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Use of investigations in the diagnosis and management of alcohol use disorders

Colin Drummond & Hamid Ghodse

The purpose of this review is to familiarise the reader with the clinical utility of investigations in the diagnosis and management of alcohol use disorders (AUDs). Many biochemical and haematological tests are widely available, and can improve significantly the quality of diagnosis and management. However, there is no single test that can detect AUDs with complete accuracy. Further, the validity of a test will vary depending on the clinical application. Such tests should never be relied on in isolation. Adequate clinical evaluation also needs to include a combination of interview and examination of the patient, and interview of other informants (Cantwell & Chick, 1994; Edwards *et al*, 1997). In the research setting, self-report is generally a valid and reliable method of assessing alcohol consumption (Babor *et al*, 1987), particularly when it is elicited by a standardised method (e.g. Sobell *et al*, 1980) and the information is provided in confidence. In the clinical setting, however, the patient may report his or her version of past drinking subject to the demand characteristics of the situation, particularly if adverse consequences are likely to ensue (e.g. discharge from a treatment programme).

This review will not be concerned with the full gamut of examinations available to investigate physical and psychiatric disorders associated with alcohol misuse, such as brain scanning or liver ultrasound. Rather, this review is intended to provide up-to-date information on biochemical and haematological markers of excessive drinking, and their application in clinical diagnosis and management.

Purpose of investigations

The choice and application of a test will depend to some extent on the purpose for which the test is being used. Other factors in the choice of test will be the cost and invasiveness of the procedure involved and the type of personnel carrying out the test.

Screening and diagnosis

The most typical and cost-effective method of screening in the primary care or general medical setting, currently, is the administration of standardised questionnaires. In the past, the CAGE questionnaire (Mayfield *et al*, 1974) and the Michigan Alcoholism Screening Test (MAST; Selzer, 1971)) have been the most commonly used screening questionnaires. However, with the development of the theory and practice of screening methods, the Alcohol Use Disorders Identification Test (AUDIT; Saunders *et al*, 1993) developed by the World Health Organization, is now generally regarded as the standard approach in these settings. The AUDIT provides a measure of multiple dimensions of AUDs including

Colin Drummond is a Reader in Addiction Psychiatry and has carried out extensive research in the addiction field. He is an Assistant Editor of the journal *Addiction* and is the consultant responsible for alcohol services in South West London and St George's Mental Health NHS Trust (Department of Addictive Behaviour and Psychological Medicine, St George's Hospital Medical School, University of London, Hunter Wing, Cranmer Terrace, London SW17 0RE). He is extensively involved in College activities as a member of the Faculty of Substance Misuse and is currently Academic Secretary. Hamid Ghodse is Professor of Addiction Psychiatry and is well known in the field for his research and teaching activities. He has published extensively in the areas of addiction epidemiology, diagnosis, treatment, policy and prevention. He is a Member of Council of the College and his extensive international work includes membership of several World Health Organization Expert Committees. He is President of the United Nations International Narcotics Control Board.

alcohol consumption, alcohol-related problems and symptoms of dependence. It has the advantage of being relatively short (12 items) and easy to administer by non-alcohol specialist personnel, and it has a sensitivity and specificity as high as 92% and 93%, respectively (Chick *et al*, 1993) (for definitions of sensitivity and specificity, see below).

Questionnaire screening methods are often supplemented with biochemical investigations, typically gamma glutamyl transferase (GGT), mean cell volume (MCV) and alanine amino transferase (ALT). Serum ethanol can also aid diagnosis, particularly if a high level is found in a morning specimen. The characteristics of these tests are described in Table 1.

Clinical management

Biochemical methods are particularly useful in the context of clinical management of patients with AUDs. The most usual application is breath alcohol concentration measurement using a hand-held breath analyser (e.g. Alcometer; Lion Laboratories Ltd) which can provide an immediate and accurate measurement. Often, alcohol detoxification programmes will routinely include random breath alcohol testing. It is not appropriate to continue to prescribe medication for detoxification in cases where an individual has relapsed to drinking, and breath testing provides a means to detect this at an early stage. Further, feedback of improved biochemical test results can be used to good effect in enhancing motivation to maintain change (either abstinence or controlled drinking), and can be useful within a motivational interviewing framework (Miller & Rollnick, 1991).

