THE DIAGNOSIS AND TREATMENT OF ACUTE PANCREATITIS

by

HENRY WAPSHAW, M.B.,Ch.B.

May 1946.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

ACKNOWLEDGMENTS.

My thanks are due to the many colleagues who were so kind as to place their clinical material at my disposal. A personal acknowledgment is made to each in the clinical reports. I am especially indebted to Professor C. F. W. Illingworth, at whose instigation the work was started and who has been throughout my association with him an ever-ready source of help and encouragement. Special thanks are also owed to Professor Noah Morris and Professor George Wishart for initiating me into the ways of biochemical research.

Expenses incurred by the investigations were defrayed by the Rankin Fund of the University of Glasgow.

I N D E X.

A STATEMENT ON THE DIAGNOSTIC PROBLEM.

"It may seem a slight to the pancreas to pass it over without noticing the diseases to which it is subject but really these diseases appear to be but few and they do not signify their existence by any plain or intelligible signs" (Watson, 1871).

Since the middle of the last century we have passed many milestones on the way to a more complete understanding of the main diseases of the pancreas. Those that seem to stand out most prominently are Fitz's monograph on acute pancreatitis, Wohlgemuth's researches into the functional disorders of the external secretion and Banting and Best's brilliant achievement, the isolation of insulin. Credit is also due to Whipple and other contemporary surgeons who have broadened the operative horizon in cases of malignancy. It is disconcerting, however, to discover that our imaginary path of progress fades into fields of controversy when we consider the recent developments in the treatment of acute pancreatitis.

The question at issue is whether we ought to operate or not during the early critical days of illness. It is still the orthodox teaching that the more destructive forms of the condition call for prompt surgical attention. Within recent times some surgeons have arrived at the conclusion that

such cases fare much better under expectant treatment. In spite of the promising results reported by this new school of thought, its policy has not as yet been received in the standard textbooks because there is some doubt as to whether the cures really belong to the seriously affected group. Nevertheless, the fact that only one out of every two cases survives operative treatment gives cause for sober reflection. As for those who are surgically minded, they seem to find solace in the thought that the death rate would be much higher if patients were not so treated.

It is apparent, then, that the first step towards a solution of this problem is to sound the principles on which each school of thought bases its diagnosis. The following are the main questions awaiting consideration:-

What assurance can the operating surgeons give that their diagnosis has been clinical and not operative?

How do those who practice the expectant line of treatment differentiate the severe from the mild cases?

When we read the works of the better known surgical authorities, we receive rather mixed impressions, but generally speaking most of them are quite confident of their clinical diagnosis of acute pancreatitis. Halsted (1901), the associate of Opie

in the Johns Hopkins Hospital, was of the opinion that "the clinical picture was so definite as to be recognizable by the general practitioner", Moynihan (1925) looked on it as "unmistakable", and Kemp (1917), Love (1926), Finney (1933) and Ogilvie (1939) express themselves in somewhat similar terms. We must not, however, overlook the fact that these authors have based their opinion on cases subjected to operation and not on general statistical evidence. It may even be said that they were so unshakable in their conviction that operative treatment was so necessary that they were inclined to accept a tentative diagnosis of pancreatitis and to underrate the difficulties in reaching a diagnosis of certainty. The following quotations from Moynihan's paper illustrate this point. He directly admits that "there is no doubt that recovery from acute pancreatitis of all grades except the more severe is possible without operation. In a number of cases in which I have operated for stones in the gall-bladder or common duct very extensive areas of fat necrosis have been found and the pancreas has been large and infiltrated with blood and oedema around ..." and yet he draws the conclusion that "it is equally certain that recovery from this disease apart from operation is so rare that no case should be left untouched." Those

who have checked the accuracy of their original diagnoses after the presence of pancreatitis became known have shown that the majority are wrongly diagnosed. Abell (1938), who found 30 cases in an experience embracing 2,000 operations on the biliary tract, made a correct diagnosis in only 12 cases, the other suggestions being acute cholecystitis (14 cases), acute appendicitis (2), intestinal obstruction (1), unknown (1). These findings agree with those in other statistical surveys. Thus, Schmieden and Sebenung (1928) found 21.8% of their collective series correctly diagnosed, Cole (1938) was right in 30% of 54 cases, McWhorter (1932) in 14% of 64 cases, Foged (1935) in 54% of 71 cases, and Lewison (1940) in 11% of 35 cases. I succeeded in reaching a correct diagnosis in 30% of 26 cases.

A short résumé of my own clinical findings will serve to show where the difficulty in establishing a diagnosis arises. The full records may be found in the appendix (see page 116). The series comprised 17 severely affected patients, 6 with subacute lesions and 3 in whom the existing pathological conditions were unknown.

The disease usually presents itself in a middle aged female somewhat given to stoutness. Abdominal pain dominates the clinical picture. It comes on

with alarming suddenness often after a meal and originates most commonly in the supra-umbilical zone. The pain is referred often to the lower dorsal region and sometimes to other parts of the abdomen. It is a vicious, throbbing kind of pain, the usual pain relieving remedies such as morphia and the local application of heat being of little avail. It shows a distinct tendency to pass off abruptly, leaving a dull epigastric ache, and to recur with renewed intensity. The other common symptom is sickness, the bouts of vomiting coinciding with the accesses of pain. This persists until the stomach is completely empty and then the patient is troubled with retching. The patients do not adopt any set position. Some are very restless, others lie on the back with knees drawn up, while a few lie listless with an apathetic look on their faces which belies the depths of their sufferings. Mild jaundice and cyanosis may be observed but only in the minority of patients.

There seems little point in recounting in detail the physical findings or those of the special examinations, as any abnormalities found could not always be related to the existing pathological conditions. In my experience, the true severity of the disease does not become manifest until towards the end of the first week of illness. The subacute cases

generally subside spontaneously, while those with extensive destruction of pancreatic substance either die within a few days or they may survive the initial toxaemia, shock, or whatever causes their prostration. Those in the third category usually have a prolonged convalescence marked by poor appetite, loss in weight and generaly debility, although it should be mentioned that a few enjoy an early return to comparatively sound health. Suppurative pancreatitis appears to be an exceptionally uncommon complication. In a certain number of the cases with haemorrhagic necrosis there develops a palpable or visible swelling in the upper abdomen which may assume enormous proportions due to a collection of fluid in the lesser sac. It naturally causes displacement and distortion of the stomach and transverse colon as viewed radiologically. This, to my mind, is the surest indication of the presence of a severe degree of acute pancreatitis, but unfortunately it does not make its appearance until the acute stage has passed.

Some of my clinical observations are given in the table below along with those of other authors to emphasise the irregularity of the findings (see Table 1).

TABLE 1.

The Incidence of certain Physical Signs given on a percentage basis as found by an unselected group of Authors.

Author	No.of Cases	Percentage with Cyanosis	Percentage with Jaundice	Percentage with Palpable Mass	The presence of discolouration in the flanks or umbilical areas
Love (1926)	51	23.5	3.9	17.6	-
Finney (1933)	32	15.9	37.5	9.3	-
Henderson (1935)	60	8.3	13.0	1.6	-
Lewison (1940)	35	5.7	42.8	8.5	-
Present Series	25	24.0	28.0	28.0	-

The quest for some sign or test on which a more secure diagnosis could be based began early in this century. In 1911, Körte concluded a personal study of 44 cases with this remark:- "The greatest advance will be the discovery of a pathognomonic reaction that will definitely indicate disease of the pancreas." This author was evidently unaware that Wohlgemuth, one of his own countrymen, had discovered and made known such a reaction three years previously. Wohlgemuth showed that in acute pancreatitis the diastase content of the faeces fell, while that

of the blood and urine mounted to high levels, and his findings have been confirmed numerous times. Although this demonstration of faulty pancreatic function is a valuable link in the chain of evidence pointing to the existence of this disease, the surgeons in this country have never shown much enthusiasm for the tests devised by Wohlgemuth and other biochemists; the same lack of interest prevailed until recently in surgical circles in America. The laboratory aids to diagnosis are now very much in vogue abroad and it seems to be more than a coincidence that their popularity should date from about the same time as when surgical opinion began to question the need for early operative treatment in acute pancreatitis. Indeed, Smead (1936) in his vigorous defence of the conservative policy actually puts the question, "Is it not probable that the real problem of lowering the terrible mortality of acute pancreatic necrosis is more likely to be solved by the biological chemist than by the surgeon?"

This brings me to the main subject of controversy, namely, the efficacy of these enzyme tests as a means of differentiating the severe cases from the mild. The remainder of the first part of this thesis is devoted to the study of this question. It takes the form of an evaluation of the individual

and combined worth of two tests, one of which estimates the serum diastatic activity, and the other, the serum lipolytic activity. The work opens with a general account of the digestive properties of the blood and a statement of my own findings under normal conditions.

INTRODUCTION TO THE BIOCHEMICAL STUDIES.

The investigations about to be presented involve the study of a group of enzymes derived in part from the pancreas and having digestive properties in vitro but whose function in the tissue fluids is still unknown. It is a branch of functional pathology which owes its origin to the French School of physiologists who first drew attention to the vital share contributed by the pancreas to the body's economy. In 1846, Magendie demonstrated the presence in the blood of a substance with starch-splitting properties. Its existence was deduced by the appearance of a notable rise in the blood sugar content of an animal after the intravenous injection of a starch solution. While engaged in his researches into the digestive function of the pancreas, Bernard (1856) confirmed his colleague's findings and also noted that saliva had the same properties. These investigators chose to call the ferment responsible for the break-down of starch "diastase", a name originally applied by Payen and Persoz in 1833 to a substance with a similar action which they had isolated from malt.

Magendie (1846) and Foster (1867) in this country showed that a starch-splitting substance was widely distributed throughout the tissues of the body. The

latter was probably the first to measure the diastatic content of tissue extracts; the estimates admitted by himself to be only approximately accurate were obtained by noting the time taken to hydrolyse a given quantity of starch. In 1908, Wohlgemuth introduced a more accurate method for the quantitative estimation of the diastatic activity of the urine. His contribution received the approval of both clinician and laboratory worker alike. To the surgeon, it suggested a means of providing a more consistently correct diagnosis of acute pancreatitis. To the physician, it held out the promise of being a reliable test of renal function. Some even entertained the hope that this test might unravel the secrets of carbo-hydrate metabolism and so lead to the discovery of a cure for diabetes mellitus. Wohlgemuth's main interest lay in the variations in diastatic activity of the blood and the urine which were caused by damage to the pancreas. Although his method is applicable to both blood and urine, only the latter seems to be used as the test fluid in British clinics and until quite recently the American workers also were mainly concerned with the output of diastase in the urine. According to a report issued by the American Gastro-enterological Association in 1934, only one of its 150 members made use of serum enzyme

tests. Marslow and Davison (1926) had previously compared the iodometric, copper reduction, polariscopic and viscometric methods for measuring the rate of hydrolysis of starch and dextrin by taka-diastase. In effect, their conclusion was that there was little to choose between them as methods of determining diastatic activity. In certain authoritative circles, however, the results of the Wohlgemuth test are viewed with some dissatisfaction. The Danish School represented by Mikkelsen (1934) and Foged (1935) prefer to determine the diastatic content of the urine by the Fabricius-Møller modification of Wohlgemuth's method. According to Elman and McCaughan (1927), the Wohlgemuth test in its original form gives a poor endpoint and duplicate specimens of blood may give divergent values. Myers and Reid (1933), in a comparative study, also encountered discrepancies with this test and in the end favoured the viscometric and copper reduction methods. In the leading gastroenterological clinics of the U.S.A. such as those of the Barnes and St Louis General Hospitals, the Mount Sinai Hospital and the Mayo Clinic, there has been a tendency for the Wohlgemuth test to be supplanted by the more delicate iodometric procedures or by the still less subjective copper reduction method. These clinics, especially the last named, also tend

to make more use of the serum lipase test. So far as can be judged from the literature, none of the serum enzyme tests referred to has been employed in every day clinical practice in this country.

Before proceeding to a detailed account of the methods employed in this investigation, it is necessary to relate a few facts concerning the behaviour of the starch and fat-splitting enzymes of the blood and urine under normal conditions.

Diastase (syn: amylase).

The property of digesting starch seems to be inherent in most of the tissue fluids. In 1908, Carlson and Luckhardt stated that the following fluids, arranged in descending series, normally exhibit diastatic activity: blood serum, thoracic lymph, cervical lymph, peripheral lymph, pericardial fluid and cerebrospinal fluid. These authors were struck by the constant level of diastatic activity maintained in the blood. Cumulative evidence of this feature of the serum diastase is to be found in the papers of Corbett (1912), Stockes (1916), Lewis and Mason (1920), Cohen (1925), Somogyi (1934), Comfort and Osterberg (1940) and Lewison (1941). Somogyi kept 100 normal persons under observation for over two and a half years and he found but little variation in the serum amylase values of any one individual although the

estimations as a whole were spread over a very wide range. He was unable to establish any correlation between the enzyme values and nutritional factors, age or sex. Lewison, also, found uniformity in serum amylase concentration of normal individuals but in an extensive investigation which entailed a study of 720 patients with diverse conditions unrelated to the pancreas, a few of his results were above the limits of normality and others fell below. In the majority of these instances, repeated estimations made within 24 hours showed that the normal activity had again become stabilised. He was unable to account for these isolated and transient rises of amylolytic activity. That these irregular readings were unimportant was shown by the fact that 94% of the whole series were within the normal range.

The function of these blood ferments is not yet fully understood. Nor do we know the nature of the regulating mechanism which maintains their activity at a relatively constant level. Oelgoetz, Oelgoetz and Wittekind (1935) have brought forward the view that diastase is absorbed into the lymph and blood streams in order to complete the digestion of partially split food products which have likewise been absorbed. Others have reason to doubt that the bowel contents constitute the main source of this enzyme.

Elman and McCaughan (1927) based their criticism on the finding that the formation of a total external pancreatic fistula had little effect on the serum diastase activity of the dog. Crandall (1935) tried the effect of introducing 200 cc. or more of fresh active pancreatic juice or saliva by way of a jejunal fistula. The results were for the most part negative though in a few experiments the increases of concentration of serum amylase and serum lipase were beyond the normal limits of variation. After due consideration of his results, however, this author came to the conclusion that the quantities absorbed under ordinary conditions could hardly be sufficient to influence the blood enzyme levels. Crandall also disagreed with the suggestion made by Oelgoetz et al. that the process of digestion is continued into the blood stream. Most authors incline to the view, originally expressed by Carlson and Luckhardt (1908), that diastase is a by-product of tissue metabolism and that once the ferment has entered the tissue fluids it is destined either to destruction or elimination. King (1914) also held with this idea although he suggested that it may be a contributing factor in the maintenance of the colloid equilibrium of the blood. If this were so, it would adequately explain the relative constancy of its concentration.

As already stated the factors regulating the diastatic activity are still unknown. It may be mentioned, however, that the view has recently been expressed that the pituitary gland may exercise some control over their production and elimination. This idea has arisen from the work of Cope, Hagstromer and Blatt, who reported in 1938 that hypophysectomy in dogs was followed by a twofold rise in the diastatic power of the blood.

A detailed study of the sources of diastase would take one well beyond the scope of this investigation, and there seems to be no real need to extend the investigations beyond the territory of the pancreas. For the present, it is sufficient to state that the share contributed by the pancreas appears to be considerable as is implied by the rapid accumulation of diastase which follows pancreatic injury or ligation of its major ducts, and by the subnormal values obtained after complete pancreatectomy (Gould and Carlson, 1911; King, 1914; Zucker et al., 1932; McCaughan, 1934). The fall in values after the removal of the pancreas in the dog may be, according to McCaughan, as low as 20% of the pre-operative values. This author, moreover, made the interesting observation that the return to normality or its near approximation occurred

in about the same length of time as was noted by him in the other experiments which resulted in greatly augmented serum diastase estimates. His abnormal findings were present until about the 10th day. In general, the findings of the other authors agree with the foregoing observations. These experimental observations infer not only that the enzymes are in part derived from the pancreas but that there is a regulating mechanism which is capable of re-establishing the original level even if the body is deprived of this source of supply. It is relevant to add that, since the dog was the most common species used for observing the effects of pancreatectomy, the responsibility for keeping up the supply could not have fallen to the parotid because canine saliva is deficient in diastase (King, 1914).

In contrast to what has been said about the constancy of the diastase content of the blood, there is ample evidence to show that the amount normally present in the urine is a variable quantity. The works of Foster (1867), Stockes (1916), Cohen (1925), Grey and Somogyi (1937) and Dozzi (1941) may be cited in support of this statement. Cohen found that during the day the rate of output rose and fell without apparent reason; meals seemed to produce an immediate increase which was more pronounced in some individuals

than in others. Readings taken during a fasting phase were irregular. Mecklar (1941) has recently stated that he could place little reliance on a single estimation of the amount of diastasuria. Zucker and his associates (1932), who also doubt the value of one reading, point out a discrepancy of 30% in results which may arise through deterioration in enzyme activity of specimens left standing a few hours.

Grey and Somogyi (1937), in a detailed study of the relative merits of serum diastase and urinary diastase determinations as a diagnostic aid in cases of acute pancreatitis, put forward the following argument in favour of the latter. Firstly, they pointed out that normal urine generally contains a greater quantity of the enzyme than the blood. They found, taking into account the fluctuations in level of output of urinary diastase, that there was a variation in the ratio of urinary diastase/blood diastase of 2/1 to 6/1. Secondly, they stated that the abnormally high enzyme activity exhibited by the urine in acute pancreatic disease is usually sustained for about a day longer than the associated increase in the serum diastase. This difference in the rate of fall of the two enzyme rises is in accordance with the later observations made by Lewison (1941). The

Continental authorities Foged (1935) and Millbourn (1936), who are chiefly interested in the urinary tests, do not refer to a lag on the part of the urinary values; they find instead that normal values are common after the second day in acute pancreatitis. As the present investigations are primarily concerned with the serum diastase changes, no further parallel need be drawn. In conclusion, however, it may be stated that practical value of the argument as to whether it is better to estimate diastase content of the urine or in the blood becomes of importance in cases of chronic renal disease developing acute pancreatitis. It has long been known that faulty renal function may affect the elimination of diastase as well as certain other constituents of the blood. I have given this some consideration in the course of the investigations.

Lipase.

The terms "lipase" and "esterase" seem to be used synonymously to signify the group of enzymes capable of hydrolysing the ester linkage. They cover the group that acts on ethyl butyrate, tributyrin, true fats, oils, cholesterol esters and waxes. These fat-splitting ferments have been found in the liver, pancreas, brain, lungs, spleen, intestinal mucosa, kidneys and muscle. Cherry and Crandall (1932) have

stressed the need for a more concise terminology when referring to this group of enzymes. These observers demonstrated for the first time that the blood assumed marked lipolytic properties after experimental ligation of the main pancreatic duct of the dog. They observed the same changes in the blood of patients who were in the early stages of acute pancreatitis. It was noticed, however, that not all of the substrates already mentioned were equally satisfactory for the demonstration of the rise in the fat-splitting activity. Thus, when ethyl butyrate was employed for the purpose, no increase was demonstrable in dogs subjected to duct ligation or in established cases of acute pancreatitis, but with olive oil, peanut oil, cotton-seed oil, that is to say, any triglyceride of the higher fatty acids, an increase became evident. Comfort and Osterberg (1934) also tried a variety of fatty substrates and their results were in accord with those of Cherry and Crandall. There would, therefore, seem to be good reason for adopting the suggestion made by the latter that the name "esterase" be retained as the generic term for all fat-splitting enzymes and the name "lipase" reserved for the type that is particularly active on fats and oils. Cherry and Crandall also approve of the designation "olive oil splitting" ferment since

an emulsion of that oil is the substrate generally used in the performance of the lipase test.

There is some doubt as to whether the blood of normal persons is capable of splitting olive oil in vitro. The earlier French workers Doyon and Morel (1902) and Arthus (1902) denied the existence of a lipolytic ferment, and Cherry and Crandall (1932) have endorsed this view despite the finding of positive values in a few of their controls. More recent contributors to this branch of enzymology have succeeded in proving to their satisfaction that lipase may be considered a normal constituent of the blood. They are, however, prepared to admit that in a certain number of controls, certainly not the majority, the enzyme is absent from the peripheral blood (Comfort and Osterberg, 1934, 1940; Johnson and Bockus, 1940).

Summary.

Starch splitting ferments may be found in many of the tissue fluids, particularly the blood, the lymph and the urine. While their digestive function can be demonstrated in experiments in vitro and while the pancreas may be an important source of these enzymes, the general view is that they are a form of tissue discard. The diastatic power of the urine varies under physiological conditions, whereas that of the blood stays at a steady level. The

blood values are constant for any one individual but in a group of persons, they may be spread over a very wide range.

In classifying the fat-splitting enzymes, it has been proposed that the term "lipase" should be specifically applied to the ferment which acts on olive oil or/and allied fats. Pancreatic obstruction causes an increase in the olive oil splitting ferment without a parallel change in the serum esterase. Views are sharply divided on the question of the lipolytic power of human blood in normal conditions.

BIOCHEMICAL METHODS EMPLOYED IN THE INVESTIGATIONS.

The serum diastase activity was estimated by the iodometric method of Somogyi (1938). The method of carrying out the test may be briefly summarised as follows: the patient's serum is incubated with a starch solution at 40° C. and at short intervals portions of this mixture are added to a weak solution of iodine measured out in small test-tubes. The end-point is reached when the colour, changing from blue to purple, becomes reduced to reddish brown as viewed by transmitted light from a standard source. The appearance of this colour indicates that the starch has been reduced to erythro-dextrin. The tints are so delicate that only clear serum or plasma can be used; icteric blood cannot be satisfactorily tested.

The time taken for this colour to appear having been noted, the diastatic activity of the serum can be calculated by a simple formula and the result expressed as a number. According to Somogyi, the indices of the normal enzyme activity of the blood range between 70-200 arbitrary units per ml. of serum.

In order to set my own normal standards, 83 "normal" patients were chosen, that is to say

patients in whom there was no reason to suspect the presence of pancreatic disease. The protocol of the individual findings may be found in the appendix. From a study of the accompanying table (No. 2) it will be noted that the mean value was 100.5 arbitrary units per millilitre of serum (Standard Deviation = 43.85). The highest value obtained was 228 units and the lowest was 40 units. An analysis of the findings failed to show any correlation with sex, age or the constitutional makeup of the individual.

The serum lipase activity was estimated by the Loewenhardt method as modified by Cherry and Crandall (1932) and further modified in certain details by Johnson and Bockus (1940). This is measured in terms of the amount of N/20 NaOH per millilitre of serum required to neutralize the fatty acids which are freed during the hydrolysis of an olive oil emulsion. The enzyme is allowed to act during a 24 hour period under optimum conditions of pH and temperature. The analyses were made in duplicate except for the few occasions when there was insufficient serum.

As already stated, certain observers maintain that there is no lipase in the blood of healthy persons. Crandall (1935) has re-stated this view and regards reports to the contrary as being due to differences in technique. Johnson and Bockus (1940)

concede this point when they stated that the serum lipase test is somewhat short of the ideal from the standpoint of quantitative biochemistry. They pointed out two potential sources of error - variations in the composition of the olive oil emulsion and the difficulty of pipetting with accuracy 2 ml. of this viscid substrate. In spite of these supposed imperfections, Johnson and Bockus were able to report not only that the blood of most of their controls contained a lipase but that duplicate estimates carried out on the same specimen of blood were remarkably close. An analyses of their results indicated to them that values over 1.0 ml. might be regarded as pathological. In an earlier report, Comfort and Osterberg (1934) accepted 2.0 ml. as their upper normal limit. They now evidently attach importance to figures above 1.5 ml. according to a more recent report published in 1940.

In my own series of 76 controls, the mean value was 0.45 ml. N/20 NaOH per ml. serum (Standard Deviation = 0.35). The highest titre was 1.6 ml. but the vast majority of the readings were below 1.0 ml. In five subjects the presence of lipase could not be detected. It will be observed that the titrations of duplicate estimations were in close agreement (see Appendix, table No. I.).

TABLE 2.

Serum Enzymes in
a Control Series of "Normal" Patients.

Serum Enzyme	No. of Controls	Range of Readings	Mean of Readings	Standard Deviation
Diastase	83	40-228 units per ml. serum	100.5	43.85
Lipase	76	0-1.6 ml. N/20 NaOH per ml. serum	0.45	0.35

THE INFLUENCE OF DIET ON SERUM ENZYMES.

The earlier references to the constancy of the serum diastatic activity as found in a particular person implied that the intake of food or its deprivations left it unaffected. In 1908, Carlson and Luckhardt stated that there was no correlation between the concentration of the blood diastase and the relative abundance of carbohydrate in the natural diet of a species. Wohlgemuth (1908) found that fasting dogs had in their blood as much diastase as

a well fed one. Nor did the enzyme's activity vary with the state of nutrition. McCaughan (1934) confirmed these observations. According to Lewis and Mason (1920), Cohen (1925) and Somogyi (1934), the diastatic activity of human blood is undisturbed by dietetic or nutritional factors. It would appear that no one has recorded the influence of diet on serum lipase.

Personal Observations.

Seven normal patients were given a puree consisting of 100 g. of starchy food and 100 g. of fatty food. This was given about 3 hours after the previous meal. Blood samples were taken before the meal and at one and two hours after. During the period of observation the subject was confined to bed. An eighth experiment was carried out on a normal person who was given a balanced meal and whose activities were not restricted. The starch and fat contents of the meal were roughly 73 g : 44 g respectively.

TABLE 3.

Effect of Diet on Serum Enzymes of 8 Subjects.

Control Patient	Times of Observations	Serum Enzymes	
		Diastase units/ml. (40-228)	Lipase ml.N/20 NaOH/ml. (0-1.6)
Those fed on puree (Carbohydrate content = 100 g; fat content = 100 g)			
1. Renal colic	Meal at 11.30 a.m.		
	Before	88	zero
	1 hour after	133	zero
	2 hours after	88	zero
2. Appendicectomy	Meal at 11.30 a.m.		
	Before	100	0.3
	1 hour after	106	0.56
	2 hours after	100	0.24
3. Epididymitis	Meal at 11.30 a.m.		
	Before		0.23
	1 hour after		0.39
	2 hours after		0.43
4. Fractured ribs	Meal at 11.30 a.m.		
	Before		0.13
	1 hour after		0.16
	2 hours after		0.09
5. Burn of foot	Meal at 10.30 a.m.		
	Before	177	0.03
	1 hour after	177	0.27
	2 hours after	160	0.18
6. Hernia	Meal at 10.30 a.m.		
	Before	160	zero
	1 hour after	123	0.1
	2 hours after	113	zero
7. Hernia	Meal at 10.30 a.m.		
	Before	160	zero
	1 hour after	123	zero
	2 hours after	123	zero
8. Normal person fed on a balanced meal - Porridge, milk cold ham, toast, butter, marmalade, tea with sugar (Carbohydrate content = 73 g; fat content = 44 g)			
	Meal at 9 a.m.		
	Before		0.74
	$2\frac{3}{4}$ hours after		0.66

Comment: Except for the findings in Nos. 1 and 4, both the serum diastase and lipase values remained more or less constant after food. An appreciable rise in the serum diastase content occurred in the first subject although the values kept within the normal range. A rise of 0.1 ml. was observed in the 1st hour specimen of No. 4, but this seemed too small to be of any significance.

The Constancy of Serum Lipase Activity.

