diagnosed as winter vomiting disease. I have noticed similar disturbances of the gastro-intestinal tract in small children undergoing poliovirus infection.

Summary

Virological studies are reported on cases of infections of the central nervous system during a two-year period. Poliovirus type 1 was dominant during 1959, whereas Coxsackie viruses types B2 and B5 were more commonly isolated in 1960.

In 1959 62 paralytic cases occurred. From 53 of these, viruses were isolated, all polioviruses. In contrast, in 1960, from 24 paralytic cases 21 virus isolations were made but only 17 (81%) of these were polioviruses; the rest (19%) were Coxsackie virus types B2 and B5.

In aseptic meningitis, virus diagnosis was made in less than half the patients. In 1959 Coxsackie, Echo, and mumps viruses caused almost as many cases as did poliovirus, and during 1960 Coxsackie viruses were responsible for most. During both years mumps caused about 10% of cases.

Cases of unusual symptomatology associated with Coxsackie infection are described. These include not only paralysis but also meningo-encephalitis and rash. In young children there were cases of myocarditis, croup, and a number of indeterminate but severe illnesses difficult to diagnose clinically.

I am indebted to Professor A. C. Dornhorst, of St. George's Hospital, Dr. J. C. McEntee, of the Grove Hospital, Dr. Ursula James, of the Victoria Hospital for Children, and Dr. G. D. W. McKendrick, of St. Anne's Hospital, whose patients comprise the present study. I am also grateful to Professor S. D. Elek, Professor T. Crawford, and Professor A. C. Dornhorst for their interest and help in the construction of the paper, and to the Board of Governors of St. George's Hospital for the grant towards the carrying out of the work.

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PERFORATION OF INTERVENTRICULAR SEPTUM AFTER MYOCARDIAL INFARCTION

BY

R. J. HARRISON, M.R.C.P.

Consultant Physician, St. James' Hospital, London

J. P. SHILLINGFORD, M.D., F.R.C.P.

Hammersmith Hospital and Postgraduate Medical School, London

G. T. ALLEN, M.D.

Pathologist, Wandsworth Hospital Group, London

AND

D. TEARE, M.D., M.R.C.P.

Department of Forensic Medicine, St. George's Hospital, London

Perforation of the interventricular septum occurring after myocardial infarction is being reported more frequently. In a few cases cardiac catheterization has been used for confirmation and to help in deciding the degree of shunt (Muller *et al.*, 1950; Cooley *et al.*, 1957; Gottsegen *et al.*, 1957; Shickman *et al.*, 1959). In at least three patients the defect has been closed surgically (Cooley *et al.*, 1957; Shickman *et al.*, 1959; Romanoff and Cooley, 1960). After septal perforation, although the patient may survive for a few days, the prognosis is generally poor: Sanders *et al.* (1956), in a collective review of 133 cases, found that 50% died within the first week, and that only 13% lived for more than two months. In occasional instances a patient has lived for some years afterwards (Wood and Livezey, 1942; Zucker *et al.*, 1952; Briggs and Holt, 1954). The longest recorded survival time was that of a patient of Schlappi and Landale's (1954), whose acquired ventricular septal defect occurred in 1947, she eventually died from a non-cardiac condition at the age of 83 (Schlappi, 1960, personal communication).

Historical Note

Dr. P. Mere Latham (1846) gave a detailed account of the terminal illness of a patient who can now be diagnosed from the history as having suffered an attack of myocardial infarction. On the fifth day (Friday) after the onset of his patient's cardiac pain there was a recurrence of a more severe attack of pain, and Dr. Latham wrote:

"But on the next day, Friday, I was suddenly called to him. It was six p.m. I found that, about an hour before, the pain had returned with far greater severity than ever. He was deadly pale, and from the centre to the extremities of his body he was cold as marble, and streaming with perspiration; but his pulse was of a good strength, and his heart was contracting regularly and forcibly, and now, for the first time (according to my observation), with a loud systolic murmur, audible in the precordial region, and not in the arteries. I administered a large dose of opium with ether and ammonia. Visiting him again in an hour or two, I

