clinical picture conformed to the diagnosis of Tay-Sachs disease, the cherry-red spot at the macula was missing.

Summary

Two cases of cerebromacular degeneration of Tay-Sachs type are described in Sinhalese children. They showed mental retardation, myoclonic fits, blindness with a dark purple patch at the fovea centralis surrounded by a white halo of avascular degenerated tissue, and primary optic atrophy. In one case, which started at 2 months of age, the duration of the illness was two years and eight months; in the other case, which started at 2 years, the duration was only two months. The usual microscopical changes described by others were found. The only unusual feature was the presence of large hyaline masses undergoing calcification in some parts of the brain substance and in the pia arachnoid. The nature of these is unknown.

We wish to thank Dr. K. J. de S. Devaditya for his report on the optic fundi, and Professor G. H. Cooray, Dr. S. Ponnadurai and Dr. Rajeswari Sathasivam for their help in the preparation of this paper.

REFERENCES

- de Silva, C. C. (1951). *J. Ceylon Br. Brit. med. Ass.*, 46, 81.
 Epstein (1917). Quoted by Hassin (1951).
 Franceschetti, A., and Klein, D. (1951). *XVI Concilium Ophthalmologicum 1950, Britannia, Acta*, 1, 158. B.M.A., London.
 Hassin, G. B. (1951). In *Brennemann's Practice of Pediatrics*, vol. 4, Ch. 9 and 10. Prior, Hagerstown, Md., U.S.A.
 — and Parmelee, A. H. (1928). *Amer. J. Dis. Child.*, 35, 87.
 Koller, C. (1896). *Med. Rec. (N.Y.)*, 50, 266.
 Mülberger, A. (1903). *Münch. med. Wschr.*, 50, 1968.
 Ostertag, B. (1925). *Arch. Psychiat. Nervenkr.*, 75, 355.
 Roos, A. (1935). *J. Pediat.*, 7, 488.
 van Creveld, S. (1953). *Advances in Pediatrics*, 6, 202. Year Book Publishers, Chicago.

SERUM AMYLASE AND ACUTE ABDOMINAL DISEASE

BY

W. BURNETT, M.B., F.R.C.S.

AND

T. D. NESS, M.B., Ch.B.

(From the Department of Surgery, University of Aberdeen)

The clinical features of the early stages of acute pancreatitis are often confusing. There may be close resemblance to those found in perforated peptic ulcer, intestinal obstruction, or other abdominal crises. We made the correct diagnosis only at laparotomy in 14 out of a consecutive series of 24 cases of acute pancreatitis. A diagnosis of perforated duodenal ulcer was incorrectly made on six occasions. Among the various tests recommended in the diagnosis of pancreatitis, the estimation of serum amylase has become recognized as a standard laboratory procedure, an increase in the level being normally found in this disease. Occasionally, however, high values are reported in other acute abdominal conditions, particularly perforated peptic ulcer, and some doubt has been cast on the diagnostic importance of the test. MacKenzie (1954), while recognizing it as a reliable indicator of pancreatitis, also found values above normal in a case of small-intestine obstruction and in two cases of perforated duodenal ulcer, in one of which the pancreas had been eroded. The present study was undertaken to assess the merit of the estimation of serum amylase as a diagnostic aid in acute pancreatitis, and to determine whether it could be adopted as a side-room test to be used by ward staff when required in the diagnosis of the acute abdomen.

A further interest lay in the incidence of acute pancreatitis in relation to other acute abdominal conditions, as we had formed the impression that this rare disease was not uncommon in this region.

Methods

Serum amylase was determined in a consecutive series of 350 patients admitted to hospital as abdominal emergency cases. Blood was obtained for analysis before any operation and also before the use of any drug, particularly morphine, which may cause spasm of the sphincter of Oddi. Pfeffer *et al.* (1953) have pointed out that morphine, in the presence of an actively secreting pancreas, can cause significant elevation in the level of serum amylase. The method of estimation was that described by Somogyi (1938); this measures the rate of destruction of a standard solution of starch by serum amylase, being recorded by the disappearance of the starch-iodine blue colour as hydrolysis progresses. The starch used was soluble starch (Analar grade, B.D.H.).