So far it has been shown that lipase is a not uncommon constituent of the blood and that its values remain reasonably constant up to three hours after a meal. Further proof of a prevailing state of equilibrium such as has been noted in respect of serum diastase is found in the other results obtained in subject No. 8. This person's blood was examined three times over a period of several months, during which time different batches of olive oil were prepared. The results tabulated below will be seen to have altered little throughout the period of observation.

TABLE 4.

Repeated Estimations of Serum Lipase on a Normal Individual (in the fasting state)

Date of Estimation	Serum Lipase ml. N/20 NaOH per ml. serum (Normal: 0 - 1.6)
25th July, 1943	0.75
14th October, 1943	1.0
21st February, 1944	0.75

THE EFFECT OF ANAESTHESIA AND COMMON SURGICAL PROCEDURES ON SERUM ENZYMES.

In some of the clinical studies to be reported later, several of the enzyme estimations were carried out during or soon after operation. A control series was, therefore, examined to find out the effect of general anaesthesia and to supply information on the biochemical effect of surgical trauma to tissues other than the pancreas.

Contradictory reports are to be found in the

literature regarding the influence of ether anaesthesia on the serum diastase. Carlson and Lockhardt (1908) noted decreased diastatic activity during the administration of ether. Watanabe (1918) anaesthetised four rabbits for one hour and took samples of blood immediately before the drug was given, immediately after, and one later. The diastase content was slightly increased in the post-anaesthetic sample but not markedly so on the average. The blood drawn off one hour after the termination of the anaesthesia showed a slight lowering in diastatic activity. ~~Ross~~ Davis and ~~Davis~~ Ross (1921) found negative or equivocal results in their experiments carried out on dogs, the period of observation being from 30 minutes to 24 hours after the giving of the anaesthetic. Karsner, Koeckert and Wohl (1921) observed a minor rise in the serum diastase values in dogs after the inhalation of ether. Zucker et al. (1932) found that a slight but insignificant rise in the serum diastase content occurred in dogs subjected to ether anaesthesia and that this reached maximal values about seven to nine hours later. In another paper published in the same year, the same group of investigators described a series of experiments on dogs which had had their pancreatic ducts cannulated. Zucker and his associates found that ether might completely inhibit the

flow of pancreatic juice. Assuming that the function of the pancreas depended, as Anrep (1924) suggested earlier, on a double mechanism of formation and transport of external secretion, they supposed that the drug tended to slow down its transport and created thereby conditions favourable for absorption of the stagnant secretions into the blood stream. It is of passing interest to note that chloroform given for as short a time as 30 minutes or to the extent of causing liver damage lowers the diastatic content of the blood (Davis and Ross, 1921; Zucker et al., 1932) and raises slightly its lipase content. Lewison (1941) considered the problem in humans but he was unable to find any difference in the serum amylase activity after general anaesthesia given according to modern standards or even after intra-abdominal handling of the pancreas.

The effect of loss of blood on the serum diastase content has received the attention of Karsner et al. (1921). Using rabbits, they noted that repeated small haemorrhages of 5 ml. at a time produced no effect until the animals were visibly exsanguinated, at which stage there occurred a slight tendency for the diastatic activity to rise.

Personal Observations.

In the cases studied, the operations were carried out on areas remote from the territory of the pancreas. The anaesthetic used in all instances was nitrous oxide, ether and oxygen, and the time during which the patients were exposed to its action averaged half an hour. The premedication in some was morphine sulphate gr. ¼ and atropine sulphate gr. 1/100th and in others Nembutal in gr. 3 doses combined with atropine sulphate gr. 1/100th. The serum diastase and serum lipase findings obtained before and after operation are set out in the accompanying table (Table No. 5).

The pre- and post-operative values in each case were substantially the same. With such a small series of cases, a definite conclusion cannot be drawn but there seemed some justification for the view that the values of the serum enzymes quoted above and later were unlikely to be vitiated by the operation or the anaesthetic.

Action of Nitrous Oxide, Oxygen and Ether on Serum Enzymes of 7 Normal Patients subjected to various operative procedures unconnected with the Pancreas.

Operation	Premedication used	Serum Enzymes — Somogyi Units (40-228) / Lipase ml. N/20 NaOH/ml. (0-1.6)						
		Before Anaesthesia	Time of Observation in hours after anaesthesia commences					
			1	2	3	4	5	6	10
Case 1 Hernia	Morphia gr.¼ Atropine gr.1/100	114	106			119			
Case 2 Appendicectomy	Ditto	100 0.58	94 0.58			114 0.33			
Case 3 Circumcision	Ditto	64 0.34	64 0.17		50 0.59				
Case 4 Appendicectomy	Nembutal gr.3 Atropine gr.1/100	0.23						0.42	
Case 5 Appendicectomy	Ditto	69 Zero							64 Zero
Case 6 Appendicectomy	Ditto	Zero					Zero		
Case 7 Appendicectomy	Ditto	0.35				0.67			

Summary.

The two methods employed in this thesis are briefly described and the results of control studies presented.

The range of normality for serum diastase in 83 controls was 40 - 228 arbitrary units per mil. serum, and for serum lipase was zero to 1.6 ml. N/20 NaOH per ml. serum in 76 controls.

The state of diastase and lipase equilibrium which exists in the blood is apparently unaffected by physiological considerations such as age, sex and dietetic factors. The range of normal particularly in regard to serum diastase is a wide one owing to the fact that the level of enzyme activity is an individual characteristic. Lipolytic activity of the blood serum was a common feature among the controls personally studied.

The serum enzymes were not materially disturbed by ordinary surgical procedures nor by nitrous oxide, ether and oxygen anaesthesia.

AN EVALUATION OF SERUM DIASTASE AND SERUM LIPASE TESTS AS INDICATORS OF PANCREATIC DYSFUNCTION.

The Scope of Study:

This investigation is an analysis of the serum enzyme findings in 15 cases of acute pancreatitis. Its aim is twofold: (1) to establish diagnostic standards, and (2) to find out whether the results obtained offer a measureable index of the pancreatic damage. The series includes 14 cases who were examined during the first ten days of illness and one other who was admitted for treatment two months after its onset, a pseudo-pancreatic cyst having developed by that time.

Serum diastase and serum lipase estimations were carried out concurrently on duplicate specimens of the same sample of serum and in each case a varying number of serial observations were made. To complete the records, the diastatic activity of the urine was also taken into account. The combined study of the serum and the urinary diastase was especially profitable in one particular case because it brought attention to bear on a latent defect in the kidneys as well as on unsuspected pancreatitis. This led one to take up the study of the effects of impaired renal function on serum enzymes. Special

consideration was also given to the biochemical changes in pancreatitis complicating mumps and in parotid affections per se. Finally as a complementary study, observations were made on the enzyme content of the peritoneal effusion which was present in some acute pancreatitis cases.

Biochemical Findings.

The results seemed to fall naturally into four main groups - the very high values, the moderately high values, those which were slightly raised and those which were normal. This arbitrary arrangement was particularly apt in so far as the range of values for diastase in one particular group of cases corresponded with the range of values for lipase in the same group (see Table 6).

TABLE 6.

Arbitrary Grouping of the Acute Pancreatitis Cases according to Enzyme Values.

Grade of Values	Serum Diastase		Serum Lipase	
	No.of Cases	Units per ml. serum (Normal: 40-228)	No.of Cases	Ml. N/20 NaOH per ml. serum (Normal 0-1.6)
1. Very high	2	4,000-5,500	2	5.3 -9.8
2. Moderately high	4	800-1,600	3	2.6 -3.4
3. Slightly raised	4	255-457	3	1.92-2.13
4. Normal	3	94-114	7	0.99-1.40

The findings presented in the foregoing table show that values approximating 20 times and 10 times the upper normal limits for serum diastase and serum lipase respectively are the maxima for the series.

Those of next group also seemed to be sufficiently raised to merit being called "pathological". At the present stage in the analysis, it is not possible to give an opinion as to the significance

of slightly raised or normal value in proven cases of acute pancreatitis. A collective review of the cases will show that there was in many instances a certain disparity between the degree of functional upset, as portrayed by the tests employed, and the pathological conditions of the pancreas. The tests seemed non-discriminative in so far as they sometimes gave very high readings in mildly affected cases and at other times normal values were found in patients whose pancreas was grossly diseased. To find the cause of these discrepancies, each case was then given individual attention. The biochemical findings and the essential data relating to the clinical and pathological features of each patient were collated and set out below in Table 7. The series comprised 6 cases which were found at operation to be grossly affected (group A), 5 cases also submitted to operation which were of the mild type (group B) and 4 cases in whom the diagnosis rested solely on a consideration of the clinical and biochemical findings (group C).

TABLE 7.

(A) Serum Enzymes in Acute Pancreatitis Cases with Gross Pathological Changes.

Operative Findings	Time of Observation	Serum Enzymes		Urinary Diastase Wohlgemuth Units/ml.
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)	
Case 11. WH., male, 65 years. June 1941.	14 hours	4,000	5.30	200
Operation on 1st day of illness.	2nd day	2,130		
Acute haemorrhagic pancreatic necrosis with scattered areas of fat necrosis and free fluid of dark brown colour.	3rd "	475	0.50	
	7th "	320	0.50	20
Died after 8 weeks, with suppurative pancreatitis.	27th "	290	1.00	
	57th "	46	Zero	
Case 14. R.S., male, 66 years. December 1941.	15 hours		3.10	
Operation on 1st day of illness.	2nd day	1,600	1.30	
Acute haemorrhagic pancreatitis of caudal half. No fat necrosis or free fluid.	3rd "	860		250
Patient survived.	4th "	530	1.80	
	12th "	320		100
	15th "	406	0.20	
Case 20. F.McD., female, 63 years. November 1942.				
Operation on 4th day.	4th day	110	0.21	16
Pancreas hidden by matted, swollen omentum. Numerous points of fat necrosis. Brownish effusion.	5th "	80	0.35	
Patient lived.				
Case 16. R.McL., male, 70 years. April 1942.				
Operation on 15th day.	4th day	457	2.13	
Pancreas hidden by matted, swollen omentum.	7th "	84	0.21	40
Small deep abscess - ? necrosed pancreatic tissue	12th "	106	0.08	
Areas of fat necrosis on surface of omentum. False cyst containing 2 pints turbid fluid.	15th "	57	0.3	16
Patient survived.				

TABLE 7.

(A) Serum Enzymes in Acute Pancreatitis Cases with Gross Pathological Changes (Contd.)

Operative Findings	Time of Observation	Serum Enzymes		Urinary Diastase Wohlgemuth Units/ml.
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)	
Case 19. I.C., female, 48 years. October 1942. Operation on 8th day. Pancreas was extensively necrosed. No sign of haemorrhage or free fluid. Numerous areas of fat necrosis on great omentum and in vicinity of pancreas. Patient survived.	8th day 18th "	94 145	0.98 1.36	
Case 25. M.B., female, 52 years. February 1944. Patient sent in as an acute appendicitis by her doctor. Severe epigastric pain of sudden onset. Later spread over whole abdomen. Vomiting from start of illness. She was very obese, and seemed to be free of pain on admission. She was pale, sweating profusely but her skin was warm to touch. There was neither jaundice nor cyanosis. Generalised tenderness especially in epigastric and right hypochondrium. Operation on 2nd day. Acute haemorrhagic pancreatic necrosis, with a gross amount of haemorrhagic bile stained exudate. Gall-stones and septic bile in gall-bladder. Cholecystostomy performed and lesser sac drained. Case died on 3rd day of illness.	3rd day	-	1.08	

TABLE 7.

(B) Enzymes in Acute Pancreatitis Cases with Minimal Pathological Changes.

Clinical Synopses and Operative Findings	Time of Observation	Serum Enzymes		Urinary Diastase Wohlgemuth Units/ml. (6-60)
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)	
Case 23. M.L., female, 49 years. June 1943.				
Epigastric pain and sickness of 6 hours' duration. Sl. jaundice. Collapsed. Acute condition settled and jaundice cleared in few days.	6 hours	5,300	9.8	
	3rd day	460	5.8	
Operation after 21 days. Pancreas slightly nodular and firmer than normal. Otherwise looked normal.	6th "	228	2.94	
Biopsy revealed focal areas of necrosis histologically. Gall-bladder showed early chronic change. It contained one pigmented stone 1.5 cm. in diameter.	48th "		1.35	
Patient survived.				
Case 21. J.W., female, 52 years. November 1942.				
Intermittent accesses of severe epigastric pain that passed to left sub-costal region and sickness over a period of 5 days. Mass palpable in left hypochondrium. Slight jaundice.	5th day			100
	6th "	255		50
Cholecystectomy done 4 months previously.	7th "			40
Barium Enema revealed downward displacement of splenic flexure of colon (? fluid lesser sac).	8th "	133		
Laparotomy 8 weeks later. Pancreas felt normal. Patient survived.				
Case 18. I.D., female, 45 years. June 1942.				
Abdominal colic vomiting and jaundice.	5th day	114	0.84	
Cholecystography: Gall bladder not visualised.				
Readmitted August 1942 with similar symptoms.				
Operation on 5th day. The pancreas was diffusely swollen and indurated throughout its length. No signs of haemorrhage or fat necrosis.	5th day (Re-admitted)		0.98	
Gall bladder was slightly oedematous, but neither it nor common duct contained stones.				
Patient survived.				

TABLE 7.

(B) Enzymes in Acute Pancreatitis Cases with Minimal Pathological Changes (Contd.)

Clinical Synopses and Operative Findings	Time of Observation	Serum Enzymes		Urinary Diastase Wohlgemuth Units/ml. (6-60)
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)	
Case 12. H.C., female. June 1941. (See section on acute pancreatitis and chronic nephritis, page 65)	10th day	1,184	3.40	
	12th "	640	3.00	
	15th "	533	2.60	5
	25th "	800	4.10	10
Case 24. R.McA., male, 49 years. January 1944. Severe pain, of a constant gnawing type, in right hypochondrium for 2 days. It was referred to the back between shoulder blades and to right shoulder tip. On examination, he looked toxic, and there was a slight degree of both cyanosis and jaundice. Abdominal movements were restricted. Tender in epigastrium. Laparotomy on 2nd day. Pancreas hard and nodular. No sign of fat necrosis. Gall-bladder distended but free of stones. Cholecysto-duodenostomy performed. Biopsy of pancreas showed subacute pancreatitis. Case survived.	10th day	-	1.4	-

TABLE 7.

(C) Serum Enzymes in Acute Pancreatitis Cases treated Conservatively.

Clinical Synopses	Time of Observation	Serum Enzymes		Urinary Diastase Wohlgemuth Units/ml. (6-60)
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)	
Case 13. A.C., female, 57 years. July 1941. Severe upper abdominal pain for 3 days. Slight jaundice. Tender right subcostal region. Cholecystogram: Non-functioning gall bladder. Patient survived.	4th day	1,280	2.60	
	6th "	228	1.70	
	8th "	228	1.70	
Case 22. J.W., female, 56 years. November 1942. Severe abdominal pain and sickness for 4 days. Admitted comatosed. Advanced diabetes mellitus. Re-admitted 3 months later in diabetic coma. Patient survived.	7th day	430		
	10th "	66	0.09	12.8
Case 15. F.F., male, 21 years. March 1942. On the 7th day of mumps, developed severe pain in left upper quadrant which passed to left loin. These symptoms lasted 3 days. No sickness. Tender left subcostally. Patient survived.	3rd day (abdominal illness)	800	0.84	80
	5th day	400	1.29	20
	7th "			6
Case 17. M.M., female, 51 years. May 1942. Acute illness 2 months previously. Abdominal pain and sickness very severe. Original diagnosis was coronary thrombosis. Illness lasted 14 days. Swelling in left upper quadrant (see Photograph page). Barium meal showed presence of a lesser sac cyst (see Skiagraph page). Diagnosis: False pancreatic cyst. Cholecystectomy had been done in September 1941. Patient survived.	2 months after acute illness	284	1.92	60
	3 days later	228	0.76	
	20 days later	237	0.96	6.6

Comment: Considering first of all the initial readings, it will be seen that the highest estimates were recorded in case 23. There were two noteworthy features in this case - it was investigated sooner than any of the others, the symptoms having been present for only 6 hours prior to biochemical investigation and when operated upon three weeks later the pancreas was only slightly nodular but otherwise normal; a biopsy of the pancreas was necessary to demonstrate the presence of the lesion. A case of acute haemorrhagic pancreatic necrosis (case 11) which was operated on 14 hours after the onset of illness gave readings of a slightly lower order. The third highest estimates were obtained in case 14, another with gross changes; the lesion was most evident in the caudal end of the gland. The symptoms in this case had lasted for 15 hours when the serum lipase estimations were carried out; the serum diastase activity was determined on the following day. Leaving case 12 out of account for the present as it was complicated by renal disease, the fourth day readings in case 13, which was regarded clinically as a biliary colic, were of still a lower order. The cases observed thereafter approximated to or lay within the normal limits.

When attention was next directed to the serial

estimations, it became evident that the increase in serum enzyme values was a very temporary episode. The highest values were found on the first day and normal values by the end of the first week. Thus it would seem logical to assume that the previous values in case 7 had probably been of a much higher gradation judging by the observation that the third day diastase readings in case 23 and in case 11 and the fourth day diastase readings in case 16 were all much the same. Another observation in favour of this argument was the finding of normal lipase titres on the third day in the two seriously ill cases nos. 11 and 25.

On the face of these findings there seemed good grounds for believing that the enzyme response bore little relation to the intensity of the stimulus; rather did it seem that the element of time was the more important point to be considered when placing an interpretation on the results. In the subsequent discussion, it is proposed to weigh these two factors - the pathological picture and the element of time - against one another.

Discussion.

There is a considerable weight of experimental evidence to support the belief that the enzyme response furnishes a reasonably accurate index of the degree of functional derangement. Wohlgemuth (1910) and McCaughan (1934) using different methods compared the effects of ligating the two main pancreatic ducts with those of ligature of one duct and both came to the conclusion that a complete block of the pancreatic duct system produced a higher and more lasting increase in the blood diastase than partial blockage. According to McCaughan and Clasen, Johnstone and Orr (1934), the height of the rise in serum diastase levels is directly proportional to the amount of destruction caused by the injection of chemical irritants into the pancreatic ducts. Baxter, Baxter and McIntosh (1938) claim to be the first to investigate the serum lipase changes in experimental pancreatitis which they produced in dogs by the intraduct injections of bile. They obtained a marked rise in the serum lipase titres comparable to the diastase changes found in experimentally produced pancreatitis. In some experiments, however, they found low values for which there was no obvious cause. Baxter and his co-workers advanced the suggestion that the lesions

in the latter group of animals might have been so extensive that the lymphatic channels and capillaries, the pathways by which the escaping pancreatic juice reaches the peripheral blood, were also engulfed in the destructive process. To draw a close parallel between these experimental findings and the clinical observations is scarcely justified since in the former the stimulus that elicits the enzyme reaction is known and to a certain extent controlled. Such a comparison would also introduce the assumption that all the clinical cases were due to interference with the pancreatic ducts with or without the entry of an irritant. It would not be irrelevant to discuss further at this juncture the mechanism of the enzyme changes and their aetiological significance but in view of the limited amount of clinical data available in the present study, it has been considered advisable to leave the discussion of these problems until later.

There are a few who believe that the biochemical findings are a reflection of the underlying pathological picture and that they may even foretell the course of the illness. Wohlgemuth (1929) has commented on the wide variations to be found in the diastase content of the urine in cases which seem on direct inspection of the pancreas to be of equal

severity. He thought that the departure from the normal levels was mediated largely by the extent and locus of the lesion. He reasoned that the functional disturbance would be greater if the main ducts were involved than if the lesion were confined to the superficial parts of the gland. Unger and Heuss (1927) held the view that the gradient of the rise in urinary diastase content was commensurate with the clinical condition, having been influenced by the fact that all their cases which had a diastatic index of 1,000 units (Wohlgemuth) and over died within a few hours of operation.

In interpreting my own observations, I came up against the difficulty of selecting a suitable pathological classification, a problem to which reference will be made later. The cases whose pancreas had been inspected were classified into two main groups: (1) those with gross signs of haemorrhages and necrosis, and (2) those little affected, the pancreas being only slightly enlarged and indurated. No attempt was made to hazard a guess as to the pathological conditions which existed in those in which operative treatment had been withheld. I refrained from doing so because on clinical examination the so-called subacute cases appeared in some instances to experience just as severe symptoms as those with extensive haemorrhagic and

necrotic lesions. The clinical findings in cases 23, 24, 25 may be cited in support of this viewpoint. A synthesis of the biochemical, clinical and pathological data set out in table 7 clearly shows that the range of the initial values could not be correlated with the pathological findings nor the clinical picture. Since one did not feel inclined to make relief incisions into the markedly affected glands nor saw the need for doing so in the subacute cases, information as to the real extent of the disease, and in particular its proximity to the major duct, could not be obtained that would substantiate Wohlgemuth's hypothesis. One can say, however, with reasonable confidence that the rise in serum enzyme levels at any given time during the acute stages stood in inverse proportion to the duration of the illness. Arguing along these lines, it may be assumed that the unfortunate experience of Unger and Heuss referred to in the preceding paragraph is really an indictment of early operative treatment in acute pancreatitis and not an indication that the enzyme values are prognostically significant.

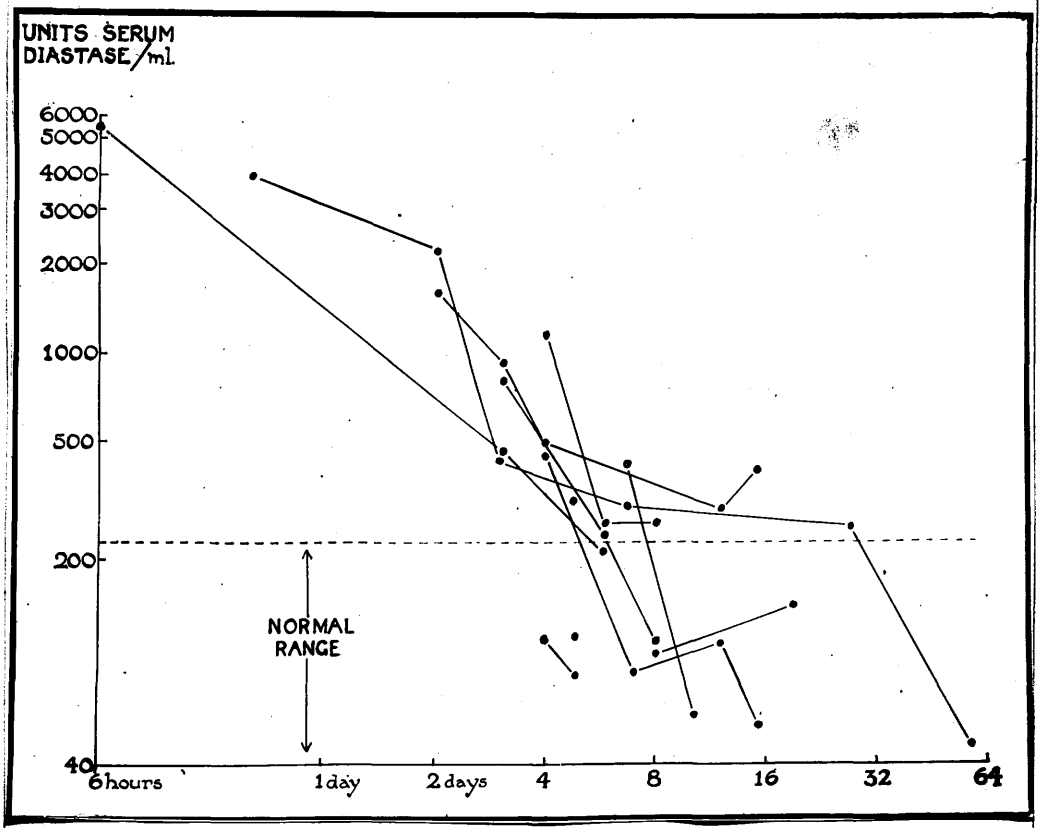
Most authorities are agreed that the enzyme levels estimated in any given case depend to a large extent on the time lag between the onset of illness and the period of observation. In 1920, Garrod

speaking with reference to the urinary diastase in acute pancreatitis, said: "The diastase increase is a temporary incident, most conspicuous in the early stages of a case. Repeated examinations at intervals may reveal a quicker or slower decline of the diastase output until normal or even subnormal figures are reached. Thus, it comes about that whereas a conspicuous excess of diastase in the urine is strongly suggestive of disease of the pancreas, a normal excretion in no way excludes even advanced disease of the gland." Mikkelsen (1934), Foged (1935) and Millbourn (1936) also noted increased diastasuria only in the initial stages; normal values after one and a half days were not considered by them to be incompatible with a diagnosis of acute pancreatitis. Those who have made a study of the serum diastase in this condition (Morton and Widger, 1940; Lewison, 1941; Elman, 1937, 1942; Sorkin, 1943, and others) and serum lipase (Bernard, 1933; Lewison, 1941) have shared much the same experience. It is of singular interest to note that Mikkelsen (1934) has recorded two cases which were seen so early that the output of diastase in the urine was still at a normal level. He first examined his cases within three hours of the onset of symptoms but when re-examined one hour later the characteristic rise had occurred. Thus comparing

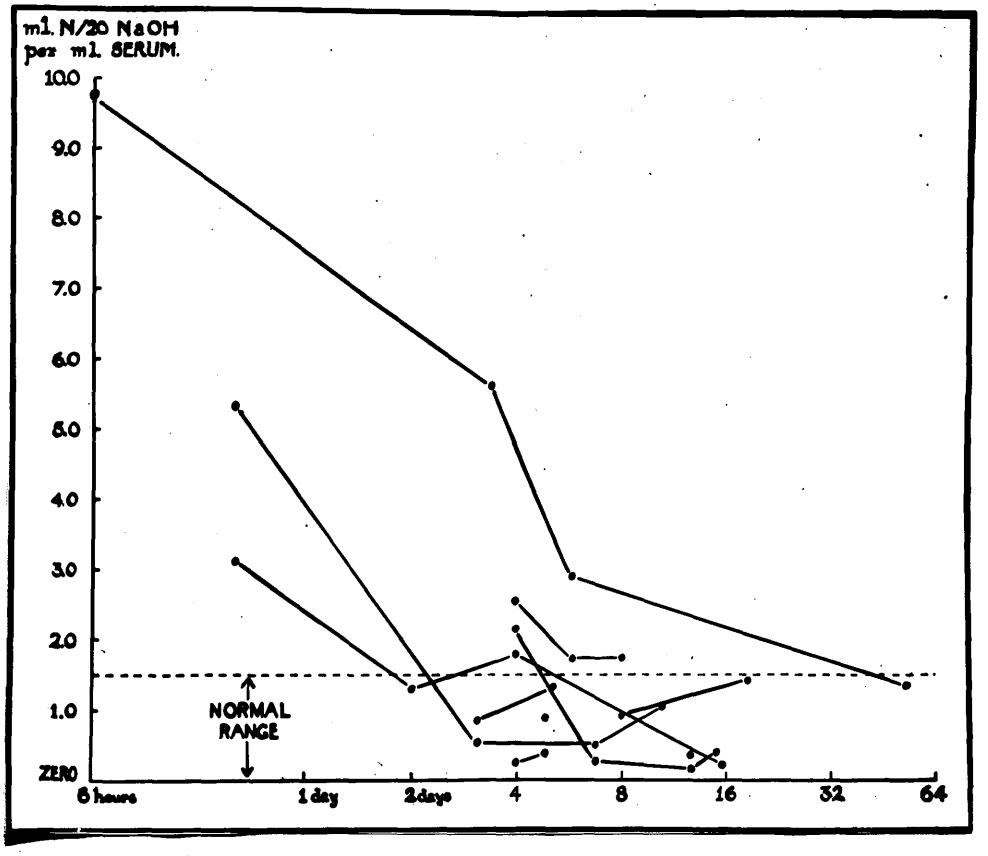
the findings in these cases with my own it would appear that the peak values, for diastase, at least, are to be found round about the fourth to the sixth hours of illness, and it seems reasonable to assume that the same holds good for serum lipase.

