.

We are grateful to Mr. J. B. Hume for permission to publish this case, and to the Pathology Department of St. Bartholomew's Hospital for the histological report.

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Provocative Emetine in Diagnosis of Amoebiasis

It has often been suggested that examination of the stools after a "provocative" dose of emetine may yield a positive result in patients whose stools have previously been negative for *Entamoeba histolytica*. Hill (1946) recommended this method and stated that it was used in the Services as a routine in suspect but unproved cases. He regarded the effect of emetine in small doses as "provocative or stimulatory to the trophozoite." In 1947 he again stressed this, while evaluating various methods of diagnosis for intestinal amoebiasis. Brown (1946) was even more emphatic; he practised this method for eighteen years and found it to "have rarely failed." He stated that when conditions become unfavourable for amoebae (due to emetine) cysts are passed out to seek a more accommodating host.

Uninucleate and binucleate cysts were seen by him, the reason for this, he believed, being that the parasites were "finding a new host in a hurry."

However, Lawrence (1946) and Wenyon (1947) thought this method to be irrational and based on a mistaken analogy with the provocative dose of neoarsphenamine in serological diagnosis of syphilis. Dobell and Laidlaw (1926) reported that, in liquid medium, 1 in 5,000,000 of emetine hydrochloride was lethal to *E. histolytica*. The mode of amoebicidal action of emetine hydrochloride is not well known. However, there is nothing on record to show that emetine in small amounts is stimulatory to the parasite *in vitro*.

The data for or against the use of "provocative" emetine in the diagnosis of amoebiasis cannot be regarded as satisfactory. The object of the present study is to place on record our observation on the value of this method.

MATERIAL AND TECHNIQUE

Two groups were studied. We selected 18 patients who had shown signs and symptoms suggestive of intestinal amoebiasis, but in whom a single stool examination was negative. Three of them had been positive for *E. histolytica* in the past, but the symptoms had relapsed after varying periods of treatment, and two had an enlarged and tender liver. They were given 3 gr. (0.2 g.) of emetine bismuth iodide, and the next day, after a saline purgative—1 oz. (28 ml.) of saturated solution of sodium sulphate—as recommended by Hill (1946), the stools were examined. A similar test was carried out on 18 positive cases of amoebiasis passing cysts or trophozoites, or both, of *E. histolytica*.

In the first group, only one case was rendered positive for *E. histolytica*. Both cysts and trophozoites were found (Table I). The other 17 cases were negative. The test was repeated in the positive case, and after a second dose of emetine the stool was found to be negative.

In the second group only five remained positive for *E. histolytica* after "provocative" emetine (Table II). In the other 13 cases the stools were rendered negative. Even in the five cases which were still positive, the number of parasites was considerably reduced, and they appeared to have degenerated.

TABLE I.—Provocative Emetine in 18 Suspected Cases of Amoebiasis

Positive after provocative dose of emetine	..	..	..	1
Negative	..	..	..	17

TABLE II.—Provocative Emetine in 18 Positive Cases of Amoebiasis

Positive after provocative dose of emetine	..	..	..	5
Negative	..	..	..	13

DISCUSSION

The above study shows that small doses of emetine have no stimulatory effect on *E. histolytica*. On the other hand, they have apparently rendered scanty infection still more scanty and diagnosis more difficult. This is amply borne out in the second group, where "provocative" emetine made the stools amoebae-free in 13 cases and in the remaining 5 the number of amoebae was considerably reduced and they appeared to be degenerating. In one case in the first group, however, *E. histolytica* was found after giving a dose of "provocative" emetine. This may be attributed to the effect of the purgative administered the next day. This method of administering "provocative" emetine cannot be recommended for diagnosis of suspected cases of amoebiasis in which ordinary smear examination is negative.

Our thanks are due to Sri B. M. Chakravarty for his assistance in this work.

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