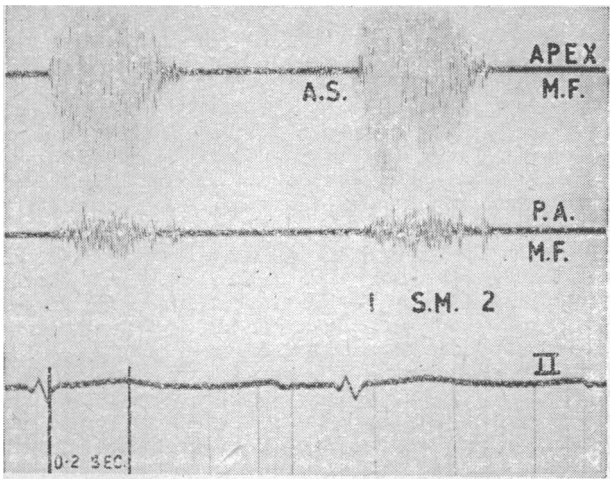

FIG. 1.—Case 1. Phonocardiogram showing (upper record) loud pansystolic murmur at the apex with small atrial sound and (lower record taken over pulmonary area) transmitted systolic murmur with pulmonary second sound. A.S.=Atrial sound. S.M.=Systolic murmur. M.F.=Medium frequency. P.A.=Pulmonary artery.

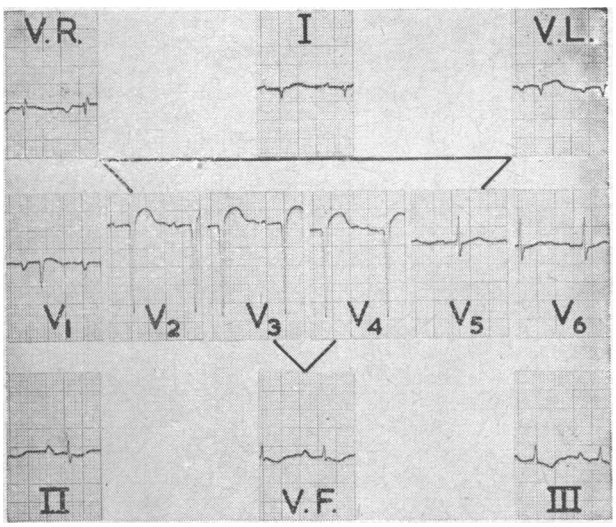

FIG. 2.—Electrocardiogram showing antero-septal myocardial infarction with suggestion in leads V_2–V_4 of ventricular aneurysm.

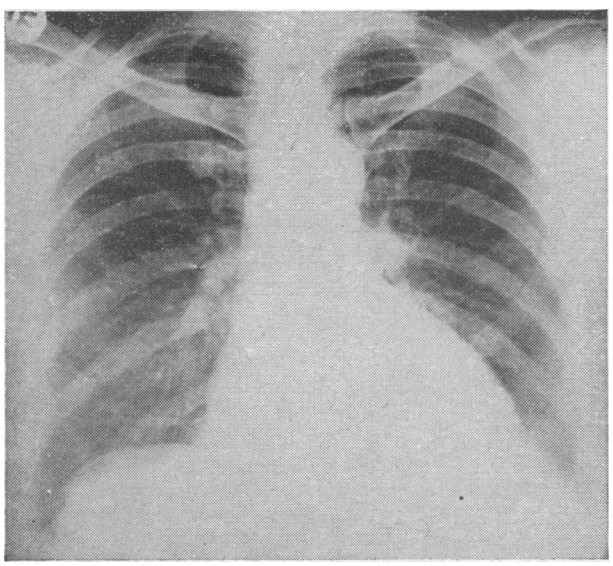

FIG. 3.—Case 1. Radiograph of chest showing size of heart two years prior to admission.

found the pain unabated, and his pulse beginning to sink. I staid with him through the night, still giving at intervals opium and ether and ammonia, and applying external warmth, but all to no purpose. Still the pain did not lessen. Still he looked and he felt like a corpse, he was so pale and so cold. At four in the morning (Saturday) the pulse finally ceased to be felt in the arteries, while yet the heart was perceived by the ear to move, but not by the hand. In this state he survived seven hours longer, until, with his mind clear to the last, he died at 11 a.m. Let me add, what I shall not soon forget, that this good man endured eighteen hours of mortal agony with wonderful patience and resignation.