Some importance has been assigned to the rate of fall of the diastase values but unfortunately the views expressed are diametrically opposed to one another. Mikkelsen (1934) takes the view that if massive necrosis of the pancreas occurs, biochemical changes may not become evident in the urine, or if they do, a speedy return to the normal output is to be expected. On the other hand, Elman (1937, 1942), who is particularly interested in the less fulminating, and in his opinion the more common, form of pancreatitis, states that a transitory rise in the serum diastase values irrespective of the height attained tends to indicate a subacute lesion and that a slow subsidence indicates continued activity of the diseased process. For that reason he regarded a slow fall as a bad prognostic sign. Wide currency is given to the view that the abnormal titres for serum lipase remain raised for a longer time than is usual for serum diastase values (Crandall, 1935; Comfort and Osterberg, 1940). Lewison (1941), on the other hand, was unable to convince himself that a gradual

diminution in the serum lipase activity was a common feature. He did report, however, that the fluctuations in the serum lipase values paralleled those for serum diastase in all his acute cases.



Graph No. 1 showing the serum diastase findings in 11 cases of acute pancreatitis.



Graph No. 2 showing the serum lipase findings in 11 cases of acute pancreatitis.

The influence of the time factor becomes more evident when the results of the serial observations given in Table 7 are presented graphically (see above figures). The peaks of the enzyme curves are found a few hours from the onset of illness while the values plotted between the 4th to the 10th days approach or lie within the normal limits. A striking feature is the way in which the serum lipase values,

taken by and large, fluctuate pari passu with the serum diastase values. The former did not exhibit a tendency to remain elevated longer than the latter. This observation, though it fits in with Lewison's experience, runs counter to the generally accepted view on the behaviour of the lipolytic ferment. Indeed, the graphic presentation of my findings suggests that the return to normality occurred sooner in the lipase studies than in the diastase studies.

Elman's dictum that a slow fall in serum diastase indicates a continuance of the disease process was supported by cases 11 and 14, each of which had prolonged convalescence, and case 17 whose illness had started two months previously and by the time this patient came under observation a pseudo-pancreatic cyst had developed. Case 11 deserves detailed mention since it was the only one which progressed to the suppurative stage, a complication which is now considered to be rather uncommon (Douglas, 1935). This patient was re-admitted to hospital with a large abscess in the right loin, eight weeks from the date on which he was first examined. He was in a moribund condition and the presence of glycosuria which had not hitherto been noted pointed with a high degree of probability to almost total destruction of the pancreas. Serum enzyme values were subnormal.

The patient died soon after evacuation of the abscess. At autopsy, no trace of pancreatic tissue could be found. It was replaced by a large collection of pus which had tracked in several directions in the retroperitoneal tissue plane.

The aforementioned correlation between the rate of fall of enzyme values and the progress of the disease did not always hold in all the serious cases. In Case 7, for example, massive necrosis of the pancreas was encountered at operation and yet there was only a slight departure from the normal values when the patient was investigated on the 4th day of illness. Nor could it be said that the rate of fall of the enzyme curves afforded a reliable guide to the prognosis in the present series.

The final point to be mentioned in this discussion is the occurrence of slight exacerbations in enzyme activity about the 10th day. A study of the graphs Nos. 1 and 2 will show the phenomenon as it appeared in my own cases. It was observed on three occasions. Except in one case (No. 14) whose values had not reached the upper normal limit (for diastase), the secondary rises kept within the normal ranges for both diastase and lipase. Secondary and even tertiary rises in serum diastase have been reported after experimental ligation of the pancreatic ducts by

some authors (Gould and Carlson, 1911; McCaughan, 1934); and Cherry and Crandall (1932) observed a similar rise in serum lipase titres in one dog similarly treated. Crandall (1935) found these late effects in clinical cases of acute pancreatitis. This author regarded this finding as a basis for criticising the current view that the blood enzyme determinations can only be expected to be significant within a brief period after the onset of the condition. Crandall saw in these late aberrations a cogent argument for carrying out serial studies, particularly in those patients who have sought treatment after the critical stage of acute pancreatitis has passed.

A Case of Mumps complicated by Pancreatitis.

A case of epidemic parotitis who was believed to have had a pancreatic complication has been included in the pancreatitis series. The patient, a young adult male, started to complain of upper abdominal pain on the 7th day of illness, by which time there was no clinical evidence of swelling of the face. The pain, which was very severe, was felt in the left

upper quadrant and left loin. It was unattended by vomiting but there was loss of appetite. The possibility of a chest or renal lesion being the cause of his symptoms seemed unlikely. The patient was not investigated until three days after the commencement of the abdominal complaint and by that time he only felt a dull ache in the left hypochondrium.

The biochemical findings in this case (No. 15) will be found in Table 7 (C). The first diastase estimate was 800 units, but the corresponding lipase reading was normal. Repeat readings carried out two days later revealed a drop to half the previous diastase level and a decided rise in the lipase level. A progressive drop in the output of urinary diastase from a moderately high level to normal values was also noted.

The question which presented itself was whether the present findings were really due to pancreatitis or merely a sequel to the mumps. Lewison (1941) met this difficulty by carrying out simultaneous studies of the serum diastase and serum lipase activity. In a series of 12 patients with epidemic parotitis and one of infective parotitis, he found that all the lipase levels were normal whereas the amylase levels were considerably raised in all except those where the parotitis was unusually mild or where

the determinations had been made late in the disease. None of these cases presented symptoms to suggest a pancreatic lesion. On the other hand, cases in which this complication had occurred exhibited a parallel rise in the lipase content of the blood. This author was led to the conclusion that the lipase test afforded more conclusive evidence of a pancreatic complication than the diastase test.

It was unfortunate that my personal observations had not been made earlier than the 3rd day of the abdominal illness, but there were two points of evidence that favoured pancreatitis being the causal factor. Firstly the distinct rise in lipase values noted later tended to indicate that the equilibrium of this enzyme's activity had been upset and had not quite stabilised itself. Secondly, it seemed improbable that a parotitis which had developed 10 days previously and which had resolved from the clinical standpoint, would produce such a sustained disturbance of the diastase levels of the blood and urine. In order to find out just how long the diastatic response to uncomplicated parotitis might last, a small series of these cases was investigated. The results are presented in Table 8.

TABLE 8.

Enzyme Changes in Parotitis.

Type of Mumps	Time of Observation	Serum Diastase Units per ml. serum (40-228)	Urinary Diastase Wohlgemuth Units/ml. (6-60)
Case 1 - Epidemic. Both glands affected. No abdominal symptoms.	3rd day	400	100
Case 2 - Epidemic. Both glands affected. No abdominal symptoms.	3rd day	250	
Case 3 - Epidemic. Transient pain in abdomen but not regarded as pancreatic.	7th day		6
Case 4 - Infective	7th day	106	

So far as the results of this small series show, a pathological rise in the diastatic activity of the serum and the urine may be expected in parotitis. In the two patients which were seen on the 7th day, the serum diastase content in the one and the amount of diastase excreted in the urine of the other were found to be within the normal limits. These findings lend credence to the belief that the elevation encountered in case 15, Table 7, was a genuine case of pancreatitis caused by the virus of mumps.

Urinary Diastase Observations in Acute Pancreatitis.

The urinary investigations undertaken in this work were, for the most part, regarded as subsidiary to the study of the serum enzymes. A control series of experiments was not done, nor were the technical merits of the serum methods weighed against those of the urinary methods.

The Wohlgemuth test in its simplest form was used. The dilution of urine which digested 2 millilitres of an 0.1% starch solution was noted, after the mixture had been exposed to a temperature of 38°C in a water bath for 30 minutes. From this information one could calculate the amount of substrate which 1 millilitre of urine was capable of digesting. Thus the diastatic index of the urine, which is usually expressed as the figure $d\frac{38^{\circ}}{30}$, was arrived at. The range of values accepted as normal was 6 - 60 units per millilitre of urine in accordance with the suggestion made by Wohlgemuth in 1929.

The following table presents the results obtained in five patients in whom it was not possible to carry out serum studies. There were four cases of acute pancreatitis and one in which the disease persisted for two months, during which time two false cysts of the pancreas made their appearance.

TABLE 9.

Urinary Diastase Output in Acute Pancreatitis.

Case	Essential Data	Time of Observation	Urinary Diastase Wohlgemuth Units/ml. (6-60)
Case 6 - M.McD. Female 57 years Dec. 1939	Pancreas seat of widespread necrosis. False cyst in the lesser sac.	14th day	20
Case 7 - C.M. Female 61 years Dec. 1939	Pancreas seat of widespread necrosis.	8th day	14
Case 8 - E.F. Female 66 years June 1940	Acute abdominal pain and sickness. Cyanosis and jaundice. Conservative treatment.	14th hour 9th day 17th "	250 40 20
Case 9 - W.N. Male 68 years Feb. 1941	Acute abdominal pain and sickness. Large abdominal tumour appeared on 1st day of illness. At operation, found to be filled with blood in the lesser sac. Pancreas hard and spots of fat necrosis at root of jejunal mesentery.	4th day	40
Case 5 - M.G. Female 46 years Jan. 1940	Operated for pseudopanc. cyst in Nov. 1939, 4 weeks after acute attack. Re-admitted Jan. 1940 with recurrence of cyst formation.	3 months after acute attack	133

Comment: Taking into consideration the urinary findings of the present series and those presented in Table 7, it will be seen that the highest level of output for diastase in the urine is 250 units. The highest reading in the above cases was obtained in case 8, which was first investigated 14 hours after onset of symptoms. The repeat readings showed a rapid drop to normal values over the period of observation. The condition of the pancreas was not known as the patient's symptoms settled with conservative treatment. A slight rise in the diastase content was noted in case 9, who was seen on the 4th day. A special feature of this case was a large false cyst situated in the lesser sac which was filled with fairly fresh blood clot. It was presumed that a major blood vessel had been eroded by the necrotizing agent responsible for the pancreatitis. For further details relating to this patient, see Appendix, page 126. A moderate rise in value was found in case 5 three months after the original attack of acute pancreatitis, during which time two false cysts had formed. Normal values were obtained in cases 6 and 7 despite the fact that necrotic lesions were much in evidence. They had not been examined until the 14th and 8th days respectively.

This short study provides corroborative evidence of the conclusion reached earlier that the greatest deviation from the normal levels is to be found at the beginning of the disease. Case 5 lends further support to the view held by Elman that a sustained rise in diastase levels tends to indicate that the disease is slow to resolve.

If attention is again turned to Table 7 it will be noticed that the amount of diastase excreted in the urine varies directly with the amount estimated in the serum. This observation is particularly true in case 14 of Table 7 (A) wherein the serum and urinary indices remained high throughout the period of observation. These two sets of readings were, however, in obvious disagreement in Case 12, Table 7 (B). The serum values were high for both diastase and lipase whereas the urinary diastase index was, if anything, subnormal. Another noteworthy feature of this case was the relatively high level of serum enzyme concentration found on the 10th day. In view of these peculiar findings, it was decided to treat this case as a separate problem. The collected data have been set out in Table 10 and follow-up notes appended.

A Case of Acute Pancreatitis and Chronic Nephritis.

TABLE 10.

Clinical Synopsis and other data	Estimation Time	Serum Enzyme		Urinary Diastase Wohlgemuth Units/ml.
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)	
Case 12 - H.C. Female, 44 years. June 1941. Admitted on 10th day with acute upper abdom. pain, nausea and slight jaundice. Cholecystogram: Non-functioning gall bladder. Blood urea: 106 mg. %. Urea Clearance Test: 11.8% of normal function.	10th day	1,184	3.40	
	12th "	640	3.00	
	15th "	533	2.60	5
	25th "	800	4.10	10
Results of further observations:- During this period patient felt occasional twinges of pain but at no time did she have acute symptoms. Patient came out in purpuric spots on abdomen and the fingers.	Augt.1941	800	3.10	
	Sept.1941	400	3.00	
	Nov. 1941	457	2.00	
	Jan. 1942	200	Zero	
	May 1942	320	0.90	
Re-admitted in Jan. 1943 with similar symptoms, this time on the 3rd week of illness.	Jan. 1943	160	2.7	

Operation (Jan. 1943) revealed an enlarged and indurated pancreas, thought by the surgeon to be due to tumour. No areas of fat necrosis or haemorrhages. The gall bladder was drained. It contained several stones.

Patient died in coma with a blood urea of 293 mg. % a week later.

Autopsy showed that the cause of death was advanced chronic nephritis. The pancreas appeared and felt normal. On section no diseased areas found. On dissection of the ampullary region, it was noted that the common bile duct and the duct of Wirsung entered together but by separate openings at the duodenal papilla. A small pigmented stone was firmly lodged in the distal part of the bile duct and seemed to be impinging on the outlet of the pancreatic duct.

Comment on Findings in Case 12.

It seemed unusual to meet such high readings for both serum diastase and lipase on the 10th day of the acute abdominal illness, but after the results of the urinary estimation were available, attention was drawn to the likelihood that here one was dealing with a disturbance of function of both the pancreas and the kidneys. The gross reduction in the excretory capacity of the kidney for urea, as shown by the results of the urea clearance test and the estimation of the blood urea content, strengthened this view. So far as one could gather from a faecal analysis, made after the patient had been on a Schmidt diet for three days, the pancreatic secretions were gaining an entrance into the duodenum, so that chronic and complete obstruction of the pancreatic ducts was unlikely

to be responsible for the maintenance of the raised enzymatic action of the blood serum. The post-mortem examination revealed the presence of a small stone at the lower end of the common duct which probably had caused intermittent or temporary occlusion of the outlet of the duct of Wirsung. The other probability to be considered is that the enzymes were solely influenced by the renal disease and that some other condition, let us say, gall-stones, might be held responsible for the patient's symptoms. This point can only be elucidated by a study of cases which have no other disorder but advanced renal failure, and it is now proposed to pass on to a consideration of this aspect of the problem.

The Effect of Renal Disease on the Excretion of Enzymes.

In 1919, Wohlgemuth recommended that his test be used as a means of assessing renal function. It was subjected to extensive trials by several investigators, but their results were so inconsistent with the clinical course of nephritis and with the findings of other recognized renal function tests that nowadays little diagnostic or prognostic value is attached to this application of the test (Corbett, 1912; Rowantree, Marshall and Baetjer, 1915; Lewis and Mason,

1920; Reid, 1925). Stafford and Addis (1923) were unable to establish a correlation between the concentration of diastase in the blood plasma and in the urine, nor between the rate of diastase excretion and the extent of renal damage in nephritic patients, although when a large portion of the kidney tissue was rendered functionless there was noted a decrease in the ratio

$$\frac{\text{rate of diastase excretion in the urine.}}{\text{concentration of diastase in the plasma}}$$

Rowantree and his co-workers studied the qualitative determination of urinary amylase as a test of renal function and found that, while the level of urinary amylase was usually decreased in nephritic cases, values were sometimes normal in cases with grave functional involvement and low in cases in which there was improvement of renal function. Dozzi (1941) was unable to relate the amount of amylase in a 24 hour specimen of urine to the extent of renal impairment as determined by the level of non-protein nitrogen in the blood and the amount of urea excreted. Gray and Somogyi (1937), using the latter's method, express the view that carefully controlled studies of the blood and urinary diastase activity should afford an index of renal efficiency. These workers report an

inversion of the $\frac{\text{amount of diastase in urine}}{\text{serum diastase content}}$ ratio referred to in the introduction (page 18) and are at present engaged in exploring the potentialities of enzyme tests in this capacity. Nørby (1932) lends support to their views when he states that excretion of amylase in the urine is proportional to the concentration of the enzyme in the blood.

The results of experimental work carried out by Van den Erve (1911) and King (1914) cannot be reconciled with the theory that the kidneys exert a controlling influence on the excretion of the serum diastase or help to maintain its constant level of activity in the blood. The former found no change in the concentration of the blood diastase following ligation of the renal arteries of a dog, and the latter was unable to demonstrate any appreciable changes even after bilateral nephrectomy.

Finally there is disagreement with regard to the existence of a correlation between the urea content and the serum enzyme content of the blood of cases of nephritis. Myers and Killian (1917) found reason to suspect that both were proportionately raised, but Lewis and Mason and Stafford and Addis failed to establish any connexion between these blood constituents.

The investigations about to be reported are not

intended to prove the worth of enzyme estimations as tests of renal function but were undertaken merely to show the extent to which adverse renal conditions may affect the serum enzyme values. The observations were made on 13 patients with advanced renal disease. Information regarding their renal investigations is incomplete but, as will be deduced from the high incidence of uraemia and from the high death rate among the cases, the condition of the patients did not allow of much investigative interference.

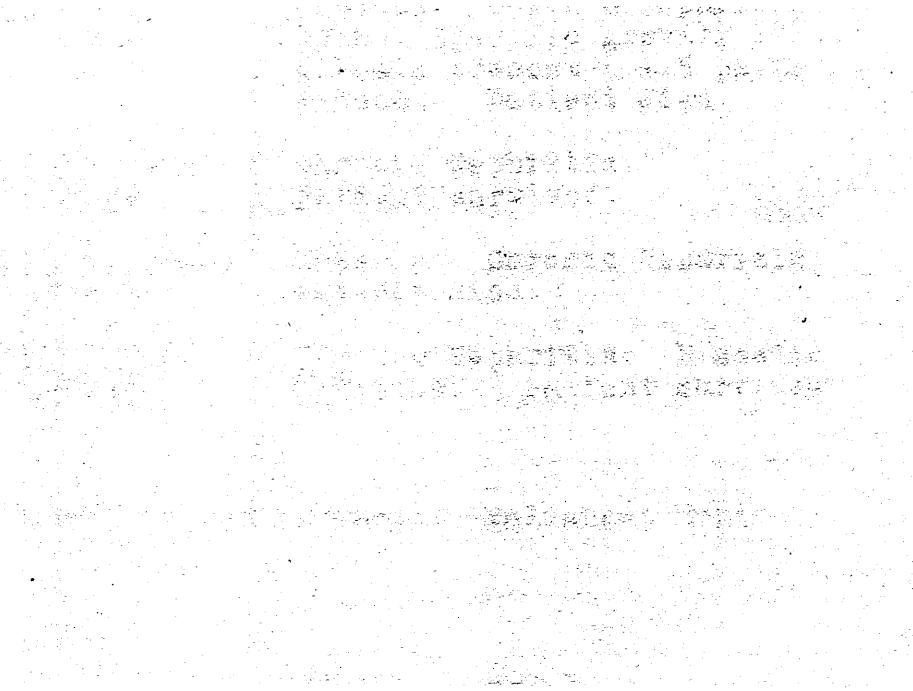


TABLE 11.

Serum Enzymes in 13 Patients with Impaired Renal Function.

Clinical Data		Blood Urea mg. per 100 c.c.	Serum Enzymes	
			Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)
Case 1 - Male 41 years	Pre-Uraemia: Pyelonephritis. Urine: Specific gravity 1012. Albumin present = 5 parts Esbach. Patient survived.	312	123	1.1
Case 2 - Female 26 years	Uraemia: Chronic Nephritis. Urine of low concentration. Patient died.	300	200	2.98
Case 3 - Male 17 years	Uraemia: ? Acute Nephritis. Anuria. Patient died.	245	133	1.61
Case 4 - Female 63 years	Uraemia: Coma for two days. Patient died.	234	376	1.62
Case 5 - Male 30 years	Uraemia: Chronic Nephritis. Patient died.	234	168	0.24
Case 6 - Male 49 years	Uraemia: Chronic Nephritis. Urine: Specific gravity 1015. Albumin present = 1.5 parts Esbach. Patient died.	160	160	1.15
Case 7 - Male 45 years	Chronic Nephritis. Patient survived.	154	228	1.12
Case 8 - Female 35 years	Uraemia: Chronic Nephritis. Patient died.	129	465	1.8
Case 9 - Male 50 years	Chronic Nephritis: Diabetes Mellitus. Patient survived.	129 92 (seven days later)		1.8 1.5
Case 10 - Female 38 years	Uraemia: Malignant Hypertension. Urea clearance for 2 hours - 24.3%. Patient died.	114	-	2.4
Case 11 - Male 45 years	Uraemia: Chronic Nephritis. Urine: Albumin present = 5 parts Esbach. Patient survived.	102	114	1.24
Case 12 - Female 60 years	Uraemia: Chronic Nephritis. Patient died.	71	-	1.02
Case 13 - Female 29 years	Carcinoma of lower Oesophagus, with secondary spread to both kidneys. Anuria. Patient died.	-	89	1.22

Comment: From the evidence presented, it seems safe to say that the serum enzyme activity is to a certain extent conditioned by the excretory capacity of the kidneys. There were only 2 cases with raised diastatic values and both happened to be quite high (Cases Nos. 4 and 8). On the other hand, 13 of the lipase estimates were in excess of 1 ml. and of these, 6 were greater than 1.6 ml., the accepted upper limit of normality.

Although it was found that renal damage can cause rises in serum enzyme activity to an appreciable extent, in no instance were the values augmented to the degree which one might expect in an early acute pancreatitis. On these grounds, the decision was reached with some confidence that the findings in case 12 indicated the presence of chronic renal disease with a superimposed acute pancreatitis.

It will also be appreciated that it is not permissible to draw a parallel between the blood urea and serum enzyme estimates from this series of observations.

Summary.

A marked rise in the serum diastase and serum lipase content is a feature of acute pancreatitis. The highest estimate for diastase was 5,500 units per ml. and for lipase 9.8 ml. N/20 NaOH/ml. The

amplitude of the increase in enzyme activity seemed to depend more on the duration of the disease rather than its grade of severity. There was a distinct parallelism between the serum diastase and serum lipase values and between the serum diastase values and the urinary diastatic indices. In certain cases, a correlation was discernible between a slow rate of fall in values and an incomplete resolution of the disease.

A rise in serum and urinary diastase values occurs in parotitis. Lipase estimations are, therefore, to be preferred if a pancreatic complication is suspected.

A case of subacute pancreatitis with advanced renal disease which gave rise to enzyme retention in the blood is discussed in detail. Evidence is given that impaired renal function may of itself occasion a slight elevation of the serum enzyme values and those of lipase in particular.

In general, the clinical usefulness of enzyme tests is limited to the first few days of acute pancreatitis; thereafter, it becomes necessary to carry out serial studies for the detection of minor fluctuations in values which may or may not be present.

THE DIAGNOSTIC VALUE OF SERUM ENZYME TESTS.

"If we cannot claim for the diagnosis of pancreatic disease the clear cut direct answers obtained in some other regions, we may none the less regard with complacency what has so far been accomplished in this field by the application of physiological discovery at the bedside, by the co-operation of the laboratory and the ward." (Garrod, 1920)

The need for ancillary methods of diagnosis does not often arise in the average run of acute abdominal cases. Even although a case does not fit in with any of the classical descriptions, the surgeon generally knows from experience what sort of treatment best suits the immediate requirements of the patient. The special aids to diagnosis find a place of practical importance in those cases that present an air of urgency and yet are so ill that a "wait and see" policy seems to offer the greater measure of safety. When confronted with such a problem, the surgeon usually turns to the radiologist for guidance. While it is true that much may be learnt from a straight film of the abdomen, the biochemist should also be consulted since his opinion is particularly helpful in the pancreatic "acute abdomen". There has been much controversy over the incidence of acute pancreatitis. As early as the beginning of this century, surgeons like Halsted (1901) and Mayo Robson

writing with Cammidge (1907), were firmly convinced that this disease was by no means a clinical rarity and in 1919 Nicoll of Glasgow published his interesting clinical study of its less acute and chronic forms emphasising their relatively frequent occurrence. Nevertheless, it has been the cumulative efforts of those who have turned to the resources of the laboratory which have supplied the evidence that pancreatitis has a considerable incidence. As proof of this assertion, one might cite the recent work of Elman (1942). This author performed routine serum diastase tests on all cases of acute abdominal pain admitted to Barnes and St Louis General Hospitals. He found that the adoption of this measure had led to an increase in the number of diagnoses of acute pancreatitis by several hundreds per cent and the total of these cases amounted to half of the number of cases with perforated peptic ulcer and a tenth of the acute appendicitis cases. The majority of his cases were of the subacute type.

The previous results have shown that the serum enzyme tests may be of considerable help in arriving at a diagnosis of acute pancreatitis, provided due regard is paid to the time factor. It is unfortunate, however, that they should have such a low differential value. This may be due to oversensitivity

of the pancreas to a nocuous stimuli. Since many of the cases so diagnosed recover without an operation, it is not beyond the bounds of possibility that some other acute lesion which has arisen adjacent to the pancreas might have a similar effect. In order to find out whether these enzyme reactions are really pathognomonic of acute pancreatitis, a series of investigations were conducted on other forms of the "acute abdomen".

The conditions selected for study were (1) disease of the biliary tract, and in particular those cases which were associated with stone formation, (2) acute intestinal obstruction, and (3) perforated peptic ulcer. These were chosen not only because of the clinical resemblance they bore to acute pancreatitis but also because each in its own way might lead to some interference with pancreatic function.

Serum Enzymes in Calculous Disease of the Gall-bladder.

Serum enzyme determinations were carried out on 19 patients. Six were diagnosed on clinical and radiographic grounds and the diagnoses of the other thirteen cases - acute cholecystitis, chronic cholecystitis with or without stones in the common bile duct - were confirmed at operation. The biochemical, pathological and essential clinical data found in each patient are given in the accompanying table (Table No.12).

Comment on the Findings: Raised enzyme values were found in only two patients out of the whole series - cases 5 and 19. The first reading for serum diastase in case 5 was approximately nine times the upper limit of normality on the second day of illness, while the corresponding reading for serum lipase, though relatively not so high was decidedly pathological. When re-investigated at intervals of two days, the diastase values showed a steady decline, normal levels being reached by the sixth day. The corresponding lipase readings, on the other hand, showed a rise to twice the original figure on the second day and then a drop in value. At operation performed 8 days later from the onset of illness,

the pancreas felt normal in size and consistency. The gall-bladder contained stones and its wall was thickened. Several facetted stones were lodged in the lower reaches of the common bile duct.

The other patient, No.19, whose serum diastatic activity was only slightly increased, reported at the out-patient clinic on the seventh day of illness. By that time her symptoms had passed off. When admitted for operation eighteen months later, a thick walled gall-bladder was found; it contained numerous small stones consisting mainly of inspissated pigment. No reference was made in the operation notes to the state of the pancreas or of the common bile duct.

Twelve of the patients, whose biochemical findings fell within the normal boundaries for either enzyme, received surgical treatment. In some, the gall-bladder was very little affected and in others, gross changes were evident. Gall-stones were present in all of the cases and in four instances, calculi occupied the common bile duct. It may be noted that none of the cases with normal readings was admitted to hospital earlier than the fourth day of illness.

TABLE 12.

Serum Enzyme Findings in 19 Cases of Biliary Disease.