The end-point was taken at the change from a violet colour to the red of erythrodextrin, but in order to avoid error the reaction was followed by repeated sampling to the final pale yellow iodine colour. Samples were withdrawn normally at two-minute intervals, but in the region of the end-point were taken every minute or half-minute. When an initial high value was obtained the test was repeated after suitable dilution of the serum to keep the enzyme-substrate ratio constant.

The quantity of iodine used as an indicator is critical. If too little is used it is consumed by various elements in the serum; if too much is used it contributes to the colour of the solution and confuses the end-point. As very little apparatus was required, the test was found to be quite adaptable for ward side-room work. With a little practice the end-point was reliably recognized in standard conditions of artificial light, and results were duplicated by persons relatively inexperienced in laboratory methods. It was found possible to carry out the test as required in the limited time available in a busy ward. A control series of 50 estimations in normals gave a range of 62 to 177 Somogyi units with an arithmetic mean of 115. Standard deviation was ± 33 . These values are similar to those described by Somogyi (1941). Wootton and King (1953), in an investigation into normal ranges, gave the range for serum amylase as 91 to 163, with extreme low and high values of 71 and 209.

Results

The distribution of the 350 cases in the series is given in Table I. The miscellaneous group included genito-urinary and gynaecological cases in addition to a substantial num-

TABLE I

Diagnosis	No. of Cases	Serum Amylase	
		> 400 Units	> 1,000 Units
Acute pancreatic disease ..	14	14	13
Acute cholecystitis ..	23	2	0
Perforated peptic ulcer ..	31	8	2
Intestinal obstruction ..	35	3	2
Acute appendicitis ..	149	2	0
Miscellaneous ..	98	3	0
Total ..	350	32	17

ber of patients who were admitted with abdominal pain which subsided spontaneously, and in whom no definitive diagnosis could be made.

In 32 cases (9.1%) the level of serum amylase was over 400 units on admission, or more than twice the upper limit of normal (Table I). Of this group, 17 had values over 1,000 units, including 13 who were diagnosed as having acute pancreatic disease, 2 with intestinal obstruction, and 2 with perforated peptic ulcer.

The results in the main groups in the series are summarized in Table II. The most important finding was that in addition to the group of 32 high values mentioned above

TABLE II.—*Distribution of Serum Amylase Levels in Main Groups of Acute Abdominal Disease. Other than Pancreatic Disease*

Diagnosis	Serum Amylase (Units)				
	<200	200-300	300-400	400-500	>500
Acute cholecystitis..	11	4	6	—	2
Perforated peptic ulcer..	17	3	3	2	6
Intestinal obstruction	16	5	11	1	2
Acute appendicitis	92	34	21	—	3
Miscellaneous ..	60	21	14	—	3
Total ..	196	67	55	3	15

TABLE III.—*Initial Levels of Serum Amylase in Acute Pancreatitis*

Case	Age	Sex	Amylase (Units)
1	60	F	1,200
2	51	F	3,200
3	47	F	1,600
4	59	F	2,560
5	28	M	6,000
6	48	M	1,600
7	67	M	4,000
8	46	M	3,200
9	70	F	2,132
10	52	F	1,600
11	57	F	3,200
12	74	F	2,285

there was a large group of 122 (32%) who had serum amylase levels below 400 units but distinctly above normal. The significance of this is discussed below, where the results are considered in more detail.