"Upon examination after death, all the interior structures of the body were found more loaded with fat than its external appearance would have led me to expect. We looked only superficially to the abdomen, where we found nothing remarkable but a vast accumulation of fat within the mesentery. Our attention was chiefly directed to the suspected seat of disease—the chest. Here the lungs were perfectly healthy. The heart was a good deal larger than natural as a whole and incased in fat. It was upon its right side that the fat was accumulated to the greatest amount, and its muscular substance was everywhere very flaccid and very thin, and became thinner and thinner as you approached the apex when it was reduced to a mere line. Yet, thin as it was, it was quite healthy in colour and preserved all the visible characters of muscle without any intermixture of fat. The fat was all exterior to it. The capacity of the right ventricle was notably larger than natural. Its internal lining was stained of a deep red. Its orifices were free, and its valves healthy. On its left side it was less covered with fat. Here the ventricle was considerably dilated. The muscular substance was considerably hypertrophied. It preserved its healthy character, both of colour and consistence in the external parietes: but in the septum it was pale and soft, manifestly in consequence of fatty degeneration. In the septum, at its posterior juncture with the parietes, there was an oblique rent passing through it from ventricle to ventricle. On the side of the left ventricle it was an inch and a half in length; on the side of the right it just opened at a point. In truth, while we were examining the right side, the rupture passed undiscovered. The orifices of the left, as of the right ventricle, were quite free, and its valves healthy. The coronary arteries contained some atheromatous deposits, but were quite pervious. The aorta was healthy as far as its arch. It began to be studded with atheromatous and earthy matter in its descending portion."

The purpose of reporting three further patients, one of whom survived for three years after a septal perforation, is to emphasize the auscultatory and haemodynamic findings in this condition. There was necropsy confirmation in each case.

Case 1

A 64-year-old housewife had experienced sharp pains under the sternum for two weeks; three days before admission these became more severe and radiated to the left side of the chest, then during the next 48 hours she had frequent attacks of acute dyspnoea, each of which lasted for about five minutes. Her husband observed that during these attacks her heart seemed to gallop; he had also felt a thrill in the centre of his wife's chest, which he described as "like the purring of a cat." When her own practitioner visited her she was in a moribund state and was admitted immediately to St. James' Hospital (May 12, 1957).

On examination she was shocked, cold, and sweating; temperature 96° F. (35.6° C.); pulse was of poor volume, 80 a minute, regular rhythm. The respirations were 20 a minute and the blood-pressure 145/80. There was a harsh, coarse systolic thrill and murmur situated between the left sternal edge and the apex; the murmur was conducted to the left axilla. An electrocardiogram showed an anterior myocardial infarction (Fig. 2). E.S.R. was 65 mm. in the first hour; the white blood count was 26,000/c.mm.

Congestive cardiac failure developed with orthopnoea, raised jugular venous pressure, and peripheral oedema. She was treated with digitalis and mersalyl; and *x*-ray examination of her chest, taken on May 16, showed her heart was enlarged to the left and right, compared with a routine chest film taken in 1955 (Fig. 3), when she was on the staff of another hospital. She remained critically ill and on May 25 had an attack of rapid auricular fibrillation lasting some hours. During these weeks she was easily exhausted, and it was not until June 5 that she was able to sit out for bed-making. At this time the jugular venous pressure became raised with marked "A" and "V" waves, and the pulmonary component of the second heart sound was accentuated (Fig. 4): an E.C.G. on June 7 showed healing of the anterior myocardial infarct, with right axis deviation. A radiograph taken on June 18 is shown in Fig. 5.

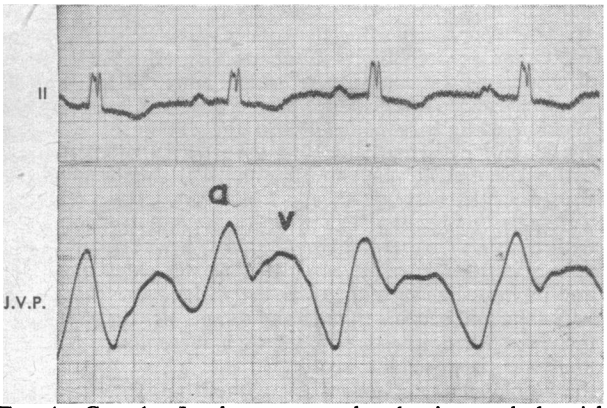

FIG. 4.—Case 1. Jugular venous pulse showing marked atrial waves.

