October, 1960. He has remained perfectly normal throughout, and the last follow-up report, on July 9, 1961, recorded that the child (then aged 1 year 10 months) was happy, was developing normally, and was growing fast. Deglutition was normal, there was no regurgitation, and the usual foods were being taken in the normal amounts.

TREATMENT

In my patient, as a result of experience of the good results I have achieved in a series of adults with achalasia of the oesophagus, I decided to perform Heller's operation through the abdominal route. I always perform the operation in this way, for it provides an easy and adequate exposure of the lower 5 cm. of the oesophagus and the fundus of the stomach.

I consider that drugs are of no real value in the treatment of achalasia. Dilatation, using a pneumatic dilator, may give temporary relief, but many patients require multiple dilatations. For instance, in Clagett's series 26 young patients were treated by dilatation. In four of them one dilatation was carried out, but symptoms recurred in less than a year. The majority required multiple dilatations—three or more—and one patient needed 18 dilatations in 15 years to maintain deglutition. Repeated dilatation is unsatisfactory for children. I prefer one operation, which, when performed correctly, will give excellent results. Clagett more recently stated that six patients were treated by a Heller type of operation, with an excellent result in five and a good result in one.

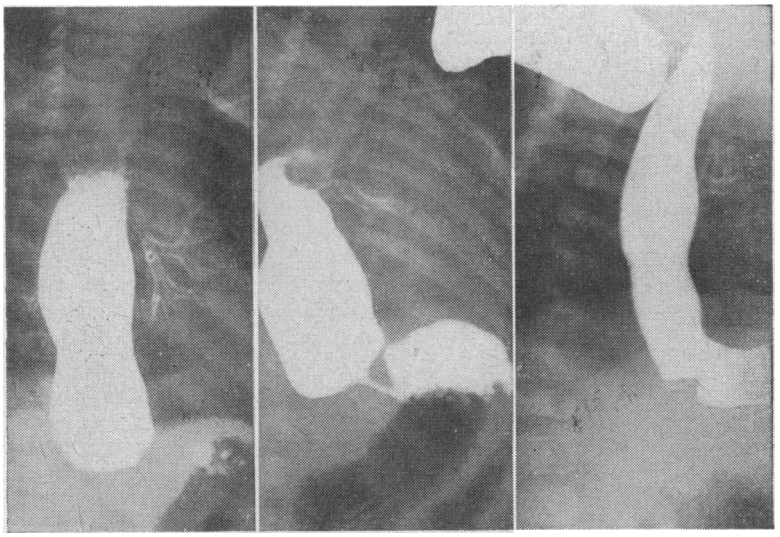

FIG. 1 FIG. 2

FIG. 1.—Pre-operative radiographs of the oesophagus with a barium swallow, showing appearances characteristic of achalasia of the oesophagus (see text).
FIG. 2.—Radiograph of the oesophagus with a barium swallow after Heller's operation. The megaoesophagus has contracted and barium flows freely in a good stream through the cardia into the stomach.

I thank Dr. I. M. Anderson for his helpful co-operation in the treatment of this patient, Dr. L. H. Morris, who gave the anaesthetic, and the nursing staff for their skilful care.

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Medical Memoranda

Peripheral Gangrene in a Case of Myocardial Infarction

Symmetrical peripheral gangrene is a rare complication of myocardial infarction. As illustrated by the case reported here, the gangrene is due to hypotension and arterial spasm in the extremities, not to arterial occlusion.

CASE REPORT

The history of the patient, a man aged 73, was obtained from relatives. He had been well until December 22, 1959, when he suddenly complained of nausea and vomited three times. The next day he complained of chest pain. He remained in bed more or less unaware of his surroundings, having little to eat or drink. On December 25 it was noted that his ears and fingers were blue. His condition remained unchanged until December 30, when he was admitted to hospital.

For five years previously he had experienced chest pain and breathlessness on climbing stairs, and occasionally his fingers had become "dead" and white on exposure to cold. Prior to this illness his health had been excellent and there was no family history of cardiovascular disease.

