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Benefits and Problems of Routine Laboratory Investigations in Adult Psychiatric Admissions

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A survey of laboratory investigations in the management of 1007 non-geriatric admissions to a district general hospital adult psychiatric unit showed a wide variation in the number of tests performed, and in the abnormal proportion between test types. Despite a policy of screening on admission, 40% of admissions had no tests. Physical illness attributable to mental illness was common, but rarely serious and usually apparent clinically. Mental illness attributable to physical illness detected by laboratory tests was rare: five cases of thyroid disease in women with affective disorder, and two cases of chest infection with raised white cell count in sustained mania. The findings show that tests are frequently used in circumstances where the result is of no apparent value. Test use might be improved by restricting screening to thyroid function and laboratory urine analysis, each in women. There are particular indications for white cell count in sustained or unexplained relapse of mental illness, and for syphilis serology when disinhibition may have exposed the patient to infection.

Mental and physical illness coexist by a number of mechanisms. Firstly, diseases cluster more than would be expected by chance (Hinkle & Wolff, 1957; Eastwood & Trevelyan, 1972). Maguire & Granville-Grossman (1968) showed 17% of 200 psychiatric admissions to have incidental physical morbidity, half of whom required transfer to a medical ward. Secondly, mental illness can have physical effects through abnormal diet or behaviour or the mechanisms of psychoimmunology (*Lancet*, 1987). Thirdly, physical illness or its treatment can have mental effects (Lloyd, 1977; Hall *et al*, 1981). Most studies of medical in-patients show a psychiatric morbidity of around 25% (*Lancet*, 1979). Fourthly, psychotropic drugs have adverse or toxic side-effects, whether used in treatment, abuse, self-harm, or by accident.

These mechanisms influence the way the laboratory is used. Tests may be used on apparently physically well patients for screening, on those with a suspected physical illness for diagnosis, and on those with a known physical illness for management. The number of tests used to investigate a disease can vary 20-fold between hospitals (Ashley *et al*, 1972; Daniels & Schroeder, 1977), and teaching and research can take investigation beyond clinical need (Griner & Glaser, 1982; Reuben, 1984). The act of testing can be therapeutic (Sox *et al*, 1981), and the laboratory may be used to generate income (Schroeder & Showstack, 1978; Moloney & Rogers, 1979). Certain criteria make tests useful: prevalence of disease must be adequate, tests must have appropriate sensitivity and specificity, and benefit must be expected from an abnormal result.

The mentally ill pose special problems. History taking, examination, and practical procedures may be difficult, and psychiatrists may be less familiar with indications and uses of tests and their interpretation. Definitive studies of the relationship of the laboratory to clinical practice exist in general medicine (Hampton *et al*, 1975; Hecker, 1975), surgery (Forrest *et al*, 1981; Kaplan *et al*, 1985), paediatrics (Leonard *et al*, 1975), geriatrics (Hodkinson, 1981), and primary care (Mills & Reilly, 1983; Hartley *et al*, 1984; Forrest *et al*, 1987), but psychiatry has received less attention.

We have examined the management of admissions to our district general hospital adult psychiatric unit. Radiology and thyroid tests are reported separately (White & Barraclough, 1986, 1988). We aim here to establish the pattern and benefits of laboratory use.

Method

The Department of Psychiatry of the Royal South Hants Hospital, Southamptom, provides a service for 200 000 people aged 16–65 years in a catchment area of 300 000. Adult psychiatry accounts for 32% of the beds and 11% of admissions; children under 16 and the elderly are treated elsewhere.

We examined the case notes of psychiatric patients admitted between 1 January 1983 and 30 April 1984, covering about 1000 admissions, and recorded the laboratory results obtained in clinical management. Routine haematology and biochemistry tests are requested by the doctor in charge of the admission at the time of clerking, and further tests are requested after review, usually at the ward round. If the test had been repeated during an admission, the first result was taken. Results falling outside the

reference range given by the laboratory were termed abnormal, and the clinical findings documented in the notes at the time were recorded. Clinical findings were termed positive if a pathological finding had been recorded in any part of the medical history or physical examination.

