good volume. The post-operative aortogram (Fig. 4) shows the graft in position and of normal calibre. There was an excellent flow of blood in the femoral arteries. In October, 1953, 14 months after his operation, he was still getting an excellent functional result and all the peripheral pulses were present.

In addition to its outstanding value in the two types of case which have been described, aortography has occasional value in other circumstances.

In one patient a lump in the left hypochondrium was particularly difficult to feel because of the build of the patient. Serious doubt existed whether the lump was an enlarged kidney or spleen. Aortography clearly demonstrated that it was an enlarged spleen (Fig. 5), for the renal outline was clearly seen and the splenic arteries spread far beyond the confines of a normal spleen. Thus, in general terms, aortography may be of value in diagnosing a doubtful abdominal tumour. It may be of value in locating the site of a suprarenal tumour in a case of Cushing's disease, but we have not yet had the opportunity of testing this. Goodwin *et al.* (1950) record its use in such a case.

Aortography has been added to the more orthodox methods of pyelography in the investigation of kidney disease, as has been fully described by Griffiths (1950). It is claimed that the pooling of dye which occurs in a hypernephroma will distinguish it from a solitary cyst, but we feel that in the absence of such an appearance it would be dangerous to make a definite diagnosis of renal cyst and not submit the patient to an exploratory operation.

Summary

The technique of aortography under sedation without anaesthesia is described and its value is illustrated.

A case in which an external iliac arterial obstruction was accurately located by aortography is reported. The artery was excised and replaced by an arterial graft, with a satisfactory result three months after the operation.

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It is estimated that at the present time out of every 100 average men and women in Great Britain only 2 have naturally perfect teeth; 16 need teeth extracted, 42 require other dental attention, and 40 have complete or partial dentures. These statistics appear in an article contributed to *Progress* by Sir William Kelsey Fry. "Dental disease is one of the consequences of civilization," he says. From examining large numbers of skulls, research workers now know that in the Middle Ages quite half the population had no carious teeth. But by fifty years ago it was unusual to see a patient with a healthy mouth, and during the 1914-18 war large numbers of men were rejected as unfit for active service on account of the state of their teeth. During the last war it was estimated that at 18 years of age 98% of the men and 90% of the women were in need of dental treatment. However, Britain has by no means the worst teeth in the world: some parts of the United States and Norway, Australia, and New Zealand have a much higher caries rate. The incidence of caries in Europe declined in both world wars, and the conclusion is drawn that this was closely linked with the reduction in sugar consumption and changes in bread texture. Nowadays dentists find themselves unable to keep pace with the alarming increase in dental disease. In England and Wales there are 10,000 practising dentists, the majority of whom are over 50 years of age. That means that one dentist is expected to keep between 3,000 and 4,000 people dentally fit.

VALUE OF SINGLE-SAMPLE TEST IN DIFFERENTIAL DIAGNOSIS OF JAUNDICE

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In the differential diagnosis of jaundice, although biochemical tests cannot take precedence over clinical findings, cases occur in which the clinical features are puzzling. For example, chronic hepatitis may in some cases present as painless jaundice simulating obstruction arising from a carcinoma of the head of the pancreas; while in other cases the main complaint may be of pain similar to that of biliary colic. In cases where the clinical picture is problematical, biochemical tests, by suggesting an earlier solution, can be of value, the importance of an early diagnosis being the necessity to decide whether surgical intervention is indicated. On the one hand, the dangers of an unnecessary exploratory operation in a case of hepatogenous jaundice must be avoided, and, on the other, the patient must be guarded from the harmful effects of prolonged extrahepatic obstruction.

The "single-sample tests" have the advantages of simplicity in obtaining the specimen with minimal discomfort to the patient, along with economy in time to the patient and the physician. Coleman (1950) has shown that such tests are reliable, irrespective of the stage of the illness. However, many such single-sample tests recommended (for example, by Schwimmer *et al.*, 1945; Shay and Siple, 1948; Mawson, 1948; Popper and Steigmann, 1948; and Hoffbauer *et al.*, 1949) involve an imposing number of biochemical determinations, employing a wide range of tests. Bearing in mind that this is a clinical problem as distinct from interesting research, the simpler tests, which can be carried out in any hospital laboratory, must be given prior consideration.

