

Economic and laboratory considerations in screening for vitamin B₁₂ deficiency in psychiatric practice

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SYNOPSIS Two alternative methods for detecting vitamin B₁₂ deficiency in a psychiatric population have been compared: the 'direct' approach by microbiological assay of serum vitamin B₁₂ levels in all patients, and the 'indirect' approach where all patients are first screened for antigastric parietal cell antibodies and thereafter all positive reactors and other 'high-risk' patients have serum vitamin B₁₂ assayed. The indirect approach was found to be cheaper.

There is increasing evidence that vitamin B₁₂ deficiency is important in the causation of various psychiatric syndromes (Rafaelsen and Schou, 1959; Edwin, Holten, Norum, Schrupf, and Skaug, 1965). This is a treatable form of mental illness, especially in its initial stages; consequently, early diagnosis is of great importance. The diagnosis will normally be considered when there is haematological or organic neurological evidence of this deficiency, but it is much more difficult where psychiatric symptoms precede other manifestations (Fraser, 1960; Strachan and Henderson, 1965). Such occult vitamin B₁₂ deficiency was found in 0.88% of patients referred to the psychiatric services of the North-Eastern (Scotland) Regional Hospital Board (Henderson, Strachan, Beck, Dawson, and Daniel, 1966). That study indicated that the Addisonian state was the most common cause of occult vitamin B₁₂ deficiency in psychiatric practice in north-east Scotland. In our experience, a reliable screening procedure for detecting all forms of occult vitamin B₁₂ deficiency has been: (1) serum antigastric parietal cell antibody test on all patients, and in addition, (2) serum vitamin B₁₂ assay in the 'high risk' group of patients, *ie*, those with antigastric parietal cell antibody, those over 60 years of age, and those with any history suggesting the possibility of non-Addisonian vitamin B₁₂ deficiency (Henderson, Strachan, Beck, and Dawson, 1967). This procedure we have called the 'indirect' method of screening for vitamin B₁₂ deficiency. The 'direct' method of

screening is the assay of serum vitamin B₁₂ level in all psychiatric patients (Hansen, Rafaelsen, and Rodbrø, 1966).

The population of psychiatric patients at risk is very large and consequently it is important to determine which clinically acceptable screening approach is the more economical. This paper considers the costs of the relevant tests in our hands.

LABORATORY METHODS

ANTIGASTRIC PARIETAL CELL ANTIBODY TEST Undiluted patient's serum was tested for antibodies to the cytoplasm of the gastric parietal cells with the indirect immunofluorescence technique described by Williams, Scott, Beck, and Blair (1966), with the important modification that sera were applied with a platinum loop that was cleaned by flaming between specimens. The fluorescein-conjugated antihuman immunoglobulin serum required for this test is available commercially. In our experience the most economical batch size is 50 specimens. The test requires a supply of fresh normal human gastric mucosa every fortnight; this can usually be obtained in a general hospital from operation specimens. It should be noted that with this procedure glassware need not be cleaned.

SERUM VITAMIN B₁₂ ASSAY We have used the *Lactobacillus leichmannii* microbiological assay (Spray, 1955) with only minor modifications (Henderson *et al*, 1966). Because of the variability inherent in microbiological assays, the whole process is repeated on the same day and the results are accepted provided there is no undue variation. We find, in a small laboratory, that the most manageable batch size is 25 specimens. It should be noted that a

great deal of cleaning and autoclaving of glassware is necessary.

The two tests are compared in Table I.

TABLE I
COMPARISON OF ANTIGASTRIC PARIETAL CELL ANTIBODY TEST AND SERUM VITAMIN B₁₂ ASSAY¹

	<i>Antigastric Parietal Cell Antibody Test</i>	<i>Serum Vitamin B₁₂ Assay</i>
Nature of test	Serological	Micro-biological
Need for sterility (containers, etc)	None	Essential
Capital cost (initial, non-recurring expenditure)	£350 (fluorescence microscope and shaking machine)	£200 (sensitive absorptiometer)
Interval to reporting	< 1 day	> 2 days
Reproducibility	Good	Variable
Number of samples one technician can deal with each week	250 to 300	100

¹Both tests were performed under optimum conditions.