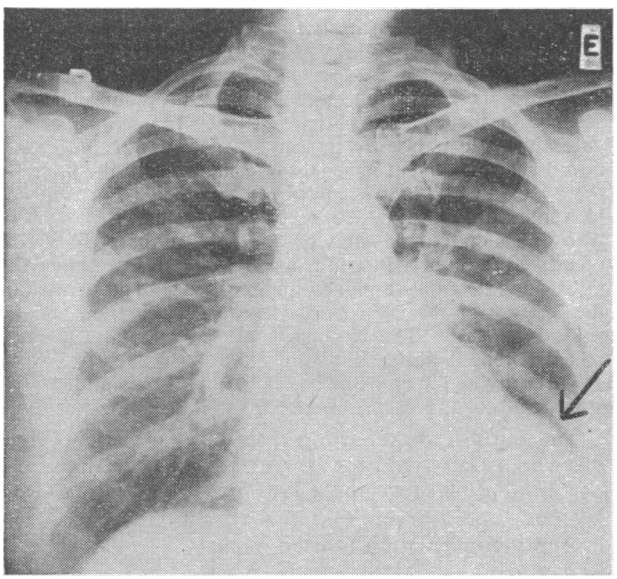

FIG. 5.—Case 1 Radiograph of chest taken five weeks after admission showing ventricular aneurysmal bulge marked by arrow.

In early July the question whether the defect might be closed surgically was discussed. As septal perforation usually occurs only when there is widespread atherosclerosis of the coronary arteries, a decision against operation was made on this account.

By September the E.C.G. showed persistent ST elevation over the septal leads, suggesting an antero-septal cardiac aneurysm with first-degree heart-block, and screening revealed a small cardiac aneurysm at the left lateral cardiac border. By December she was able to live a quiet, restricted life. A recurrence of her oedema was treated effectively with chlorothiazide. By July, 1958, the signs of pulmonary hypertension were marked with a giant "A" wave plus 6 cm. There was splitting of the second sound in the pulmonary area, with accentuation of the pulmonary component; a persistent cough with mucopurulent sputum occurred.

She was able to go out for walks, needing maintenance therapy of digitalis and chlorothiazide. She attended as an out-patient periodically, and during the next 18 months the E.C.G.s showed no change. In November, 1959, there was a recurrence of congestive heart failure, with tricuspid incompetence, which responded to increased doses of chlorothiazide.

She died suddenly at home on June 30, 1960, just over three years from the time the ventricular perforation had occurred.

Post-mortem Findings

The pericardium was adherent to the anterior surface of the heart (Fig. 6), where a very large patch of old fibrosis had undergone aneurysmal dilatation. The right ventricle was hypertrophied to twice its normal thickness. The aneurysm was actually found to constitute a ventricular septal defect; the left ventricle was also slightly hypertrophied. There was no valvular disease; advanced atheromatous changes were seen in the coronary arteries, but no clot was found.

Respiratory System.—A pint (584 ml.) of free fluid was found in each pleural cavity, and there were some adhesions at the right base: both lungs were congested and oedematous.

Intestinal System.—Cardiac cirrhosis and nutmeg changes were seen in the liver; there were several pints of free fluid in the abdominal cavity. The kidneys were finely granular. The spleen was congested and firm. The endocrines were normal.

Case 2

A 75-year-old retired man was admitted to St. James' Hospital on February 25, 1960, with a left hemiplegia, which had occurred three days previously. There was no past history of chest pain or winter cough. A diagnosis of cerebral thrombosis was made. On examination the heart sounds were normal, no thrill or murmurs were present; blood-pressure 245/140 mm. Hg; pulse 72 a minute, regular rhythm. With physiotherapy he made slow but steady progress, and after two months was walking fairly well with a stick.

On May 9 he complained for the first time of severe central, low substernal pain, which he later described as a dull ache, like a weight on his chest. On examination the heart sounds were normal, there were no murmurs

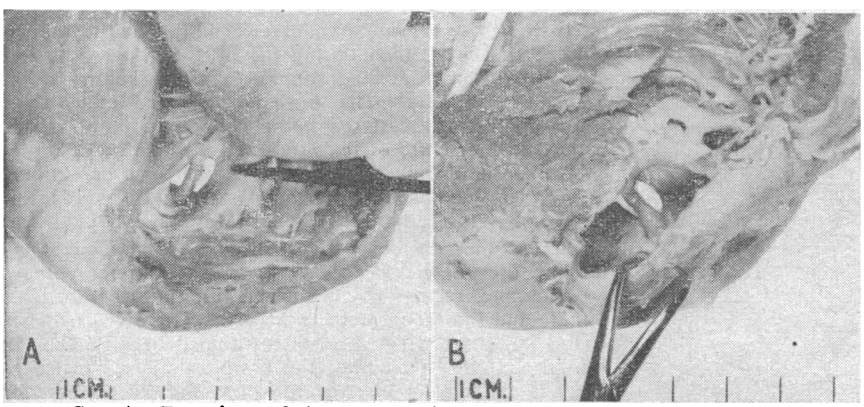

FIG. 6.—Case 1. Two views of the septal perforation: (A) from right and (B) from left ventricle showing aneurysm in the left ventricle with adherent pericardium. Note bar of intact myocardium across perforation marked by arrow.

or thrill; blood-pressure 190/115 mm. Hg; pulse 48 a minute, regular rhythm. An electrocardiogram showed a recent posterior myocardial infarction (Fig. 7), with a Q–S complex in AVF, and lead III with raised, coved ST segments and biphasic T waves.