Acute Pancreatic Disease.—There were 14 cases of acute pancreatic disease in the series. Of these, one patient whose amylase was 640 units was not seriously ill and was considered to be suffering from subacute pancreatitis; another had sustained a subcutaneous traumatic rupture of the pancreas. Here the initial level was 4,180 units. This case is discussed in detail elsewhere (Burnett, 1955). The remaining twelve patients (3.4% of the total series) were diagnosed as acute pancreatitis. All were admitted to hospital suffering from severe abdominal pain and were seriously ill. Ten patients ultimately recovered, and two died during the first few days of illness. The diagnosis was confirmed in seven cases by laparotomy in the acute phase or later, and in one case at necropsy. The admission levels of serum amylase in the 12 cases of acute pancreatitis are given in Table III. Some values are higher than are often thought to occur. This may well be due to admission to hospital within 24 hours of the onset of the disease and early estimation. It was found that the level tended to fall abruptly after 24 or 36 hours and then more gradually until normal values were reached in four to five days. This applied whether the patient was treated conservatively or by operation (Fig. 1).

FIG. 1.—Comparison of fall in the level of serum amylase in two cases of acute pancreatitis, one (x—x) treated by conservative means, and the other (· — ·) by operation. Acute pancreatitis was later confirmed as being present in the case treated conservatively.

The diagnosis was confirmed in seven cases by laparotomy in the acute phase or later, and in one case at necropsy. The admission levels of serum amylase in the 12 cases of acute pancreatitis are given in Table III. Some values are higher than are often thought to occur. This may well be due to admission to hospital within 24 hours of the onset of the disease and early estimation. It was found that the level tended to fall abruptly after 24 or 36 hours and then more gradually until normal values were reached in four to five days. This applied whether the patient was treated conservatively or by operation (Fig. 1).

Perforated Peptic Ulcer.—Of the 31 cases studied, 14 had values above normal, but only 8 were over 400 units. None of the 12 cases in which the perforation was of less than five hours' duration had an amylase above normal; in the group of eight with high values, seven had massive and one had considerable free fluid in the peritoneal cavity. Accurate estimations of peritoneal contents for amylase were often not possible, but values up to 8,000 units were obtained. It seems likely that in perforated peptic ulcer

the increased levels sometimes reported are due to absorption of spilled duodenal contents from the peritoneum, and the serum amylase level attained depends accordingly on the duration of the perforation and the peritoneal contamination. The highest values found in perforated duodenal ulcer were two of 800 units and one of 1,600 units. A very high value of 3,400 units was found in a case of perforated gastric ulcer of seven hours' duration in which 800 ml. of free fluid was found in the lesser sac.

Intestinal Obstruction.—Of the 35 cases in this series, 19 had amylase levels above normal. In all but two cases, summarized below, these were below 400 units.

A man aged 77 was admitted in a collapsed state, having had severe abdominal pain for 20 hours. Serum amylase was 2,000 units. He was suffering from an obvious severe peritonitis, and at operation most of the small intestine was found to be gangrenous as a result of thrombosis of the superior mesenteric artery.

A man aged 58 had symptoms of acute intestinal obstruction for three days before admission because of a strangulated inguinal hernia. Serum amylase was 1,600 units. At operation the hernial sac was found to contain a strangulated but viable loop of small intestine and a necrotic loop of sigmoid colon.

It seemed likely that the very high amylase levels found in these two cases was due to absorption of intestinal amylase through capillaries or lymphatics in a damaged bowel wall or from the peritoneum after seeping through the bowel wall. In addition, there may have been an element of pancreatic necrosis in the first case from involvement of the inferior pancreaticoduodenal vessels.

Acute Cholecystitis.—In 12 of the 23 cases the serum amylase was moderately elevated, but the highest values found were two at 533 units. None approached the level of the lowest value found in acute pancreatitis. On these findings the test would seem to be of considerable value in differentiating the two conditions, which are apt to be confused clinically.

Acute Appendicitis.—This group formed the largest in the series, comprising 149 cases. Moderate elevations were found in 57 (Table II), the highest value, 800 units, being found in a patient whose symptoms had lasted three days, and who was found to have an obstructed gangrenous appendix. Many other cases of acute appendicitis of apparent equal severity had normal levels. No rise was noted in six cases of appendicular abscess.