The object of the present investigation was to find out the minimal number of determinations that should be included in a single-sample test to make this of value in differentiating obstructive from hepatogenous jaundice. It is generally agreed that none of the tests employed will estimate the degree of liver damage, and this aspect of the problem is therefore not touched upon. Likewise, no attempt has been made to assess the prognostic significance, if any, of these tests.

Material and Methods

Material.—The present series consisted of 104 patients who showed signs of jaundice and whose records contained sufficient data to establish an undoubted diagnosis. This series was composed of the following:

Obstructive jaundice (67 cases)

1. Carcinoma obstructing extrahepatic bile ducts ..	27
2. Calculus in the common bile duct	17
3. Chronic pancreatitis	4
4. Stricture of common bile duct	2
5. Carcinomatosis involving liver	17

Hepatogenous jaundice (37 cases)

6. Cirrhosis of liver	20
7. Acute hepatitis	11
8. Miscellaneous cases of hepatogenous jaundice ..	6

Those grouped in "carcinomatosis involving liver" were patients in whom neoplastic metastases invading the liver

were demonstrated either clinically, at operation, or at necropsy, but where no definite extrahepatic biliary obstruction was found. The justification for including such cases among the obstructive groups was that Himsworth (1950) considered that the jaundice in such cases was due to pressure by deposits of growth upon the biliary passages. In the other obstructive groups the diagnosis of obstruction was based on operation or necropsy findings in all but two cases.

As might be expected, in the hepatogenous groups most of the diagnoses were based on clinical findings and progress. Cases in which there was doubt about the diagnosis were excluded from the series. Cases of haemolytic jaundice were also excluded, as this condition rarely presents a problem in the differential diagnosis of jaundice.

Methods.—The tests employed were serum alkaline phosphatase activity (King and Armstrong, 1934); serum total cholesterol (Bloor method as modified by Kenny, 1952); plasma protein; and thymol turbidity (MacLagan, 1944b). These determinations were carried out on a single sample of 20 ml. of venous blood divided into 10 ml. each of clotted and oxalated blood. At the same time a sample of urine was examined for urobilinogen and urobilin.

Results

The individual findings in the 104 patients are not detailed here, but the result of each determination in the patient's initial single-sample test has been classified as indicating obstructive or hepatogenous jaundice according to the criteria in Table I.

TABLE I.—Critical Levels

Test	Obstructive Jaundice	Hepatogenous Jaundice	Reference
Serum alkaline phosphatase	Over 35 units	Under 35 units	MacLagan (1944a)
Serum total cholesterol	Over 300 mg./100 ml.	Under 300 mg./100 ml.	Epstein and Greenspan (1936)
Plasma albumin	Over 3.4 g./100 ml.	Under 3.4 g./100 ml.	Gray (1950)
Plasma globulin	Under 2.9 g./100 ml.	Over 2.9 g./100 ml.	Gray (1950)
Thymol turbidity	Under 4 units	Over 4 units	MacLagan (1944b)
Urobilinogen and urobilin	Not increased	Increased	Watson (1937)

Analysis of the separate tests yielded the results summarized in Table II. The left column under each test contains the number of determinations in each group of patients suggesting an obstructive cause for the jaundice, the numbers in the right column being the determinations suggesting a hepatogenous lesion.

Serum Alkaline Phosphatase.—This was most often raised above the critical level in cases of obstruction due to carcinoma or to metastatic deposits (groups 1 and 5); but even where obstruction rose from other sources it was raised in 16 out of 23 cases (70%). In the present series, however, it was also raised in 10 out of 37 cases (27%) of hepatogenous jaundice. Using 35 units as the differential level, this test by itself would have suggested the cause of the

jaundice in 80 out of 104 cases, but would have been misleading in 24 cases. In no case of obstructive jaundice, no matter how mild, was the serum alkaline phosphatase below 20 units.