Court proceedings

Psychiatrists are increasingly asked to provide assessment of individuals in both criminal and civil proceedings in relation to the presence or absence of an AUD. Sometimes, this is to establish the contribution of alcohol in a criminal act (e.g. assault or murder). On other occasions, it may be to establish the contribution and treatability of an AUD in a repeated pattern of offending (e.g. shoplifting or driving while intoxicated (DWI)). Psychiatrists are also asked to provide an assessment of the contribution of an AUD to problems in parenting (including child neglect and abuse). These are areas probably best dealt with by specialists in the field. Biochemical investigations often play a significant part in assessment and diagnosis. It is important to be able to inform the court of the likely limitations of recommended monitoring packages and of their cost.

Employee assistance programmes

A similar application for biochemical tests is in the context of employee assistance programmes. Increasingly, employers are becoming aware of the problems of alcohol misuse in the workplace, and in some occupations (e.g. airline pilots and doctors) alcohol misuse can be particularly hazardous. Psychiatrists are often asked to diagnose, treat and monitor alcohol-misusing employees, many of whom are reluctant patients.

Sensitivity and specificity of tests

Definitions

The sensitivity of a test refers to its ability to identify 'true positives', while minimising 'false negatives'. In a screening study for alcohol misuse, for example, a test with a sensitivity of 60% would correctly identify 60% of persons who are truly misusing alcohol as diagnosed by a 'gold standard' method (usually a standardised diagnostic interview). However, by the same token, the test would 'miss' the other 40% of

Table 1. Characteristics of tests

	Sensitivity	Specificity	Duration
Aspartate amino transferase	30–50%	80–86%	1–2 months
Alanine amino transferase	30–50%	80–86%	1–2 months
Gamma glutamyl transferase	50–70%	75–85%	1–2 months
Mean cell volume	25–52%	85–95%	1–3 months
Carbohydrate deficient transferrin	40–70%	80–98%	1–3 weeks
AUDIT questionnaire	92%	93%	–

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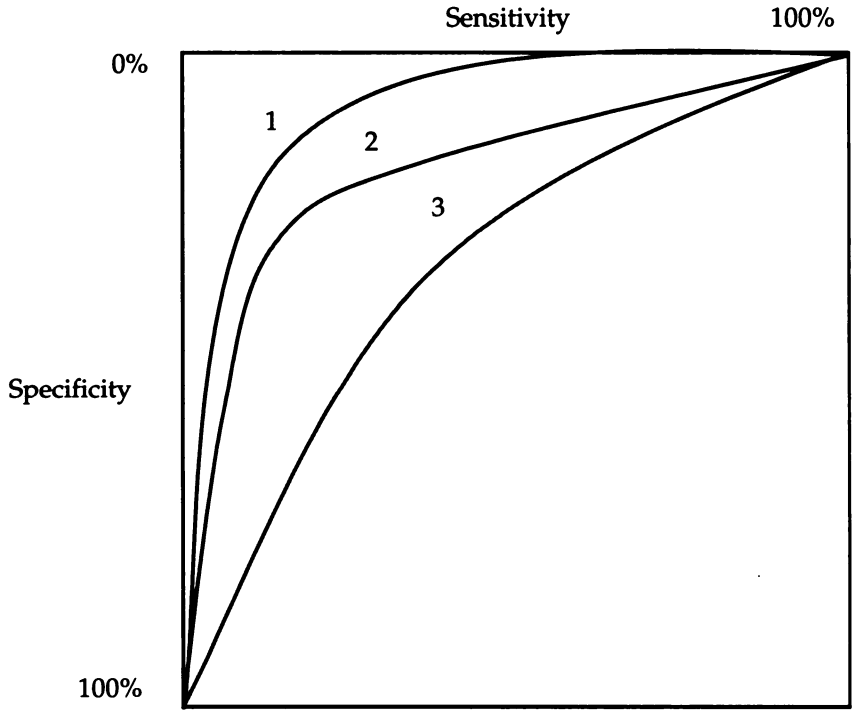
true positives (i.e. it would classify 40% of alcohol misusers as 'negative'). The higher the sensitivity of the test, the more effective it is as a screening tool.