Case	Nature and Duration of Illness	Stones in Gall bladder	Stones in Common Bile Duct	Condition of Pancreas	Serum Enzymes	
					Diastase Somogyi Units/ml.	Lipase ml. N/20 NaOH/ml.
1. Female 69 years	Acute Cholecystitis 14 days	+	-	Normal	59	0.20
2. Female 51 years	Gallbladder little affected. Biliary colic 4 days	+	-	Normal	123	0.09
3. Female 40 years	Gallbladder little affected. Bouts of pain over a period of one year.	+	-	Normal	160	-
4. Female 52 years	Gallbladder little affected. Bouts of pain over a period of one year	-	+ (one)	Normal	160	0.32
5. Female 60 years	Gallbladder little affected. Colic for one day. Severe epigastric and right hypochondriac pain began on previous day. Sickness.	+	+ (seven facetted at distal part)	Normal	1,830 (24/2/43) 464 (26/2/43) 213 (28/2/43)	2.08 4.38 1.76
6. Female 40 years	Chronic disease of gallbladder	+	+	Normal	160	0.10
7. Male 68 years	Chronic disease of gallbladder. Jaundice. Pain for 5 days.	+	+ (five facetted at distal part)	Normal		1.00
8. Female 51 years	Chronic disease of gallbladder. Bouts of pain for 2 years.	+	+	Slight induration	133	
9. Female 55 years	Chronic disease of gallbladder. Jaundice. Colic for 6 days.	+	-	Normal	80	0.10
10. Female 60 years	Chronic disease of gallbladder. Bouts of pain for 6 years.	+	-	Normal	100	
11. Female 50 years	Chronic disease of gallbladder. Bouts of pain for 5 years.	+	-	Normal		0.05
12. Male 37 years	Chronic disease of gallbladder. Bouts of pain for 5 years.	+	-	Not examined	104	0.20
13. Female 62 years	Chronic disease of gallbladder. Bouts of pain for 2 years. Recent one, 3 weeks ago.	+ (four small Stones in cystic ducts)	-	Normal		0.80

TABLE 12 (Continued)

Case	Nature and Duration of Illness	Serum Enzymes	
		Diastase Somogyi Units/ml.	Lipase ml. N/20 NaOH/ml.
	Cases diagnosed Clinically:		
14. Female 62 years	Severe upper abdominal pain lasting 3 weeks. History of typhoid fever in childhood. Cardiac decompensation. Gallbladder not examined radiologically.	104	0.80
15. Female 45 years	Biliary colic 7 days. The history of abdominal discomfort and attacks of colic dated back for 2 years. Cholecystogram: A poorly functioning gallbladder without visible stones.	76	Zero
16. Female 55 years	Abdominal pain for 7 days. Cholecystogram: A poorly functioning gallbladder. No stones seen.		Zero
17. Female 25 years	Acute pain in right hypochondrium for 1 week. Slightly jaundiced. No X-ray films taken.		0.95
18. Female 48 years	Pain in right subcostal region for 3 weeks. Cholecystogram: Functioning gallbladder and no opaque calculi.		Zero
19. Female 46 years	Severe pain in right hypochondrium for 7 days, with vomiting. Similar attacks had occurred during the preceding year. Cholecystogram: Gallbladder functioned poorly and contained multiple stones. Interval Operation - a year later. Chronic cholecystitis with numerous small pigmented stones. No other information available.	266	

Discussion.

As the incidence of pathological values in my own series of cases is so small, it is necessary for the interpretation of the results to draw on the experience of other workers in this field of investigation. A search of the literature shows that there is a possibility of the biochemical findings in certain cases of biliary disease and acute pancreatitis being so similar as to add to the clinical difficulty of discrimination.

In 1936, Comfort conducted a lengthy study of the serum lipase in various conditions. He found elevated values in 19 out of 135 biliary cases in which pancreatitis was not evident to the operating surgeon. Each of these nineteen patients had a calculus or a lesion in the common bile duct. This author ascribed his findings to impairment of either hepatic or pancreatic function. If regard is paid solely to fluctuations in lipolytic activity, there would seem to be grounds for accepting the raised lipase values in case 5 of the present series as being due to liver dysfunction. Crandall, in 1935, drew attention to slight but significant elevations in the lipase content of patients with hepatic disorders and in animals which had had their common bile ducts tied and others which had been given an over-

dose of chloroform. Comfort (1939) reported slightly raised values in 5 out of 37 cases suspected of having disease of the liver and Johnson and Bockus (1940) found 7 out of 24 cases with cirrhosis with similar enzymatic changes. In the present series, no attempt was made to find out whether the patients had disease of the liver. It seemed unlikely that this was present in case 5 at any rate, since evidence has been given that hepatic disorder either leaves the serum diastase levels undisturbed or causes a lowering in value depending on the method of study. Thus, Elman, Arneson and Graham (1929) using the viscometric method and Foged (1935) using one of the iodometric methods failed to demonstrate any appreciable deviation from the normal range of values, while Somogyi (1934), Rachmilewitz (1938) and Lewison (1941) found with the copper reduction method devised by the first named author that disease of liver tended to have a depressing effect.

A closer study of the problem has shown that raised diastase values have only been encountered in cases in which stones were present in the common bile duct. Millbourn (1936) recorded a high output of urinary diastase in as many as 53% of 74 cases with jaundice due to choledocholithiasis. A considerable number of Foged's cases reported in the previous year,

who were similarly affected, also, had increased diastasuria. According to Lewison (1941), each patient's case should be studied on its own merits. To illustrate this point, he presented the case-records of three patients who had sudden transient rises in serum amylase activity following operations on the gall-bladder and its ducts. The pre-operative observations all gave normal readings. In two patients, it was discovered that stones had been left inadvertently in the common bile duct and in the third instance, he assumed that the altered enzyme values were the result of the T-tube, which was draining the common duct, pressing on the main pancreatic duct. Lewison was led to the conclusion that such biochemical findings indicated a state of enzyme retention in the pancreas due to temporary blockage of the duct of Wirsung although it seemed to him that the rise in values was relatively of moderate amplitude in comparison with those encountered in cases of acute pancreatitis. Cholecystitis with or without stones does not, in the wide experience of Somogyi (1934) or Rachmilewitz (1938) lead to a rise in the level of serum diastatic activity. The presence of stones in the common duct has been shown by Bernhard (1933) to be associated occasionally with an excess of lipase in the blood.

Sufficient evidence has been given to show that raised pathological readings are likely to occur in patients with stones in the common bile duct in the absence of a demonstrable pancreatic lesion. A slight increase in lipase titres unaccompanied by a parallel rise in diastase values tends to signify faulty liver function. A marked increase in the activity of both enzymes would seem to suggest that the passage of a gall-stone through, or its lodgment at, the ampulla of Vater has interfered with the outflow of the pancreatic juice. Since both enzyme values in case 5 were affected, it has been regarded as a case of the latter type. The similarity that exists between the second day readings and those obtained in acute pancreatitis cases of two days' standing (see Table 7) is also in conformity with the view that the findings in this case denote some form of pancreatic dysfunction. That the same agency was at work in case 19 can only be surmised, but, in view of the diminutive size of the stones, the escape of one or more into the duodenum via the common duct was a likely probability. The suggestions offered for the normal values noted in the other four patients with choledocholithiasis are: (1) that the stones were not in a position to interfere with the main pancreatic duct or/and (2) that they were admitted too late for

pathological readings to be recorded. It may be noted that one of these cases (No. 8) had a swollen indurated pancreas which might have been either a subacute pancreatitis in the resolving stage or disease of a more chronic nature. In agreement with the findings of others, negative results were obtained in patients in whom the gall-bladder was the sole seat of disease.

Serum Enzymes in Acute Intestinal Obstruction.

So far as I can ascertain, Johnson and Bockus (1940) are the only authors who claim to have found raised enzyme values in association with intestinal obstruction. In all of the four cases of obstruction studied, they found that the serum lipase content was raised slightly above normal. No estimations of serum diastase were made.

In the present investigation the serum diastase and serum lipase activity of 6 cases was studied. There was regurgitant vomiting of ~~flocculent~~ faeculent material in each one. The other condition likely to interfere with the free flow of pancreatic juice in such cases, namely, distension of the upper coils of the small bowel, was demonstrated at operation in each case.

The findings set out below in Table 13 were all within the normal limits for both enzymes. As the cases, though few in number, seemed fair samples, the view was taken that an acute intestinal obstruction is unlikely to be mistaken on biochemical grounds for an acute pancreatitis.

TABLE 13.

Serum Enzymes in 6 Cases with Small Bowel Obstruction.

Case	Nature of Obstruction	Serum Enzymes	
		Diastase Somogyi Units per ml. serum (40-228)	Lipase ml. N/20 NaOH per ml. serum (0-1.6)
Case 1 Male 21 yrs.	Paralytic ileus. Peritonitis from ruptured appendix.	199 195 (2 days later)	0.09 0.10
Case 2 Male 58 yrs.	Small bowel obstructed from contact spread of colonic carcinoma.	210	0.08
Case 3 Male 30 yrs.	Upper ileal loop ensnared by Meckel's diverticulum.	74	0.07
Case 4 Female 40 yrs.	Tumour of transverse colon with dilatation of small bowel.	62	0.82
Case 5 Male 20 yrs.	Paralytic ileus due to peritonitis after perforation of duodenal ulcer.	100	1.12
Case 6 Male 51 yrs.	Paralytic ileus due to peritonitis after perforation of duodenal ulcer.	133	

Serum Enzymes in Acute Perforated Peptic Ulcers.

This investigation was prompted by the following case:-

A male, aged 57 years (Case 1, Appended Table III), admitted to the Western Infirmary, Glasgow, in December 1941, gave a history of 14 years periodic indigestion, culminating in a severe epigastric pain of two days' duration.

The diagnosis appeared to lie between an acute pancreatitis and a general peritonitis, probably as a result of perforation of a peptic ulcer. Both the serum diastase and serum lipase estimations showed a fourfold increase. Further help was sought from an abdominal tap, which resulted in a withdrawal of a brownish fluid also rich in digestive ferments. A confident but incorrect diagnosis of acute fulminating pancreatitis was made. The patient, however, was moribund and died a few hours later.

Autopsy revealed a perforated ulcer of the anterior wall of the first part of the duodenum. There was general peritonitis with pronounced inflammatory changes and fibrinous exudate in the vicinity of the lesion. To the naked eye, the pancreas appeared normal.

Scope of the Investigations.

Serum diastase and serum lipase estimations were carried out on 32 patients with anterior peptic ulcer perforations. The majority of the readings were taken prior to operation, the others while it was in progress. In the course of the inquiry, information

was also sought concerning the factors likely to lead to changes in the enzyme levels. These were: (1) the site of perforation, (2) the activity of the pancreas and (3) the ferment content of the peritoneal fluid.

Biochemical Findings.

A perusal of Table III on pages 168-170 will show that out of 32 cases there were 7 patients with abnormally high diastase activity and 4 with hyperlipaemia. The values accepted as abnormal are compared with the normal in Table 14 (below). The former ranged from 248-720 units (diastase) and 1.69-4.10 ml. (lipase) whereas the latter's limits were 46-184 units and 0.01-1.49 ml. respectively. Those with raised lipase levels (nos. 1, 3, 13, 14) belonged to the same group as had raised diastase levels, and there was a certain

TABLE 14.

Showing the Range of Values for the Normal and Abnormal Readings.

Type of Cases	Range of Readings Serum Diastase units/ml. (40-228)	No. of Cases	Range of Readings Serum Lipase ml.N/20 NaOH/ml. (0-1.6)	No. of Cases
Normal	46-184	23	0.01-1.49	26
Abnormal	248-720	7	1.69-4.10	4

correlation between the extent of deviation from the normal. In numbers 8, 11 and 12 the diastase content only was altered. It will also be noted that the duration of illness prior to operation may be a factor of importance. This hypothesis is based on the observation that a 7-hour perforation was the earliest to exhibit raised readings and the others were of longer standing - 9 to 48 hours, and by far the highest values were found in the 15- and 48-hour old cases. Those that had been missed in the acute stage (nos. 31 and 32) gave normal readings.

To investigate the time factor more fully, it was decided to repeat the tests 24 hours after operation. This was done in 15 cases and the findings are presented in a separate table for convenience of study. Table 15a gives the results which were initially raised or became so, and Table 15b those that fluctuated within the normal limits. It is clear from these tables that there is a wide individual variation in the results: some rise, others fall, while yet a third group remain the same. Even so the findings as a whole do suggest that pancreatic function may be disordered in cases of peptic ulcer perforation. The rest of the investigation concerns the ways by which this may occur.

TABLE 15 (a)

Results obtained in 8 Perforation Cases with raised Serum Enzyme Values.

The repeat readings were taken 24 hours later.

Case Number	Duration	Serum Diastase Somogyi Units per ml. serum (40-228)	Serum Lipase ml. N/20 NaOH per ml. serum (0-1.6)
12	4 hrs.	-	0.13
		260	1.02
14	7 hrs.	355	1.69
		355	0.07
11	9 hrs.	266	0.14
		80	Zero
8	10½ hrs.	248	0.75
		80	0.89
13	11 hrs.	266	2.07
		160	0.55
24	12½ hrs.	88	1.25
		300 (24 hrs. later)	1.40
		22 (2 days later)	0.66

TABLE 15 (b)

Results obtained in 9 Perforation Cases with normal values.

The repeat readings were taken 24 hours later.

Case Number	Duration	Serum Diastase Somogyi Units per ml. serum (40-228)	Serum Lipase ml. N/20 NaOH per ml. serum (0-1.6)
9	4 hrs.	145 190	0.22 0.99
26	4 hrs.		0.60 0.80
7	4½ hrs.	184 84	0.42 0.42
10	6 hrs.	84 56	0.01 0.10
18	7 hrs.	88 84	0.13 0.22
17	7 hrs.	66 80	0.67 0.52
25	7 hrs.	168 200	0.10 0.32
30	11 hrs.	66 123	0.06 0.08
19	12 hrs.	88 106	0.03 0.81

Pathological Findings: (The Site of Perforation.)

The site incidence of the ulcers was as follows:

Plate I. Perforated duodenal ulcer with bile-staining of the surrounding tissues. Spots of fat necrosis are to be seen in the lesser omentum.
(See text page 93).

pyloro-duodenal - 29; gastric - 2; anastomotic - 1. All the perforations were situated anteriorly. In 5 of the 6 cases with raised values, the perforations were just distal to the pyloric sphincter, and in the remaining 1, the lesion was at the sphincter. No signs indicative of disease of the pancreas were found at any of the operations.

In one of the series with normal readings, autopsy revealed, in addition to an anterior ulcer of the duodenum, a posterior ulcer superficially attached to the pancreas. There were a few flecks of fat necrosis in the adjacent part of the lesser omentum of this patient. Since no evidence of pancreatitis could be seen on direct inspection of the gland, I presumed that the fat necrosis was due to the lipase of the escaping duodenal juice. (See photograph facing page 93)

Time of Previous Meal: It was considered that this information would furnish some indication as to the functional state of the pancreas at the time that the duodenum perforated. The interval between the previous meal and the onset of abdominal pain was known in 23 patients.

It was estimated that on an average the lapse of time was just over four hours. One of the series actually perforated during a meal, but this was an

exceptional occurrence. The longest intervening period was six hours.

There appeared to be no connexion between the time of the previous meal and the variations in serum enzyme activity noted in certain cases.

The Ferment Content of the Peritoneal Fluid: It is necessary to preface this investigation by referring to some observations which were made on the peritoneal exudate of acute pancreatitis cases. These results obtained in 4 cases are given in the appended Table II, page 167. They show that the pancreatic ferments tend to diffuse into the general peritoneal cavity or are borne there in the blood which may be present in considerable amounts in the more destructive forms of the disease.

The case presented at the beginning of this study illustrates how perforated peptic ulcer might be mistaken for an acute pancreatitis if too much stress is given to the chemical properties of abdominal fluid.

The present investigation concerns only the enzyme content of the peritoneal fluid in perforated peptic ulcer cases. It was taken up with the possibility in mind that absorption of the duodenal and pancreatic ferments lying free in the peritoneal cavity might be the cause of the biochemical findings

encountered in certain of the cases. It entailed the carrying out of diastase and lipase estimations on the peritoneal fluid of 21 cases. In one case the sample of fluid was obtained by paracentesis abdominis; in all the others, the samples were taken at operation. The results are to be found in Table III. of the Appendix, page 168.

The range of values was, as expected, a very wide one. Except for one patient (case 14) whose initial blood readings were raised and whose enzyme content was very high, there seemed to be a general lack of correlation between the blood and peritoneal fluid findings. For reasons to be discussed later, a detailed analysis of the results was not carried out.

Discussion.

Little prominence has been assigned to the enzyme variations in cases of perforated peptic ulcer of the common anterior type, due no doubt to the relative ease with which a bedside diagnosis can be made. It would seem that only two authors have hitherto reported raised values in this condition and in both instances, the urinary diastase was studied. In 1936, Millbourn reported moderately increased level of output. The pathological details

of his cases were not given in his paper. Hughes presented four such cases before the Royal Society of Medicine in 1942. The total number of cases studied by him was forty and all were of the anterior variety. The values obtained in these four patients were so high as to suggest a diagnosis of acute pancreatitis. An arresting feature noted in three out of the four cases was the presence of fat necrosis in the field of operation. Although the idea was entertained that the saponification of fatty tissue was due to a co-existing pancreatitis, further exploration ruled this out. Autopsy carried out on the fourth case revealed a normal pancreas. Other observers have not found any material alteration in the blood or uninary diastatic indices in acute anterior perforation cases (Foged, 1935; Probstein, Wheeler and Grey, 1939; Elman, 1942). Probstein et al. did find pathological findings in 4 out of 18 cases of anterior perforations but the ulcers in those which gave these readings proved at operation to be gastric and lying contiguous with the pancreas. They did not think that the common anterior duodenal perforations were ever associated with abnormal enzyme readings. In their conclusions, they suggested that blood diastase tests should be carried out on all acute abdominal cases not only for the differentiation and recognition of

acute pancreatitis but also as a means of locating the site of a peptic ulcer should one exist. It would appear from the results of Hughes' studies and my own that the clinician is apt to be misled should too much reliance be placed on such diagnostic criteria since no pancreatic involvement had occurred in our cases.

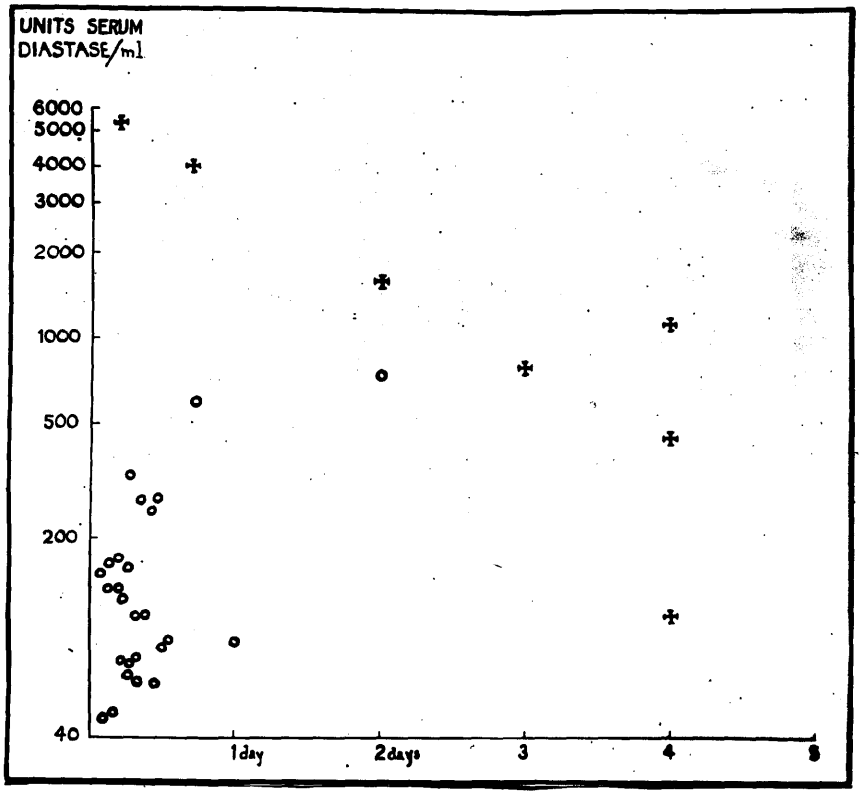
No suggestions were made either by Millbourn or by Hughes as to the probable causes of the occasional occurrence of abnormal enzyme findings in perforations of the anterior variety, nor the conditions under which they may be found. Though in close proximity to the pancreas, an anatomical connexion between the lesion and the pancreas was not obvious at any of ~~the~~ my operations. Nor could the biochemical findings be explained on a physiological basis. The notes taken on the incidence of perforation in relation to meals suggested that peptic ulcer cases are prone to develop this complication at a time when the stomach is well nigh empty and when presumably the pancreas is entering a quiescent phase of secretory activity. Illingworth, Scott and Jamieson (1944), in their statistical survey on the subject of perforated peptic ulcer, reported that the incidence of the condition was highest toward the end of the working day and lowest during the period of rest. Thus, it would

seem that fasting may be a contributory factor but, as they pointed out, more definite data are necessary to elucidate this problem. Substantial support is given to their belief by the present findings. Although the results do not offer a solution to my own problem, they have been the means of drawing attention to a fine point in the differential diagnosis of this condition from acute pancreatitis since the latter occurs in its classical form soon after a meal and is said to be particularly common in corpulent individuals who have a taste for high living.

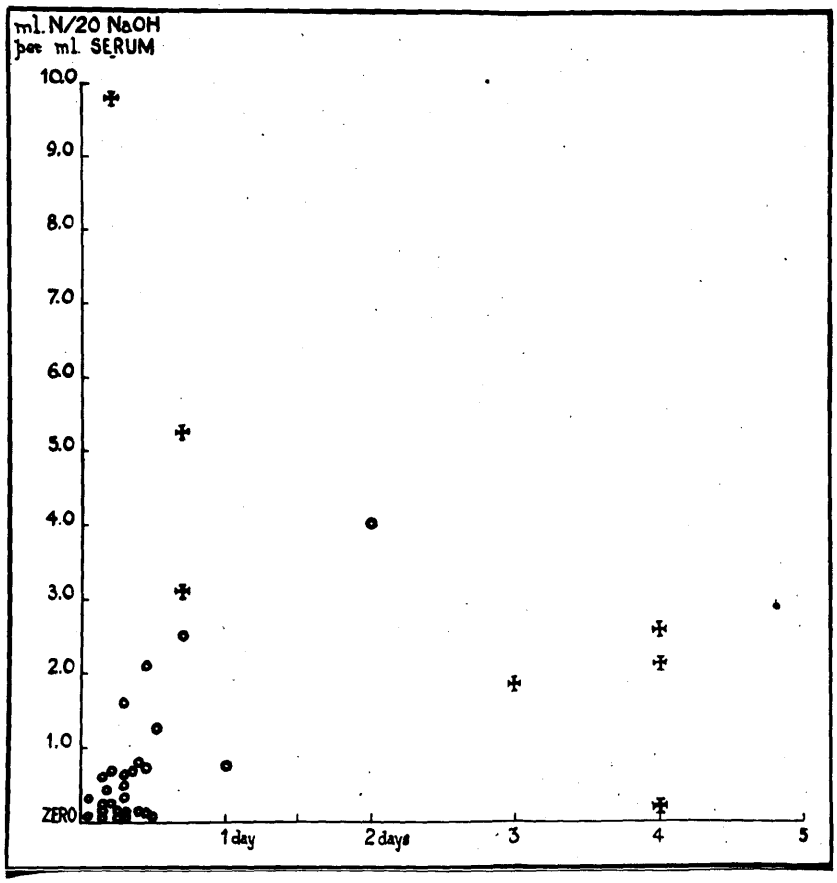
It seemed reasonable to assume that during the absorption of the peritoneal fluid, digestive ferments, which were still active, had been carried into the bloodstream. Conclusive evidence could not be obtained that this did in fact occur. A detailed analysis of the results was not entered upon owing to the existence of factors which were variable, such as the quantity of the duodenal or gastric contents which escaped, and the extent of their dilution by peritoneal transudate. Alternatively it is suggested that the contact with these irritating fluids or the development of peritonitis had adversely affected the pancreas. In keeping with the latter suggestion are the post-mortem findings in case 1. As few surgeons pay much attention to the pancreas during an

operation for the closure of a perforation, the difficulty of collecting evidence to support this theory is considerable.

In the interpretation of the results from the clinical standpoint, it was possible to reach more definite conclusions. The unexpected discovery of pathological values raised issues of signal importance because if a perforation is obscure enough to be taken for an acute pancreatitis such a finding might weigh against operative treatment. An analysis of the results seemed to indicate that in contradistinction to what happens in acute pancreatitis, the serum enzyme levels have a tendency to rise the longer operation is withheld. This applied to both the serum diastase and serum lipase findings. The contrast in behaviour of the serum enzymes as found in these two conditions is well shown graphically (see Graphs Nos. 3 and 4).



Graph No. 3 presents the serum diastase values of 26 perforation cases (o) and of 7 cases of acute pancreatitis (-) during the first four days of illness.



Graph No. 4 presents the serum lipase values of 27 perforation cases (o) and of 7 cases of acute pancreatitis (-) during the first four days of illness.

Thus, it would appear that the serum enzyme readings are most likely to be normal or only slightly increased in perforation cases which have been seen within 12 hours of the onset of symptoms, whereas in acute pancreatitis they are greatly raised during that period. However, between 15 and 48 hours the enzyme content of the blood may be augmented to a moderately high level during which time that of most cases of acute pancreatitis is tending to fall to about same levels. This is precisely the time that the clinical features of a perforated peptic ulcer case become so modified by general peritonitis as to cause real difficulty in diagnosis. It would seem to make little odds which method of treatment is instituted at this late stage because, unless the perforation happens to be of the self sealing variety, the patient's chances of recovery are by then very poor.

Summary.

The findings in cases of calculous disease of the biliary tract, small bowel obstruction and perforated peptic ulcer of the anterior type are presented.

Raised values were obtained in two of the biliary cases and in six of the perforation cases. The obstructed patients gave normal readings.

The view was accepted that a high serum diastase estimate is found only in cases of choledocholithiasis

and that the causal mechanism is obstruction of the pancreatic duct. When the serum lipase titre is raised the cause may either be a pancreatic disorder or a hepatic disorder. Consequently in the differentiation of these two conditions, weight should be given to the diastase findings.

The biochemical findings were normal in the majority of the perforation cases. Taking an arbitrary division of time, it seemed that normal or slightly raised values may be expected during the first twelve hours; thereafter moderately raised values are liable to occur, if the case is still untreated. No satisfactory explanation could be offered for the positive findings.

In short, the biochemical findings in the more common forms of the "acute abdomen" do not seriously impair the diagnostic value of enzyme tests as applied to acute pancreatitis. The possibility of a perforation case being mistaken for one of acute pancreatitis only arose at a time when such an error was unlikely to affect the fate of the patient. With regard to the findings in biliary affections, the study has thrown an interesting light on the mechanism of raised enzyme readings and has at the same time fortified the view that these are merely a sign of pancreatic distress and not a measure of the resultant damage.

THE MANAGEMENT OF ACUTE PANCREATITIS.

The care of those affected with acute haemorrhagic necrosis of the pancreas still constitutes a very serious problem. When first seen they are usually overwhelmed with pain and in a state of extreme prostration.

At operation the lesion presents differing characteristics and seems to follow no set course which precludes any attempts to predict what the outcome is likely to be. And moreover, should recovery take place, there is no guarantee that another attack will not occur, nor is there any reliable preventive measure which we can take. The problem that really concerns us is whether or not it is within our power to control the disease process once it is established. The prevailing belief is that this can be done with the aid of surgery.