Haematological tests of haemoglobin, mean corpuscular volume, and total white cell count are measured by automated counter, which also computes red cell indices. The laboratory reference range is taken from a standard text, Dacie & Lewis (1975), which itself takes a consensus of several surveys. Erythrocyte sedimentation rate was not recorded, as the reference range is unclear, and the test is not useful for screening (Sox & Liang, 1986). Chemical pathology is performed on 6-channel and 13-channel autoanalysers. The number and type of tests performed by these machines may vary from day to day. Other tests are undertaken singly. The reference ranges are those used by the laboratory for healthy adults. Psychiatric diagnoses were taken from the Southampton psychiatric case register.

Results

Demography

The 1007 admissions were accounted for by 719 patients, 182 having one or more readmissions during the period. Compared with the catchment population, the admissions comprised more men over and fewer under 25, and more women over and fewer under 35. Only 19 admissions were aged 65 or over (Table I).

Investigation rates

The 1843 requests produced 8663 results, the difference attributable to the use of autoanalysers. Forty per cent of admissions had no results, a rate similar to that in other admission screening programmes in psychiatry (Bannister *et al*, 1987). A further 40% had one haematology and one biochemistry automated analysis each, accounting for 90% of all results; the remaining 20% had single investigations alone or in addition.

A mean of 14 results were obtained from each of the 60% of admissions investigated, a rate similar to that in Whitehead & Wootton's (1974) study in general medicine.

The rate of investigation was related to diagnosis ($\chi^2 = 24.5$, d.f. = 6, $P < 0.001$); the diagnoses with most and least investigations, affective and personality disorder respectively, contributed most of the variance. When these two diagnoses were eliminated from the calculation, the difference between the remaining diagnoses was not significant.

Investigation varied little with age until increasing for patients aged over 55 years (Table I).

Abnormality rates

Of the 8663 results, 887 (10.2%) were reported to be abnormal. Of the 610 admissions tested, 374 (61%) had at least one abnormal result. The modal number of abnormal results was two, which is expected with multiple tests, even in the healthy (Sackett, 1973). The percentage abnormal was associated with diagnosis ($\chi^2 = 44.8$, d.f. = 6 $P < 0.001$); the diagnoses with most and least percentage abnormal, alcoholism and schizophrenia respectively, contributed most. When these two diagnoses were eliminated from the calculation, the difference was not significant. The percentage abnormal varied little with age, until increasing for patients aged over 65 years (Table I). Our rate of 10.2% of tests giving abnormal results is lower than that in other studies in psychiatry – Thomas (1979) found 13% of 2895 results abnormal, and Ferguson & Dudleston (1986) 17% of 2753 abnormal. Positive clinical findings accompanied fewest abnormal test results in the 25–34-year-olds and most in the 55–64-year-olds (Table I).

Important results

Described below are the tests that yielded the 73 abnormal results making important contributions to diagnosis or management (compare with Table II).

Thyroid function tests

The 300 thyroid function tests were accounted for by 259 patients. Ten results were abnormal, accounted for by

TABLE I
Age and sex distribution of admissions, and test results

Age: years	*Population*		*Admissions*			*No. of tests*			
	% male	*% female*	*% male (n)*	*% female (n)*	*% having any test (n)*	*Total*	*Average per admission*	*Abnormal results (n)*	*Clinical findings positive (% of abnormal results)*
15–24	25	24	11 (58)	13 (66)	62 (76)	957	7.7	7 (67)	46
25–34	24	23	26 (128)	16 (81)	53 (109)	1525	7.3	9 (135)	42
35–44	18	19	28 (137)	23 (116)	53 (133)	1835	7.2	11 (209)	56
45–54	16	18	22 (113)	22 (110)	64 (42)	2147	9.6	10 (221)	61
55–64	16	18	13 (68)	22 (111)	75 (133)	1941	10.8	11 (218)	64
>65			2 (8)	3 (11)	79 (15)	258	13.6	14 (37)	63