COSTS OF LABORATORY TESTS

The assessment of the cost of any laboratory investigation has previously been found to be extremely complex (Ministry of Health, 1963). No attempt has been made in the present paper to deduce the absolute cost of the antigastric parietal cell antibody test or of assay of serum vitamin B₁₂ levels. The ordinary laboratory overheads, and the procedures common to both tests, namely, the separation of serum, the clerical work of issuing reports, and the time spent in liaison with the wards, have not been considered. The costs of these two tests have been compared only in so far as they differ. In making this estimate, we have assumed that the tests will be performed in an established clinical pathology laboratory by appropriately trained staff and that, whenever possible, commercially available reagents will be used. The cost of screening tests for detection of occult vitamin B₁₂ deficiency can be considered in terms of working time or money. (For the cost in terms of money see Appendix.)

In our experience (Table II), the total working time required for serum vitamin B₁₂ assays is considerably greater than that for antigastric parietal cell antibody tests, but relatively more graduate time is required in the latter.

COST OF SCREENING PSYCHIATRIC PATIENTS

The relative costs of the direct and indirect methods for screening can be calculated either in terms of working time or cost of labour and chemicals from the estimate deduced for antigastric parietal cell

TABLE II
RELATIVE WORKING TIMES FOR TESTING 100 BLOOD SAMPLES
Working Time

	<i>Antigastric Parietal Cell Antibody Test</i>	<i>Serum Vitamin B₁₂ Assay</i>
No. of batches of tests	2	8 (4 batches of samples in duplicate)
Time taken by:		
Graduate (reading and/or checking)	3 hours 20 minutes	1 hour 20 minutes
Technician (preparation and reading)	9 hours 50 minutes	32 hours
Attendant (washing and sterilizing)	—	10 hours
Total work time for 100 samples	13 hours 10 minutes	43 hours 20 minutes
Average work time for each sample	7.9 minutes	26.0 minutes

antibody test and the vitamin B₁₂ assay (see Appendix).

Thus if 100 patients are to be screened and of these, *x* are 'low risk' patients, then the number of 'high risk' patients will be (100 - *x*). If *n*% of the 'low risk' patients are positive in the antigastric parietal cell antibody test and if the cost of each test is *A* and of each serum vitamin B₁₂ assay is *B* then

$$\begin{aligned} \text{cost of 'direct' approach} &= 100B \\ \text{and cost of 'indirect' approach} &= \end{aligned}$$

$$100A + \left[100 - \frac{(100 - n)x}{100} \right] B.$$

The indirect approach will be cheaper when

$$100A + \left[100 - \frac{(100 - n)x}{100} \right] B < 100B$$

$$\text{that is, when } x > \left[\frac{10^4}{(100 - n)} \right] \frac{A}{B}.$$

In our recent experience (see below), *n* has been low (< 5%) therefore

$$(100 - n) \longrightarrow 100.$$

With this approximation, the indirect approach will be cheaper when

$$x > \left[\frac{A}{B} \right] 100.$$

In terms of work time, *A* = 7.9 minutes and *B* = 26.0 minutes, therefore the indirect approach will be more economical when less than 70% of the patients are 'high risk'. When, however, working costs (British) are compared, *A* = 3s 1d and *B* = 5s 10d (or *B* is almost twice as expensive as *A*), so that the indirect approach will be cheaper in monetary terms when less than 47% of the patients are 'high risk'.

There are considerable regional variations in the prevalence of gastrointestinal disease, in fashions in gastrointestinal surgery, and possibly also in age distribution of patients with psychiatric disease. It is, therefore, not possible to predict the percentage of 'high risk' patients in the population served by any psychiatric service. So long as this is less than 47% the indirect screening procedure will be more economical. (An example of costing is given in the Appendix.)