Serum Total Cholesterol.—In contrast to the above, hypercholesterolaemia was present most frequently where obstruction was due to causes other than malignant neoplasm. It failed to appear in more than half of the cases of obstruction where neoplasm was present, but in many of these cases cachexia, which tends to lower the blood cholesterol, was evident. Although positive in obstructive jaundice less often than the serum alkaline phosphatase, it was misleadingly raised in only three cases of hepatogenous jaundice. The results in Table II show that absence of hypercholesterolaemia need not indicate the absence of obstruction, but where hypercholesterolaemia is present obstruction is probable. Using hypercholesterolaemia as an indication of obstruction, and disregarding a serum total cholesterol of under 300 mg. per 100 ml. as of no differentiating value, this test would have diagnosed correctly only 35 out of 66 cases (53%) of obstructive jaundice, but would have been misleading in only 3 out of 35 cases (9%) of hepatogenous jaundice.

Plasma Albumin.—Hypo-albuminaemia was present in 40% of the cases of hepatogenous jaundice, but was also present in 41% of the obstructive cases. This test was obviously of no differentiating value in the present series.

Plasma Globulin.—Hyperglobulinaemia was present in 81% of the cases of hepatogenous jaundice, but was present also in 81% of the obstructive cases. This test also was obviously of no differentiating value.

Thymol Turbidity Test.—In hepatogenous jaundice this test was more often within normal limits than raised. A normal thymol turbidity is therefore no indication of the absence of liver-cell damage. When abnormally raised, however, it indicated correctly the nature of the jaundice in 16 out of 37 cases (43%) of hepatogenous jaundice, and was misleading in only 7 out of 67 cases (9%) of obstructive jaundice. In obstructive jaundice the level of 9 units was never exceeded in the present series.

Urinary Urobilinogen and Urobilin.—The anticipated absence of urobilinogen and/or urobilin from the urine in cases of obstructive jaundice was shown in 42 out of 62 cases (66%), while in hepatogenous jaundice only 8 out of 36 cases (22%) failed to show either in increased amounts.

Discussion

Serum Alkaline Phosphatase

Although its mechanism is still not clearly understood, this test has repeatedly proved its value since its use in the differential diagnosis of jaundice was described by Roberts (1930, 1933). In the present series there was a similar degree of overlap at the usual differentiating point at 35 units to that reported by Giordano *et al.* (1939), Gutman *et al.* (1940), Higgins *et al.* (1944), and MacLagan (1944a).

The present observation that the rise in serum alkaline phosphatase is most pronounced in the presence of malignant neoplasm has also been noted by Higgins *et al.* (1944),

TABLE II.—Analysis of Results

Group	No. Cases	Serum Alkaline Phosphatase		Serum Total Cholesterol		Plasma Albumin		Plasma Globulin		Thymol Turbidity		Urobilin and/or Urobilinogen	
		35 +	35 -	300 +	300 -	3.4 +	3.4 -	2.9 -	2.9 +	4 -	4 +	-	+
1. Carcinoma obstructing ducts	27	22	5	14	13	14	13	5	22	26	1	20	6
2. Calculus in common bile duct	17	11	6	12	5	11	5	1	15	16	1	10	7
3. Chronic pancreatitis	4	3	1	3	1	3	1	1	3	4	—	3	—
4. Stricture of common bile duct	2	2	—	—	2	2	—	1	1	1	1	—	2
5. Carcinomatosis involving liver	17	15	2	6	10	8	8	4	12	13	4	9	5
Total obstructive	67	53	14	35	31	38	27	12	53	60	7	42	20
6. Cirrhosis of liver	20	8	12	2	17	10	10	2	18	11	9	4	16
7. Acute hepatitis	11	2	9	1	10	9	2	4	7	5	6	4	7
8. Miscellaneous hepatogenous	6	—	6	—	5	3	3	1	5	5	1	—	5
Total hepatogenous	37	10	27	3	32	22	15	7	30	21	16	8	28

Schwimmer *et al.* (1945), and Hoffbauer *et al.* (1949). This observation cannot be explained. Cleveland *et al.* (1950) found no detectable phosphatase activity in neoplastic cells in the liver.