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TABLE II

Test	*Total no. of tests*	*No. abnormally low (%)*	*No. abnormally high (%)*	*Total no. abnormal n (%)*	*Clinical findings positive (% of abnormal results)*
Haematology					
Haemoglobin[1]	504	20 (4)	1 (0)	21 (4)	45
Mean corpuscular volume[1]	503	10 (2)	40 (8)	50 (8)	66
White cell count[1]	504	5 (1)	72 (14)	77 (15)	58
Blood film	40	- -	- -	18 (45)	67
Vitamin B_{12}	22	1 (5)	- -	1 (5)	0
Folate	20	1 (5)	- -	1 (5)	0
Chemical pathology					
Sodium[1]	517	17 (3)	6 (1)	23 (5)	65
Potassium[1]	514	44 (9)	7 (1)	51 (10)	69
Chloride[1]	481	17 (4)	35 (7)	52 (11)	37
Bicarbonate[1]	507	115 (23)	6 (1)	121 (24)	44
Creatinine[1]	517	- -	15 (3)	15 (3)	80
Urea[1]	523	- -	91 (17)	91 (17)	41
Calcium total[1]	462	10 (2)	36 (8)	46 (10)	47
adjusted	462	7 (2)	5 (1)	12 (3)	23
Inorganic phosphate[1]	444	69 (16)	0 -	69 (16)	42
Total protein[1]	457	5 (1)	35 (8)	40 (9)	45
Albumin[1]	455	1	5 (1)	6 (1)	67
Bilirubin[1]	465	- -	34 (7)	34 (7)	59
Alkaline phosphatase[1]	462	- -	31 (7)	31 (7)	81
Aspartate transaminase[1]	454	- -	66 (15)	66 (15)	77
Glutamyl transpeptidase	54	- -	22 (41)	22 (41)	91
Glucose	136	0 -	13 (10)	13 (10)	77
Syphilis serology	136	- -	- -	5 (4)	60
Thyroid function tests	300	5 (2)	5 (2)	10 (3)	80
Autoimmune screen	24	- -	- -	9 (38)	100
Porphyrins	6	- -	- -	0 -	0

1. Components of autoanalysers.

nine patients. Two of the nine settled spontaneously, and were probably due to the euthyroid sick syndrome, a transient abnormality of thyroid hormone during non-thyroid illness, which seems to be under-recognised (Gooch *et al*, 1982). Five of the nine were known cases, and the remaining two were new diagnoses. All seven cases were women with an affective disorder, four of whom had a past history and two of whom had a family history of thyroid disease. No patients giving abnormal results were taking lithium. Thyroid disease was thought to have precipitated the mental illness in five patients, including the two newly diagnosed with thyroid disorder. They are described elsewhere (White & Barraclough, 1988).

Syphilis serology

One patient with active and one with treated syphilis acquired their infection while disinhibited through mental illness. Three other patients had positive results from treated infection. Psychiatric patients appear at risk of infection because of their mental illness, rather than vice versa. Selective screening of those exposed to risk is indicated (Hart, 1986).

Urinalysis in women

Of 97 biochemical and bacteriological tests of urine in women and 59 in men, 15 in women showed infection. Five of the 15 were asymptomatic, their infection detected only by screening.

White cell count

Seventy were raised and five were low. Many raised results were accounted for by smoking (Howell, 1970) or lithium treatment (Murphy *et al*, 1971). Underlying pathology may also be unmasked; 12 raised counts were associated with chest infection, of which two had intractable mania which only resolved when the chest infection was treated. Selective screening may be warranted when clinical signs are present or the psychiatric illness becomes protracted.

Glucose

The 13 abnormal results included three new diagnoses of diabetes of mature onset; each was suspected from clinical findings, and the test was necessary for diagnosis. In ten known cases the test was necessary for management.

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Mean corpuscular volume

Fifty results were abnormal, 10 microcytic, and 40 macrocytic. Forty-eight of the 50 were suspected from alcohol abuse or other clinical findings, or from low levels of haemoglobin. The remaining two were not clinically important.

Blood film examination

All 18 abnormal patients had positive clinical findings (12 cases), abnormal blood count (13), or both (7). Screening appears unnecessary, but the usual medical indications are shown to be worthwhile (Hamblin, 1983).

