LIVER FUNCTION TESTS

A Survey of Some Recent Work

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TABLE I

Test	Indication	Alternate or Supplementary Procedure
Plasma alkaline phosphatase Total serum bilirubin Total serum cholesterol Urine bilirubin	To assess the degree of biliary obstruction	Duodenal intubation
Direct bilirubin percentage		LIVER BIOPSY
{ Bromsulphalein clearance Plasma cholinesterase level Galactose tolerance Benzoic acid detoxication Plasma prothrombin level Urinary urobilinogen	Specific tests of parenchymatous liver damage	
<i>Flocculation Tests:</i> (A) { Thymol turbidity Cephalin-cholesterol Thymol flocculation (B) { Zinc sulphate turbidity Gamma flocculation	Non-specific tests of parenchymatous liver damage	SERUM PROTEIN IONOPHORESIS (on filter paper)

For the last 30 years an evaluation of liver function has been attempted by various chemical and physiological tests. Many of these are now obsolete and reference to them is omitted. In recent years an interim study has been undertaken by a variety of new methods of investigation, notably electrophoresis, which have materially assisted in the diagnosis and treatment of liver disorders. For the purpose of this survey, therefore, only work of recent date is included.

Much information is contained in the excellent reviews of this subject that have appeared in the last three years; in particular the paper by Popper and Schaffner (1950), the Ciba Foundation Symposium on Liver Disease (Sherlock and Wolstenholme, 1951), the survey of cirrhosis by Sherlock (this journal, 1950) and the infective hepatitis report of the Medical Research Council (No. 273, 1951). The difficulties encountered in the neonatal period with respect to liver function tests have been summarized by Harris (1952). In addition, a number of important contributions have been made to our knowledge of the behaviour of

the serum protein fractions in liver disease, in particular the electrophoretic studies of Popper *et al.* (1951), Franklin *et al.* (1951), Ricketts and Sterling (1949, 1951) and Wuhrmann *et al.* (1950).

It is not without significance that during the same period at least three papers have appeared with the sole object of pointing out the pitfalls (Kramer, 1950) and misuses of liver function tests. At the same time the number of new tests is increasing every year. The biochemist has no easy task as he has to decide which of the many tests mean precisely the same thing and are therefore redundant, as unnecessary laboratory investigations have often resulted in confusion rather than increased clarity in diagnosis. Should we have six, nine or 20 simultaneous tests of liver function? With the ever widening circle of suspected liver damage (e.g. infectious mononucleosis) a restriction of tests becomes necessary unless especial facilities for these investigations are provided. Table I is an attempt to classify approximately equivalent tests. In the writer's opinion tests grouped together in a bracket though different in

character have approximately the same clinical value, in other words only one from each group need to be done in any particular investigation.

Biliary Obstruction

It is not sufficient to assess the extent of biliary obstruction alone as in every case of jaundice hepatocellular damage may be present as well. The pure form of extrahepatic obstruction is at least four times less common than intrahepatic obstruction with concomitant cell pathology. Severe parenchymatous liver damage is a strong contraindication to any form of surgical intervention including needle biopsy. Hence, a complete investigation has to be made in every case.

Total serum bilirubin and the direct reacting bilirubin percentage. The amount of bilirubin diazotizing within one, ten or 15 minutes in the van den Bergh reaction is measured quantitatively. This direct (or prompt) reacting bilirubin is independent of the concentration of circulating bilirubin and when expressed as a percentage of the total gives more useful information than the former vague designations 'direct,' 'biphasic' and 'indirect' van den Bergh reaction. The direct reacting bilirubin (Na-bilirubinate) reaches the highest levels in complete extrahepatic obstruction. Incomplete extrahepatic obstruction and obstruction arising from acute or chronic inflammatory liver disease gives rise to high or moderate increases in total bilirubin of which half or more is of the fast diazotizing form. There is much overlapping of results, and an estimation of the direct reacting bilirubin percentage is of little use in the differential diagnosis of jaundice whether haemolytic, obstructive or viral in origin (Klatskin and Drill, 1950). All that one can say is that when the ratio of the direct reacting bilirubin to the total bilirubin is less than 40, obstructive jaundice can be excluded (Gray, 1947).