In the present series none of the 67 cases of obstructive jaundice showed a serum alkaline phosphatase below 20 units, irrespective of the duration or degree of jaundice. Maclagan (1944a) reported only 3 out of 43 cases of obstructive jaundice as falling below 24 units. It would therefore appear that a serum alkaline phosphatase of under 20 units, in the presence of jaundice, strongly indicates a non-obstructive cause.

Concurrent serum bilirubin determinations with the serum alkaline phosphatase results reported in this paper showed that there was no tendency towards inverse relation with the height of the serum bilirubin in the two groups of jaundice. This is in keeping with the findings of Flood *et al.* (1937), Sherlock (1946), and Mawson (1948). Therefore interpretation of the serum alkaline phosphatase determination should not be influenced by the serum bilirubin level.

Serum Total Cholesterol

The value of this test has been doubted in the past. Sherlock (1946) regarded it as of no value, but her limits for hypercholesterolaemia were low. Hoffbauer *et al.* (1949), using 225 mg. per 100 ml. as the differentiating level, were also not impressed by this test. When, however, their figures are reviewed using 300 mg. per 100 ml. as the point of hypercholesterolaemia it can be seen that only 6 out of their 57 cases (10.5%) of hepatogenous jaundice showed hypercholesterolaemia. This value of 300 mg. per 100 ml. was the level above which Epstein and Greenspan (1936) considered significant hypercholesterolaemia to be present. They found that this level was exceeded by 78% of their cases of obstructive jaundice, while only 10% of their cases of hepatogenous jaundice showed hypercholesterolaemia. The comparable figures in the present series were 53% and 9% respectively. Cantarow and Nelson (1937) recorded that 11 of 28 cases (40%) of obstructive jaundice exceeded 300 mg. per 100 ml., while none of their 22 cases of hepatogenous jaundice showed hypercholesterolaemia. From these figures it would appear that a hypercholesterolaemia of over 300 mg. per 100 ml. is suggestive of obstruction, but that figures below this level are of no diagnostic value.

Determination of the serum total cholesterol is of value not only in confirming the more frequently positive serum alkaline phosphatase test, but also in picking up the case of obstructive jaundice missed, especially in the non-malignant groups, by the phosphatase test. In the present series the cholesterol test indicated the presence of obstruction correctly in six cases in which the phosphatase test had failed.

Estimation of cholesterol esters has been advocated, but, as this estimation is time-consuming and has been shown by Hoffbauer *et al.* (1949) to be of little value, it was not carried out in the present investigation.

Plasma Protein

The present results showed that determination of plasma albumin and globulin is of no differentiating value. This is in accordance with the results and opinion of Schwimmer *et al.* (1945) and Sherlock (1946). There is therefore a clear indication for the omission of these determinations from a single-sample test intended only for the differential diagnosis of jaundice.

Thymol Turbidity

This empirical test, first described by Maclagan (1944a, 1944b), has the advantages of being easy to perform, rapid in giving a result, and clear in its numerical assessment of the reaction. Maizels (1946) considered it to be the most useful of a number of empirical tests compared by him. Watson and Rappaport (1945) believed it to be more uniformly negative in obstructive jaundice than the cephalin-

cholesterol test. Franklin *et al.* (1948) found that this test showed statistically the most significant correlation with liver-cell damage.

The test has been criticized for being insufficiently sensitive (Mateer *et al.*, 1947), and this is confirmed by the present results, there being only 16 positive tests in 37 patients (43%) suffering from hepatogenous jaundice. The present results, however, also showed that it was reliable, only 7 misleading results being obtained out of 67 cases (9%) of obstructive jaundice.