Liver function tests

Of 1435 liver function tests, 153 were abnormal; 117 were associated with positive clinical findings, in 79 with alcohol abuse. As almost all newly admitted patients receive psychotropic drugs, the abnormal results can be attributed to alcohol, and can be expected. Only raised aspartate transaminase levels were significantly associated with alcoholism ($\chi^2 = 71$, d.f. $= 6$, $P < 0.001$). All bilirubin and alkaline phosphatase estimations repeated at follow-up were normal, except for one patient newly diagnosed with Gilbert's syndrome. Of 41 repeated aspartate transaminase tests, 12 of the 16 patients who remained abnormal were known to have continued to abuse alcohol.

In summary, clinical findings are so regularly present that use of liver function tests for screening or diagnosis of alcoholism is unwarranted. The laboratory may occasionally help management (Latchman, 1986; Skinner *et al*, 1986).

Potassium

Forty-four results were low and seven raised. There was an unexplained association between a low result and a psychiatric diagnosis of personality disorder ($\chi^2 = 14.4$, d.f. $= 6$, $P < 0.001$). Low results may arise in the specimen stored warm, when potassium passes into red cells with glucose, or in the patient with chronic hyperventilation causing a respiratory alkalosis and kaliuresis. Screening is not necessary as most abnormal results are not clinically important.

Bicarbonate

One hundred and fifteen were low and six raised. Low results may arise from respiratory alkalosis in the chronic hyperventilation syndrome or from ketosis of starvation. Screening is not necessary as most abnormal results are not clinically important.

Urea

Ninety-one were raised, with a significant association with a psychiatric diagnosis of organic disorder ($\chi^2 = 12.7$, d.f. $= 6$, $P < 0.001$). Mental illness, particularly organic psychosis, may contribute through dehydration. Only seven patients also had raised creatinine levels. No renal failure or unsuspected pathology was detected. Screening is unnecessary.

Phosphate

Sixty-nine were low. Hypophosphataemia may arise from menstruation, drugs such as barbiturates, antacids or oral contraceptives, or eating after starvation (Ritz, 1982; Cumming *et al*, 1987). Screening is unnecessary, but the test is indicated when sudden resumption of eating accompanies psychiatric treatment.

Discussion

The role of tests

A test has a screening role when an abnormal result is not expected, and a diagnostic or management role when the result is expected from clinical findings. Ideally, tests of high sensitivity are used for screening, and of high specificity for diagnosis. Sensitivity and specificity can be varied by having a choice of reference ranges which allow the same test to be used for different roles.

Criteria for abnormality

Reference ranges are conventionally two standard deviations either side of the mean, covering 95% of results, as most variables have a normal or log-normal distribution which enables use of parametric statistics. Many of the remaining 5% fall just outside the reference range and are false positives which are abnormal only statistically (Fig. 1).

Problems arise because of rigid interpretation of the reference range by clinicians who are remote from the laboratory sciences. A result tends to be noted as abnormal irrespective of its magnitude, context, and meaning, and further investigation is instigated. A wider reference range, say three standard deviations, would encompass 99.7% of values and reduce the number of false positives. The use of alternative reference ranges or 'action limits' would involve the clinician in selecting the appropriate cut-off for his particular situation. However, action limits have disadvantages; for example, the laboratory must know the distribution of results more precisely, and true positives may be missed.

A choice of reference range is not routinely available, and results are interpreted here as they are in practice, as normal or abnormal. Not all abnormal results are important, as 5% of these are to be expected; in addition, many results have a bias to their distribution that invalidates the reference range supplied, as Fig. 1 demonstrates. Tests can be considered according to whether the abnormal exceed this expected 5%.