The position is different where a diagnosis has been established or where the aim is to differentiate extrahepatic obstruction from some other intra-abdominal condition, e.g. pancreatitis. Here positive not negative findings lead in diagnosis and prognosis. Schalm (1952), using as criterion a high 10 minute direct reacting bilirubin percentage, has shown that this may be used to confirm an attack of cholelithiasis in the absence of visible jaundice and bilirubinuria.

Whether one postulates a renal threshold for bilirubin (Neye, 1952) or not (Watson, 1946, 1951; Pollock, 1951) the direct reacting bilirubin always appears early in the urine where it can be identified by the sensitive Harrison-Fouchet or Hunter reaction. These urine tests are useful before frank jaundice develops and during convalescence.

Total serum cholesterol. In progressive portal cirrhosis and hepatic insufficiency cholesterol values are normal or low, but in biliary cirrhosis and extrahepatic obstruction values are generally high. It is a useful confirmatory test especially when obstruction occurs in early infancy. In adults a high serum cholesterol value should be interpreted with care even in the presence of jaundice as numerous other conditions may cause a rise in serum cholesterol, e.g. hypothyroidism.

Alkaline phosphatase. It is a normal function of the polygonal cells of the liver to excrete serum alkaline phosphatase through the bile channels (LaVeen *et al.*, 1950). Obstruction of these passages causes failure of excretion of the enzyme and correspondingly high levels in the blood, the amount being roughly proportional to the degree of obstruction. Hence, moderate elevations are seen in hepatitis and very high values in extrahepatic obstruction.

Freeman (1951) has shown in dogs that common bile duct obstruction gives rise to a much higher alkaline phosphatase concentration in the blood than total hepatectomy. This has been interpreted to mean that the liver cells themselves synthesize the enzyme and add a contribution to the serum. It must be remembered, however, that Sherlock and Walshe (1947) in their very searching study did not find any histological evidence to support this suggestion, though they admit that histological studies of material from cases of obstructive jaundice can yield little information on this point.

At present, therefore, it does not seem unreasonable to assume that serum alkaline phosphatase is of multiple origin, the major contributions being derived from the tissues that most actively secrete it, notably bone, intestines, the kidneys and liver.

A dual function on part of the liver cells (secretion and excretion) would fit the clinical evidence best. In infective hepatitis we deal with a partial failure of both mechanisms. The observed enzyme rise in the serum representing the balance between the enzyme lowering effect of hepatocellular failure on the one hand and the enzyme raising effect of intrahepatic obstruction on the other. In extrahepatic obstruction the excretory mechanism may fail completely whereas the secretory mechanism since it is mainly non-hepatic remains undisturbed.

Twenty-five King-Armstrong units of alkaline phosphatase have been taken as the dividing line between obstructive and non-obstructive jaundice. Baker (1951b), in conformity with other workers, found that in infective hepatitis the serum alkaline phosphatase values were below 30 units. In biliary obstruction he found that cases of malig-

nant obstruction gave more consistently high values than cases of mechanical obstruction. This is in agreement with the observations by Ricketts (1951) who found that even cases of metastatic carcinoma with practically normal liver function tests had a raised serum alkaline phosphatase though there was no direct evidence of obstruction.

Many forms of bone disease, e.g. rickets, Paget's disease, malignancy, etc., may give rise to a high serum alkaline phosphatase level and these conditions should be excluded before the test is considered in the differential diagnosis of liver disease.

Damage to Liver Cells. Specific Tests

Many of the metabolic functions of the liver have been made the basis of a function test. All these tests are handicapped from the start as they rely on either single or serial estimations of the plasma concentration of a liver metabolite. The specificity of the test is thereby reduced as the plasma level of liver metabolites is controlled apart from factors regulating circulatory volume and the metabolic activity of other organs, by diverse hormonal influences. It is not surprising, therefore, that relatively uncommon substances to the liver like galactose and complete strangers like bromsulphalein have yielded more reliable evidence of liver dysfunction than tests employing glucose, fructose or benzoic acid.

Much work has been done with these more specific tests for parenchymatous liver damage, but it has not always been realized that these tests must be performed under standard conditions. Previous dietary regimen, recumbency whilst the test is being done, size of the test dose, whether the patient is afebrile or not and other factors affect the reproducibility of results (Kramer, 1950). Under comparable conditions repeat tests show good agreement (Mendeloff *et al.*, 1949).