None of the 67 cases of obstructive jaundice exceeded 9 units. Maclagan (1947) found none of 56 cases of obstructive jaundice to exceed 8 units; and Hoffbauer *et al.* (1949) found none of 77 cases of obstructive jaundice to exceed 9 units. It would therefore appear that a thymol turbidity of 10 units or over indicates hepatogenous jaundice, irrespective of other findings.

Urinary Urobilinogen and Urobilin

The present findings are similar to those of Cantarow and Nelson (1937). Snell (1947) and Coleman (1950) believed these tests to be of much value. However, as an increase of urinary urobilinogen and urobilin can occur in incomplete obstruction with secondary liver damage, as well as in hepatogenous jaundice, and as absence of both these substances can be found in hepatogenous jaundice at the height of the disease, less reliance can be placed on these urinary tests than on the blood tests. Nevertheless, where the latter are equivocal, the urinary tests may give a hint regarding the cause of the jaundice.

Serial Tests

Repetition of tests has been advocated by many authorities. Although not detailed in the present investigation, 82 tests were carried out on 28 patients. In 22 of these patients the initial biochemical interpretations were subsequently proved to be correct. In five cases with equivocal initial results, subsequent tests altered sufficiently to give a final interpretation later proved correct. In one case, the tests remained equivocal on all three occasions.

Combination of Tests

The present series once again confirms that no single test is absolutely reliable in the differential diagnosis of jaundice. Maclagan (1947), however, combining serum alkaline phosphatase with thymol turbidity results, obtained 68% accuracy. Using the same tests, Hoffbauer *et al.* (1949) had no erroneous results, but their interpretations were equivocal in 30% of cases; and Coleman (1950) found four misleading interpretations in 70 cases. Gutman and Hanger (1941), using serum alkaline phosphatase and cephalin-cholesterol tests in combination, obtained 72% accuracy.

In the present investigation, serum alkaline phosphatase, serum total cholesterol, and thymol turbidity tests have been found to be of most value. The present results have shown the following:

- (a) Serum alkaline phosphatase
  - Under 20 units indicated hepatogenous jaundice
  - Under 35 units suggested hepatogenous jaundice
  - Over 35 units suggested obstructive jaundice
- (b) Serum total cholesterol
  - Over 300 mg. per 100 ml. suggested obstructive jaundice
  - Under 300 mg. per 100 ml.—no value
- (c) Thymol turbidity test
  - Over 10 units indicated hepatogenous jaundice
  - Over 4 units suggested hepatogenous jaundice
  - Under 4 units—no value

Obstructive jaundice was therefore suggested by either serum alkaline phosphatase over 35 units or serum total cholesterol over 300 mg. per 100 ml., or by both, when thymol turbidity was not more than 4 units.

Hepatogenous jaundice was suggested by: (1) serum alkaline phosphatase under 20 units, irrespective of other results; (2) thymol turbidity of over 10 units, irrespective of other

results; (3) thymol turbidity over 4 units when serum alkaline phosphatase was under 35 units, and serum total cholesterol under 300 mg. per 100 ml.

The results were interpreted as equivocal when: (1) either serum alkaline phosphatase was over 35 units or the serum total cholesterol over 300 mg. per 100 ml., or by both, with thymol turbidity between 4 and 10 units; (2) both serum alkaline phosphatase was between 20 and 35 units and serum total cholesterol was under 300 mg. per 100 ml., with thymol turbidity under 4 units.

Applying these rules to the individual results, this combination of tests can be correlated with the final diagnosis as in Table III.