Miscellaneous.—Minor elevations occurred in a number of varied conditions—for instance, in 10 out of 15 cases of urinary infection, none of which had any symptoms or signs of renal failure. Values of 800 units were obtained in a case of Meckel's diverticulitis and in a case of abdominal carcinomatosis arising from a carcinoma of the caecum. No increase was found in a small series of six cases of diverticulitis.

Discussion

This investigation has confirmed that the level of serum amylase is consistently high in acute pancreatitis. Very high values were found in the first 24 hours of the disease. Unfortunately, high values are not pathognomonic of pancreatitis, as similar levels were found in perforated peptic ulcer and intestinal obstruction on four occasions. It is our impression, however, that the test, which can be quickly performed in the side-room, is well worth doing in an acute abdominal case where the diagnosis is in doubt. In particular, it should help in differentiating acute cholecystitis from pancreatitis.

The incidence of acute pancreatitis—3.4% in this series of 350 cases, or in one case seen for every three of perforated peptic ulcer—suggests that the diagnosis should be seriously considered in the differential diagnosis of acute abdominal pain.

It seems reasonable to postulate peritoneal absorption as the cause of the increased serum amylase in perforated ulcer, and absorption of pancreatic amylase in the intestine may occur through the damaged bowel wall or the peritoneum

in intestinal obstruction. This is supported by the report of hyperlipasaemia in intestinal obstruction (Johnson and Bockus, 1940). However, no clear explanation can be given for the minor elevations found in appendicitis, cholecystitis, urinary infections without uraemia, etc. Baker *et al.* (1950) demonstrated a number of amylase-producing organisms in the human intestine. It is possible that, with the altered bacterial flora occurring in appendicitis and other abdominal infections, enough bacterial amylase may be absorbed through areas of increased vascularity in the affected region to produce a small increase in serum

FIG. 2.—Thirty-six-hour culture of contents of the lumen of an acutely inflamed appendix, grown on nutrient agar with 0.5% starch; photographed after application of solution of iodine to show zones of amylolytic activity round colonies.

amylase. This possibility is now being investigated. As a preliminary, it has been shown that many amylase-producing colonies are to be found in a culture from an acutely inflamed appendix grown on nutrient agar containing starch (Fig. 2).

Summary

Serum amylase was estimated in a consecutive series of 350 patients admitted to hospital with acute abdominal pain. The test was found suitable for use in a ward side-room. There were 12 cases of acute pancreatitis—an incidence of 3.4%. Serum amylase levels in these 12 cases varied from 1,200 to 6,000 Somogyi units. The test is very useful in differential diagnosis, but is not pathognomonic of pancreatitis, as high values were found in perforated peptic ulcer and intestinal obstruction.

We would like to express our thanks to Professor W. C. Wilson for his interest and advice, to Dr. R. Menzies for the appendix culture, to Mr. R. Drummond for the photograph, and, finally, to the house-surgeons of ward 8, Aberdeen Royal Infirmary, for their co-operation during this study.

REFERENCES

- Baker, F., Nasr, H., Morrice, F., and Bruce, J. (1950). *J. Path. Bact.*, **62**, 617.
 Burnett, W. (1955). *British Medical Journal*, **1**, 1455.
 Johnson, T. A., and Bockus, H. L. (1940). *Arch. Intern. Med.*, **66**, 62.
 MacKenzie, W. C. (1954). *Ann. roy. Coll. Surg. Engl.*, **15**, 220.
 Pfeffer, R. B., Stephenson, H. E., and Hinton, J. W. (1953). *Gastroenterology*, **23**, 482.
 Somogyi, M. (1938). *J. biol. Chem.*, **125**, 399.
 — (1941). *Arch. intern. Med.*, **67**, 665.
 Wootton, I. D. P., and King, E. J. (1953). *Lancet*, **1**, 470.