The direct reacting bilirubin percentage. Liver cells transform indirect bilirubin into the direct form and excrete the latter. This mechanism becomes deranged when the parenchyma is affected and the direct reacting bilirubin accumulates in the blood. This increase apparently occurs at the expense of the indirect bilirubin fraction as the change takes place before there is a significant rise in total bilirubin. In infective hepatitis the direct reacting bilirubin increases early and reaches a peak value during the pre-icteric stage of the illness. An estimation of this fraction is therefore a most valuable test in the early diagnosis of the disease (Pollock, 1945, 1951). Similarly, the test may be employed during convalescence from infective hepatitis, when a persistently high direct reacting fraction in spite of a normal total bilirubin level indicates continuous activity of the pathological process (Schaffner *et al.*, 1950).

The bromsulphalein test. This is considered the best general screening test. It will reveal the immaturity of liver function during the neonatal period (Mollison and Cutbush, 1949), detect parenchymatous liver damage in cases of latent cirrhosis (Ricketts and Kirsner, 1951) and hepatitis without jaundice and show a positive correlation with liver disease arising from focal lesions, e.g. cysts, metastatic nodules, etc. (Ricketts, 1951). The test should always be performed in suspected malignancy as when positive it is a strong contra-indication to surgical intervention (Magath, 1951).

The usual test dose is 5 mg. per kg. of body weight. This large amount has been objected to by Lorber and Shay (1951) on the grounds that it gives rise to a marked entero-hepatic circulation of the dye, which interferes with the interpretation of results. Owen (1951), however, could not detect any evidence of an entero-hepatic circulation after introducing bromsulphalein into the stomach or duodenum and only the 5 mg. dose imposes a sufficient load on the liver to make the test clinically reliable. The liver clearance rate for bromsulphalein is approximately the same as for bilirubin (Cantarow *et al.*, 1948).

The results can be expressed either as the amount of dye retained, for which calculation a plasma volume of 50 ml. per kg. is assumed, or they can be given as the clearance rate employing the method of Goodman (1952), which is based on the formulas developed by Lewis (1950).

The test bears a good relationship to morphological changes in the liver except during the recovery period when the test may remain unaltered for years despite steady clinical improvement (Patek, 1950).

The detoxication tests. Quick's hippuric acid test has often been criticized, but newer detoxication tests employing *p*-aminobenzoic acid (Deiss and Cohen, 1950) or *p*-hydroxyphenylpyruvic acid (Felix *et al.*, 1951) do not present a material advance from the clinical point of view, however interesting the biochemical findings. The general trend in parenchymatous liver disease is for glycine and sulphuric acid conjugation to fail and to become replaced by the glucuronic acid mechanism (Hartmann, 1951). In response to the standard test dose of benzoic acid, therefore, hippuric acid excretion is diminished with a corresponding increase in the excretion of benzoylglucuronide (Snapper *et al.*, 1951). As the kidneys also take part in hippuric acid synthesis the test has to be interpreted with care. Its main value is in the evaluation of liver function when jaundice renders other tests unsuitable and in prognosis. Where the test is employed routinely throughout the course of the illness it serves as a reliable index

to the rate of recovery. It is valueless as a means of differential diagnosis (Peters *et al.*, 1950).

The galactose tolerance and index tests. The blood galactose level is less affected by hormonal influences than the blood glucose level as is seen from the absence of the physiological Staub-Traugott phenomenon (Lauchenaue, 1950). Both the intravenous and oral tests yield reliable results, though abnormal findings should not be interpreted on a quantitative basis, i.e. the test lacks prognostic significance. In differential diagnosis it is only of value when cases of uncomplicated early extrahepatic obstruction are considered as there is a considerable overlapping of results between the hepatitis, cirrhosis and late obstructive group of conditions. As this test has a better physiological basis than the bromsulphalein test it has been employed preferentially in testing drugs suspected of hepatotoxic action (Boström and Gardell, 1950).