On examination he appeared alert but could only answer "yes" or "no." He was not breathless at rest. Except for the tips of his fingers and toes his limbs were red and warm. There was superficial gangrene of the toes affecting the skin over the terminal phalanges. The skin of the fingers was similarly affected at the tips for about ½ in. (1.3 cm.) from the nail. A small area of gangrene was present on the septum of the nose. The pulse was regular (100 a minute), the blood-pressure 105/75 mm. Hg, and the respiratory rate 16 a minute. There was no clinical cardiac enlargement. The heart sounds were faint but otherwise normal, and there were no signs of congestive heart failure. All peripheral pulses were palpable. Crepitations were heard at both lung bases, but no other abnormal signs were found in the respiratory system and no abnormality on examination of the abdomen. The tendon jerks were present and equal, the plantar response was bilaterally flexor, and there was no loss of power in the limbs.

The Hb was 105% (15 g./100 ml.), the E.S.R. was raised slightly (22 mm. in one hour Westergren), and the white-cell count was raised to 17,000/c.mm., with a neutrophil leucocytosis. The urine contained a trace of albumin with hyaline casts. The blood urea was raised to 125 mg./100 ml. A chest *x*-ray film showed slight cardiac enlargement, but the lung fields appeared clear. The electrocardiogram showed changes of an extensive myocardial infarct.

He was treated with anticoagulants but not with pressor agents. He survived until January 6, 1960, when he died suddenly.

Necropsy Findings (Dr. J. L. Edwards).—*External:* Edentulous; purple discoloration of fingers and toes; several scabs on back of right calf, 1 cm. each. *Internal:* Fat 2 cm. Atheroma of circle of Willis (moderate). Gross oedema of choroid plexuses. Emphysema. Moderate oedema of lungs. Moderate atheroma of pulmonary artery. Senile changes in heart valves. Petechiae on pericardium. No lumen of left coronary artery could be found over 1 cm. from ostium; heavily calcified. Most of left ventricle was

necrotic and yellow, only reddish portion was towards posterior cusp of mitral valve. Mural thrombus in left ventricle 5 by 3 by 5 cm. Thrombosis of right coronary artery 1 cm. from ostium. Mottling of right ventricle. Gross atheroma of aorta. Slight fibrosis of testes. Diverticulosis of sigmoid. Solid appendix. Prostate measured 3 cm. and showed hyperplasia. Anatomical diagnosis: myocardial infarction; atheroma and thrombosis of coronary arteries; peripheral gangrene. (Dorsalis pedis artery left taken for section.) *Histology:* Heart showed recent infarct and fibrosis. Dorsalis pedis artery appears substantially normal. Lung, spleen, kidney, and pituitary showed little of interest.

COMMENT

In this case the symmetrical nature of the lesions, the presence of all peripheral pulses, and the absence of disease in the artery examined histologically indicate that gangrene resulted from either prolonged hypotension or peripheral vasoconstriction, or both in combination. Non-occlusive symmetrical peripheral gangrene, an uncommon disorder, has been reviewed by Cotton and Bedford (1956). It is nearly always a complication of cardiovascular disease in which there is reduced cardiac output.

The patient was admitted to hospital under the care of Dr. T. E. Gumpert, senior physician, Sheffield Royal Hospital, whom I thank for permission to report the case. I also thank Dr. J. L. Edwards for allowing me to publish his necropsy report.

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REFERENCE

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Fatal Jaundice after Administration of Pheniprazine

A case is presented where the patient developed fatal liver failure after the administration of pheniprazine ("cavodil"), a mono-amine oxidase inhibitor. The significance of certain contributory factors is discussed.

CASE REPORT

The patient, a woman of 43, was admitted to hospital in hepatic precoma in April, 1961. She had been referred to the out-patient department three months previously complaining of chest pain which had the characteristic clinical features of angina of effort, though the electrocardiogram was normal. Pheniprazine was prescribed in a dose of 6 mg. daily. Three weeks before admission, when she had been receiving pheniprazine for two months, she developed intense nausea followed in a few days by jaundice. At this stage she was given, in addition, perphenazine ("fentazin") 2 mg. q.d.s. to combat her nausea, but this and the pheniprazine were discontinued 14 days later when the jaundice deepened. It had been thought that she was suffering from infective hepatitis as there had been several other cases of this in the same district about this time.