This idea was engendered by Fitz (1889), Halsted (1901), Egdahl (1907) and Körte (1911), the earlier authorities on the subject, who were firmly convinced that the best hope of survival lay with early recourse to laparotomy and the promotion of free drainage. The succeeding generation of surgeons, the more notable being Moynihan (1925), Waring (1923), Love (1926) and Finney (1933), pursued the same active line of

treatment and the enthusiasm with which they did so is reflected in their writings. Unfortunately, success did not attend their efforts to lower the mortality rate of their predecessors for according to the statistical analyses available at the time the operative mortality rate still remained forbiddingly high (Schmieden and Sebenung, 1928). It was about this time that doubts began to be aired as to advisability of surgical therapy. These emanated from a new school of thought represented by Nordmann (1938), Mikkelsen (1934), Waltzel (1934), Smead (1936) and others who had switched over to the adoption of a more conservative policy. Their published results were most impressive and encouraged the bold suggestion that acute pancreatitis might possibly be a self-limiting disease, which was in a sense tantamount to calling it a medical condition. Indeed, Trasoff and Scarf (1937) go so far as to give this challenging title to their paper, "Acute Pancreatitis; a Medical Problem". Speaking very generally, the conservative line of treatment is widely practised on the Continent, but in the United States it would still seem to be under trial and according to available information Morley (1939) is the sole exponent in this country. The standard textbooks both in America and in this country, perhaps with the exception of Bailey and

Love (1943), have so far completely ignored its possibilities and continue to set great store by surgery as a life-saving measure. This teaching is fully endorsed by Ogilvie (1939) and in America by Casberg (1939), Abell (1938) and Cole and Elman (1939). The main objection all along to the acceptance of the conservative policy has been, to use the words of Rowlands, and Turner (1937) ~~Rowland (1934)~~, "the difficulty of accurate diagnosis which makes it difficult to withhold laparotomy and renders statistics of cases not operated on of questionable value".

As evidence of the good that may come of this form of treatment, let me quote Mikkelsen (1934) who had only three deaths out of a series of 39 cases. They were all critically ill when first observed, but it was obvious from the reading of his paper that the biochemical findings formed the basis of diagnosis. That some of his cases were of the milder sort is quite probable, for this author chose to operate only in those who proved subsequently to have disease of the biliary tract.

The whole problem becomes much simpler once we realise how little is known of the aetiology of acute pancreatitis. Granted experimental research has done a great deal to clarify the position, but much of the information placed at our disposal is probably

of greater interest to the physiologist than to the practising surgeon. It is easy to understand why clinical research has lagged so far behind. In the first place the surgeon is hampered in his investigations by tactical necessity. Secondly, even supposing he were to try to probe the secrets of this disease, he can never carry out an organised inquiry.

To explain this point, let us consider the recognised predisposing factors, namely, a vascular accident, and an obstruction somewhere in the pancreatic duct system. He may, within reason, be able to exclude an apoplexy of the gland, but there remains the difficulty of distinguishing between a lesion caused by some obstructive agent such as an ampullary gall-stone or possibly a roving nematode and a lesion due to epithelial hyperplasia of the lesser ducts (Rich and Duff, 1934). It may again be conceded that the ampullary region is well within reach, but the surgeon even denies himself the satisfaction of exploring that area by choosing, in the interests of the patient, the simpler expedient of cholecystostomy. This procedure is calculated to help the patient in two ways, first by ridding him of any gall-stones that may be present, and second by diverting the bile flow away from the meeting place of the two duct systems. The "common channel" theory was postulated

in 1901 by Opie. It rapidly gained recognition and has maintained its ascendency until the present time. We would do well to bear in mind, however, that it is no longer accepted in the School whence it originated. Rich and Duff (1936) surveyed the autopsy ~~dates~~ cases of the Johns Hopkin's Medical School in which they included Opie's celebrated case. The following extract epitomises their views on the subject. They stated that "while the underlying obstruction in some cases of haemorrhagic pancreatitis is caused by a gallstone lodged at or near the ampulla of Vater, in most cases the main pancreatic duct is unobstructed and the obstruction is situated in branches of the duct within the pancreas. Retrojection of bile into the pancreatic duct is an infrequent cause of haemorrhagic pancreatitis in our experience, and proved cases in the literature are scarce."

No further comment on the bile question seems to be called for. It may be stated, however, that if the benefit conferred by cholecystostomy is so doubtful, then would it not be better to postpone the removal of calculi to a time when exploration of the biliary system could be done under less testing circumstances?

Let us next consider the more specific aims of surgical treatment. It is convenient to start at

the time when abdominal surgery was in its infancy. In these days, the lesion that holds our interest was regarded as a sort of visceral carbuncle and the practice was to make bold incisions into the pancreatic substance. This mutilating procedure fell out of favour when it became known that the condition was essentially a process of auto-digestion. Surgeons then became motivated with the idea that some benefit might be derived from "decompressing" the gland by incising its peritoneal covering. Nowadays even this is regarded as not only an ineffective but also an irrational means of providing drainage, and we content ourselves with evacuating the contents of the lesser sac and the insertion of a drain down to the surface of the pancreas. This reversal of policy is interesting for it manifestly shows that those responsible for its direction have gone a long way to admitting that the pancreas is capable within limits of looking after its own affairs. We may well ask next, why drain at all? No one seems to be clear on this point. The danger of microbic invasion is, in my experience, very slight indeed. The peritoneal exudate is either absorbed within the first week or it becomes trapped in the lesser sac and may develop into an enormous encysted collection. None of my cases with such cysts went septic. This peculiar

brownish exudate which on standing presents the appearance of shot milk is not found in all cases; only in those where haemorrhages dominate the pathological picture. Personal studies have shown that it usually possesses starch-splitting and fat-splitting properties. On microscopic examination, there are to be seen red blood cells, leucocytes intermingled with floating globules of fat which give its surface the characteristic sheen. Experimental research has failed to substantiate the view that it contains toxic substances when inoculated into the peritoneal cavity or the blood stream of healthy animals (Iraneus, 1941). Taking all these points into consideration, it is obviously stretching factual data rather far to assert that the drainage of this fluid is a life-saving measure. The truth of the matter is that the results of surgery are so bad that we think of them only in terms of the mortality rate.

There is no escaping the conclusion that this controversy has been carried too far beyond the boundaries of clinical reality. Too often has it been assumed that the difficulties of diagnosis invalidate the cures of conservative treatment. Surely the mere fact that the operating surgeon has first hand information does not mean so very much because

in the majority of cases his diagnosis is fortuitous and unexpected. Indeed, it is almost as if he arrived at his diagnosis, to quote the motto of a daring branch of the Royal Navy, "by guess and by God". On the other hand, if the conservative policy is to obtain recognition, then its supporters must produce facts as well as figures. Biochemical evidence alone is not acceptable because, as has been demonstrated, the tests are not a means of differentiating the severe from the mild lesions. The results must be judged principally on definite physical signs, such as a pseudo-pancreatic cyst or discoloration in the flanks, and on the pathological data of autopsies and late operations. The following Table No.16 is a presentation of the data relating to eleven of my own cases which were treated expectantly. Out of these there were two deaths. The first three cases (Nos. 8, 12, 14), all of whom survived, were essentially biochemical diagnoses and might perhaps be discounted. Even so, to have only 2 deaths out of 8 cases with demonstrably severe lesions is quite a fair reckoning.

TABLE 16.

The Results of 11 Cases of Acute Pancreatitis

"+" = significantly increased values.

Management of the Case	Diagnostic Evid		
	Clinical	Biochemical	Opera
Conservative		+	
Conservative (1st attack)		+	
Conservative		+	
Conservative			
Conservative			
Conservative	False Cyst		
Conservative	False Cyst	+	
Exploration biliary system 4 weeks later	False Cyst		Necro panc
Exploration biliary system 4 weeks later	False Cyst		Pancreas but not eye. N spots fa aro
Exploration biliary system 14 days later			Necrosi creas. fat ne
Exploration biliary system 14 days later	False Cyst	+	Haemo necro pan

TABLE 16.

The Results of 11 Cases of Acute Pancreatitis treated Conservatively.

"+" = significantly increased values.

Case No.	Management of the Case	Diagnostic Evidence				Result
		Clinical	Biochemical	Operative	Autopsy	
8	Conservative		+			Recovered
12	Conservative (1st attack)		+			Recovered
14	Conservative		+			Recovered
2	Conservative				Haemorrhagic necrosis of pancreas	Died
26	Conservative				Haemorrhagic necrosis of pancreas	Died
1	Conservative	False Cyst				Recovered
17	Conservative	False Cyst	+			Recovered
4	Exploration biliary system 4 weeks later	False Cyst		Necrosis of pancreas		Recovered
5	Exploration biliary system 4 weeks later	False Cyst		Pancreas felt hard but not seen naked eye. Numerous spots fat necrosis around		Recovered
6	Exploration biliary system 14 days later			Necrosis of pancreas. Spots of fat necrosis		Recovered
16	Exploration biliary system 14 days later	False Cyst	+	Haemorrhagic necrosis of pancreas		Recovered

My operative experience was more limited. There were 5 severely affected patients, none of whom were diagnosed correctly beforehand, who received emergency surgical treatment within the first three days of illness. The procedures carried out were cholecystostomy and the insertion of a drain down to the pancreas. Three recovered, one died soon afterwards, and the fifth developed suppurative pancreatitis eight weeks later.

My own view on the matter is simply this, that acute pancreatitis is a medical condition which for practical reasons must remain a surgical responsibility. It is suggested that all of the obscurer forms of the acute abdomen might be considered suspect and confirmatory biochemical evidence sought. A positive result does not tell us how far the digestive process has gone, but that, to my mind, need not move us to satisfy our curiosity. My clinical experience has convinced me that a goodly proportion of those whose pancreas has been grossly affected do recover without operative interference. The suggestion is tentatively made that those who are so fortunate and who show evidence of biliary disease might be well advised to submit to a laparotomy when their general health permits.

A P P E N D I X.

A P P E N D I X.

CASE RECORDS.

CASE No. 1.

CLINICAL DIAGNOSIS - False Pancreatic Cyst
RESULT - Well

Clinical History: Mrs E.D., aged 78, was admitted to the Western Infirmary, Glasgow, in October 1937. Ten days prior to admission the patient experienced a sudden access of upper abdominal pain which was mostly felt in the right hypochondriac region. She felt a shivery sensation and there was an increase in pulse rate. The acute pain persisted for two days, then passed off only to return with increased severity and with extreme sickness and vomiting. These symptoms continued until her admission to hospital.

On Examination: The patient was small and on the stout side. Her general condition was poor. Temperature and pulse rate were normal. Leucocyte count = 7,600 per cu.mm.

The abdomen was grossly distended by a large round tumour that occupied a central position in the upper abdomen. It had a smooth contour and was of firm consistency. The overlying muscles were moderately resistant but there was no tenderness. The mass was tympanitic over its dome and dull on the periphery, merging on the right with hepatic dullness.

Barium Meal Investigation was carried out by Dr S. D. S. Park, who reported that the stomach was displaced to the left by a tumour lying above the lesser curvature, but intrinsically normal.

Progress Notes: The patient made an uninterrupted recovery with general nursing care, and by two months' time the mass had completely disappeared.

Seen by Professor A. E. Whipple, of New York, who suggested the diagnosis of false pancreatic cyst following acute pancreatitis.

CASE No. 2.

CLINICAL DIAGNOSIS - Acute Cholecystitis
AUTOPSY - Acute haemorrhagic pancreatic necrosis.

Clinical History: Mrs J.R., aged 45, was admitted to the Western Infirmary in April 1938. The patient had suffered abdominal pain for 3 days but was so desperately ill that she could not be interrogated. It was learned that four years previously she had been treated conservatively for biliary colic. She was never jaundiced.

On Examination: The patient was found to be in a state of collapse and most restless. The temperature was 99° F.; the pulse rate 100 per minute. She was fat.

The abdomen was rigid over the left rectus and over the right rectus in its lower half. No other points were noted at the examination.

Progress Note: The pain remained with unabated severity throughout the night and was quite unrelieved by gr.¼ morphia. She died on the following day.

Synopsis of Autopsy: The peritoneal cavity contained 700 c.c. of blood-stained fluid and numerous areas of fat necrosis were scattered throughout the omenta, the left renal and pancreatic regions. Pancreas was greatly swollen, haemorrhagic, and its surface studded with fat necrosis. Its main duct was patent. On section the gland was congested and haemorrhagic with massive necrosis of the body. Gall-bladder was distended and thin-walled. It contained numerous mixed, pigmented and cholesterol stones. A minor degree of cholesterosis was present. Ampulla of Vater was patent and admitted passage of a probe. It looked rather prominent. The bile duct was slightly dilated but contained no stones. Intestine contained a small gallstone 3 mm. in maximum diameter at the level of the pelvic colon and embedded in a faecal mass. ? Causal factor. The stomach and duodenum were normal.

CASE No. 3.

CLINICAL DIAGNOSIS - Acute Cholecystitis
OPERATIVE FINDINGS - Acute Pancreatitis
RESULT - Well

Clinical History: Mrs A.H., aged 37, was admitted to the Western Infirmary in May 1938, complaining of severe abdominal pain. This pain had come on two days previously with alarming suddenness, lasted two hours and had then passed off. Four hours before admission she had another exacerbation which was much more violent. She described it as a persistent pain but coming in paroxysms. She had vomited five times within the four hours.

She gave a history of flatulence and heartburn extending over many years. There had never been any jaundice.

On Examination: The patient was lying in great pain with her knees drawn up. The temperature was 99.4° F. and pulse rate 88 per minute. There was a peculiar state of carpo-pedal spasm. Her skin betrayed no sign of cyanosis or jaundice. She was fat.

The abdomen was tender over the epigastrium, particularly on the left side. The right hypochondriac muscles were en garde.

Operation by Mr A. W. Mackey on the day of admission:- The pancreas was extensively necrosed but pale in colour and not stained with blood or bile. The gall-bladder was tense and avascular. It was opened and found to be full of stones. Cholecystostomy was done and a drain placed down to the pancreas. Saline and glucose venoclysis.

Bacteriology of the Bile done by Dr Kyles:- There were no organisms on films. On culture a growth of staphylococcus albus was obtained.

Progress Note: The patient developed acute pulmonary oedema, but recovered. The sinus of the wound after leaking for many weeks eventually dried up. She was dismissed feeling well.

CASE No. 4.

CLINICAL DIAGNOSIS	-	Doubtful
OPERATIVE FINDINGS	-	False Pancreatic Cyst Later - Resolving Acute Pancreatitis
RESULT	-	Well

Clinical History: Mrs M.Y., aged 43, was admitted three times to the Western Infirmary, Glasgow, during the latter part of 1938. She was first seen in July 1938 during an acute attack of abdominal pain which had lasted for 24 hours. This pain was particularly severe in the mid-epigastric and right hypochondriac areas with a tendency to spread through to the back. Repeated retching was a concomitant symptom.

On Examination: The patient, who was very stout, lay in great distress. Her tongue was dry but clean. The temperature was 101° F.; pulse rate 124 per minute. She was neither cyanosed nor jaundiced.

Her abdominal respiratory movements were undisturbed and no distension could be detected. There was tenderness in the right hypochondrium and periumbilical areas, without rigidity.

Her urine was alkaline with a specific gravity of 1028; traces of albumin and bile were found.

Cholecystographic Investigation was carried out by Dr J. S. Fulton, who reported that the gall-bladder was functioning normally.

Progress Notes: The pain gradually abated but there was a tendency to retch at times. She ran a mild pyrexia with moderate increase of pulse rate for a few weeks. Dismissed in a debilitated state.

RE-ADMITTED in September 1938 complaining not of her previous symptoms but of poor general health and abdominal discomfort.

On Examination: An irregular mass was palpable associated with increased muscular resistance in the right hypochondrium. The mass was not tender.

Barium Meal Investigation was carried out by Dr S. D. S. Park, who reported "no intrinsic lesion of

stomach or duodenum. It was noted even gentle palpation over the pars media of stomach produced the appearance of a filling defect suggestive of the presence of a mass behind the stomach."

Operation by Mr W. A. Mackey:- There was found extensive calcifying fat necrosis in the great omentum. The gall-bladder and head of pancreas were enveloped in a mass of vascular adhesions. Further exploration was impossible and the wound was closed.

Post-operative course was uneventful.

RE-ADMITTED in November 1938, again feeling vague abdominal discomfort.

On Examination of the abdomen a large visible tumour was noted in the upper abdomen. The main bulk of the swelling was in the right of the midline but apparently dissociated from the liver dulness. A marked fluid thrill was demonstrable.

A Barium Series was carried out by Dr S. D. S. Park once more, and his report was: "The stomach and duodenum empty normally. The palpable mass lies above and below the pyloric antrum. At 24 hours the mass is situated above the colon."

Operation by Mr J. L. Orr and H. Wapshaw:- A large cyst was found pressing forwards behind and above the stomach. Amber-coloured fluid was evacuated along with sloughs, probably of pancreatic origin. The edges of cyst wall were sutured to edges of the abdominal wound.

The patient made a good recovery.

Biochemistry of the Cyst Fluid was studied by Dr S. V. Telfer, who reported that the fluid contained albumen and proteoses, indicating proteolytic change. The diastatic activity was estimated at 400 units (Wohlgemuth) and lipolytic changes had also taken place.

Bacteriology of the Cyst Fluid (Dr Kyles) - Sterile.

CASE No. 5.

CLINICAL DIAGNOSIS - (False Pancreatic Cyst
(Acute Pancreatitis
OPERATIVE FINDINGS - As above
RESULT - Well

Clinical History: Mrs M.G., aged 46, was admitted in November 1939 to the Western Infirmary complaining of epigastric pain and sickness that had lasted with varying intensity for four weeks. The pain had come on suddenly and was of considerable severity. This illness was one of many similar bouts experienced during the preceding twelve months, but these had always been of milder degree. They recurred about every five weeks.

Her pain was of a paroxysmal nature and radiated through to the back. Nausea and retching were also present.

She had noticed her abdomen had been swelling of late.

On Examination the patient did not look as if she were acutely ill. She was stout. Cyanosis and jaundice were absent. The temperature was 99.6°; pulse rate 98 per minute.

The left upper quadrant of her abdomen was greatly distended by a large globoid swelling. It was not tender and the overlying muscles were lax.

Operation by Professor C. F. W. Illingworth with H. Wapshaw assisting:- Numerous points of fat necrosis, apparently of some considerable duration, were found on the great omentum. The lesser sac contained about one pint of clear faintly straw-coloured fluid and a few small masses of fibrin. The pancreas could not be definitely palpated, but did not appear to show gross enlargement. The gall-bladder contained one large and several small facetted stones. It was thick-walled but not acutely inflamed. The common duct did not contain any stones. Tubes were inserted into the gall-bladder and common bile duct.

Post-operative course was satisfactory.

Biochemistry of Cyst Fluid as reported by Mr S. V. Telfer:- "The fluid had a diastatic activity of over 200 units (Wohlgemuth) but very little proteolytic property."

Bacteriology of Cyst Fluid and Bile (Dr Kyles): Both were sterile.

RE-ADMITTED in January 1940 with another large globular mass in the epigastrium. She had obviously lost weight and was lacking in energy. The appetite was poor. These symptoms suggested a recurrence of the pseudo-pancreatic cyst and pancreatic insufficiency. Her urinary diastase was 133 units (Wohlgemuth).

Operation by Professor C. F. W. Illingworth and H. Wapshaw:- A very large cyst was found occupying the lesser sac and bulging below stomach. The cyst had a fibrous wall and contained about one gallon of turbid watery fluid in which were several small sloughs. The fluid was evacuated and the cyst sutured to the wound margin.

Post-operative course was satisfactory.

CASE No. 6.

CLINICAL DIAGNOSIS	-	Acute Biliary Disease
OPERATIVE FINDINGS	-	Diffuse Pancreatic Necrosis False pancreatic cyst
RESULT	-	Well

Clinical History: Mrs M. McD., aged 57, was admitted to the Western Infirmary in December 1939 with acute abdominal symptoms of 14 days' duration. She complained of severe pain in the upper abdomen and also in the lumbar and interscapular regions. This was attended by vomiting turns.

Previous History: She had been in another ward four months previously with a similar attack from which she had not quite recovered.

For as long as 10 years she had been subject to bilious attacks, coming on about every three weeks, and for that reason she avoided fatty foods. No history of jaundice present.

On Examination: The patient, a rather stout individual, was found lying doubled up with pain. She

was of sallow complexion with a tinge of lividity about the lips. The temperature was 98.5° F.; pulse rate 100 per minute.

The epigastric area of the abdomen was distended by a large globular cyst-like swelling which had a smooth contour. The abdominal movements were replaced by thoracic breathing. The upper abdomen was moderately tender and rigid.

Loewi Mydriatic Test - Negative.

Urine was acid, of 1020 specific gravity, and contained albumen.

Urinary Diastase = 20 units (Wohlgemuth) on the 14th day.

Blood Sugar = 0.09 mg.% (fasting level).

Operation on the 14th day by Professor C. F. W. Illingworth and H. Wapshaw as assistant:- A thick-walled false pancreatic cyst was present in the lesser sac lying above the lesser curvature of the stomach. It contained several large brownish masses of solid material.

The pancreas was indurated throughout and much altered in appearance. The head and tail were replaced by white necrotic material and the latter was surrounded by adhesions. A piece from the tail was taken for examination. There were none of the characteristic spots of fat necrosis or haemorrhages in the pancreas, its vicinity, or distantly.

The gall-bladder was small, thick-walled and on being opened contained a number of small pigment stones. The common bile duct, which was also thick-walled, contained clear bile but no stones. A bougie introduced into it could be readily passed into the duodenum.

The stomach and duodenum were normal.

The gall-bladder and common bile duct were drained by tubes, the cyst by a rubber dam drain.

Biochemical Findings as found by Dr S. V. Telfer were as follows:- "The cyst fluid was faintly alkaline. It had no proteolytic effect on egg albumen." Other enzymes not mentioned.

Bacteriological Findings of Dr Kyles were:-

(1) Bile from the common bile duct was infected fairly heavily by coliform bacilli.

(2) Fluid from the cyst showed no organisms on film and culture.

(3) Wall of cyst showed staphylococcus albus on culture.

(4) Piece of pancreas showed staphylococcus albus on culture.

Histology of Pancreas: The piece of tissue consisted of areolar tissue.

Post-operative Progress was satisfactory.

CASE No. 7.

CLINICAL DIAGNOSIS - Gall-bladder Disease.
OPERATIVE FINDINGS - Resolving acute pancreatitis
RESULT - Well

Clinical History: Miss C.M., aged 61, was admitted to the Western Infirmary in December 1939 complaining of abdominal pain and sickness. Her pain, which was preceded by some nausea, began suddenly in the epigastrium seven days previously. It later radiated to the back and the left shoulder blade. It was paroxysmal in character. When very severe paroxysms came on the patient tossed about in bed and felt shivery, and as these abated she continued to feel a persistent ache. Nausea, with retching and occasional vomiting, was also a prominent feature of the case.

Seven years previously the patient had a similar attack but of lesser degree. A transient icteric tinge was noted at that time. She has otherwise enjoyed good health except for mild flatulent dyspepsia intolerant to fatty food.

On Examination the patient was in an exhausted state. Her temperature was 99.6° F.; pulse rate 88 per minute. There was neither cyanosis nor jaundice.

The abdomen was not distended but did not show any movements. It was, on the whole, lax with a

moderate degree of rigidity in the right hypochondrium. There was no clinical evidence of intraperitoneal effusion.

Loewi Mydriatic Test was positive.
Urinary Diastase was 14 units (Wohlgemuth) on 8th day of illness.
Blood Sugar (fasting level) 0.08 mg. %.
Urine was acid, of 1030 specific gravity, and contained albumen.

Operation by Professor C. F. W. Illingworth with H. Wapshaw assisting, on 13th day of illness. The pancreas was enlarged and nodular, and on its exposure was found to be the seat of widespread necrosis. Outside the pancreas and in the remainder of the abdomen there was no evidence of either fat necrosis or haemorrhage. The gall-bladder was normal in appearance and free from stones on palpation. The common duct was opened and from it escaped clear green bile. It was also free of calculi and a bougie could be readily passed into the duodenum. It was drained by a tube.

A small active ulcer was discovered on the anterior wall of the duodenum just beyond the pylorus.

A piece of pancreas was removed for examination.

Progress Note: Uneventful.

Histology of Pancreas: "The tissue stains poorly and consists of hyaline fibrous tissue and degenerate parenchyma. Extravasated erythrocytes, some mononuclears and a collection of lymphocytes are also seen."

CASE No. 8.

CLINICAL DIAGNOSIS - Acute Pancreatitis
RESULT - Well

Clinical History: Mrs E.F., aged 66, was admitted to the Western Infirmary in June 1940 complaining of abdominal pain and sickness of 14 hours' duration. The pain came on abruptly without warning and was of violent severity. It started in the epigastrium

and spread later to the rest of the abdomen and through to the back. Morphia gr. ¼ gave her no relief. The patient was also violently sick while the pain lasted.

Previous History: Similar attacks but of shorter duration and milder in degree had occurred during the previous 8 months. During one which occurred 6 months previously she noticed that she was jaundiced, but the stools and urine seem to have been normal in colour.

On Examination: The patient was suffering great pain and was rather dehydrated. Her pulse was of good tension and its rate was 92 per minute. Her temperature was 99° F. She was generally cyanosed and her sclerotics were yellow.

The abdomen was symmetrically shaped and not distended. It was immobile. No masses were palpable. She was very tender in the epigastrium and around the umbilicus. Free fluid could not be found on percussion.

Loewi Mydriatic Test was negative.
Urinary Diastase was 250 units (Wohlgemuth) on 1st day of illness.
Urine was neutral, of 1030 specific gravity, and contained albumen and bile.

Progress Note: The patient's symptoms gradually settled under conservative care, and she was dismissed well.

CASE No. 9.

CLINICAL DIAGNOSIS - (False Cyst of Pancreas
(Acute Pancreatitis
OPERATIVE FINDINGS - Blood Cyst, probably of same nature.
RESULT - Died.

Clinical History: Mr W.N., aged 51, was an inpatient in the Western Infirmary in July 1940 recuperating from a hernia operation when he took ill.

He was seized by a sudden and severe pain in the left hypochondrium and began to vomit copious amounts of fluid at frequent intervals. An acute dilatation of stomach or some type of high obstruction was at first suspected, and in order to relieve him the apparatus for continual duodenal lavage and drainage was set up on the third day, and salines were supplied by the rectal route. There was considerable improvement from this treatment and by the sixth day pain and sickness had left him; he was much relieved but in a very weak and dehydrated state.

On Examination: The patient was very thin and wizened. His temperature and pulse rate were slightly raised. He was neither cyanosed nor jaundiced.

The patient was found to have a large visible swelling in the left upper quadrant of his abdomen when examined a few days after the commencement of symptoms. It was tense, dull to percussion, and had a smooth round contour. Gaseous distension of bowel was also noted (see photographs).

Urinary Diastase = 40 units (Wohlgemuth) on 4th day of illness.

Barium X-ray Series was carried out by Dr S. D. S. Park, who reported:- "The stomach functions normally and seems to be healthy. It is, however, displaced upwards by a large mass lying behind and below in the lesser sac. The barium enema tended to be held up at the splenic flexure by the same mass."