The specificity of a test is the extent to which it only identifies 'true positives' and minimises 'false positives'. In the same hypothetical screening study, a test that has a specificity of 90% will correctly classify 90% of 'positives' as alcohol misusers. However, 10% of those who are identified as 'positive' are not suffering from alcohol misuse (as defined by the 'gold standard' interview method) and are, in reality, 'true negatives'.

In general, most tests used in screening for alcohol misuse (as in the hypothetical test above) have a relatively high specificity but a moderate sensitivity. In other words, they yield relatively few false positives at the expense of a relatively large number of false negatives (although there will be more false positives in the medical ward setting owing to, for example, liver disease or prescribed drugs). This is to some extent the result of a relatively large variation in the normal range in the non-alcohol-misusing population.

Normal ranges and measurement error

The setting of the upper limit of the normal range for a test is crucial in determining the sensitivity and specificity. As the cut-off point for the upper limit of the normal range increases, the specificity will increase as the sensitivity decreases. In other words, there will be fewer false positives but more false negatives. As the upper limit of normal is reduced the converse applies – there will be fewer false negatives at the expense of more false positives. For



1. Screening test with a relatively high and approximately equal level of sensitivity and specificity. This would result in a relatively low proportion of false negatives and false positives.
2. Screening test with unequal sensitivity and specificity.
3. Screening test with a relatively low and approximately equal sensitivity and specificity. This would result in a relatively high proportion of false positives and false negatives at any given cut-off point.

ROC curves can be used to choose the optimal cut-off point for a given screening test, a point that maximises sensitivity and specificity. The area under the ROC curve provides a measure of the overall performance of the test: the greater the area, the greater its positive predictive value.

Fig. 1 Receiver operating characteristics (ROC) of three hypothetical screening tests

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any given test, a Receiver Operating Characteristics (ROC) curve can be determined to provide the optimal cut-off point to maximise sensitivity and specificity. Figure 1 shows a hypothetical set of ROC curves for a range of tests.

In practice, the normal range for a given test varies from one laboratory to another and depends on a variety of factors including the type of analysis used to measure the parameter and the population used to calibrate the normal range. Ideally the population used should contain no alcohol misusers or patients with biochemical abnormalities due to any other physical causes. Box 1 shows the physical factors that can affect the interpretation of tests used to identify alcohol misuse. The Blood Transfusion Service donor population is an ideal source of specimens for test calibration, but it cannot be guaranteed to provide a totally healthy population. However, it is considerably better than using clinical populations to define normal ranges. The reference ranges for St George's Hospital laboratories are shown in Table 2.

Within any laboratory, there will be a degree of measurement error, and most laboratories calibrate the method regularly to provide quality control data. Usually measurement error is approximately ± 1–2%. It is important to bear this in mind when interpreting test results that are marginally outside the laboratory's reference range.

Specific tests

Ethanol

Direct estimation of ethanol concentration in body fluids is typically used by law enforcement agencies and accident and emergency departments to establish recent alcohol ingestion, and is commonly

Box 1. Sources of false positives

Alanine amino transferase
Very high:
- Viral hepatitis
- Toxic hepatic necrosis
- Shock

Moderately high:
- Cirrhosis
- Cholestatic jaundice
- Liver congestion secondary to congestive cardiac failure
- Infectious mononucleosis
- Extensive trauma
- Barbiturates
- Drug-induced liver damage (e.g. paracetamol, disulfiram)
- Some antidepressants (e.g. lofepramine)

Aspartate amino transferase
Very high:
- Myocardial infarction
- Viral hepatitis
- Toxic liver necrosis
- Circulatory failure

Moderately high:
- Cirrhosis
- Cholestatic jaundice
- Malignant infiltration of the liver
- Skeletal muscle disease
- Trauma