TABLE III.—*Interpretation of Combined Tests Correlated with Final Clinical Diagnosis*

Group	In Agreement with Diagnosis	Equivocal Interpretations	Erroneous Interpretations
1. Carcinoma—obstructing ducts ..	22	5	0
2. Calculus in common bile duct ..	14	3	0
3. Chronic pancreatitis ..	4	0	0
4. Stricture of bile duct ..	1	1	0
5. Carcinoma—metastases in liver ..	11	6	0
6. Cirrhosis of liver ..	9	6	5
7. Acute hepatitis ..	8	2	1
8. Miscellaneous cases of hepatogenous jaundice ..	5	1	0
	74	24	6

Although the present accuracy of 71% shows no significant improvement over the figures obtained by Gutman and Hanger (1941), MacLagan (1947), and Hoffbauer *et al.* (1949), despite the addition of the serum total cholesterol determination to the tests, it is felt that this test is justified, as it correctly indicated obstruction in six cases where the serum alkaline phosphatase had failed, and yet on only one occasion was it misleading by itself. Furthermore, as has been shown in Table II, hypercholesterolaemia is more often present in non-malignant causes of obstruction, the type in which the serum alkaline phosphatase is less often helpful.

When the urinary tests were taken into account in those cases with equivocal blood results, in the obstructive groups 10 out of 15 cases showed absence of both urobilinogen and urobilin, three cases showed a misleading increase of these substances, and in the remaining two cases these tests were not carried out. In the hepatogenous groups, seven cases out of nine showed increase of urobilinogen and urobilin; in two cases neither was increased.

After applying the less accurate urinary tests, the final interpretation of the biochemical tests showed:

In agreement with diagnosis					
Blood tests	..	..	..	74	91
Suggestive urinary tests	..	..	..	17	
Disagreement with diagnosis					
Suggestive urinary tests	..	..	..	5	11
Blood tests	..	..	..	6	
Equivocal (urinary tests not done)	..	..	..	2	

The erroneous blood tests were limited to cirrhosis and acute hepatitis, and the proportion to the total number in the series was similar to that reported by Coleman (1950).

Summary

A series of blood tests was investigated regarding the value of these determinations for inclusion in a single sample test for the differential diagnosis of jaundice.

Of the tests employed, the serum alkaline phosphatase activity, serum total cholesterol, and thymol turbidity were found to be of most significance. Deter-

mination of the plasma protein fractions was of no value and should be omitted from any single-sample test.

Tests for urobilinogen and urobilin in the urine were found to be of value as supplementary information where the results of the blood tests were equivocal.

Critical levels in the blood tests for the differentiation of hepatogenous from obstructive jaundice are suggested. Applying these criteria in a series of 104 cases of jaundice, the correct diagnosis of the type of jaundice was made in 91 cases. Of the remaining 13 cases, two gave equivocal results, while in 11 the biochemical findings were frankly misleading.

This paper was made possible only through the generosity of Dr. Ian A. Anderson, who gave me free access to the biochemical records of these tests. I cannot adequately express my thanks for his unstinted help and advice. I am also indebted to the physicians and surgeons of the Victoria Infirmary for allowing me the use of their clinical records.

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In his annual report for 1952 the medical officer of health for the County Borough of Smethwick, Dr. Hugh Paul, comments on the rapid decline in infectious diseases, in particular tuberculosis, since the war. He attributes the decline mainly to the use of antibiotics, but, he continues: "On the other hand, one cannot withhold a meed of praise to the conscientious chest physicians throughout this country who have achieved remarkable success during the past two generations. Many of us feared when the regional board took over our schemes in 1948 that the glamour of cure would swamp the infinitely more useful but infinitely less attractive aspects of prevention, and that the tuberculosis service would sink to the level of other branches of hospital cure. We have built better than we knew, however, and it would appear that the tuberculosis officers trained by us in the olden days, soaked in the gospel of prevention from their early days and imbued with the desire to look upon their task in the broadest possible light, are continuing in the olden ways, and have evaded the blandishments of the sirens of curative medicine. One can only hope that the new generation of chest physicians will be trained in the same way, but one cannot help but feel uneasy when one reads advertisements for chest physicians stating that the M.R.C.P. is necessary and that previous experience in tuberculosis is desirable. We must not sink to cure."