The plasma prothrombin level in response to vitamin K. This test though not a very sensitive one gives a fair quantitative indication of parenchymatous damage; a level 15 per cent. below normal being considered slight damage and 25 per cent. below normal severe damage. The results are affected to some extent by the method of estimation, some authors having declared Quick's original method unsuitable for the purpose (Perlick, 1951). Positive findings alone are useful. The main value of the test is to the surgeon who will be unwise to operate when faced with an unfavourable laboratory report. The test is not sensitive enough to reveal the extent of parenchymatous damage in infective hepatitis, at least 50 per cent. of the cases giving a normal response (Gottlebe, 1950).

The plasma cholinesterase level. The protagonists of this comparatively new test are uniformly in agreement with its value in liver disease (Alcalde, 1950; Wilson *et al.*, 1952). It is, they say, the best means of testing the liver's ability to synthesize protein. A low level of plasma cholinesterase indicates parenchymatous damage, provided myasthenia gravis has been excluded from the diagnosis. The test is of greatest value in the chronic case, especially in portal cirrhosis. The plasma enzyme level is low during the active stage of infective hepatitis and during a relapse. Normal values are encountered in cholangiohepatitis unless infection supervenes. In extrahepatic obstruction the low values are not seen until the obstruction has persisted for at least two months. The test is valuable both from a diagnostic and prognostic view and with the simplified technique for measuring the enzyme that was introduced by Michel (1949) deserves greater popularity in the future and might well replace some of the less specific flocculation tests.

Urinary urobilinogen excretion. Baumgärtel (1950) maintains that bilirubin is reduced to stercobilin in the gut and not to urobilinogen and he does not believe in an enterohepatic circulation of urobilinogen. His ideas though gaining ground on the Continent have not been accepted here or in America, where Watson has refuted Baumgärtel's claims (see Ciba Symposium, p. 221). Healthy liver cells re-oxidize urobilinogen to bilirubin.

An interruption of the enterohepatic circulation of urobilinogen may be due either to biliary obstruction or a hepato-cellular 'block,' the former being associated with a total lack of urinary urobilinogen and the latter with an augmented blood level and renal excretion of this substance. The peak of urobilinogen excretion is in the early afternoon (Suavely and Unglaub, 1952), hence specimens for routine testing should be collected at this time.

In infective hepatitis urinary urobilinogen excretion is increased in the pre-icteric stage and when jaundice is on the decline, but fails at the height of jaundice on account of intrahepatic obstruction. This gives rise to the characteristic camel's back curve in serial excretion studies. Obstruction from stone is rarely complete, hence some urobilinogen can be detected in the urine. In malignant obstruction, however, the test is usually quite negative (Baker, 1951a). This distinctive behaviour is of considerable diagnostic importance to the surgeon. In progressive and active cirrhosis parenchymatous damage blocks the path and the amount of urobilinogen found in the urine is an indication of the severity of the damage.

Non-specific Tests

These tests depend on alterations in the serum protein fractions and they are called non-specific because as F. Wuhrmann has rightly pointed out (Ciba Symposium, p. 72), 'all disease without exception decreases serum albumin and simultaneously increases the globulin, never the contrary.' The liver, however, plays the dominant role in plasma protein synthesis and manufactures exclusively all the albumin, prothrombin, alpha-globulin and some enzyme proteins (Roberts and White, 1949). Isotope studies in the rat have shown that most of the fibrinogen and 80 per cent. of the remaining globulins are also synthesized by the liver (Miller *et al.*, 1951).

We have several methods for studying the serum protein fractions but only two will be discussed here. First, the flocculation tests which depend less on quantitative than qualitative alterations of the proteins, and secondly the ionophoretic method (electrophoresis) which principally measures quantitative alterations but may

detect qualitative changes when they are pronounced. The two methods, therefore, are to some extent complementary to each other.

The flocculation tests. The literature is too vast to be reviewed here in detail, and for recent discussions of this topic the reader is referred to the papers by Sophian and Connolly (1952), Kihn *et al.* (1951), Popper *et al.* (1951), Popper and Schaffner (1950) and MacLagan (1948; Ciba Symposium, 1951).