Discussing some of the causes of failure in medico-social experiments, Dr. J. L. BURN, medical officer of health of Salford, has this to say about housing: "Another failure has been in the rehousing of families for what may be termed mental health reasons. Parents have come to me in emotional states begging for rehousing, blaming their obviously poor housing accommodation for psychological disturbances. How carefully one must assess these cases in order to be just, for I can recall two families in particular in which rehousing made not a whit of difference. There was an underlying mental and emotional instability and infidelity which were not cured but rather worsened on rehousing. Patients in the families really needed psychological and mental treatment as well as the provision of a new roof over their heads" (*Public Health*, 1955, **68**, 150).

Medical Memoranda

A Case of Myxoedema with Serous Effusions

From a study of the literature it appears that multiple serous effusions are a rare complication of myxoedema. The following case may therefore be found of interest.

CASE REPORT

A housewife aged 52 was admitted to hospital in February, 1953, because of gross ascites. Five years previously she had had a partial thyroidectomy for thyrotoxicosis. Since that time she had been slowly gaining weight, and during the last two to three years had noticed that her hair was falling out excessively, that her voice was becoming hoarse, and that she could not tolerate the cold.

On examination her voice was hoarse and she was moderately dyspnoeic; she also had the classical appearance of myxoedema. The smooth, pale, waxy appearance of the skin of her face was relieved by a malar flush; her eyelids were puffy; the little hair that remained on her head was dry and coarse, and the eyebrows were almost absent; the hands and forearms were puffy. Her pulse rate was 66 a minute. Her heart was enlarged to the left, but the apex beat could not be located accurately; the heart sounds were faint and there was a soft apical systolic murmur. Her blood pressure was 160/110. There were signs of a left basal effusion. Her abdomen was grossly distended from ascites, and marked pitting oedema was present over the sacrum and legs. The central nervous system was normal.

Investigation.—Haemoglobin, 82% ; R.B.C., 3,930,000 per c.mm.; leucocytes, 5,200 (polymorphs 63%, lymphocytes 37%); plasma cholesterol, 450 mg. per 100 ml. E.C.G.: flat T waves in all leads. An x-ray report on the chest was as follows: "There is considerable increase in the cardiac diameters. The cardiac outline, as far as it can be seen, suggests a pericardial effusion. There is considerable basal congestion, while there is a moderate effusion on the left."

The patient's abdomen was tapped and 20 pints (11.4 litres) of amber-coloured fluid removed. Unfortunately, no fluid was sent to the laboratory for protein estimation. (Mussio-Fournier *et al.* (1949) have reported a case in which the protein content of the ascitic fluid was abnormally high.) Her breathing became easier, and the following morning she had a moderate diuresis. During the next eight days, however, the urinary output became progressively less and the patient gained 5 lb. (2.3 kg.) in weight. She was then given dried thyroid, $\frac{1}{2}$ gr. (30 mg.) twice daily. The dose was increased by $\frac{1}{2}$ gr. (30 mg.) weekly. Within a week her urinary output began to increase and her general condition to improve. She was discharged six weeks later on a maintenance dose of 4 gr. (0.26 g.) of thyroid. Her condition was much improved and her appearance was normal apart from baldness. No ascites or oedema was detectable. An x-ray film of the chest showed the lung fields to be clear. The heart shadow, though still enlarged, was much smaller than initially, and there were no signs of a pericardial effusion. The E.C.G. was within normal limits.

When last seen in January, 1955, she was leading an active life and was free from symptoms. The hair of her head had grown. Her pulse rate was 70 a minute. Her heart was still somewhat enlarged, probably owing to hypertension, her blood pressure being 210/110.

COMMENT

Gross abnormalities in the heart in myxoedema were first described by W. M. Ord in 1880, but not until Zondek's report in 1918 was the association of myxoedema with certain cardiac phenomena generally recognized. Gordon (1929) described the first proved case of myxoedema complicated by a pericardial effusion. Since that time 17 additional reports bring the total number of recorded cases to 24.