Operation by Mr H. Wapshaw on the 13th day of illness. A large globular cyst occupied the lower part of the lesser sac and bulged from under the transverse colon. It had a deep attachment to the pancreas about its body. Around the base of the cyst there was a sprinkling of fat necrosis that spread on to the root of the jejunal mesentery. In the exposure an adhesion to the cyst broke with brisk bleeding.

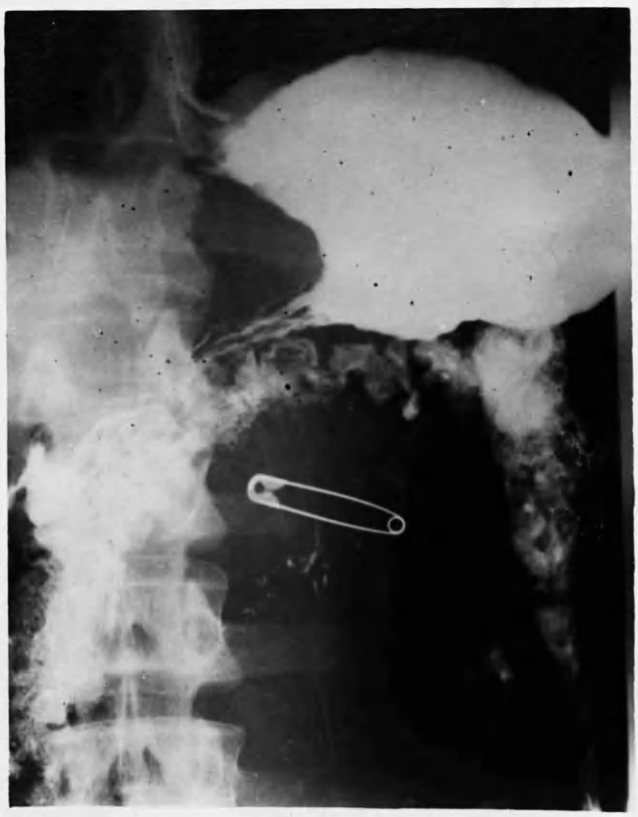
The cyst was unilocular and about 10" in diameter; on opening it the interior was found to be filled with blood clot from a bleeding of fairly recent date. This clot was gently scooped out but as the depths of the cyst were being cleared of clot a persistent haemorrhage began. Since its source could not be traced, reliance was placed on firm gauze packing.

The pancreas was firm and nodular but could not

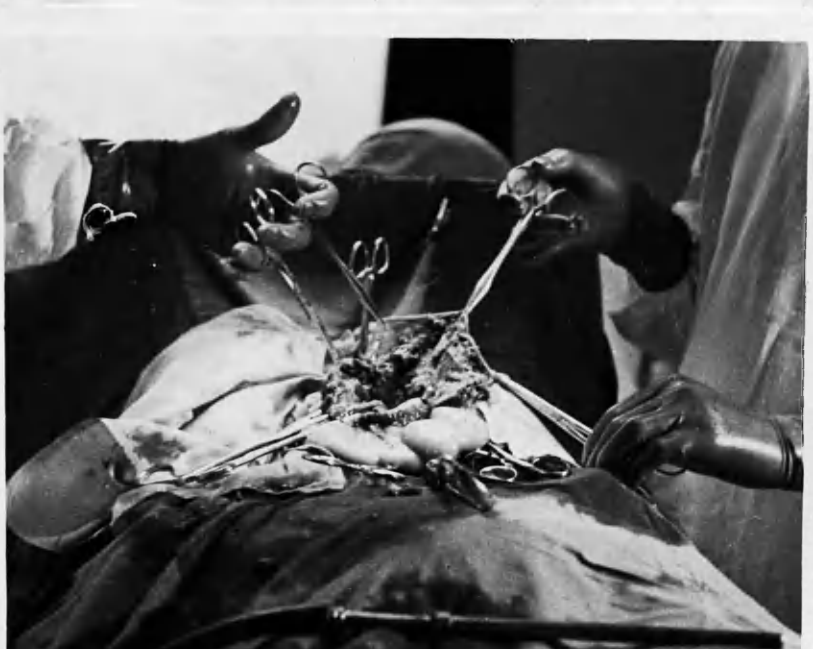
be brought into view. The gall-bladder was thin-walled, distended, and to palpation was full of stones. It was left undisturbed.

Post-operative Course: The patient died from haemorrhage which continued to issue from the depths of the cyst despite packing and hot irrigations. Its source was in all probability a splenic or large pancreatic vessel.

Photograph No. 1, showing the immense globular swelling in the left upper quadrant.



Barium Investigation: Film showing upward displacement of the stomach and transverse colon. The pin marks the centre of the cyst.



Photograph No. 3 taken at operation. The cyst has been opened and walls held apart to show masses of blood clot.

CASE No. 10.

CLINICAL DIAGNOSIS - Doubtful
OPERATIVE FINDINGS - Gangrenous Pancreatitis
RESULT - Died

Clinical History: Mr W.B., aged 68, was admitted to the Western Infirmary in February 1941 with severe pain of 10 hours' duration in his left loin and left subcostal regions. This pain had come on just after he had taken his breakfast. It remained with unremitting severity and with occasional paroxysms on the left side, and later spread to the epigastrium. He had vomited four times.

Previous History: For 2 years the patient had suffered from peptic ulcer which was proven to be prepyloric in position, but he had not complained of indigestion during the past few months. Prostatectomy had been performed two months ago with success for a simple enlargement of the gland.

On Examination: The patient was of thin build, pale, drowsy and non-co-operative. He was suffering severe pain which came on in spasms. Temperature 98° F.; pulse rate 108 per minute. Blood pressure was 200/130 mg. Hg. He was neither cyanosed nor jaundiced.

His abdomen looked symmetrical, moved freely with respiration but on deep inspiration left hypochondriac pain was evoked. There was no obvious distension. He was dull to percussion and tender in the left subcostal region and left loin. There was slight rigidity over these areas. Signs of fluid were not elicited.

Loewi Mydriatic Test - Positive on the day of his death.

Urine was acid, of 1020 specific gravity, and contained albumen, granular casts and white cells.

Blood Urea = 0.105 gm. %.

Progress Note: The patient was placed in Fowler's position and given a saline infusion. He improved a little during the subsequent week, although he remained very listless and continued to suffer pain in the left loin. A swelling gradually became palpable in this area and operative treatment was then considered.

Operation by Mr J. S. Buchanan (after 8 days' illness). The peritoneum and surfaces of jejunal loops were congested and the latter had a matting of fibrinous lymph. The pancreas felt nodular and was suspected of being acutely diseased. In the left flank there was a collection of blood-stained fluid and the abdomen was drained by a tube leading to the pancreatic tail through the flank.

Saline venoclysis given, but the patient died in coma on the following day.

Synopsis of Autopsy: The whole of the pancreas was necrotic and nearby fatty tissues were covered with small areas of fat necrosis. The terminal part of the main pancreatic duct contained bile but was not dilated. A small duodenal diverticulum was found just above the ampulla of Vater. Both stomach and duodenum showed signs of peptic ulceration. The gall-bladder was markedly dilated; its lining was healthy and it did not harbour stones. The common bile duct was dilated for no apparent reason, and the ampulla of Vater was unobstructed. A slight roughening of the ampullary lining was noted. The bladder urine was semi-purulent and the wall of the viscus contracted. The liver and spleen were the seat of infarcts and their respective veins were extensively thrombosed.

CASE No. 11.

CLINICAL DIAGNOSIS	-	? Perforated Duodenal Ulcer
OPERATIVE FINDINGS	-	Acute Haemorrhagic Pancreatic Necrosis
RESULT	-	Died later from Suppurative Pancreatitis

Clinical History: Mr W.H., aged 61, was admitted to the Western Infirmary in June 1941 complaining of severe pain in the upper abdomen which had been present for 14 hours. It came on suddenly about one hour after a full meal which included two eggs. The pain continued with great severity, coming and going in spasms, and passing through to the back. When gr. $\frac{1}{4}$ of morphia was given on admission it had but little effect on this pain. Another outstanding

symptom was vomiting which was more persistent than would be expected in a case of duodenal perforation.

The patient's past health had been good apart from occasional flatulent dyspepsia. He did not take alcohol and smoked in moderation.

On Examination: The patient was obese and lay in considerable distress. He was neither cyanosed nor jaundiced. His pulse rate and temperature were normal; blood pressure 130/95 mg. Hg.

The abdomen was distended but its movements were quite free. Tenderness and moderate rigidity were found across the upper abdomen.

Loewi Mydriatic Test - Negative.

Urine was acid, of 1026 specific gravity, and contained albumen and diminished chlorides.

Urinary Diastase = 200 units (Wohlgemuth)

Blood Diastase = 4000 units per ml. serum (Somogyi)

Blood Lipase = 5.3 ml. N/20 NaOH per ml. serum.

Operation by H. Wapshaw on day of admission: Acute haemorrhagic necrosis was found in the head and body of the pancreas, and numerous spots of fat necrosis were scattered throughout the omentum and other fatty tissues. The stomach and duodenum were dilated and congested. The gall-bladder was thin-walled and tense, but contained no calculi. The common duct was free of any palpable gall-stones. A considerable amount of brownish effusion flowed out of the peritoneal cavity. A tube was placed in the gall-bladder, and a rubber drain placed down to the pancreas. Saline venoclysis performed.

Bacteriology of the Bile as reported by Dr Kyles: "No organisms on films or culture."

Post-Operative Notes: He recovered from the effects of operation but remained listless and apathetic. Cholangiogram was taken on the 10th day after lipiodol had been injected into the cholecystostomy tube. The pancreatic duct was visualised and was seen to enter the ampulla of Vater in conjunction with the common bile duct. Lipiodol passed freely into the duodenum. Dismissed after 6 weeks stay, very debilitated.

RE-ADMITTED ten days after in a dying condition. He had developed a large left-sided perinephric abscess which was pointing. There was oedema of both feet and lumbar region consequent upon either cardiac failure or interference with venous flow in the inferior vena cava.

His heart sounds were poor, pulse impalpable at the wrist, and his temperature was slightly elevated.

Leucocyte count = 22,000 per c.mm.
Urine - contained sugar.
Blood diastase = 45.7 units per ml. serum (Somogyi).
Blood lipase = Zero reading.

Operation by H. Wapshaw: While the patient lay in his bed the pus was let out by a small oblique loin incision. It flowed out in great quantity, was of a sickly smell and contained large sloughs (? pancreatic sequestra). The abscess cavity lay in the retroperitoneal tissues adjacent to the tail of the pancreas. The wound was drained by a wide bore tube.

Blood and plasma were administered plus 20 units of insulin, but he died on the following day.

Bacteriology of Pus as reported by Dr Kyles: Heavy growth of B. Coli and Streptococci.

Autopsy: The pancreatic gland was found to have been completely destroyed by the suppurative process which had spread widely in the retroperitoneal tissues.

CASE No. 12.

CLINICAL DIAGNOSIS - Acute Pancreatitis: Chronic Nephritis.
RESULT - Died after second attack in uraemic coma.

Clinical History: Mrs H.C., aged 44, was admitted to the Western Infirmary in June 1941 with abdominal pain and sickness of 10 days' duration. Her pain came on suddenly in the upper abdomen and was transmitted through to the back. Sickness with retching

was an associated and persistent feature of the case. After four days these symptoms, which were only partly relieved by morphia, abated to some extent, with only a dull ache remaining. There was an acute exacerbation of intense pain and sickness two days later, and these symptoms continued until she was admitted to hospital.

Previous History: She had been troubled with 'bilious' attacks, painless in character, over the previous six years, although she could enjoy an ordinary diet without any disagreeable effects.

On Examination: The patient was in acute distress, fatigued and dehydrated. The temperature was normal, pulse rate 108 per minute, and blood pressure 100/110 mm. Hg. There was a sclerotic icterus; cyanosis was absent.

There was slight meteorism and limitation of movement of the abdomen. Tenderness with some rigidity was elicited in the upper half, especially in the right hypochondrium. Clinically there was no peritoneal effusion, nor was any tapped by an abdominal puncture.

Leucocyte Count = 8,000 per cu.mm.
Loewi Mydriatic Test - Negative.
Urine was acid, of 1009 specific gravity, and contained albumen and diminished chlorides.
Urinary diastase = 5 units (Wohlgemuth)
Blood diastase = 1184 units per ml. serum (Somogyi).
Blood lipase = 3.4 ml. N/20 NaOH per ml. serum.
Blood sugar (fasting level) = 0.09 gm. %.
Blood urea = 0.166 gm. %.

Cholecystographic Examination was done by Dr S. D. S. Park, who reported a non-functioning gall-bladder.

Progress Note: The patient was given normal saline by venous and rectal routes and by the second day she was put on a graduated fat-free diet.

She was dismissed after 4 weeks, improved but still feeling very weak. A record was kept of her progress and repeated enzyme estimations were carried out. She was able to carry on with light domestic duties but readily became fatigued and her ankles were swollen by night time. She continually complained of a bad taste in her mouth. Four weeks after dismissal

she experienced two transient attacks of abdominal pain. It was unaccompanied by sickness and jaundice was absent. Later she developed scattered subcutaneous haemorrhages on her arms and legs. There was no vitamin C deficiency as judged by ascorbic acid estimation. It was concluded that poor renal function was responsible for the ecchymosis.

Renal Function: Using the Urea Clearance Test the mean of readings = 10.8% of average normal renal efficiency.

Schmidt's Diet was given for three days and the following results were obtained from an examination of the stool as reported by Dr A. B. Anderson:

Dry matter	13.5%
Fat	10.8%
Neutral fat	3.8%
Fatty acid	7.0%

As the results were within normal limit, it was assumed that the pancreatic ferments had a free entry into the duodenum.

Blood Examination:

Haemoglobin (Sahli)	57%
Red blood cells	3,200,000 per cu.mm.
Colour index	0.89

Blaud's pill was prescribed.

RE-ADMITTED in January 1943 with a repeat of her acute illness. Her pain, which was again in the epigastrium and right hypochondrium, had been present for three weeks before admission. Vomiting and retching were again severe. She complained of frontal headaches and spots passing before her eyes. The region between the shoulder blades ached badly.

On Examination: She was thin and anxious and her dried features betrayed a tinge of jaundice. The temperature, pulse and respiratory rates were normal.

The abdomen was distended below the umbilicus and generally resistant over the umbilical and epigastric zones.

Urine was neutral, of 1010 specific gravity, and contained albumen; chlorides were diminished.

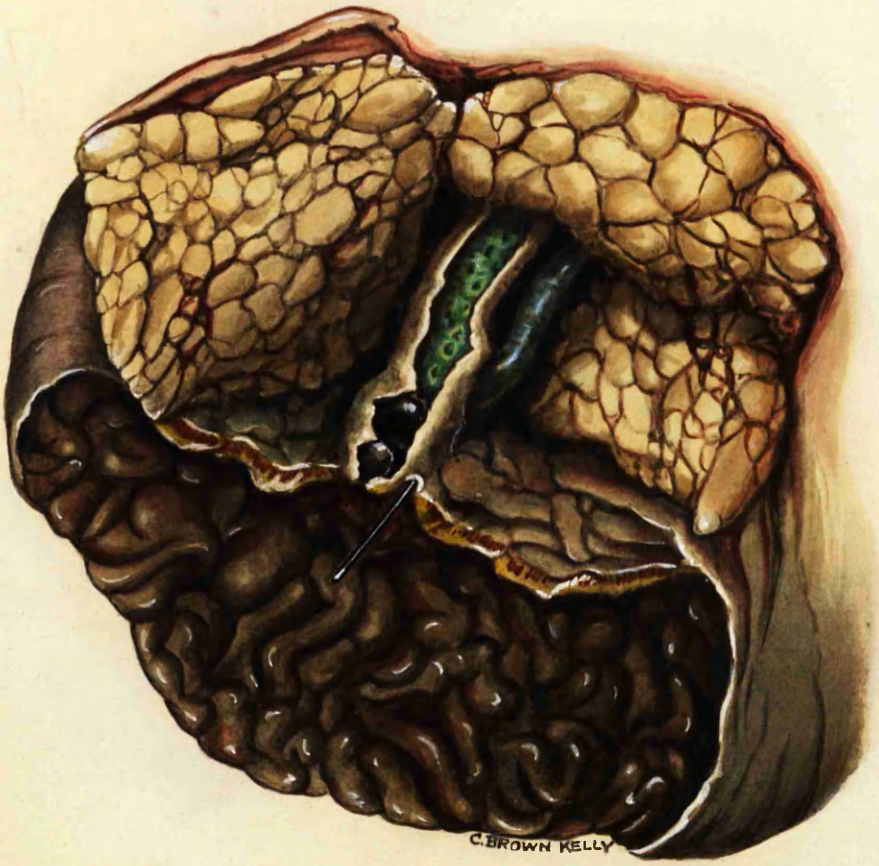


Plate II. Gallstones in ampulla of Vater, the duct of Wirsung shown by probe is seen to enter duodenum separately. The pancreatic tissue appears normal. (See text page 136).

Leucocyte count was 12,000 per cu.mm.
Loewi Mydriatic Test - Negative
Blood diastase = 160 units per ml. serum (Somogyi)
Blood Lipase = 2.7 ml. N/20 NaOH per ml. serum
Blood Urea = 0.293 gm. %.

Operation by Mr J. P. Fleming: The pancreas was very swollen and indurated. The gall-bladder was slightly distended. A few gall-stones were extracted from it and a tube inserted.

Post-Operative Progress: The patient developed delusional insanity and died in coma 10 days later.

Synopsis of Autopsy: The pancreas was slightly firm but otherwise normal outwardly and on section. The dissection of the terminations of the bile and pancreatic ducts was interesting. They entered the duodenum separately but were in close contiguity for about 1.5 cm. Two small irregular pigmented stones were lodged at the lower end of the common bile duct. If the pancreatic disorder were due to the gall-stones, a reflux of bile could not have been the cause, but temporary occlusion of the pancreatic duct was a distinct possibility as a result of pressure from the nearby gallstones. The kidneys were both shrivelled and their capsules adherent.
See Plate II.

CASE No. 13.

CLINICAL DIAGNOSIS - Transient Pancreatitis
RESULT - Well

Clinical History: Mrs A.C., aged 57, was admitted to the Western Infirmary in July 1941 complaining of upper abdominal pain and sickness of three days' duration. The pain began in the lower thoracic region behind, and later shifted round to the right hypochondrium and epigastrium. It did not reach its maximum of intensity until one hour after its onset, about which time she became violently sick, vomiting and retching. She described sensations of being alternately "hot and cold". These symptoms

passed off on the morning of admission, leaving a dull ache at the right subcostal margin. Previous health was good.

On Examination: She was stout and did not suffer much pain. Her temperature, the pulse and respiratory rates were all normal. The blood pressure was 145/80 mm. Hg. She was mildly jaundiced.

The abdomen was lax and very stout. She was tender but not rigid in the right hypochondrium.

Leucocyte count = 7,000 per cu. mm.
Loewi Mydriatic Test - Negative.
Urine had a specific gravity of 1022, and contained both albumen and bile.
Blood Diastase = 1,280 units per ml. serum (Somogyi)
Blood Lipase = 2.6 ml. N/20 NaOH per ml. serum
Blood Sugar = 0.09 gm. % (Hagedorn & Jansen)

Cholecystographic Examination was carried out by Dr S. D. S. Park, who reported a non-functioning gall-bladder.

Progress Note: The patient recovered rapidly and had no further trouble.

CASE No. 14.

CLINICAL DIAGNOSIS was doubtful - ? Perforated Duodenal Ulcer
OPERATIVE FINDINGS - Acute Pancreatitis localised to the tail of the gland
RESULT - Well

Clinical History: Mr R.S., aged 61, was admitted to the Western Infirmary in December 1941 with epigastric pain of 15 hours' duration. It did not reach the maximum intensity for about three hours, and was propagated through to the lower dorsal region. He was very sick and retching repeatedly. He had

enjoyed a heavy meal 1½ hours prior to the onset of the illness.

Previous History: He had had dyspepsia about one hour after a meal for about 15 years, but his appetite was in no way blunted.

On Examination: He was obviously very ill, lying with his knees drawn up and restless. He was inarticulate with the pain. Temperature was 97° F.; pulse rate 99 per minute. He was neither cyanosed nor jaundiced.

His abdominal movements were restrained and he was tender and very rigid above the umbilicus.

Loewi Mydriatic Test - Positive
Urine was acid, of specific gravity 1042; it contained no abnormal constituents.
Urinary Diastase = 250 units (Wohlgemuth)
Blood Diastase = 1,600 units per ml. serum (Somogyi)
Blood Lipase = 3.1 ml. N/20 NaOH per ml. serum.

Operation performed by Mr T. M. Newton on day of admission:- Acute pancreatitis, localised to the tail piece, was discovered, without any visible fat necrosis. The gall-bladder was normal and did not seem to contain calculi. A large ulcer 1½" in diameter was felt on the posterior wall of the stomach, and its rolled edge raised the question of malignancy. No metastases, however, were evident.

Wound closed completely.

Post-Operative Course: He continued to have pain and sickness on the following day but these subsided thereafter and when seen five months later he looked very fit.

Cholecystographic Examination was carried out by Dr S. D. S. Park, who reported that the gall-bladder was functioning normally.

Ward Chart of Case No. 15.

Name F. FAYE.

Age 21 YRS.

Ward.....

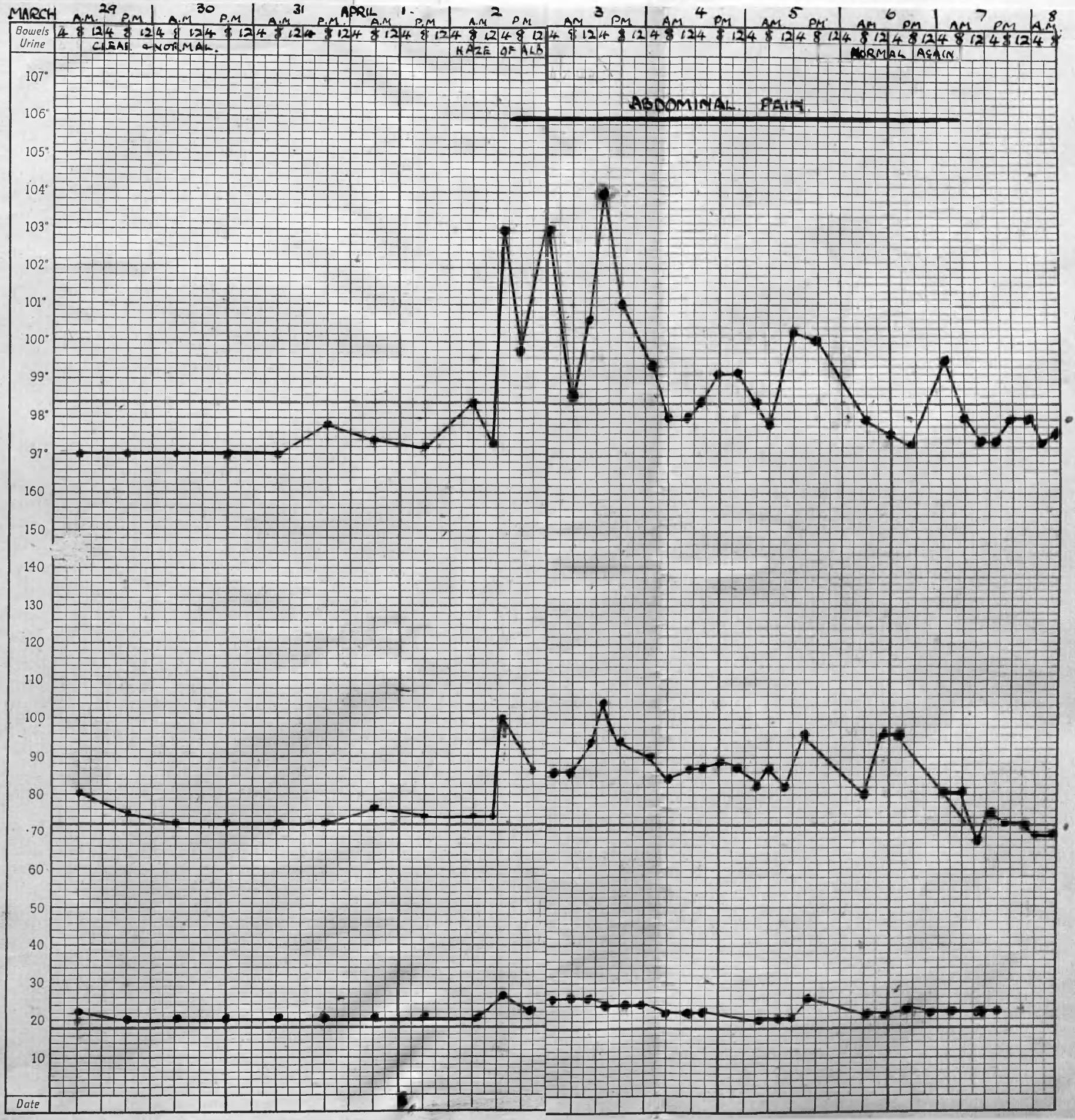
Journal.....

Page .....

MUMPS BEGAN.
27th March.

PANCREATITIS ?
2nd April.

Date of Admission
.....



CASE No. 15.

CLINICAL DIAGNOSIS - Epidemic Mumps: Pancreatitis.
RESULT - Well

Clinical History: Mr F.F., aged 21 years, was admitted to Knightswood Fever Hospital feeling moderately ill with mumps of two days' standing. Both parotid glands were affected.

When this infection was becoming quiescent and had reached the seventh day of the disease there developed a very severe pain in the epigastric and left subcostal regions and the left loin. He had no symptoms to suggest a pulmonary infection. Deep inspiration, however, made the pain worse. His appetite became poor but at no time did he feel sick.

On Examination: The patient looked healthy and did not appear to be suffering extreme pain when seen on the third day of his abdominal illness. His parotids were no longer swollen, nor was his scrotum affected. He was neither cyanosed nor jaundiced.

The abdomen looked normal in shape and movement. It was slightly tender and rigid in the left hypochondrium.

Leucocyte count = 14,000 per cu. mm.
Loewi Mydriatic Test was negative.
Urine was acid, of 1020 specific gravity, and contained trace of albumen.
Urinary Diastase = 80 units (Wohlgemuth)
Blood Diastase = 800 units per ml. serum (Somogyi) on 3rd day of abdominal illness.
Blood Lipase = 0.84 ml. N/20 NaOH per ml. serum on 3rd day of abdominal illness.

Progress Note: The patient had completely recovered by the sixth day.

CASE No. 16.

CLINICAL DIAGNOSIS - Acute Pancreatitis: False Cyst.
OPERATIVE FINDINGS - As above.
RESULT - Diabetes Mellitus

Clinical History: Mr R.McL., aged 70, was admitted to the Western Infirmary in April 1942. He first became aware of an uncomfortable feeling which came on in his epigastrium about an hour after food on the day before admission. This discomfort was soon replaced by a pain of exceptional severity that spread to both the right and left hypochondriac areas. Morphia provided but little sedative effect. There was attendant nausea with persistent retching.

Previous History: For many years he had had mild ill-defined dyspeptic symptoms. He was a whisky drinker.

On Examination: The patient lay quiet on his back but when disturbed he experienced acute pain. He looked well-nourished; slightly jaundiced and cyanosed about the face. His breath emitted a smell of acetone. Temperature 98° F.; pulse rate 68 per minute; blood pressure 145/105 mm. Hg.

The abdominal movements were restricted but the contour seemed normal. There was both tenderness and rigidity in the epigastrium and right hypochondrium. No sign of free fluid in the peritoneal cavity.