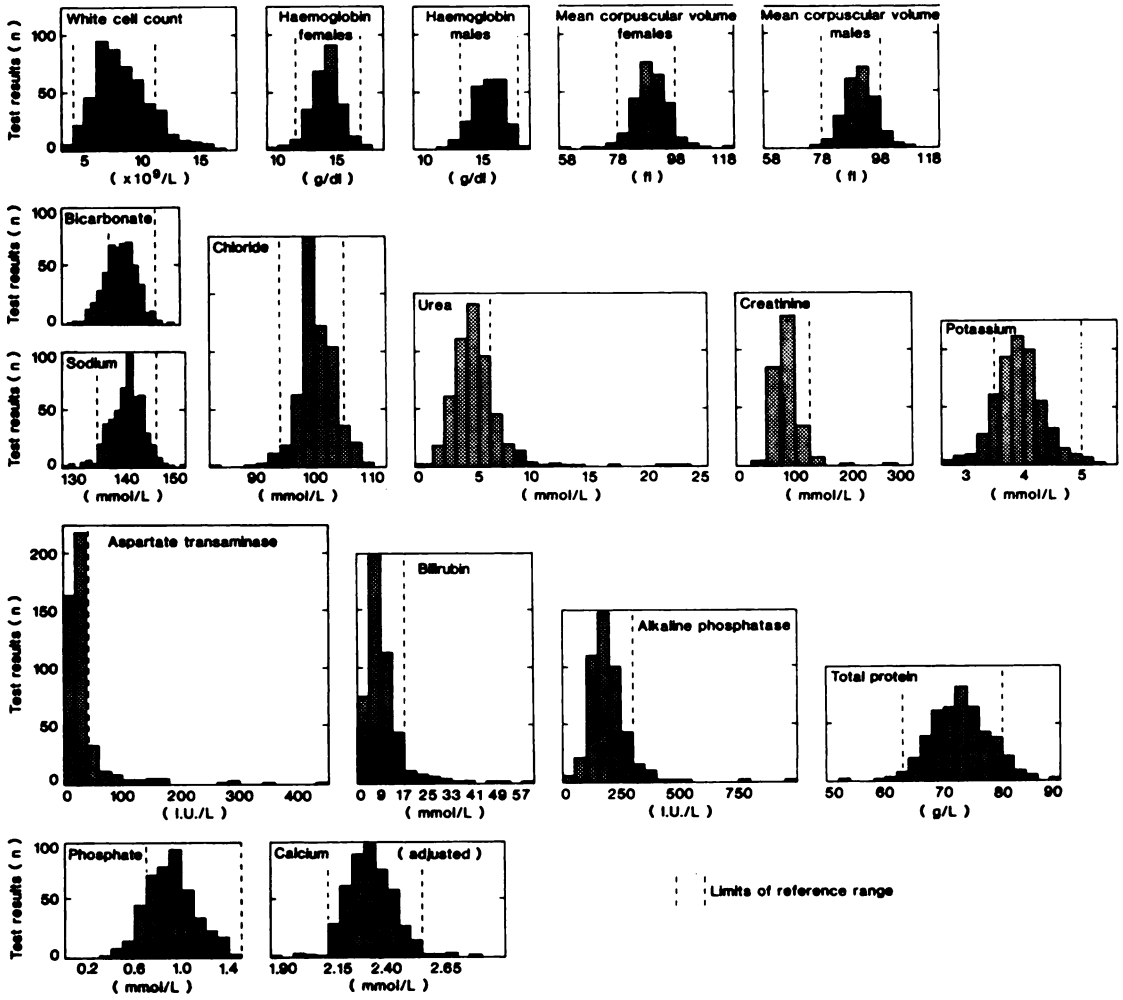

FIG. 1 Distribution of results for individual tests.

(a) Tests with only the expected rate abnormal. Tests with less than 5% abnormal may be necessary for management, as with creatinine in lithium treatment, or for diagnosis, as with thyroid function and syphilis serology. Tests are unnecessary where no important pathology or cause of mental illness is detected, as here with haemoglobin, vitamin B_{12}, folate, sodium, calcium, and porphyrins.

(b) Tests with anticipated increase in percentage abnormal. Some results are necessary for diagnosis or management even when expected from clinical findings, as with glucose or autoantibodies. Others are so predictably abnormal that they are unnecessary, as with mean corpuscular volume, blood film, or liver function tests.

(c) Tests with unanticipated increase in percentage abnormal. Where the excess beyond 5% is not expected from clinical findings, the role of the test continues to be screening. A few results have clinical importance, as with urinalysis for women. In most cases the excess is likely to be due to spurious effects on the distribution of results in psychiatric patients, as with protein, potassium, chloride, bicarbonate, urea, and phosphate (Fig. 1).