Sufficient data have accumulated since the introduction of most of the flocculation tests to put us into a position to do some rigorous pruning. It is the writer's considered opinion that for one reason or another that cannot be discussed here in detail we can now afford to discard the following as liver function tests: The formol gel and Takata-Ara reactions, the Weltmann coagulation band, the colloidal gold and colloidal silver reactions and probably the cephalin-cholesterol and cadmium sulphate reactions. The remainder of the flocculation tests can be divided into two groups: (A) the hypersensitive and (B) the sensitive group (see Table 1). To the former belong the thymol turbidity and cephalin-cholesterol tests and to the latter the gamma flocculation, thymol flocculation and zinc sulphate tests.

Group (A) tests will detect a minimal amount of liver damage but owing to their high sensitivity lack specificity and are less useful in differential diagnosis. Hence, when the aim is to differentiate between infective hepatitis and extrahepatic obstruction, group (B) tests give more reliable information.

In a positive flocculation test visible colloid aggregates are formed. This is due to a reduction in serum albumin and a simultaneous increase in the gamma (and beta) globulins. A positive flocculation test can be reversed by addition of sufficient albumin which is said to exert a protective action on the colloid system. The magnitude of the thymol reaction depends in addition on the amount of serum lipid; it is a more complex reaction.

It is not always realized that the tests in group (A) and the thymol flocculation test must be performed under standard conditions, i.e. blood from a fasting patient must be used and heparin must not be used as the anticoagulant. The laboratory reagents should be standardized (Kibrick *et al.*, 1952) when possible.

Fatty metamorphosis of the liver and fibrous tissue infiltration unaccompanied by infection or inflammatory reaction do not give rise to positive flocculation tests (Moyer and Wurl, 1951; Ricketts, 1951). A general mesenchymal reaction with increased activity and proliferation of the Kupffer cells must take place before flocculation tests be-

come positive, and such a reaction is not exclusive to liver disease. This explains on the one hand the negative tests obtained in biliary cirrhosis, portal cirrhosis without symptoms (Baker, 1951a), Banti's disease (Nussey, 1949) and focal lesions of the liver; and on the other, the so-called false positive reactions that may be witnessed in myelomatosis, Kala-azar, rheumatoid arthritis, etc. Kupffer cells also proliferate in biliary obstruction but they are devoid of cytoplasmic basophilic granules, which suggests that the loading with regurgitated biliary products (lecithin) suppresses their specific activity (Popper, Ciba Symposium, 1951), and in consequence the flocculation tests remain negative. A false negative flocculation reaction may also occur when there is a great increase in the alpha-one-globulin as it appears to be able to exert a protective influence on the test similar to albumin (Seitz, 1950).

In summing up one may say that to follow the course of acute infective hepatitis a test of group (A) is best. The latter should be substituted by one of the tests of group (B) during convalescence as they more clearly indicate smouldering activity, a slow rise in gamma globulins and the transition to cirrhosis.

Serum protein ionophoresis. For clinical purposes the classical Tiselius method has been superseded by the filter paper method which is best known in this country from the work of Flynn and de Mayo (1951). Filter paper ionophoresis is now used routinely in some laboratories for the separate estimation of the serum protein fractions. Parallel determinations by the two methods have shown that the filter paper method gives basically the same results as the classical method (Köiw *et al.*, 1952), except for the beta-globulin, for which a truer value is obtained by the paper method. It seems profitable, therefore, to review as briefly as possible what has been learned from the classical method as most of this knowledge can be applied directly to the interpretation of results obtained by the paper method.

A good ionophoretic separation shows us at least six distinct fractions, which in order of speed of movement read as follow: albumin, alpha-one-globulin, alpha-two-globulin, beta-globulin, gamma-one-globulin and gamma-two-globulin. Some pathological sera may show a double beta fraction. The early hopes that individual patterns might be detected for the various liver diseases have not been fulfilled; nevertheless, information of considerable value can be derived from the fractionation. It enables us to determine correctly the albumin:gamma-globulin ratio, which is difficult to obtain by the single stage salting-out procedure as the latter method precipitates the alpha-one-globulin with the albumin fraction. A

true albumin: gamma-globulin ratio has considerable diagnostic and prognostic value (Popper *et al.*, 1951), whereas the ordinary albumin:globulin ratio is of little value in liver disease (Rafsky *et al.*, 1950; Baker, 1951; Sophian and Connolly, 1952). The failure of the crude albumin:globulin ratio is largely due to the erratic behaviour of both the alpha-globulins as also to the fact that the beta fraction is increased in obstructive jaundice as well as in toxic and infective hepatitis (Popper *et al.*, 1951).