On admission she was deeply jaundiced, very drowsy, and confused. Her condition steadily deteriorated, she became deeply unconscious, and died 48 hours after admission.

Laboratory investigations on admission had shown serum albumin 3.4 g./100 ml.; serum globulin 3.4 g./100 ml.; total serum bilirubin 20 mg./100 ml.; serum thymol turbidity 4 units; serum alkaline phosphatase 15 K.A. units/100 ml.; serum transaminase levels: S.G.O.T. 205 units/ml., S.G.P.T. 720 units/ml.

At necropsy the body was jaundiced. Visceral abnormalities were confined to the liver and gall-bladder. The liver was shrunken, weighing only 780 g. The capsule was smooth, and cut surfaces showed that for the most part the lobules had disappeared and only a few small pale-brown areas persisted where the lobular architecture was preserved. There was a mucocele of the gall-bladder. It contained four faceted stones. The common bile-duct was patent and healthy throughout its length.

Histological examination of the liver showed gross disorganization of its architecture. In most areas the parenchymatous cells had completely disappeared; the portal tracts had become approximated, and contained only red blood cells in the place of the former liver cells. The few surviving liver lobules did not demonstrate any particular pattern of zonal damage. There were many bile plugs in the canaliculi and also in the Kupffer cells of these lobules. In relation to the portal tracts there was both bile-duct proliferation and aggregation due to the collapse of the lobular framework. The portal tracts were only slightly infiltrated by inflammatory cells, which consisted of lymphocytes, plasma cells, and polymorphs. Macrophages containing lipofuscin were also present, indicating the acuity of the process. The histological appearances were those of a massive hepatic necrosis with only a slight cellular reaction.

DISCUSSION

Other reports of liver damage have come from the United States, where pheniprazine is used under the names of "catron" or "JB 516." Beer and Schaffner (1959) described a case of fatal hepatic damage from catron. Greenblatt and Kahn (1959), in a toxicity study of the effects of JB 516 on 37 patients, included a case of "irreversible jaundice" in their description of six cases showing changes in liver function. Berkowitz *et al.* (1961) described a non-fatal case of catron-induced jaundice. Dosage was not in excess of therapeutic levels; they had given 18 mg. daily for two weeks.

Pheniprazine is a potent mono-amine oxidase inhibitor with a more selective action on the brain than iproniazid (Gogerty and Horita, 1959). This property should theoretically allow effective inhibition of the brain enzyme by doses small enough to have no significant effect on the liver. However, no relationship has been established between total dosage of iproniazid and hepatic toxicity, and it is well established that iproniazid is capable of producing severe liver damage in therapeutic doses (Popper, 1958).

In the present case the pathology of the liver is similar to that observed in the cases of iproniazid-induced jaundice studied by Popper (1958) and in the fatal case of catron-induced jaundice reported by Beer and Schaffner (1959), who had only a needle-core of post-mortem liver tissue for study. These authors noted the similarity to infective hepatitis. Our case occurred in a district where there had been several cases of infective hepatitis. From his studies, Popper (1958) concludes that iproniazid may effect its toxic action by the activation of a subclinical viral hepatitis. Pheniprazine may well have a similar action. It would also potentiate an overt attack.

The part played by pheniprazine in the fatal outcome of the illness is complicated by the fact that perphenazine was administered for 10 days, beginning shortly after the onset of jaundice. Perphenazine, a phenothiazine derivative, has only once been reported as producing jaundice (Berkowitz *et al.*, 1961); hepatic biopsy showed hepatic cholestasis. There was some cholestasis in our case, but in the presence of such gross parenchymal necrosis it probably played an insignificant part in producing the fatality.

The possibility of potentiation of pheniprazine by the perphenazine is more difficult to assess. The