Gamma glutamyl transferase
- Hepatitis
- Cirrhosis
- Cholestatic jaundice
- Metastatic carcinoma
- Hepatic infiltration
- Anticonvulsant therapy
- Barbiturates
- Simvastatin
- Drug-induced liver damage (e.g. paracetamol, disulfiram)

Mean cell volume
- B_{12}, folate deficiency
- Pernicious anaemia
- Pregnancy
- Smoking
- Leukaemia
- Folate antagonists (e.g. methotrexate)
- Phenytoin, primidone

Carbohydrate-deficient transferrin
- Severe liver disease
- Primary biliary cirrhosis
- Chronic active hepatitis
- Genetic D variants of transferrin
- Inborn error of glycoprotein metabolism
- Severe haemolytic anaemia
- Infectious mononucleosis
- Drug-induced liver damage (e.g. paracetamol, disulfiram)

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used in criminal proceedings as evidence of, for example, DWI. Ethanol measurement is also used as a means of corroborating self-reported drinking in alcohol treatment programmes and in some research studies. Its utility as a means of screening for alcohol misuse is, however, somewhat limited owing to the relatively rapid elimination of ethanol.

The metabolism of ethanol is subject to large individual variation. The rate of absorption of ethanol is dependent upon many factors including: the type of drink; alcohol concentration in the drink; rate of alcohol consumption; recency of food intake; body mass; gender; and the presence of certain disease states (Sellers & Kalant, 1976). Even when most of these factors are controlled for, the time taken to reach peak alcohol levels can vary between 10 and 100 minutes depending on the dose administered (Jones, 1995). However, once absorbed the rate of elimination is near linear (zero order kinetics) with approximately 1 unit of ethanol eliminated per hour (1 unit = 8 g ethanol = ½ pint of 4% beer = 25 ml (or one pub measure) of 40% spirits), although this too is subject to wide individual variation and is dependent on body mass, gender and alcohol tolerance (Holford, 1987). Thus, it is easy to see how a person drinking 15 units of alcohol in an evening (approximately eight pints of beer) could remain above the legal limit for driving the following morning. However, even in very heavy drinkers, serum ethanol is unlikely to be positive after about 24 hours following the last intake of alcohol.

Table 2. Laboratory reference ranges

Substance	Range	Units
Sodium	135–145	mmol/l
Potassium	3.5–4.7	mmol/l
Urea	2.5–8.0	mmol/l
Creatinine	60–110	mmol/l
Bilirubin	0–17	mmol/l
Alanine amino transferase	5–40	u/l
Alkaline phosphatase	30–100	u/l
Albumin	38–48	g/l
Gamma glutamyl transferase	0–30	u/l (women)
	0–60	u/l (men)
Serum B_{12}	150–1000	ng/l
Red cell folate	150–750	µg/l
Serum folate	2.5–10	µg/l
Mean cell volume	78–95	fl (women)
	80–95	fl (men)
Mean cell haemoglobin	27–32.5	pg
Mean cell haemoglobin concentration	32–35.8	g/dl
White cell count	4–11	10^9/l
Neutrophils	1.8–8.0	10^9/l
Lymphocytes	1–4	10^9/l
Monocytes	0.4–1.1	10^9/l
Eosinophils	0.1–0.8	10^9/l
Basophils	0–0.4	10^9/l
Platelets	150–450	10^9/l
Haemoglobin	12–16	g/dl (women)
	13–17	g/dl (men)
Haematocrit	0.37–0.47	(women)
	0.41–0.52	(men)
%CDT (Axis)	0–6	%

NB All values provided by the Biochemistry and Haematology Departments, St George's Hospital, London. Normal ranges established from specimens taken from the South West London Blood Transfusion Service donor specimens. It is important to compare all results with the reference ranges provided by the laboratories in which the tests have been conducted.