He was treated by bed rest, and 50 mg. of pethidine gave relief; he had no more severe pain. On May 26, at 3.15 a.m. he wakened suddenly, intensely dyspnoeic, complaining of abdominal pain; he was cyanosed; blood-pressure 140/110, pulse 136 a minute and regular. There was now a loud, coarse systolic thrill and murmur at the lower left sternal edge (Fig. 8). He was given pethidine, aminophyllin, digitalis, and mersalyl. After a few hours the dyspnoea had improved, and it was seen that the jugular venous pressure was raised to the angle of the jaw, with marked "A" waves. An electrocardiogram on May 26 showed a tachycardia of 116 a minute with healing of a posterior infarction. Treatment with digitalis and mersalyl was continued. His jugular venous pressure fell to normal, blood-pressure 100/70 mm. Hg, pulse 72 a minute, regular rhythm. No peripheral oedema; he continued fairly well until July 31, when at 6.45 a.m. he suddenly collapsed and died, 83 days after his myocardial infarction and 66 days after the perforation of his ventricular septum.

Post-mortem Findings

Cardiovascular System.—The heart weighed 420 g.; the pericardium was adherent over a small area posteriorly: there was atherosclerotic thickening of the mitral and aortic valves; the posterior wall of the interventricular septum had an ovoid perforation 1.5 by 1 cm., surrounded by a ring of dense fibrosis (Fig. 9). The coronary vessels were narrowed by calcific atherosclerosis. The aorta showed calcific atherosclerosis with much ulceration and thrombosis of the left common iliac artery: the main vessels showed a similar picture.

Respiratory System.—Both pleural cavities were full of pale green fluid; the lungs were oedematous and showed basal congestion.

Alimentary System.—A constriction was found in mid-stomach due to scarring from previous ulceration.

The liver showed early nutmeg change. The endocrines and the spleen were normal.

Genito-urinary System.—Severe bilateral nephrosclerosis with cortical cysts and reduction of the cortices; the capsule stripped, leaving a granular surface; the bladder was dilated and the prostate enlarged.

Central Nervous System.—Two small cysts were found in the right cerebral hemisphere.

Case 3

A 66-year-old housewife was first admitted to St. James' Hospital in March, 1960 in hypoglycaemia. She rapidly recovered after the administration of glucose, and then gave a history of diabetes mellitus, treated by diet and insulin, for the previous 16 years: during this period she had been admitted to various hospitals on about four occasions for hypoglycaemic attacks.

On examination there was no diabetic retinopathy. Cardiovascular system: heart sounds were normal, with a short aortic ejection systolic murmur; rhythm regular. The pedal pulses were not felt. The central nervous system showed no evidence of peripheral neuropathy.

Investigations.—Urine: a faint trace of albumin. Chest radiography, normal. Blood count, normal. Serum cholesterol and liver-function tests within normal limits: fasting blood sugar, 179 mg./100 ml.

Her diet and insulin were adjusted and she was discharged home on May 4. She remained well until she was again admitted as an emergency case on September 29, with a history of precordial pain, radiating to her neck, for one week prior to admission.

On examination she was acutely ill: the jugular venous pressure was not raised; the pulse was of poor volume, regular rhythm, rate 100 a minute; blood-pressure, 120/85 mm. Hg. On auscultation there was a triple rhythm at the apex and a pericordial friction rub audible over an area to the left border of the sternum in the fourth intercostal space; there was ankle oedema. An electrocardiogram

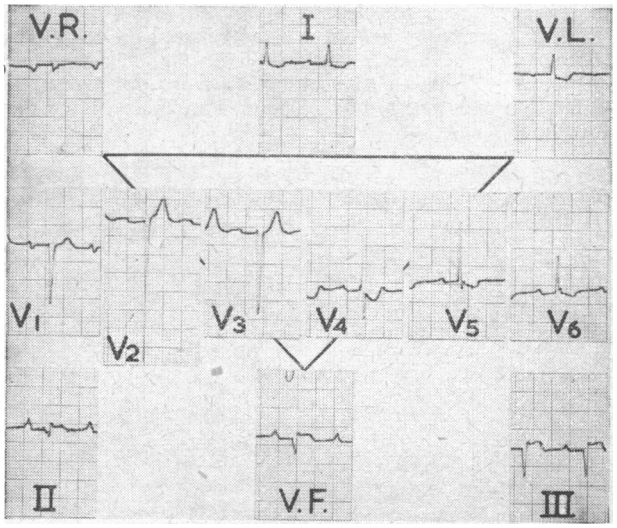

FIG. 7.—Case 2. Electrocardiogram showing posterior cardiac infarction.