Sources of error

Psychiatric patients may differ from other populations in effects of diagnosis, age, sex, season, activity, posture, diet, and use of drugs and alcohol. A fundamental factor such as mobility may influence

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levels of plasma proteins and protein-bound anions as psychiatric patients, who are not bed bound, have higher levels (Fig. 1).

Individual patients may have results influenced by hyperventilation, pregnancy, or menstruation. Individual specimens may be influenced by haemostasis during sampling, by delay, contamination, agitation or temperature during transport, or analytical errors. Therefore excess abnormal results may be either truly pathological or false positive artefacts.

Relationship between physical and mental illness

Mental illness causing physical illness accounts for many abnormal results. Deliberate self-harm, usually overdose, can require medical treatment. Abuse of drugs or alcohol influences mean corpuscular volume and liver function. Dietary neglect disturbs fluid and electrolytes. Bizarre or disinhibited behaviour can lead to any abnormality; two patients contracted syphilis. Transiently abnormal results related to disturbed behaviour and emotions are also seen, here with thyroid function in two patients and with glucose in another.

Physical illness causing mental illness is rare but important. In five cases thyroid disease appeared to cause mental illness. Chest infection apparently perpetuated two cases of mania and possibly ten other episodes of mental illness. Other studies vary widely; Willett & King (1977) found no physical cause in 636 admissions, Herridge (1970) found 21% in 209 admissions, and Hall *et al* (1978) 49% in 100 severely ill compulsory admissions in the USA.

Mental and physical illness may be unrelated, either as false positives or as incidental morbidity.

Costs

Good practice involves the correct level of investigation; too much is bad, as well as too little, as resources are diverted away from other needs, known in health economics as 'opportunity cost' (Fleming & Zilva, 1981; Mooney & Drummond, 1982; Thurow, 1985). What has been the actual cost of detecting the 73 clinically important findings here? Available methods of costing remain very artificial, and the cost is apparently small. Relying chiefly on Tarbit's (1986) methods gives £7499.33 for the 8663 investigations.

Reservations should be borne in mind about this figure. Firstly, Tarbit notes some indirect costs are not included. Secondly, testing may affect management in ways that elude measurement, such as prolonging hospital stay. Thirdly, testing has various non-financial disadvantages: unsolicited results pose problems of confidentiality and ethics (Knight, 1986). If some are false positives, the problems are compounded (Bradwell *et al*, 1974).

Benefits

Tests give benefits other than the detection of disease. Patients may be reassured by investigation (Sox *et al*, 1981), and doctors may feel more confident with investigations rather than a history and examination, particularly if severe mental illness impairs co-operation, although this will depend on the experience and skills of the individual. Results may also have a role in clinical teaching.

Further inquiries

The opposing pressures of budgetary restraint on the one hand, and litigation on the other, may require justification of practice by clinical audit. The effectiveness of audit has been established in medicine (Cohen *et al*, 1982; Everett *et al*, 1983; Fowkes, 1985; Fowkes *et al*, 1986) but not in psychiatry.

This study makes the initial step of an audit of current practice, but a prospective survey is desirable. In psychiatry the distribution of results and reference

TABLE III

Recommendations for routine use of the laboratory in in-patient adult psychiatry

Test	*Indications*	*Comment*
Thyroid function tests	Women with affective disorder. Past or family history of thyroid disease	In all cases delay testing until or repeat in the third week after admission to avoid transitory rise of euthyroid sick syndrome
Laboratory 'urinalysis'	Women	Even when asymptomatic
White cell count	Unexplained unremitting episode of psychiatric illness	
Syphilis serology	Exposure to risk of infection	
Other investigations		Use for medical diagnosis or management as opposed to screening

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ranges may be unique, and could be established by testing every patient admitted, a recognised research strategy (Hecker, 1975; Hampton, 1983; Reuben, 1984).

Conclusions

This survey does not support the extent of investigation commonly seen in adult psychiatry: the findings justify only those tests in Table III. Others may be indicated when physical treatments require management. Use of these guidelines would eliminate expense and risk without sacrificing detection.

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