Serum ethanol concentration is the most accurate method used in estimation. Several other body fluids have been studied and are relatively highly correlated with serum ethanol concentrations. Urine can be used as an alternative and is commonly used in DWI cases. Urine and blood ethanol measures are subject to similar metabolic factors. Breath ethanol concentration using a hand-held electronic analyser (e.g. Alcometer) provides a rapid and less invasive measurement. Breath ethanol is highly correlated with serum ethanol, if the manufacturer's instructions are followed, including providing an adequate specimen of alveolar air, regular calibration of the analyser, and not taking measurements immediately after consuming alcohol or other chemicals, including cigarettes and some mouthwashes containing alcohol. The best method is to wash the mouth with water and then wait for 15 minutes before taking a measurement. Serum and breath ethanol concentrations are, however, markedly different in absolute terms. In the UK, the legal limit for driving is 35 µg/100 ml breath, equivalent to 80 mg/100 ml blood (blood–breath ratio is assumed to be 2300 : 1 in the UK). However, most handheld analysers convert breath measurements into serum ethanol equivalent concentrations.

Ethanol can also be measured in saliva and sweat. For saliva, ethanol dipsticks have been developed which have a correlation of 0.90–0.98 with serum and breath ethanol methods (Bates & Martin, 1997). As saliva tests become more widely available they may prove more cost-effective than buying a breath analyser (about £3 per test compared to an analyser costing about £650), particularly for practitioners who need to measure ethanol relatively infrequently.

Only about 0.1% of ethanol is excreted in sweat (compared with 0.7% excreted in breath, 0.3% in urine and over 99% metabolised by the liver). It is possible to measure ethanol in sweat using sweat

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patches or biosensors. These methods are, however, still under development and are probably more likely to find application in research studies than in the clinical setting at present.

Overall, most methods of ethanol measurement are useful in detecting recent alcohol intake, with the less invasive techniques providing a reliable, valid and more acceptable method of repeated analysis in the clinical setting. The sensitivity of ethanol measures as screening methods for alcohol misuse is low because of the short half-life of ethanol in the body. Further, the specificity is relatively low as a means of detecting AUDs, as approximately 90% of the UK population consume alcohol. Nevertheless, very high serum ethanol concentrations of 200 mg/100 ml or more – particularly in the morning or when there is little clinical evidence of intoxication – is indicative of a significant degree of alcohol dependence.

In terms of monitoring progress in the clinical setting, breath ethanol provides the most rapid and easily repeated measure, particularly to monitor abstinence during detoxification. In this context, breath ethanol should be monitored on a daily or random basis, and detoxification discontinued and the treatment plan re-formulated if a positive specimen is returned. It should be noted, however, that it may be hazardous to insist that severely alcohol-dependent individuals can only commence detoxification when no ethanol is detectable in their breath since they can develop severe withdrawal symptoms even with a high, but falling, serum ethanol concentration (relative withdrawal).

Liver enzymes

Three liver enzymes are commonly used in screening for AUDs: aspartate amino transferase (AST), alanine amino transferase (ALT), and gamma glutamyl transferase (GGT). Some laboratories do not routinely provide all three tests and it is sometimes necessary to request them specifically.

The amino transferases (AST, ALT) are found in many body tissues apart from the liver (including the heart, skeletal muscle, kidney, brain, erythrocytes and lungs), but it is the ability of alcohol to damage liver cells that provides their utility as a marker of excessive drinking. Early elevations of liver enzymes (including GGT) may be due to enzyme induction by alcohol. ALT is more specific for liver damage than AST, and hence is a more useful test of excessive drinking. There are many possible causes of liver disease other than alcohol, and a range of factors gives rise to increases in amino transferases (see Box 1). However, an AST : ALT ratio of >2 in a patient with liver disease diagnosed on clinical grounds is highly suggestive of alcohol as a cause (Marshall & Bangert, 1995).

The sensitivities of AST and ALT are relatively low for AUDs, typically between 30% and 50%. One recent study comparing the sensitivity and specificity of different biochemical screening tests in 502 medical patients found the sensitivities of AST and ALT to be 50% and 35%, respectively (Bell *et al*, 1994). Specificities are generally higher (80%–86% for AST and ALT).