Leucocyte count - 11,800 per cu. mm.
Loewi Mydriatic Test - Negative.
Urine was acid, of 1028 specific gravity, and contained sugar and acetone per
Urinary Diastase = 40 units (Wyi) emuth)
Blood Diastase = 457 units per ml. serum (Somogyi)
Blood Lipase = 2.13 ml. N/20 NaOH per ml. serum.

Progress Notes: On admission glucose saline venoclysis was arranged; he received 5 pints given slowly with 10 units of insulin added to the pint.

On the third day the abdomen became moderately distended, yet his general condition had improved. He still felt slight abdominal discomfort and occasionally retched. Dr L. W. D. Scott examined him and thought that his glycosuria was due to gross pancreatic damage.

On the seventh day a globular mass became palpable, but barely visible, on the left of the midepigastrium. It was about 12 cm. in diameter, had a smooth contour and was not tender. The mass was

dull to percussion and apparently unrelated to liver or spleen.

Cholecystographic Examination was done by Dr S. D. S. Park, who reported a normally functioning gall-bladder.

Blood Sugar Curve (Hagedorn & Jansen) on 10th day of illness:-

Fasting level	9.00 a.m.	...	191 mg. %
50 gm. glucose	9.30 a.m.	...	211 "
	10.00 a.m.	...	245 "
	10.30 a.m.	...	270 "
	11.00 a.m.	...	251 "

Operation by H. Wapshaw on the 14th day of illness:- The palpable mass consisted of a matting of great omentum, thickened, oedematous and congested, overlying the greater curvature of stomach. Behind the stomach there was an encysted collection of fluid in the lesser sac. Numerous areas of fat necrosis were scattered over the omentum. The transverse colon was tacked down through shortening of the meso-colon to the region of the pancreas. The gland itself could only be partly seen owing to altered structures that enveloped it, and a small abscess was encountered in its vicinity containing ¼ oz. of yellowish necrotic matter. The pancreas was enlarged, indurated along its whole extent, and a small piece was removed for biopsy.

About 2 pints of whitish, turbid, watery fluid were evacuated from the false cyst in the lesser sac. The foramen of Winslow was blocked by fibrous adhesions.

The gall-bladder was greyish, slightly thickened and not distended. It contained no stones. A cholecystostomy was performed. The common duct looked and felt normal.

Biochemical Findings of Cyst Fluid:

No proteolytic action on casein.
Diastatic activity = 2,280 units per ml. fluid (Somogyi)
Lipolytic activity = 7.35 ml. N/20 NaOH per ml. fluid.

Bacteriological Examination was done by Dr Kyles, who reported non-specific coliform organisms in the

bile. The cyst fluid was sterile. The pus from the pancreatic abscess contained enterococci.

Pancreatic Biopsy: The tissue consisted of necrotic acini.

Post-Operative Progress: The patient's recovery was very tardy because of either persistent sepsis of his wound, which was infected with streptococcus pyogenes, or pancreatic cachexia. Small areas of altered fat and small pancreatic sloughs were discharged.

CASE No. 17.

CLINICAL DIAGNOSIS - (False Cyst of the Pancreas
(Resolving Pancreatitis

RESULT - Well

Clinical History: Miss M.M., aged 51 years, was admitted to the Western Infirmary in May 1942. She had not been well since her acute illness, which occurred two months before her admission. This was ushered in by a severe bout of vomiting that came on soon after a meal and lasted for half an hour. As the sickness subsided she was seized with an acute pain in the left hypochondrium. There was some pain over the rest of the abdomen. Her doctor was inclined to regard the seizure as a coronary thrombosis, and found that morphia gr.$\frac{1}{4}$ only partially sedated her. Her acute symptoms gradually wore off in the course of the next 14 days.

In the interim she had felt occasional twinges of pain in the left side but the main complaint was constant malaise unaccompanied by vomiting.

Previous History: Three years previously she had severe typical attacks of biliary colic and for eighteen months she had freedom from symptoms. After another biliary attack in January 1941 Professor C. F. W. Illingworth removed the gall-bladder, which was thin-walled and contained a number of rather large facetted stones. The common duct was healthy. Apart from a small healed duodenal ulcer, the other

viscera, including the pancreas, were normal at that operation.

On Examination: The patient, a well nourished, diminutive person, lay comfortably in bed. Temperature and pulse rate were normal. She was not jaundiced. Her stools were normally coloured.

The only abnormal finding in the abdomen was a visible and palpable mass in the left upper quadrant. It was globular in outline, dull to percussion, fixed and not tender.

Leucocyte count	=	3,600 per cu.mm.
Loewi Mydriatic Test	-	Negative.
Urinary analysis was normal.		
Urinary Diastase	=	60 units (Wohlgemuth)
Blood Diastase	=	284 units per ml. serum (Somogyi)
Blood Lipase	=	1.92 ml. N/20 NaOH per ml. serum
Blood Sugar (fasting level)	=	0.136 gm.%.

Progress Notes: The mass completely disappeared in the course of time, and her general improvement made operative intervention quite unnecessary.

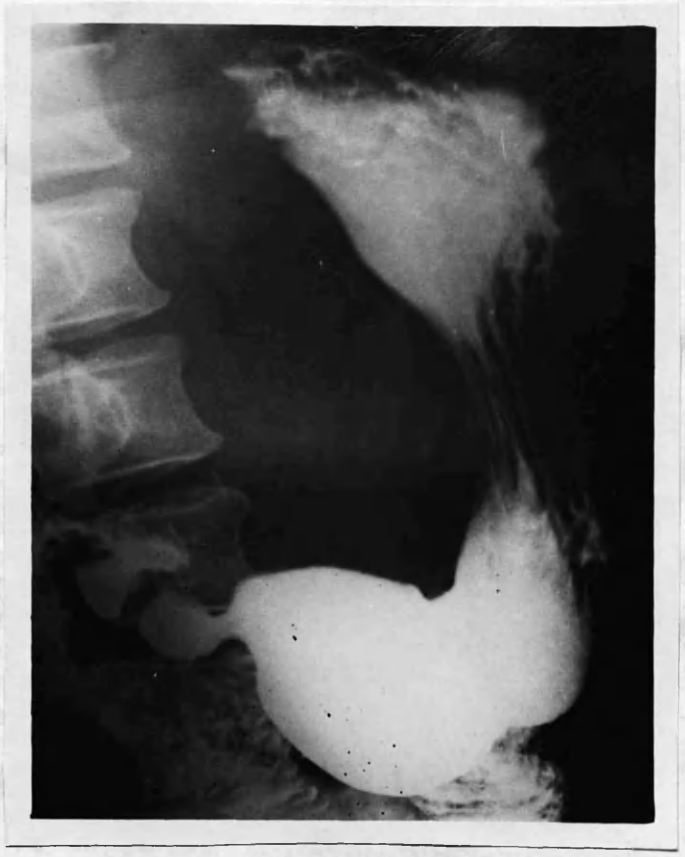
Barium Meal Investigation was carried out and the stomach was reported to be functioning well and of normal appearance. An oblique view showed a mass pushing the pars media forwards.

Paracentesis of the Cyst: 45 ml. of straw-coloured fluid, free of sediment, were aspirated. It was neutral in reaction and proteolytically inactive with 1% casein.

Diastatic Activity	=	16,000 units per ml. fluid (Somogyi)
Lipolytic Activity	=	14.7 ml. N/20 NaOH per ml. fluid.
Bacteriology of fluid	=	No organisms found in films on culture (Dr Kyles).

Photograph No. 4, showing slight swelling of the left upper quadrant.

Case No. 17.



Photograph No. 5. X-ray film taken obliquely after barium meal to show forward displacement of the stomach.
Case No. 17.

CASE No. 18.

CLINICAL DIAGNOSIS - ? Acute Biliary Disease
OPERATIVE FINDINGS - ? Interstitial Pancreatitis
RESULT - Well

Clinical History: Mrs I.D., aged 45, was admitted to the Western Infirmary in June 1942 after five days' illness. The patient had been slightly delirious for two days prior to admission, consequently her history was lacking in detail. She complained of severe upper abdominal pain, associated with considerable gastric upset - flatulence and vomiting.

She had headaches and felt extremely weak.

Previous History: In June 1940 she was laid up with a severe attack of epigastric pain which spread across the upper abdomen, through to the lumbar region and interscapular area. It was of a colicky nature and was accompanied by vomiting. She remembered being very restless at that time, and on the following day her skin became yellow, the presence of jaundice being evidenced by the dark colour of the urine and lack of pigment in the stools. The pain came on intermittently thereafter and lasted, but diminishing in its severity, for ten days.

She remained well until April 1942 when she was again stricken with a similar illness but the symptoms of pain and vomiting were more marked than on the previous occasion. Slight jaundice was again a feature of the case. She never recovered completely from this attack, being lacking in appetite, feeling easily tired and breathless on exertion.

On Examination: The patient was a well nourished woman. She was restless in bed but at the same time seemed to be rather drowsy. Yet she answered questions intelligently. There was a slight tinge of jaundice. Her tongue was red and dry, breath foul, and her thirst was extreme. Her pulse was of good volume; rate 108 per minute. The temperature was 102° F. Blood pressure was 118/70 mm. Hg.

The abdomen was symmetrical and free in its movements except in the right upper quadrant where there was a slight fullness. She was rigid and tender to the right of the epigastrium. The liver was enlarged to two finger breadths below the costal margin and slightly tender on pressure.

Leucocyte Count = 6,800 per cu. mm.
Urine contained albumen and blood.
Stools were pale.
Blood Diastase = 114 units per ml. (Somogyi) on 5th day.
Blood Lipase = 0.84 ml. N/20 NaOH per ml. serum.

Cholecystographic study done by Dr S. D. S. Park revealed a non-functioning gall-bladder but the presence of one stone was suspected.

Progress Note: Patient remained drowsy and jaundiced for a few days. Her pain and sickness

gradually eased off, and after 18 days' stay in hospital she was dismissed feeling much improved.

RE-ADMITTED in August 1942 with yet another attack of pain, vomiting and jaundice. Her temperature was 97° F. and pulse rate 84 per minute.

Blood Lipase = 0.98 ml. N/20 NaOH per ml. serum (on 5th day).

Operation by Professor Illingworth on the 5th day of illness:- The gall-bladder was thick-walled and somewhat oedematous but contained no stones. The common bile duct was exposed via the cystic duct and no stone was found. A bougie passed freely into the duodenum. The pancreas was diffusely swollen and indurated; it presented no sign of fat necrosis. The liver was somewhat enlarged and slightly nodular. The stomach and duodenum were normal.

The gall-bladder was removed and a tube inserted into the common bile duct. A portion of the pancreas was removed but the specimen was misplaced.

Culture of the Wall of the Gall-bladder revealed a pure growth of Friedländer bacilli.

Post-operative Course was uneventful.

CASE No. 19.

CLINICAL DIAGNOSIS - Acute Biliary Disease
OPERATIVE FINDINGS - Resolving Acute Pancreatic Necrosis
RESULT - Well

Clinical History: Mrs I.C., aged 48, was admitted to the Western Infirmary in October 1942 complaining of abdominal pain and sickness for four days. The pain was situated in the right hypochondrium and was referred to the lumbar region. On admission the acute symptoms had left her and only a dull lumbar ache remained.

Previous History: In April 1942 she was laid up for about three weeks with acute pain in the right

hypochondrium and epigastrium accompanied with sickness. A deep jaundice came on during this illness and later passed off. A strong distaste for fatty foods followed this "biliary attack".

On Examination: The patient was very stout. She lay comfortably and in no way distressed in bed. The temperature and pulse rate were within normal limits. Her skin had a jaundiced tinge.

The abdomen was not appreciably distended; its movements were restricted in the upper half. She was tender in the right iliac fossa and rigid over the right hypochondrium.

Urine was acid, of specific gravity 1030, and contained a trace of bile.
Blood diastase = 94 units per ml. serum (Somogyi) on the 8th day.
Blood Lipase = 0.98 ml. N/20 NaOH per ml. serum on the 8th day.

Operation by Professor C. F. W. Illingworth on the 8th day:- The pancreas showed very extensive degree of recent acute necrosis. It was uniformly swollen, indurated and covered with numerous spots of fat necrosis. These were also scattered throughout the great omentum. There was no haemorrhage or free fluid.

The gall-bladder was somewhat thickened and contained eight small mulberry cholesterol stones. The common bile duct appeared a little dilated; it contained clear bile and no stones. It was drained by a tube.

Post-Operative Course was uneventful.

CASE No. 20.

CLINICAL DIAGNOSIS - Doubtful
OPERATIVE FINDINGS - Acute Pancreatitis
RESULT - Well

Clinical History: Mrs F.McD., aged 63 years, was admitted to the Western Infirmary, Glasgow, in

November 1942. She complained of a pain in the epigastric region which had come on three days before admission to hospital. It had started soon after a meal, was severe in character and tended to spread to the rest of the abdomen but nowhere else. Shortly after the onset of illness she began to vomit and continued doing so, bringing up mouthfuls of dark brown material resembling coffee grounds. Her symptoms were slightly relieved by poultices. Constipation present but only during the current illness.

Antecedent History: During the previous month the patient had had an uncomfortable feeling in the epigastrium after meals, and she was troubled with slight indigestion which took the form of a sense of fulness in the abdomen. Appetite good, but fatty foods were inclined to upset her. No history of jaundice.

On Examination: She lay still in bed and was reluctant to move. She looked ill, with features drawn, sunken eyes and hollow cheeks. The pallor of the mucous membranes was suggestive of an anaemic state. There was a certain tinge of cyanosis about the lips, but no evidence of jaundice.

The temperature was 97.8°F., pulse rate 88 per min. and respirations 20 per min.

The appearance of the abdomen suggested distension of the transverse colon. The abdomen moved little on respiration. There was some muscle guarding over the right hypochondrium just beyond the mid line. Tenderness was also most marked in this area but was present in other parts as well: no rebound tenderness. No free fluid percussible and no abnormal masses felt.

Urine Examination: Neutral in reaction, a specific gravity of 1020, and deficient in chlorides.

Operation: By Mr A. Kay on the 4th day of illness. Free blood stained fluid in abdominal cavity and multiple areas of fat necrosis. The pancreas hidden by matted smaller omentum. The lesser sac was opened and was found to contain free fluid. A gauze drain inserted. Gall-bladder, although it appeared normal, was opened and drained; no stones found therein.

CASE No. 21.

CLINICAL DIAGNOSIS - Acute Pancreatitis
OPERATIVE FINDINGS - Negative
RESULT - Well

Clinical History: Mrs J.W., aged 52 years, was admitted to the Royal Infirmary, Glasgow, in November 1942. Her trouble dated from June 1942, when she had an emergency cholecystectomy performed in Dumfries Infirmary. An acute cholecystitis without stone was found. The pancreas was not examined. She had been confined to bed since her dismissal in August 1942 with general debility and loss of appetite.

When she was making her first attempt to rise out of bed there developed a "terrific" pain just to the right of the mid-epigastrium, spreading later across the upper abdomen to the left lower chest and posteriorly to the lumbar region. It lasted ten hours, attended by severe vomiting. Her symptoms recurred two days later and again passed off. When seen on the 5th day she complained of a dull ache in the left hypochondrium and lumbar region. She retched occasionally.

On Examination: The patient was restless and felt very thirsty. Her temperature fluctuated between 98.6° F. and 102.8° F.; her pulse rate between 105 and 110 beats per minute in the first few days. Both observations were normal thereafter. Blood pressure = 130/65 mm. Hg. Her lips were cyanosed and she presented a mild degree of generalised jaundice.

Her abdominal movements were slightly restricted owing to the aggravation of the left hypochondriac pain with deep breathing. A degree of meteorism was noted. She was tender in the supraumbilical zone, particularly at the left hypochondrium, where a deep mass of indefinite outline was palpable. The abdominal wall was moderately rigid in its upper half.

Leucocyte Count = (a) 24,800 per cu. mm. (on admission, 9.11.42)
(b) 5,000 per cu. mm. (17.11.42).
Loewi Mydriatic Test - Negative.
Urine contained bile.
Urinary Diastase = 100 units (Wohlgemuth)
Blood Diastase = 255 units per ml. serum (Somogyi) on 6th day.

Progress Notes: The patient's condition varied almost from day to day. About the 9th day the presence of a mass (? false cyst of pancreas) was verified

beyond doubt in the left upper quadrant. During the fourth week of December another bout of acute pain, accompanied by jaundice, came on, but by the beginning of the year she was considerably improved and free of jaundice. The abdominal swelling had resolved completely.

Barium Investigation was carried out by Dr J.Harper on 24.11.42, who reported that the stomach and duodenum were functioning normally and not deformed. The splenic flexure, however, was pushed downwards and to the left.

Sugar Tolerance Tests carried out by Dr A. B. Anderson on 22.12.42 showed:-

Fasting sugar level	=	111 mg.	%
½ hour specimen	=	143 "	"
1 " "	=	167 "	"
1½ " "	=	176 "	"
2 " "	=	178 "	"

Operation performed by Mr George Stevenson 8 weeks after the patient's admission failed to reveal any abnormalities except adhesions near the site of the cholecystectomy. The pancreas felt normal. The common bile duct contained no stones and was not dilated.

Post-Operative Course was rather protracted but the patient ultimately made a satisfactory recovery.

CASE No. 22.

CLINICAL DIAGNOSIS - ? Acute Pancreatitis: Diabetes Mellitus

RESULT - Unsatisfactory

Clinical History: Mrs J.W., aged 56, was admitted to the Western Infirmary in November 1942 with abdominal pain and sickness of four days' duration. The pain developed in the mid abdomen soon after a meal, and was referred to the left flank. The pain and sickness persisted for three days, during which time she had a constant thirst and was completely lacking in appetite. By the fourth day she had a dull belly ache.

The patient did not give a lucid account of her previous history. She denied having been abnormally thirsty at any time, though she thought she passed urine rather often. This was her first acute illness.

On Examination: The patient was very stout. When first examined, she was semi-conscious and restless. The breath emitted a smell of acetone. The temperature was 98.8° F., and the pulse rate 98 per minute. She was cyanosed about the lips.

She was too fat for any meteorism to be detected. She was tender on both sides of the abdomen, particularly in the left flank. Rigidity was not present.

Urine had a specific gravity of 1040 and contained diacetic acid, acetone and sugar (at 1 drop).

Blood Diastase = 430 units per ml. serum (Somogyi).

Progress Note: The patient was treated as a case of diabetes mellitus.

RE-ADMITTED in January 1943 in a diabetic coma. The details of treatment were as follows:-

30.1.43	12 noon	Blood Sugar = 740 mg.%	40 units Insulin		
	6 p.m.	" " = 872 mg.%	100	"	"
	11 p.m.	" " = 540 mg.%	20	"	"
31.1.43	11 a.m.	" " = 185 mg.%			

Patient survived but proved a refractory type of diabetes to treat.

CASE No. 23.

CLINICAL DIAGNOSIS - Acute Pancreatitis
OPERATIVE FINDINGS - Interstitial Pancreatitis
RESULT - Well

Clinical History: Mrs M.L., aged 49, was admitted to Killearn Emergency Hospital in June 1943 with abdominal pain and sickness of six hours' duration. On the preceding evening she had felt mildly sick, with pains in her abdomen and back. She passed a reasonably quiet night and was given a light breakfast of tea, toast and poached egg about 8.30 a.m. There followed in about 1½ hours' time a dull pain in the upper abdomen which soon assumed agonizing proportions. It was most severe just above the umbilicus and radiated to other parts of the abdomen and to the lumbar region. While the pain lasted it

was of unremitting severity and paroxysmal in character. She was also very sick and retched a lot.

Previous History: During the previous six weeks the patient had not been in the best of health. Her indisposition began, while at lunch one day, with a violent spasm of epigastric pain attended by sickness. In the succeeding four weeks these episodes were frequent and were usually induced by eating food. Each time the pain came on it was always referred to the back. She consumed a considerable amount of alkali powders without the desired effect, and in time they too caused her to vomit. She admitted to feeling very hungry on occasions but abstained from eating much for fear of incurring further sickness. She attended the Western Infirmary Out-Patient Department and was diagnosed as a case of appendiceal colic. There followed two weeks of good health.

About four years previously the patient received medical attention for glossitis and "bilious" turns.

On Examination: The patient was in a collapsed state, with cold extremities, poor circulation, and a blood pressure of 110/70 mg. Hg. Her face presented a peculiar melange of lividity and jaundice. She preferred to lie on her side but could not find effective relief in any one position. Pulse rate was 92 per minute; temperature 100° F.

The abdominal outline was normal though its movements were decidedly restricted. Moderately severe tenderness was present in the midline just above the umbilicus, and some tenderness was elicited in other parts with the exception of the right hypochondrium. Some rigidity was also noted. Both renal angles were tender on pressure. The presence of free fluid was confirmed.

Her heart sounds were faintly audible and almost tic-tac in rhythm.

Leucocyte Count = 5,200 per cu. mm.
Erythrocytic Sedimentation Rate = 16 mm. in 1st hr.
Loewi Mydriatic Test - Negative.
Urine was acid, of 1022 specific gravity, and contained albumen.
Test for bile was not done.
Blood Diastase = 5,300 units per ml. serum (Somogyi)
Blood Lipase = 9.8 ml. N/20 NaOH per ml. serum.
(serum was tinted with bile)

Progress Notes: Symptoms subsided and jaundice cleared in about four days' time.

Barium Investigation carried out by Dr D. Stenhouse:- Stomach and duodenum normal.

Cholecystography showed faulty function of gall-bladder.

Blood Sugar Curve performed on 12th day (Folin Wu):

Fasting Sugar Level	=	100 mg. %
½ hour specimen	=	80 " "
1 " "	=	100 " "
1½ " "	=	90 " "
2 " "	=	90 " "

Operation performed by H. Wapshaw on the 21st day: The pancreas was slightly enlarged and nodular with no superficial signs of haemorrhage or necrosis. There were no spots of fat necrosis anywhere. The gall-bladder was slightly thick-walled and infiltrated with some fat. It contained one pigmented stone 1 cm. in its greatest diameter. The bile was rather glairy in appearance. Stomach and duodenum were normal.

The common bile duct felt normal and was left intact. Cholecystectomy performed and a piece of tissue taken from the body of the pancreas.

Post-Operative Course was uneventful.

Histology of Pancreas: The tissue shows some fatty infiltration and slight increase of interlobular fibrous tissue with round cell infiltration. Here and there masses of acini have undergone necrosis and disintegration. At other places considerable dilatation of small intra-acinar spaces can be seen. The islets are well represented and a few are larger than normal.

Bacteriology of Bile: A heavy growth of Gram negative coliform bacilli.

CASE No. 24)
) For essential data, see text
) (Table 7, pages 43 and 41.
CASE No. 25)

CASE No. 26.

CLINICAL DIAGNOSIS - Acute Pancreatitis (Provisional)
AUTOPSY FINDINGS - Acute haemorrhagic Necrosis confined to head of Pancreas.

Clinical History: Mrs A.B., aged 40, was admitted to Stracathro E.M.S. Hospital in August 1944 while in a state of marked prostration. She was suffering from acute pain in the upper abdomen which had come on with dramatic suddenness two days previously. It had the effect of doubling her up and was so extreme as to lead to collapse. She was quite lucid on admission but in such a poor state that a proper detailed story could not be elicited. Apparently the pain, which was of a "steady" nature, was localised to the epigastric and umbilical regions. Since the onset of illness she had vomited five or six times, the material being of a brownish colour.

There were no other relevant points to the history of the case.

On Examination: She was noted to be grossly fat and mentally alert or seemingly so. The extremities were blue and cold. She perspired profusely. No jaundice visible. She preferred to lie curled up on her side. Temperature 98° F.; pulse rate 96 per minute (feeble); respirations 26 per minute. Only the systolic blood pressure could be recorded: it was 80 mm. Hg.

The abdominal wall was very obese and showed a pattern of distended venules; it moved slightly on respiration. There was tenderness in the upper abdomen, particularly in mid-epigastrium, but no rebound tenderness. A fixed dulness was present in the right flank.

Conservative Treatment instituted. The sedative chosen was morphia gr. $\frac{1}{4}$ and atropine gr. 1/100, but the effect was unsatisfactory. One pint of plasma

and one pint of saline were administered intravenously, but the patient gradually became unconscious and died 7 hours after admission.

Autopsy: Several pints of dark brown fluid were found lying free in the peritoneal cavity. The great omentum and other fat-laden areas were studded with spots of fat necrosis. The lesion was found to be acute haemorrhagic pancreatic necrosis affecting the head of the gland. The body and caudal parts were shown to be free of disease both to naked eye inspection and on histological examination.

The ampulla of Vater was occupied by a small gall-stone about 0.5 cm. in greatest diameter. The anatomy of the region and its probable bearing on the etiology of the case ~~has already been discussed in the text (see page 81)~~. is communicated in diagram below.

The gall-bladder wall was apparently normal. It contained clear bile and numerous small cholesterol stones.

Liver: A moderate degree of fatty infiltration was apparent to naked eye inspection. Histologically the liver cells showed advanced fatty changes but no evidence of necrosis. There was a moderate degree of round-cell infiltration of the portal tracts.

(Indebtedness is owed to Professor J. S. Young of Aberdeen for carrying out the histology of this case.)

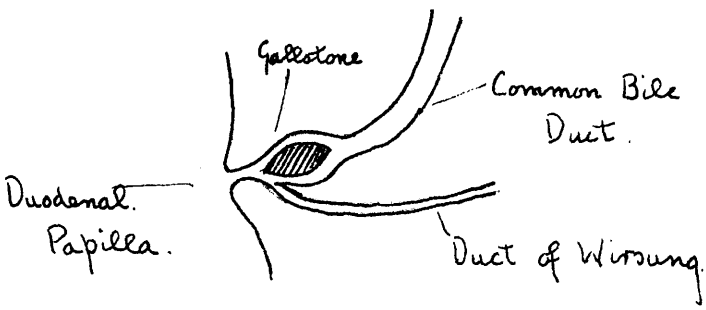


Diagram of Case No. 26: Showing the location of the gallstone and the configuration of the ducts at the ampulla of Vater. Note that the pancreatic duct enters the distal end of the ampulla. Consequently the stone would require to be driven hard against, or into the papilla before the two ducts came into direct communication.

METHOD OF ESTIMATING THE DIASTATIC ACTIVITY OF BLOOD SERUM.

The following extracts taken from Somogyi's paper (1938) on the "Micro-Methods for the Estimation of Diastase" describe his method of preparing the starch substrate and the detailed steps of the iodometric test to which preference was given.

"Purification of Starch. We employ pure rice starch. The starch is washed as follows: 100 gm. of starch are suspended and frequently agitated for about an hour in 1 liter of approximately 0.01 N HCl. After sedimentation the acid is poured off and the starch is stirred up in 1 liter of approx. 0.05 per cent. NaCl solution. After sedimentation and decantation washing with salt solution is repeated once more; then the starch is spread out and allowed to dry in air."

"Preparation of Starch Solution. This reagent contains 75 mg. of starch and 250 mg. of NaCl per 100 c.c. of solution. It is prepared of the same washed corn-starch as is used in the copper reduction method. In preparing a paste as the first step, 15 to 20 gm. of the starch are rubbed up in a mortar with 100 c.c. of water and the suspension is poured with vigorous agitation into 900 c.c. of boiling water. After this has boiled for about 1 min. under continuous stirring, 10 c.c. of 25 per cent. NaCl sol. are added and the flask is immersed for 30 min. in a boiling water bath, the mouth of the flask being covered with an inverted beaker. After standing (covered with the beaker to keep the solution sterile) at room temp. for a day (or longer if necessary), the greater part of the starch separates out, forming a sediment. The limpid supernatant fluid is removed by syphoning or, in order to obtain a better yield, by centrifugation. The dilute starch paste is the stock solution which, properly diluted with 0.25% NaCl sol., furnishes the substrate." (The reagent must be kept sterile.)