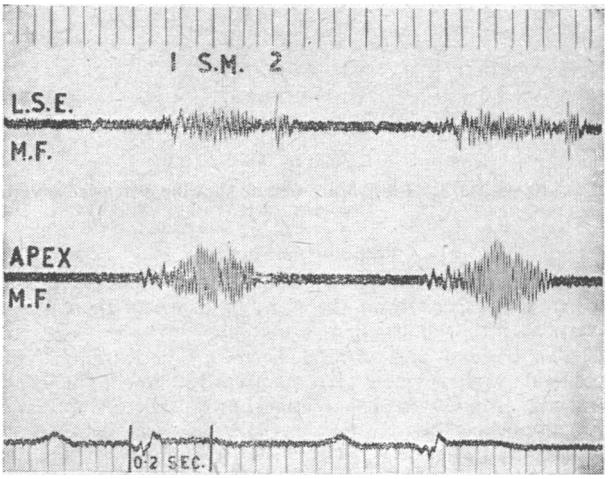

FIG. 8.—Case 2. Phonocardiogram. Lower record: medium frequency at apex showing pansystolic murmur. Upper record: medium frequency left sternal edge fourth interspace. S.M.=Systolic murmur. L.S.E.=Left sternal edge. M.F.=Medium frequency.

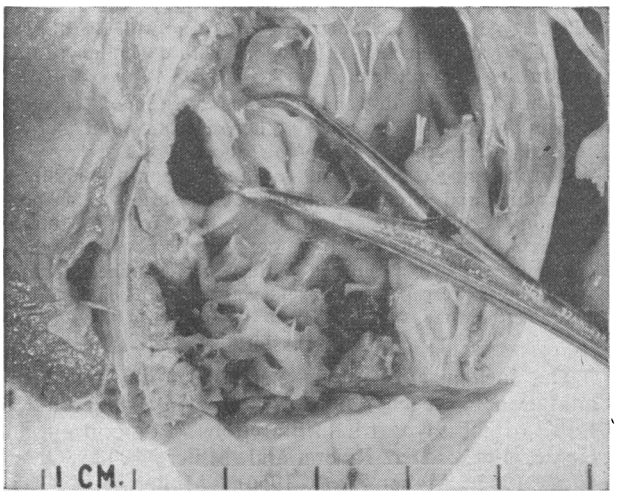

FIG. 9.—Case 2. Septal perforation view from the right ventricle.

showed a recent extensive anterior myocardial infarction with right bundle-branch block (Fig. 10). Soluble insulin was given for her diabetes, the pulse remained rapid and weak; the area over which a pericardial friction rub was audible increased in size. On October 3 her blood-pressure fell to 110/80 mm. Hg and a left hemiparesis developed; a few hours later she became dyspnoeic, and a pansystolic thrill and murmur occurred midway between the left sternal border and the apex. Perforation of the interventricular septum was diagnosed after an extensive anterior myocardial infarction with pericarditis. The patient collapsed and died two hours later.

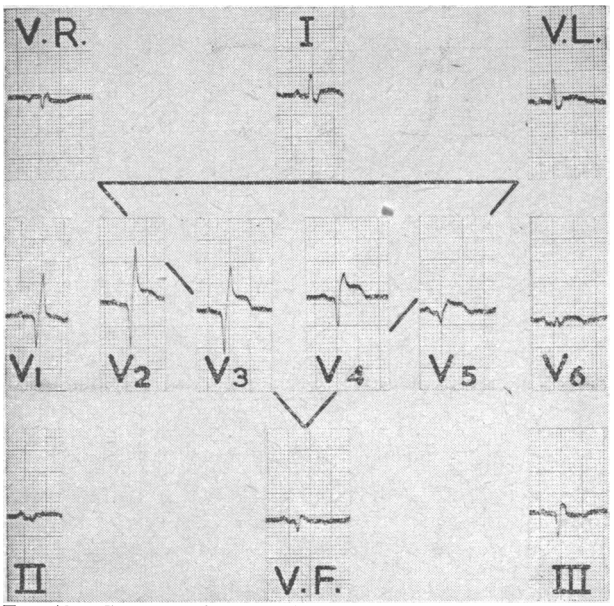

FIG. 10.—Case 3. Electrocardiogram showing extensive antero-septal infarct.