GGT is a microsomal enzyme mainly found in the liver, although it is distributed widely in most organs except muscle. GGT adds little information to AST and alkaline phosphatase (ALP) in the diagnosis of liver disease, however it can help to locate the origin of elevated ALP to the liver. GGT is more sensitive to enzyme induction by alcohol than AST or ALT in excessive drinkers, but can also be elevated due to liver damage. False positive results can be due to enzyme-inducing drugs (e.g. anti-convulsants). Box 1 shows possible sources of false positives. Nevertheless, the sensitivity and specificity of GGT is typically higher than for AST and ALT. The sensitivity of GGT ranges between 50% and 70%, and the specificity between 75% and 85%. The upper limit of the normal range for GGT is typically higher for men than for women (at St George's Hospital, London the normal range for men is 0–60 u/l compared with 0–30 u/l for women). However, in patients attending an alcohol treatment clinic, it is not unusual to see GGT levels of 300 u/l or more in the absence of evidence of hepatocellular damage. The GGT level is moderately correlated with the quantity and frequency of heavy drinking.

In practice, of the three liver enzymes, GGT is the most useful, widely available test for the detection of AUDs. Where AST, ALT or GGT are elevated owing to alcohol misuse, they normally return to normal after 1–2 months of abstinence, although this is subject to individual variation and is dependent on the starting level. A higher initial level will take longer to return to normal, and the tests will take longer to return to normal where there is significant hepatocellular damage or cholestasis. However, it is safe to assume that the results of these tests only refer reliably to excessive drinking in the month prior to the tests. Finally, it is also important to note that liver enzymes can be affected by drug-induced liver damage, importantly in AUDs, including paracetamol overdose and disulfiram toxicity. The latter is relatively rare, with the number of adverse reactions including all types of reaction being 1 per 200–2000 treatment years (Wright *et al*, 1988; Enghusen-Poulsen *et al*, 1992). Usually there is evidence of gross liver impairment (hepatitis) with a distinct peak incidence at two months of treatment,

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but occasionally, isolated minor increases in amino transferases have been reported. It is, therefore, important to monitor liver function, particularly in the initial stages of disulfiram treatment.

Mean cell volume

Mean cell volume is commonly used as a marker for excessive drinking in screening. The precise mechanism for macrocytosis (increased corpuscular volume) in alcohol misuse is unclear, but is believed to be related to a toxic effect of alcohol on the bone marrow, leading to the release of immature and abnormally large cells. Sometimes in alcohol misusers, other evidence of bone marrow toxicity will be evident, with reduction in the number and function of granulocytes and macrophages as well as reduction in the number and function of platelets (thrombocytopaenia, or occasionally thrombocytosis) (Estruch, 1996) (low platelet count can occur in AUDs in the absence of significant liver disease). However, chronic excessive drinking is also associated with various vitamin deficiencies, notably vitamins B_{12} and folate, which in turn are associated with macrocytic anaemia. Thus, in practice, it is important to examine the full range of haematological results and request serum B_{12} and folate levels to exclude macrocytic anaemia as a cause of macrocytosis. Disorders that may lead to false positive MCV results are shown in Box 1.

The sensitivity of MCV is typically less than for GGT. Sensitivities of between 25% and 52% have been found, but specificity is typically 85–95%. MCV takes longer than liver enzymes to return to normal following abstinence owing to the half-life of red blood cells. As with liver enzymes, the speed of recovery depends on the initial starting level but can take between one and three months.

High-density lipoproteins

The relationship between alcohol consumption and high-density lipoproteins (HDL) is complex, but correlations between the two have been found (Skinner *et al*, 1985). The sensitivity and specificity of HDL is relatively low compared to other available markers, and it is therefore seldom used as a screening method.

Carbohydrate-deficient transferrin

Carbohydrate-deficient transferrin (CDT) is an isoform of transferrin and, in comparison to liver enzymes, appears to be relatively unaffected by liver disease. Early research with CDT suggested a high sensitivity and specificity in the detection of AUDs of 82% and 97%, respectively (Stibler, 1991). However, more recent studies have found lower sensitivity of between 40% and 70%. Specificity is typically high across a range of studies at 80–98%. It has also been suggested that CDT is more sensitive than GGT in detecting relapse in alcohol-dependent patients in treatment than as a screening method to detect AUDs in moderately heavy drinkers (Rosman *et al*, 1995; Mitchell *et al*, 1997; Schmidt *et al*, 1997).