The range of normal values for the individual protein fractions is quoted from the paper of Popper, Beán, de la Huerger, Franklin, Tsumagari, Routh and Steigmann (1951).

Albumin: In normal people this should be above 3.8 per cent., though in old age the normal limit is somewhat lower (Rafsky *et al.*, 1952). Albumin diminishes rapidly in acute infective hepatitis and keeps at a level above 3.5 per cent. only in the mildest cases. The lowest values are seen in portal cirrhosis with symptoms, though in portal cirrhosis without symptoms and in biliary cirrhosis where the lesions are often well compensated by regeneration, normal or borderline values are frequently encountered. A. J. Patek (1950) has shown that in dealing with liver failure the effect of treatment is better reflected in the serum albumin level than in the bromsulphalein test and serves as a reliable guide to prognosis.

Alpha-globulins: The normal range is 0.7 to 1.5 per cent. with the alpha-two fraction being slightly more than double the alpha-one-globulin. These two fractions are raised in a great number of miscellaneous conditions and therefore without significance in liver disease.

Beta-globulin: The normal range is 0.5 to 1.0 per cent., though at present it is not certain whether these figures are also true for the paper ionophoresis method. Sudan III staining lipid moves with the beta-globulin fraction (Kunkel and Slater, 1952) and in pathological sera both are usually found increased together when the beta fraction is raised. They are raised early in viral hepatitis, almost in proportion to the severity of the illness. Such a relationship is not found in toxic hepatitis or cirrhosis. Some striking elevations are seen in biliary cirrhosis when the classical method is used (lipid plus beta-globulin) (Nicola, Wuhrmann and Wunderly, 1950). According to Popper *et al.* (1951), the beta-globulins are elevated in portal cirrhosis and more so in the jaundiced than the non-jaundiced patient, though Martin (1949) reports low or normal values in these cases.

Fibrinogen: Fibrinogen is difficult to determine by the electrophoretic method as it travels at the same speed as the gamma-one-globulin (Franklin *et al.*, 1951). Fibrinogen is decreased in liver failure and increased in portal cirrhosis.

Gamma-globulin: Values above 1.25 per cent. should be considered with suspicion though upper normal values of 1.44 per cent. are occasionally seen. The gamma-one fraction was shown by Deutsch *et al.* (1946) to possess antibody properties; it is normally present in serum. In the ionophoresis diagram it shows up as a plateau rather than a peak. Gamma-one globulin is raised a little in infective hepatitis and grossly in cirrhosis where it may reach values of 6 per cent. or more. Values over 6 per cent. are usually only encountered in fatal cases of hepatic failure (Viollier, Ciba Symposium, 1951). The gamma-one plateau when raised tends to

overlap with the gamma-two fraction, hence most authors only quote total gamma-globulin values.

The gamma-globulins are greatly augmented in the serum during the first three months of life and this fact accounts for the false positive flocculation tests encountered during this period (Longworth *et al.*, 1945; Moore *et al.*, 1949).

In summing up one may say that not every peak in the ionophoresis diagram has always the same interpretation but that some diseases tend to be associated with a similar pattern from case to case (e.g. progressive portal cirrhosis with symptoms). The clinician should look at the diagram as well as consider the result in percentage or absolute figures, as the same figure may equally result from a tall peak as from a wide plateau, e.g. the tall gamma-globulin peak of multiple myelomatosis and the broad gamma plateau of cirrhosis. The ionophoretic serum protein fractionation is of especial value in the chronic cases when repeated flocculation tests and other investigations over a period of time have remained unaltered or given equivocal results. In these cases serial serum protein analysis by ionophoresis are the best guide to prognosis.

With the wider application of filter paper ionophoresis, no doubt more data of critical value will emerge, but even now the opinion has been voiced that flocculation tests can be dispensed with when one uses this method (Grassmann, Hannig and Knedel, 1951). This opinion is not shared by MacLagan (Ciba Symposium, 1951) but space forbids a full discussion of this controversy.