"Iodine Solution. This is a 0.002 N aqueous iodine solution containing 2% KI. It is prepared by dilution of 10 c.c. of a 0.1 N aqueous iodine sol. to 500 c.c. with a 2% KI sol."

"Analytical Procedure. Into a test-tube of 14 to 16 mm. diam., 4 c.c. of the starch sol. (which contains 3.0 mg. of starch) are introduced, and the tube is immersed in the constant temp. (40°C.) water bath. A few mins. later, when the reagent has assumed the standard temp., 1 c.c. of the blood plasma (serum) under examination is added, and simultaneously a stop-watch is started. The mixing of the plasma and starch is expedited by blowing the plasma from a 1 c.c. pipette ("to contain") into the reagent and rinsing the pipette once with the mixture.

While the reaction mixture is being incubated, 0.5 c.c. portions of the iodine solution are measured into test-tubes. These test-tubes are of about 7 mm. inside diameter and should be fairly uniform. After about 5-6 mins. of incubation a 0.5 c.c. portion of the reaction mixture is withdrawn with a pipette and added to one of the iodine tubes for observation of the reaction. The test-tube is viewed in transmitted light, coming from a standard source. This consists of a 100 Watt frosted elec. light bulb covered by a cardboard screen with a slit in the front. At subsequent time intervals further 0.5 c.c. samples are withdrawn from the reaction mixture for color tests with iodine, until the red-brown color of erythrodextrin is seen with barely a perceptible tint of purple. At this point, the end-point, the duration of the reaction is registered on the stop-watch." (On the event of a very high enzyme content, the serum was diluted with 0.5% NaCl solution.)

"Calculation of Results: From the equation $D = K \times 1/(t \times v)$, the diastatic activity can be obtained once K, the constant factor, has been experimentally determined. As stated before, under the standard conditions described, K = 1600. Thus, for example, when 12 mins. are required for 1 c.c. of plasma to digest 3 mg. of starch to the selected end-point of the reaction, D = 1600/12 = 133; or, when the reaction time for 1 c.c. of a 1:4 dilution of plasma (actually 0.25 c.c. of plasma) is 13 mins., D = 1600/(13 x 0.25) = 492. In case 1.5 mg. of starch are employed for the assay of very low diastatic activity, K = 800, provided that the reaction time does not exceed 30 mins.

The values obtained in this manner are in close agreement with those obtained by the copper reduction method. There is no need, therefore, to introduce any specific "diastase unit" to express diastatic activity as determined on the basis of the amyloclastic activity of the enzyme."

METHOD OF ESTIMATING THE LIPOLYTIC ACTIVITY OF BLOOD SERUM.

The method was the modification of the Loewenhardt method suggested by Cherry & Crandall (1932) and further modified by Johnson & Bockus (1940). The last named authors' method differs in respect of the buffer solution employed. Their mode of preparation is as follows:-

Preparation of Buffer Solution: Mix 10.00 c.c. of a one-third molar solution of disodium hydrogen phosphate (Na_2HPO_4) and 3 c.c. of a one-third molar solution of potassium dihydrogen phosphate (KH_2PO_4).

Preparation of Olive Oil Substrate: The emulsion was made up of olive oil 50%, acacia 5%, sodium benzoate 0.5% as preservative made up in water. With such a small amount of emulsifying agent, it was necessary to homogenize the mixture very thoroughly. The following was the technique adopted.

i. Make a primary emulsion in mortar consisting of acacia 3 drs., water 6 drs., and olive oil 12 drs.

ii. Mix the primary emulsion with the remainder of the oil and mix this thoroughly, using a glass 2 oz. syringe. This makes a fairly crude emulsion. It is not a necessary step but useful.

iii. Place the mixture in a creamer and pass through three or four times until a good emulsion is formed. Have the lower nozzle loose at first, thus giving a wider aperture, and then gradually tighten nozzle after each passage through the creamer.

iv. Finally add the sodium benzoate dissolved in some water and make up to desired volume.

Procedure:

1. Place 3 c.c. of distilled water in each of three boiling tubes marked A, B and C. A is the control tube, B and C are duplicates.

2. Add to each 1 c.c. of serum to be tested.

3. Put A in a water bath at 100° C. for 5 minutes in order to inactivate the contained lipase. Cool before proceeding to next step.
4. Add 0.5 c.c. buffer solution to each tube.
5. Place 2 c.c. of the olive oil emulsion to each tube and shake thoroughly.
6. Incubate the three of them for 24 hours at 37.5° C.
7. Thereafter add 3 c.c. of 95% alcohol and 2 drops of a 1% solution of phenolphthalein in 95% alcohol and shake the specimens thoroughly to break up the emulsion.
8. Titrate each to a faint pink colour with a twentieth normal solution of NaOH.
9. The titration figure of A is substracted from those of the two specimens B and C respectively, and the result expressed in terms of c.c. N/20 NaOH.

APPENDED TABLE No. I.

SERUM ENZYME VALUES IN "NORMAL" PATIENTS.

No.	Sex	Age in Years	Condition	Serum Enzymes		
				Diastase	Lipase	
				Somogyi Units/ml. (Normal 40-228)	Titration figure (in ml. of N/20 NaOH per 1 ml. serum)	Final Result (Normal 0-1.6)
1.	Male	50	Epigastric hernia	150		
2.	Male	35	Fracture forearm	133		
3.	Male	46	Renal colic	133	Blank = 1.60 1st reading = 2.35	0.75
4.	Male	38	Head injury	160	Blank = 1.81 1st reading = 2.28 2nd reading = 2.29	0.47
5.	Male	20	Acute appendicitis (convalescent)	123	Blank = 1.67 1st reading = 1.97 2nd reading = 2.09	0.36
6.	Male	47	Acute appendicitis (convalescent)	160	Blank = 1.85 1st reading = 2.79 2nd reading = 2.82	0.95
7.	Male	21	Head injury	110	Blank = 1.98 1st reading = 2.12 2nd reading = 2.19	0.12
8.	Male	21	Foot injury	88	Blank = 1.84 1st reading = 2.27 2nd reading = 2.32	0.46
9.	Male	21	Appendicectomy	228	Blank = 1.89 1st reading = 2.38 2nd reading = 2.35	0.47
10.	Male	45	Fracture patella	80	Blank = 1.74 1st reading = 2.31 2nd reading = 2.49	0.66
11.	Male	38	Actinomycotic peri-nephric abscess	56	Blank = 1.85 1st reading = 2.12 2nd reading = 2.19	0.30
12.	Male	19	Cut tendon and nerve at wrist	88	Blank = 2.01 1st reading = 2.68 2nd reading = 2.69	0.67
13.	Female	22	Acute appendicitis	61	Blank = 2.25 1st reading = 2.46	0.21
14.	Female	74	Fractured skull	80	Blank = 2.1 1st reading = 2.21 2nd reading = 2.53	0.27
15.	Female	68	Cancer of breast	114	Blank = 2.11 1st reading = 2.42 2nd reading = 2.35	0.27
16.	Male	33	Epigastric hernia	100		

APPENDED TABLE No. I (Contd.)

SERUM ENZYME VALUES IN "NORMAL" PATIENTS (Contd.)

No.	Sex	Age in Years	Condition	Serum Enzymes		
				Diastase	Lipase	
				Somogyi Units/ml. (Normal 40-228)	Titration figure (in ml. of N/20 NaOH per 1 ml. serum)	Final Result (Normal 0-1.6)
17.	Male	42	Hydrocele	61		
18.	Male	38	Inguinal hernia	80		
19.	Male	14	Appendicitis (drained)	80		
20.	Male	70	Fracture, head of femur	80		
21.	Male	40	Hernia	200	Blank = 2.51 1st reading = 2.69 2nd reading = 2.69	0.18
22.	Female	29	Acute appendicitis	73	Blank = 3.0 1st reading = 3.41 2nd reading = 2.48	0.44
23.	Male	29	Fractured pelvis	114	Blank = 2.06 1st reading = 2.205 2nd reading = 2.29	0.18
24.	Female	45	Thyroid adenoma	80	Blank = 2.38 1st reading = 3.115 2nd reading = 2.535	0.44
25.	Female	26	Hernia	100	Blank = 3.099 1st reading = 3.215 2nd reading = 3.22	0.12
26.	Male	36	Chronic empyema	160	Blank = 2.51 1st reading = 2.545 2nd reading = 2.54	0.03
27.	Male	69	Burn of fingers	100	Blank = 2.49 1st reading = 2.76 2nd reading = 2.85	0.31
28.	Male	39	Spinal fracture	53	Blank = 3.145 1st reading = 3.195 2nd reading = 3.175	0.04
29.	Female	51	Appendix abscess	123	Blank = 2.69 1st reading = 3.51 2nd reading = 3.17	0.55
30.	Male	57	Renal colic	123	Blank = 2.91 1st reading = 3.01 2nd reading = 3.17	0.18
31.	Female	20	Salpingitis	228	Blank = 2.69 1st reading = 3.17 2nd reading = 3.29	0.54
32.	Male	25	Fracture of humerus		Blank = 2.2 1st reading = 1.7 2nd reading = 1.6	Zero

APPENDED TABLE No. I (Contd.)

SERUM ENZYME VALUES IN "NORMAL" PATIENTS (Contd.)

No.	Sex	Age in Years	Condition	Serum Enzymes		
				Diastase	Lipase	
				Somogyi Units/ml. (Normal 40-228)	Titration figure (in ml. of N/20 NaOH per 1 ml. serum)	Final Result (Normal 0-1.6)
33.	Male	32	Addison's disease		Blank = 1.7 1st reading = 2.3 2nd reading = 2.1	0.50
34.	Male	35	Hernia	50	Blank = 1.57 1st reading = 1.71 2nd reading = 1.63	0.10
35.	Male	32	Renal colic	88		Zero
36.	Male	35	Appendicitis	70	Blank = 1.91 1st reading = 2.12	0.21
37.	Male	30	Fracture of leg	80	Blank = 2.79 1st reading = 2.80	0.01
38.	Male	18	Appendicitis	100	Blank = 2.57 1st reading = 3.035 2nd reading = 3.275	0.58
39.	Male	56	Epididymitis		Blank = 2.97 1st reading = 3.22 2nd reading = 3.19	0.23
40.	Male	60	Fractured ribs		Blank = 2.47 1st reading = 2.65 2nd reading = 2.56	0.13
41.	Male	17	Appendicitis	100		0.32
42.	Male	42	Fractured femur	228		0.67
43.	Male	34	Cut tendons	190		0.73
44.	Male	30	Burn of foot	177		0.03
45.	Male	29	Hernia	160		Zero
46.	Male	55	Hernia	133		0.50
47.	Male	40	Hernia	85		0.18
48.	Male	59	Hernia	114		0.33
49.	Male	26	Fracture of humerus	100		0.22
50.	Male	30	Hernia	88		0.11
51.	Male	61	Fracture of tibia	48		0.01
52.	Male	30	Fracture of humerus	100		0.31

APPENDED TABLE No. I (Contd.)

SERUM ENZYME VALUES IN "NORMAL" PATIENTS (Contd.)

No.	Sex	Age in Years	Condition	Serum Enzymes		
				Diastase	Lipase	
				Somogyi Units/ml. (Normal 40-228)	Titration figure (in ml. of N/20 NaOH per 1 ml. serum)	Final Result (Normal 0-1.6)
53.	Male	33	Circumcision	64		0.34
54.	Female	20	Appendicectomy	100		0.58
55.	Male	32	Ulcer of leg	70		0.27
56.	Male	24	Deflected nasal septum	47		0.06
57.	Male	30	Fracture of humerus	100		0.26
58.	Male	30	Fracture of tibia	123		-
59.	Male	35	Fracture of tibia	133		-
60.	Male	26	Deflected nasal septum	76		-
61.	Male	36	Chronic bronchitis	168		1.08
62.	Male	35	Lateral sclerosis of cord	66		0.64
63.	Male	30	Fracture os calcis	100		0.85
64.	Male	39	Scalp wound: dislocated elbow	60		0.75
65.	Male	54	Hernia, inguinal	80		0.39
66.	Male	64	Hernia, inguinal	133		0.73
67.	Male	32	Pilonidal sinus	53		0.31
68.	Male	32	Hernia, ventral	84		1.60
69.	Male	34	Chronic sepsis in abdominal wound	123		0.45
70.	Male	35	Bursitis of elbow	100		1.21
71.	Male	26	Axillary adenitis	88		0.52
72.	Male	37	Nervous dyspepsia	69		0.56
73.	Male	19	Ulcer of leg	80		0.74
74.	Male	30	Hernia	114		
75.	Male	31	Appendicectomy	40		0.70
76.	Male	18	Hernia, inguinal	55		1.20

APPENDED TABLE No. I (Contd.)

SERUM ENZYME VALUES IN "NORMAL" PATIENTS (Contd.)

No.	Sex	Age in Years	Condition	Serum Enzymes		
				Diastase	Lipase	
				Somogyi Units/ml. (Normal 40-228)	Titration figure (in ml. of N/20 NaOH per 1 ml. serum)	Final Result (Normal 0-1.6)
77.	Male	60	Hernia, inguinal	160		0.94
78.	Female	77	Prolapse of rectum	59		0.55
79.	Female	23	Appendicectomy	55		0.80
80.	Female	24	Burn of leg	73		0.89
81.	Female	22	T.B. Ulcer of leg	50		1.07
82.	Female	28	Herniorrhaphy	84		0.54
83.	Female	39	Hernia	46		Zero
84.	Female	17	Abscess, Chest wall	55	Blank = 1.98 1st reading = 1.64 2nd reading = 1.63	Zero
85.	Male	43	Appendicectomy	66	Blank = 1.8 1st reading = 1.44 2nd reading = 1.62	Zero
86.	Male	48	Herniorrhaphy	80	Blank = 1.50 1st reading = 3.00 2nd reading = 2.60	1.30
87.	Male	28	Herniorrhaphy	46	Blank = 1.82 1st reading = 2.47 2nd reading = 2.50	0.66

APPENDED TABLE No. II.

SHOWING THE ENZYME FINDINGS IN THE BLOOD AND PERITONEAL FLUID in 4 Cases of Acute Pancreatitis.

Case	Duration of Illness at time of observation.	Blood		Peritoneal Effusion	
		Diastase Somogyi Units/ml. (40-228)	Lipase ml. N/20 NaOH/ml. (0-1.6)	Diastase Somogyi Units/ml.	Lipase ml. N/20 NaOH/ml.
Case 11 Acute Haem. Necrosis. Operation Case	1st day	4,000	5.3	1,600	4.40
Case 16 Acute Haem. Necrosis. Operation Case	15 days	57	0.30	2,285	7.35
Case 19 Acute Haem. Necrosis. Operation Case	4 days	110	0.21	320	2.92
Case 17 False Pancreatic Cyst. Fluid obtained by Paracentesis	2 months	284	1.92	16,000	14.70

APPENDED TABLE No. III.

FINDINGS IN 32 CASES OF PERFORATED PEPTIC ULCER
arranged according to duration of illness prior to operation.

Type	Duration of illness before Operation	Time of previous meal	Serum Enzymes		Peritoneal Fluid Enzymes	
			Diastase (Somogyi Units/ml.)	Lipase ml. N/20 NaOH/ml.	Diastase (Somogyi Units/ml.)	Lipase ml. N/20 NaOH/ml.
Case 29 - Male Anterior wall of stomach	2½ hours	-	160	-	Not available	
Case 5 - Male Anterior wall 1st part duodenum	2½ hours	5 hours	46	0.04	94	0.49
Case 2 - Male Anterior wall 1st part duodenum	3 hours	-	177	0.33	Not available	
Case 28 - Male Anterior wall of pylorus; 2nd perforation	3 hours	-	145	-	Not available	
Case 12 - Male * Anterior wall 1st part duodenum	4 hours	7 hours	- 266 (24 hrs. later)	0.13 1.02	2,400	12.33
Case 9 - Male Anterior wall 1st part duodenum	4 hours	2 hours	145 190 (24 hrs. later)	0.22 0.99	Zero	0.11
Case 26 male Pyloric ring	4 hours	4½ hours	-	0.6 0.8		6.4
Case 15 - Male Anterior wall 1st part duodenum	4 hours	¼ hour	53	0.07	200	9.05
Case 7 - Male Anterior wall 1st part duodenum	4½ hours	during meal	184 84 (24 hrs. later)	0.42 0.42	6,400	11.41
Case 16 - Male Anterior wall of stomach	5 hours	4 hours	133	0.7	3,200	9.19
Case 21 - Male Anterior wall 1st part duodenum	5 hours	3 hours	76	0.33	400	10.2
Case 4 - Male Anterior wall 1st part duodenum	6 hours	6 hours	65	0.14	Not available	
Case 10 - Male Anterior wall 1st part duodenum	6 hours	6 hours	84 56 (24 hrs. later)	0.01 0.1	Not available	
Case 18 - Male Anterior wall 1st part duodenum	7 hours	4 hours	88 84 (24 hrs. later)	0.13 0.22	710	7.52
Case 17 - Male Anterior wall 1st part duodenum	7 hours	2 hours	66 80 (24 hrs. later)	0.67 0.52	800	4.97
Case 14 - Male * Anterior wall 1st part duodenum	7 hours	5 hours	355 355	1.69 0.07	32,000	14.30

* = Cases with abnormal enzyme readings.

APPENDED TABLE No. III. (Contd.)

FINDINGS IN 32 CASES OF PERFORATED PEPTIC ULCER
arranged according to duration of illness prior to operation.

Type	Duration of illness before Operation	Time of previous meal	Serum Enzymes		Peritoneal Fluid Enzymes	
			Diastase (Somogyi Units/ml.)	Lipase ml. N/20 NaOH/ml.	Diastase (Somogyi Units/ml.)	Lipase ml. N/20 NaOH/ml.
Case 31 - Female Subhepatic abscess overlying leaking anterior duodenal perforation	10 days	-	73	0.44		
Case 32 - Female Subhepatic abscess resulting from leaking duodenal ulcer. Adhesions obscured duodenum and gall-bladder	18 days	-	106	0.27		

BIBLIOGRAPHY.

Abell, I.: (1938) Surg. Gynec. & Obstet., 66, 348.

American Gastroenterological Association Report, (1934). See Lewison, E. F. (1941)

Anrep, G. V., Lush, J. L., Palmer, M. G.: (1924) Journ. Physiol., 59, 434.

Arthus, M.: (1902) Compt. rend. soc. de Biol., 54, 381.

Bailey, H. and Love, R. J.: (1943) Textbook of Surgery. 6th Ed., London, H. K. Lewis & Co. Ltd.

Baxter, H., Baxter, S. G., and McIntosh, J. F.: (1938) Amer. Journ. Digest. Dis., 5, 423.

Bernard, C.: (1856) Mémoire sur le pancreas et sur le rôle du sac pancreatique dans les phénomènes digestifs. Paris. J. B. Baillière, page 97.

Bernhard, F.: (1933) Klin. Woch., 1, 221.

Carlson, A. J. and Luckhardt, A. B.: (1908) Amer. J. Physiol., 23, 148.

Casberg, M. A.: (1939) Arch. Surg., 39, 247.

Cherry, I. S. and Crandall, L. A.: (1932) Amer. J. Physiol., 100, 266.

Clasen, A. C., Johnstone, P. N., & Orr, T. G. (1933) J. Lab. & Clin. Med. 18, 457.

Cohen, I.: (1925) Brit. J. exp. Path., 6, 173.

Cole, W. H.: (1938) Surg. Gyn. & Obstet., 67, 31.

Cole, W. H. and Elman, R.: (1939) Textbook of General Surgery, 2nd Ed. D. Appleton-Century Coy. Inc. New York, London.

Comfort, M. W.: (1936) Amer. J. Digest. Dis. and Nutrition, 3, 815.

Comfort, M. W.: (1939) Surg. Clin. N. America, 19, 899.

Comfort, M. W. and Osterberg, A.: (1934) J. Lab. & Clin. Med., 20, 271.

Comfort, M. W. and Osterberg, A.: (1940) Med. Clin. N. America, No. 4, 1137.

Comfort, M. W., Parker, R. L. and Osterberg, A.: (1939) Amer. J. Digest. Dis., 6, 249.

Cope, O., Hagstrômer, A. and Blatt, H.: (1938) Amer. J. Physiol., 122, 428.

Corbett, D.: (1912) Quart. J. Med., 6, 351.

Crandall, L. A.: (1935) Amer. J. digest. Dis. & Nutr., 2, 230.

Davis, L. H. and Ross, E. L.: (1921) Amer. J. Physiol., 56, 22.

Douglas, J.: (1935) Amer. J. digest. Dis. & Nutr., 1, 871.

Doyen, M. and Morel, A.: (1902) Compt. rend. de soc. Biol., 54, 614.

Dozzi, D. L.: (1941) Arch. int. Med., 68, 232.

Egdahl, A.: (1907) Bull. Johns Hopkins Hosp., 18, 130.

Elman, R.: (1937) Amer. J. digest. Dis., 4, 732.

Elman, R.: (1937) Ann. Surg., 105, 379.

Elman, R.: (1942) J. Amer. med. Ass., 118, 1265.

Elman, R., Arneson, N. and Graham, E. A.: (1929) Arch. Surg. 19, 943.

Elman, R. and McCaughan, J. M.: (1927) Arch. Int. Med. 40, 58.

Finney, J. M. T.: (1933) Ann. Surg. 98, 750.

Fitz, R. H.: (1889) Med. Rec. 35, 197.

Foged, J.: (1935) Amer. J. Surg. 27, 439.

Foster, M.: (1867) Jour. Anat. & Physiol. 1, 107.

Garrod, A. E.: (1920) Lancet, 1, 749.

Gould, L. K. and Carlson, A. J.: (1911) Amer. J. Physiol. 29, 165.

Grey, S. Hand Somogyi, M.: (1937) Proc. Soc. exp. Biol. & Med. 36, 253.

Halsted, W. S.: (1901) Bull. Johns Hopkins Hosp. 12, 179.

Henderson, F. F. and King, E. S. A.: (1935) Arch. Surg. 30, 1049.

Hughes, E. B.: (1942) Proc. Roy. soc. Med. 35, 339.

Illingworth, C. F. W., Scott, L. D. M. and Jamieson, R. A.: (1944) Brit. Med. Jour. 2, 617 and 655.

Iraneus, C. Jr.: (1941) Arch. Surg. 42, 126.

Johnson, T. A. and Bockus: (1940) Arch. int. Med. 66, 62.

Karsner, H. T., Koeckert, H. L. and Wohl, S. A.: (1921) J. exp. Med. 34, 349.

Kemp, R. C.: (1917) Diseases of Stomach, Intestines and Pancreas. W. B. Saunders & Co., Philadelphia.

King, C. E.: (1914) Amer. J. Physiol. 35, 301.

Körte, W.: (1911) Arch. f. klin. Chir. 96, 557.

Lewis, D. S. and Mason, E. H.: (1920) J. biol. Chem. 44, 455.

Lewison, E. F.: (1940) Arch. Surg. 41, 1008.

Lewison, E. F.: (1941) Surg. Gynec. & Obstet. 72, 202.

Love, R.J. (1926) Lancet, 2, 1262.

Magendie, M.: (1846) Gazette medicale de Paris, 1, 3. E series.

Marslow, H. L. and Davidson, W.C.: (1926) J. biol. Chem. 68, 75.

Mayo Robson and Cammidge: (1907) The Pancreas; its Surgery and Pathology. W. B. Saunders & Co., Philadelphia.

Meklar, A.: (1941) Gastro-enterologia. 66, 12.

Mikkelsen, O.: (1934) Acta Chir. Scand. 75, 373.

Millbourn, E.: (1936) Acta Chir. Scand. 77, 523.

Morley, J., Yates, H. B. and Ogilvie, W. H.: (1939) Proc. Roy. Soc. Med. 32, 670.

Morton, J. I. and Widger, S.: (1940) Ann. Surg. iii, 851.

Moynihan, B.: (1925) Ann. Surg. 81,132.

Myers, V. C. and Killian, J. A.: (1917) J. biol. Chem. 29, 179.

Myers, V. C. and Reid, E.: (1933) J. biol. Chem. 99, 595.

McCaughan, J. M.: (1934) Surg. Gynec. & Obstet. 59, 598.

McWhorter, G. L.: (1932) Arch. Surg. 25, 958.

Nicoll, J. H.: (1919) Brit. Med. Jour. 2, 1919.

Nørby, G.: (1932) Hospitalstid. 75, 1281.

Nordmann, O.: (1938) Arch. f. klin. Chir. 193, 370.

Oelgetz, A. W., Oelgetz, P. A. and Wittekind, J.: (1935) Amer. J. digest. Dis. & Nutrition 2, 422.

Ogilvie, W. H.: (1939) see Morley.

Opie, E.: (1901) Johns Hopkins Bull. 12, 182.

Payen and Persoz: (1833) Ann. de chim. et phys. 3, 73.

Probstein, J. G., Wheeler, P. A. and Gray, S. H.: (1939) J. lab. & clin. Med. 24, 449.

Rachmilewitz, M.: (1938) Amer. J. digest. Dis. 5, 185.

Reid, C.: (1925) Brit. J. exp. Path. 6,314.

Rich, A. R., and Duff, G. L.: (1934) Proc. soc. exper. Biol. & Med. 31, 470.

Rich, A. R., and Duff, G. L.: (1936) Bull. Johns Hopkins Hosp. 58, 286.

Rowantree, L. G., Marshall, E. K., and Baltzer: (1915) Arch. int. Med. 15, 543.

Rowlands, R. P. and Turner, P. THe Operations of Surgery. page 534, 8th Ed., vol.11. London. J.& A.Churchill,Ltd. (1937).

Schmieden, V., and Sebenung, W.: (1928) Surg. Gynec. & Obstet. 46, 735.

Smead, L. F.: (1936) Amer. J. Surg. 32, 487.

Somogyi, M.: (1934) Proc. soc. exp. Biol. & Med. 32, 538.

Somogyi, M.: (1938) J. biol. Chem. 125, 399.

Sorkin, S. Z.: (1943) J. clin. Invest. 22, 329.

Stafford, D. D., and Addis, T.: (1923) Quart. J. Med. 17, 151.

Stockes, P.: (1916) Quart. J. Med. 9, 216.

Trasoff, A., and Scarf, M.: (1937) Amer. J. med. Sci. 194, 470.

Unger, E., and Heuss, H.: (1927) Zentralblf. f. Chir. 54, 770.

Van den Erve, J.: (1911) Amer. J. Physiol. 29, 182.

Walzel, P.: (1934) Med. Klin. 30, 1516.

Waring : (1923) Brit. J. Surg. 11, 476.

Watanabe, C. K.: (1918) Amer. J. Physiol. 45, 30.

Watson, Sir Thomas: (1871) Lectures on the Principles and Practice of Physio. Vol. 2, page 689.

Wohlgemuth, J.: (1908) Biochem. Ztschr. 9, 1.

Wohlgemuth, J.: (1910) Biol. klin. Woch. 67, 92.

Wohlgemuth, J.: (1929) Biol. klin. Woch. 8, 1253.

Zucker, T. F., Newburger, P. G., and Berg, B. N.: (1932) Amer. J. Physiol. 102, 209.