The sensitivity of CDT in women is lower than in men, with some studies finding values as low as 44% (Anton & Moak, 1994). Specificity in women is, however, similar to that in men. It has been hypothesised that normal fluctuations in total transferrin throughout the menstrual cycle, and in pregnancy, and changes in transferrin in anaemia or liver disease may partly account for this. It has been found that the CDT : total transferrin ratio (%CDT) has a higher sensitivity and specificity than CDT alone, particularly in women and in those patients vulnerable to fluctuations in transferrin (Keating *et al*, 1998). For this reason %CDT (Axis Biochemicals) is currently the method of choice (Sorvajarvi *et al*, 1996; Keating *et al*, 1998; Viitala *et al*, 1998).

It has been reported that CDT increases and recovers more rapidly than GGT in response to a drinking binge, within one week of onset of heavy drinking, and recovery typically in 1–3 weeks, compared with 1–2 months with GGT (Stibler, 1991). As with GGT, there is evidence that CDT is moderately correlated with alcohol consumption.

At present, CDT is available only in a small number of laboratories in the UK, and is relatively expensive compared to other routinely available measures. If, as seems likely, CDT becomes more widely used, its cost and availability should improve. However, for the time being, the use of CDT is likely to be restricted to medico-legal applications – as an investigative method where other markers are positive but there is doubt as to the cause of the elevation – and potentially as a measure to detect relapse, particularly in patients who do not show raised GGT after heavy drinking.

Combinations of tests

So far we have examined the utility of individual biochemical tests in isolation from each other. In practice, such tests are most often used in combination, and in doing so, the sensitivity of the combined tests is greater than any individual test alone (Leigh & Skinner, 1988). This can be further improved by combining biochemical tests with interview, questionnaire or physical examination

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methods. Box 2 shows our recommended testing package.

Usually, the way in which combined tests are interpreted is by counting one or more positive tests as being indicative of a positive 'case'. However, it should also be noted that if multiple tests are positive, greater weight can be placed on the 'caseness'. Further, the higher the values are above the normal reference range, the greater the likelihood of caseness and the higher the likely level of drinking. As noted above, the specificity of a test typically increases with an increasing cut-off point.

Individual baselines

Given that the sensitivity of all the tests described here is somewhat lower than their specificity, they are more useful in monitoring treatment response and in the early detection of relapse in alcohol misusers who have abnormal results on entry to treatment, than in general screening. Even when a test is within the normal range following excessive drinking, it can show changes in response to abstinence and subsequent relapse. Thus, in treatment, it is useful to establish baseline measures at initial assessment from which to monitor subsequent progress. Indeed, some studies have shown that blood markers may increase in advance of a patient's self-reported relapse (Rosman *et al*, 1995). Often, patients are reluctant to report relapse for fear of losing face or 'disappointing' their therapist. Biochemical investigations can provide a way of helping the patient to look objectively at unpalatable truths.

Other disorders associated with alcohol dependence

Throughout this paper, it has been assumed that physical illnesses that give rise to biochemical and haematological abnormalities are a confounding factor in relation to their utility in screening for AUDs. This is true. However, the same tests can be valuable in the clinical identification and

Box 2. Recommended testing package

The following approach to investigations is recommended:

Initial assessment	Liver function tests (including ALT and/or AST, and GGT) Full blood count (including MCV) Serum B_{12} and folate (or red cell folate) Serum ethanol concentration (in medico-legal cases or cases with otherwise normal results consider CDT : total transferrin ratio)
During detoxification	Breath ethanol measurement *Frequency: daily or randomly*
Clinical follow-up	Liver function tests (including ALT and/or AST, and GGT) Full blood count (including MCV) Serum ethanol concentration (Supplemented in research studies with CDT : total transferrin ratio) *Frequency: monthly*
Monitoring abstinence in medico-legal cases	Liver function tests (including ALT and/or AST, and GGT) Full blood count (including MCV) Serum ethanol concentration *Frequency: monthly* Breath, saliva or urine (depending on the availability of trained personnel) *Frequency: random (approximately weekly)* (Supplemented, if necessary, with CDT : total transferrin ratio, monthly)