Summary

The question of how many tests one should use remains unanswered. Without a careful clinical history and thorough physical examination tests are misleading. At the onset of the illness the problem is usually one of deciding whether the patient and his complaint should be treated medically or surgically. For this purpose Popper and Schaffner (1950) have suggested a scheme which is set out in Table 2. Following this initial classification no further rules can be laid down as any additional investigation will depend on the exact nature of the illness and the kind of information one is anxious to obtain.

There are several ancillary methods of investigating liver disease that cannot be discussed here in full. The various forms of liver biopsy may be most helpful and for a discussion of their value the reader is referred to the above-mentioned paper by Popper and Schaffner, the papers by Moyer and Wurl (1951) and Schiff (1951). Liver biopsy is not an infallible guide to diagnosis, prognosis or treatment and it is not an absolutely safe method. The blood picture may also assist in the

TABLE 2
(AFTER POPPER AND SCHAFFNER)

Routine Investigation	Interpretation of Results
(A) Do TWO different tests for liver cell damage and (B) ONE test for obstruction to the flow of bile (See Table 1)	(i) (A) positive and (B) negative MEDICAL Exception: A palpable mass is present or urinary urobilinogen fluctuates on consecutive examinations.
	(ii) (A) positive and (B) positive with abnormal flocculation tests with normal flocculation tests MEDICAL SURGICAL (primary hepatitis with some degree of obstruction) Exception: purulent hepatitis or cases with palpable abdominal mass Exception: few cases of toxic hepatitis (arsenic)
	(iii) (A) negative and (B) positive SURGICAL Exception: Rarely, when a toxic factor is discovered, or when a history of preceding infective hepatitis speaks for cholangiolitic cirrhosis.

diagnosis. Macrocytic anaemia being common in liver disease on account of the role the liver plays in haemopoiesis. For a detailed account of the changes in erythrocyte structure that accompany macrocytic anaemia of liver disease, the reader is referred to the careful work of Larsen (1948). The changes in the white cell picture in infective hepatitis are discussed by Miles (Medical Research Council Report, p. 84).

Conclusion

No single system of tests will meet all requirements. The puzzling case with negative liver function tests that does not reveal a tell-tale story until he comes under the classifying eyes of the morbid anatomist, will recur again and again. But this does not mean that the tests are unreliable. The evidence merely points to the imperfection of our knowledge of the basis of most of the tests we employ. It is hoped that the newer methods may throw fresh light on this perplexing problem and make our understanding more complete for the sake of the patient.

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Postgrad Med J: first published as 10.1136/pgmj.29.331.255 on 1 May 1953. Downloaded from <http://pmj.bmj.com/> on April 26, 2023 by guest. Protected by copyright.

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SOLITARY AND INFIRM OLD PEOPLE

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The experience on which I base the views expressed in this article comes from my work as a Housing Manager for two housing associations in North Kensington. Much of their property consists of old houses which can be let off in single rooms, and these are often occupied by elderly people (for the most part women) who in other districts might have to live with relations or friends. If one of these old people becomes ill, but is not bad enough for hospital and there are no relations living near, a distressing situation arises which worries doctors as well as neighbours and social workers.

Our first attempt to meet this kind of hardship was to convert two connecting houses into a hostel where 28 old people could be fed and looked after when they could no longer manage for themselves. This type of hostel is called Part III accommodation, and under the National Assistance Act the major part of the maintenance cost is met by the welfare authority if it considers the old person in need of care and attention. We provide a

Matron and an Assistant Matron who, though not qualified nurses, have had nursing experience, and we look after the old people until they die unless they become so ill that they need hospital care. It is as difficult to get old people into hospital from a hostel as it is from their homes, but it is possible to arrange direct exchanges if there are people in the hospital ready for hostel life at the time when there is a serious illness in the house.

At this hostel the old people go out as they like, help in the house if they are able, bring some of their own furniture if they want and generally look on it as their permanent home. They share bedrooms for the most part without difficulty, but if we were taking professional people it would be essential to have single bedrooms.

The fact that the hostel is run by people they know and in a district they know makes the move when it comes less worrying for old people than it would be. I cannot stress too strongly what a pity it is that, under present legislation, different authorities are responsible for old people at