DISCUSSION

In the population we studied, it has been shown that, on economic grounds, occult vitamin B₁₂ deficiency in psychiatric patients can be most conveniently diagnosed by screening with the anti-gastric parietal cell antibody test with vitamin B₁₂ assays in positive reactors and 'high risk' patients. We have previously shown that this approach is preferable on clinical grounds (Henderson *et al*, 1966; 1967). The difficulty in costing laboratory procedures is already well known. We have not solved this problem for the tests used in screening for vitamin B₁₂ deficiency. Instead, we have compared the time taken to perform these tests and deduced their relative costs. When radioisotope assays for serum vitamin B₁₂ become more generally established, with their increased reliability over microbiological assay (Spray, 1967), and their probable cheaper running costs (Matthews, Gunasegaram, and Linnell, 1967), the matter will have to be reconsidered. It is likely, however, to be some time before all laboratories are able to supply a radioisotope service, and until then, our findings will continue to be relevant.

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Appendix

MONETARY COSTS

Calculation of cost in terms of money (Table III) is based on the current salary scales in Britain. With the

TABLE III
 RELATIVE COSTS OF TESTING 100 BLOOD SAMPLES

	<i>Antigastric Parietal Cell Antibody Test</i>	<i>Serum Vitamin B₁₂ Assay</i>
Number of batches	2	8 (4 batches of samples in duplicate)
Salaries ¹		
Graduate	£5 15s 10d	£2 6s 4d
Technician	£5 13s 1d	£18 8s 0d
Attendant	—	£ 2 3s 4d
Materials		
Chemicals	£3 10s 0d	£ 4 6s 0d
Glassware	6s 9d	£ 1 16s 0d
Total cost for 100 samples	£15 5s 8d	£28 19s 8d
Average cost for one sample	3s 1d	5s 10d

¹It is assumed that (a) the graduate is a NHS consultant who works 40 hours per week for 46 weeks per year (the rate is £1 14s 9d per hour at the lower end of the scale), (b) the technician is a NHS senior technician I who works 38 hours per week for 47 weeks per year (the rate is 11s 1½d at the lower end of the scale), and (c) the laboratory attendant is paid 4s 4d per hour.

assumption that the graduate pathologist is a National Health Service consultant and the technician is a National Health Service senior technician I, the cost of labour of the anti-gastric parietal cell antibody test is approximately half that of the vitamin B₁₂ assays. The cost of reagents and replacement of breakages (mainly pipettes damaged during autoclaving) is also shown. On these grounds we estimate that in our laboratories the cost of performing an indirect immunofluorescence test for anti-gastric parietal cell antibody on each serum sample is 3s 1d whereas the corresponding cost of the assay for serum vitamin B₁₂ level is 5s 10d. We have not included any estimate of the time cost to collect gastric mucosa for the anti-gastric parietal cell antibody test, since this will obviously depend on local conditions.

AN EXAMPLE OF COSTING

These calculations can be illustrated by a hypothetical costing based on our recent experience in a study of all patients attending the psychiatric services of the north-east of Scotland over an eight-month period (Henderson

TABLE IV
 HYPOTHETICAL RELATIVE COSTING OF TWO ALTERNATIVE
 APPROACHES TO SCREENING OF 1,012 PSYCHIATRIC
 PATIENTS¹

Approach	Relative Cost	
	Money	Working-time (hr)
Direct	£295 3s 4d	438.5
Indirect	£205 5s 4d	286.7

¹Based on findings of Henderson *et al* (1966).

et al, 1966). There were 1,012 patients in this group; subsequent analysis has shown that 233 were more than 60 years of age and 91 of those less than 60 had a history of gastrointestinal symptoms, abdominal operations or inadequate diet. The 'high risk' group in Aberdeen was thus 324 or 32% of the population studied; 4.4% of the 'low risk' patients had a positive result in the antigastric parietal cell antibody test. The relative costs of the direct and indirect approaches are shown in Table IV; there is no doubt that in this population the indirect approach would have been considerably cheaper.