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management of physical complications of alcohol dependence. Many physical disorders are more common in alcohol dependence, for example, hepatitis and cirrhosis, nutritional deficiency, pancreatitis, diabetes and gastrointestinal haemorrhage, among many others (Dinan & O'Flynn, 1994; Edwards *et al*, 1997). Often, the addiction specialist will find him- or herself having an important role in the early diagnosis of serious physical pathology. On occasions, alcohol misusers are not treated or investigated with the same vigour as other patients, perhaps owing to negative attitudes towards AUDs from the medical profession (Farrell & David, 1988).

Often the diagnosis of an AUD will be made on the basis of a combination of findings, as noted above. The presence of physical stigmata typically associated with excessive drinking (e.g. spider naevi, rhinophyma, plethoric facies and pseudo-Cushing's syndrome), despite not being diagnostic in isolation, may add weight to the diagnosis in association with other evidence.

Another aspect of clinical assessment is the inclusion of urine screening for drugs, given that an increasing number of people presenting to treatment use a range of drugs including alcohol. Therefore, it is important for the addiction specialist to investigate patients with AUDs adequately (Edwards *et al*, 1997).

Conclusions

Biochemical and haematological tests can add important precision to the diagnosis and management of AUDs. The approaches recommended here should form an important part of routine clinical practice. Specialist addiction services should routinely conduct blood investigations as part of an initial comprehensive clinical assessment to obtain measures of the nature and severity of the AUD and associated clinical conditions. These investigations have an important role in enhancing patients' motivation to change their drinking behaviour. Such measures also provide a baseline from which to monitor clinical improvement and/or subsequent relapses.

Biochemical and haematological tests also have a key role to play in medico-legal and employee assistance cases, when the client's self-reporting may be especially unreliable. However, as no individual test can provide total certainty, it is important to be aware of the limitations of the methods currently at our disposal.

Further, there is a need to encourage greater use of investigations in screening in the primary care, general hospital and general psychiatric service settings, where AUDs are common but seldom detected. In doing so, a greater proportion of alcohol misusers can be identified and can be offered early interventions. While the search for more sensitive and specific markers needs to continue, it is important to bear in mind that existing measures, if used correctly and more extensively, could significantly improve the quality of diagnosis and management of AUDs.

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* Indicates key references for further reading

Multiple choice questions

1. In relation to the sensitivity and specificity of a test:
   a sensitivity refers to the ability of a test to identify true positives with few false negatives
   b if sensitivity is high but specificity is low, the test is effective in minimising false negatives, but poor in identifying true positives
   c sensitivity and specificity are usually positively correlated
   d specificity refers to the ability to identify true positives with few false positives
   e in detecting alcohol use disorders liver function tests have a high sensitivity and low specificity.

2. The following drugs can cause abnormalities of liver enzymes:
   a disulfiram
   b diazepam
   c paracetamol
   d lofepramine
   e amoxycillin.

3. The following are causes of raised mean cell volume:
   a iron deficiency anaemia
   b hypertension
   c pernicious anaemia
   d pregnancy
   e heavy smoking.

4. Which of the following tests usually remains elevated for four weeks or more after an episode of alcohol misuse?
   a aspartate amino transferase
   b carbohydrate deficient transferrin
   c white cell count
   d serum ethanol
   e gamma glutamyl transferase.

5. The following are characteristics of ethanol metabolism:
   a subject to zero order kinetics
   b peak level is achieved within three minutes following ingestion
   c it is mostly eliminated by liver metabolism.
   d ethanol is eliminated at the rate of about 10 units per hour
   e ethanol is typically not detectable 24 hours after last ingestion.

MCQ answers

1	2	3	4	5
a T	a T	a F	a T	a T
b T	b F	b F	b F	b F
c F	c T	c T	c T	c T
d T	d T	d T	d F	d F
e F	e F	e T	e T	e T

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