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, Schrumpf, 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, i.e., 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 Rodbro, 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

<table>
<thead>
<tr>
<th>Nature of test</th>
<th>Antigastric Parietal Cell Antibody Test</th>
<th>Serum Vitamin B₁₂ Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for sterility (containers, etc)</td>
<td>Serological</td>
<td>Essential</td>
</tr>
<tr>
<td>Capital cost (initial, non-recurring expenditure)</td>
<td>£350 (fluorescence microscope and shaking machine)</td>
<td>£200 (sensitive absorptiometer)</td>
</tr>
<tr>
<td>Interval to reporting</td>
<td>&lt; 1 day</td>
<td>&gt; 2 days</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>Good</td>
<td>Variable</td>
</tr>
<tr>
<td>Number of samples one technician can deal with each week</td>
<td>250 to 300</td>
<td>100</td>
</tr>
</tbody>
</table>

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 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

\[
\text{cost of 'direct' approach} = 100A + \left[ 100 - \frac{(100 - n)x}{100} \right] B.
\]

The indirect approach will be cheaper when

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

that is, when \( x > \frac{10^4}{(100 - n)} \frac{A}{B} \).

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

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

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'.
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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 antigastric 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.

We wish to thank Professors A. R. Currie, H. W. Fullerton, and W. M. Millar for their constructive advice on the preparation of this paper.

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REFERENCES


**TABLE IV**

<table>
<thead>
<tr>
<th>Approach</th>
<th>Money</th>
<th>Working-time (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td>£295 3s 4d</td>
<td>438.5</td>
</tr>
<tr>
<td>Indirect</td>
<td>£205 5s 4d</td>
<td>286.7</td>
</tr>
</tbody>
</table>

HYPOTHETICAL RELATIVE COSTING OF TWO ALTERNATIVE APPROACHES TO SCREENING OF 1,012 PSYCHIATRIC PATIENTS

<table>
<thead>
<tr>
<th>Approach</th>
<th>Relative Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td></td>
</tr>
<tr>
<td>Indirect</td>
<td></td>
</tr>
</tbody>
</table>

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.

Based on findings of Henderson et al (1966).
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