Post-mortem Findings

At necropsy (Dr. P. W. Kippax) the lungs were very congested, especially at the right base, where there was a very recent haemorrhagic infarction.

The parietal and visceral layers of pericardium were adherent and separated in some areas to show a roughened surface, in others a shaggy appearance. There were a few small pockets of yellowish necrotic material between the adherent membranes. The distal two-thirds of the left ventricle showed full-circumference infarction, some of it partially healed, but with evidence of recent haemorrhagic infarction and areas of liquefaction necrosis. The infarction had produced an interventricular septal defect towards the apical end of the septum, which was partially closed by recent mural thrombus. The myocardium at the apex was thinned to 3 mm. The anterior part of the wall of the right ventricle was infarcted, showing a picture similar to that seen in the left ventricle.

Right anterior descending and circumflex coronary arteries were all extremely atherosclerotic and showed internal haemorrhages beginning about 1.5 cm. from the ostium in the right and 1 cm. from the ostium in the anterior descending and circumflex branches. There was a mural thrombus deep to the chordae tendineae of the anterior mitral cusp, but no septal defect was demonstrated here. The liver showed a nutmeg pattern and weighed 1,480 g. The kidneys were pale and there was a small healed infarct in the left kidney.

Discussion

The incidence of septal perforation in myocardial infarction has been reported as varying from 0.9% to 1.6% of all myocardial infarctions (Edmondson and Hoxie, 1942; Diaz-Rivera and Miller, 1948; Oblath *et al.*, 1952; Maher *et al.*, 1956). Muller *et al.* (1950) stressed the difficulty in finding such perforations even when the pathologists were searching for this condition.

The clinical history is usually characterized by the cardiac pain due to the myocardial infarction, followed after a period of 3 to 16 days by a sudden change in the condition of the patient; this may present as acute pulmonary oedema, tachycardia, raised venous pressure with prominent "A" wave, enlargement of the right side of the heart, and production of loud systolic murmur, often with a thrill, maximal between the left sternal edge and the apex in the fourth and fifth left intercostal spaces. The murmur may simulate that of organic mitral incompetence in that it is pansystolic and may include the aortic element of the second sound and radiates into the axilla. This differs from the murmur of congenital septal ventricular defect, in which the murmur is usually localized to the lower left sternal edge. This difference may be due in part to the different anatomical situation of the defect and in part to the different haemodynamic situation in acute and chronic forms.

Confusion may arise between the murmur of functional mitral incompetence due to dilatation of the left ventricle, but a loud murmur with thrill appearing during the course of the recovery phase of myocardial infarction should make one consider the diagnosis of perforation of the septum. Pericardial rub and ruptured papillary muscle must also be considered in the differential diagnosis. The effect on the circulation is to produce an acute left-to-right shunt with an increase in pulmonary blood-flow and load on the right heart. The venous pressure rises with a prominent "A" wave, and the sudden increase in pulmonary flow may result in pulmonary oedema. During the course of time increasing pulmonary hypertension may occur. Although cardiac catheterization has been used to confirm an acquired septal defect in cases of traumatic septal rupture, this procedure carries a very definite risk in a patient with a recent myocardial infarct. Muller *et al.* (1950) performed cardiac catheterization in a patient six months after myocardial infarction with septal perforation: they found increased pressures in the right ventricle and pulmonary artery with an oxygen content higher than that in the right atrium; the calculated left-to-right shunt was 5.2 litres a minute. Other workers have confirmed these findings (Cooley *et al.*, 1957; Gottsegen *et al.*, 1957). The use of dye-dilution curves in our first two cases confirmed the diagnosis by showing the presence of a left-to-right shunt (Swan and Wood, 1957; Oakley *et al.*, 1960).

Pathology.—Rupture of the interventricular septum usually accompanies widespread coronary arterial disease. The immediate cause of rupture is occlusion of either the left anterior descending coronary artery or its branches, or the right coronary artery. In the former the rupture tends to be towards the anterior part of the septum, and in the latter more posteriorly. The rupture is often difficult to see and may be missed on routine post-mortem examination, especially when hidden by blood clot or covered by papillary muscles. In Case 1 a strand of intact papillary muscle actually crossed the septal perforation. It is difficult to assess the speed with which fibrosis develops after the incident, as there are usually widespread atherosclerotic changes, and fibrotic areas may well have been formed at an earlier stage. The blood supply to the area was poor in our cases, and one can only speculate on what the result of inserting sutures through this area would be.

Prognosis.—Our first patient is of interest because of the long survival period. A significant feature of septal perforation is that death does not occur immediately: Edmondson and Hoxie (1942) found an average period of survival of 7.4 days. In the series of Sanders *et al.* (1956) 13% (12 patients) lived from two months to several years.

Treatment.—The general principles of treatment are based on the knowledge that the efficiency of the heart in which septal perforation has occurred has already been impaired by coronary atherosclerosis followed by myocardial infarction. The left-to-right shunt, with increased blood-flow and raised pressure in the pulmonary circulation, throws an extra strain on the ventricles, and leads to heart failure. In our first two cases the administration of digitalis was of benefit, and diuretics were of considerable help. In Case 1, after a few weeks, there was a loss of response to mercurial diuretics: chlorothiazide with potassium supplements had an immediate beneficial effect.

Summary

Three cases of ventricular septal perforation are described. The diagnosis should be considered when a patient with an acute myocardial infarction suddenly deteriorates and develops a loud blowing pansystolic murmur between the left sternal edge and apex in the fourth and fifth left intercostal spaces. Dye-dilution curves in two cases showed the presence of a left-to-right shunt.

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About one child in every 600 born in this country is a mongol, and the National Association for Mental Health has published a booklet, *A Letter to Parents of a Mongol Baby*, prepared by a children's specialist, which will be of help to those concerned with what, how, and when to tell the parents that their child suffers from this condition. (N.A.M.H., 39 Queen Anne Street, London W.1, price 1s. 3d.)

EXPERIMENTAL AND CLINICAL OBSERVATIONS ON POLDINE IN TREATMENT OF DUODENAL ULCER

BY

J. E. LENNARD-JONES, M.A., M.B., M.R.C.P.
Member, Medical Research Council Department of Clinical Research, University College Hospital Medical School; Late Registrar, Department of Gastroenterology, Central Middlesex Hospital, London

The gastric secretion of acid by a patient with duodenal ulcer in response to a glucose test meal is about halved if an effective dose of poldine methosulphate (" nacton ") is taken beforehand (Douthwaite and Hunt, 1958). The drug also reduces gastric secretion of acid in response to a large dose of histamine (R. Seidelin, 1960, personal communication). These observations, made under strictly controlled experimental conditions, suggest that the drug might be useful in the treatment of duodenal ulcer. To investigate this possibility, the effect of the drug on the acidity of gastric contents has been investigated under the conditions of clinical use, and the drug has been subjected to a small controlled therapeutic trial.

Experimental Observations

Observations are reported on 16 patients with an uncomplicated radiologically proved duodenal ulcer. All were admitted to hospital, they were allowed up, and drugs other than poldine and sedatives were withheld unless stated otherwise. The individual dose of poldine for each patient was found by giving increasing doses until side-effects appeared. The initial dose given was 7.5 mg. daily, divided into three doses, or 12.5 mg., divided into five doses, and the total dose was increased by 7.5 or 12.5 mg. each day. If the first side-effects to appear were trivial the dose was further increased until definite side-effects developed. The dose just below that producing uncomfortable side-effects was defined as the " optimum " dose.

On the days of the test, samples of gastric contents were withdrawn every hour, on the hour, for 24 hours through a fine naso-gastric tube placed radiologically so that the aspiration holes lay in the likely position of the gastric antrum. The *p*H of the samples was measured with a sealed glass electrode. Doses of the drug, food, and drinks were given immediately after a sample was withdrawn.

Gastric Acidity of Patients Taking Gastric-type Diet

The effect of different doses of poldine was studied under these conditions in 16 patients. Observations made on a control day without poldine were compared with observations made on days when the drug was given. The control observations were made first in 13 patients and last in three patients. Four patients were studied while the dose of poldine was being increased and at a time when they were experiencing no side-effects from the drug; two patients were studied on one day at daily doses of 30 and 40 mg. respectively, the other two patients were studied on two days at daily doses of 30 and 60 mg., 30 and 90 mg., respectively. Of 10 patients taking the drug in the optimum dose, nine received five daily doses and the other patient three daily doses. Four of these patients had received the drug continuously in the optimum dose for periods of 1, 4, 9, and 12 days respectively before the test. The results in these four