Vitamin B12 is given intramuscularly in the UK despite the fact that oral vitamin B12 in sufficiently large doses is equally effective. Historically, this passive absorption mechanism provided the first treatment for pernicious anaemia. In the absence of an intact ileum or intrinsic factor, 1.2% of an oral dose of vitamin B12 will pass across the small bowel. The dose absorption ratio is remarkably constant in an oral dose range from 1 to 100 000 μg of hydroxocobalamin and adequate levels of serum vitamin B12 have resulted using oral doses above 500 μg daily. Reflecting this, most vitamin B12 replacement therapy is now given orally in Sweden and in the USA it is becoming a more popular mode of treatment. Nursing time spent on intramuscular injections is costly—an assessment of the costs of administering injections of vitamin B12 made in 1997 to the 89 patients in our combined inner city practice of 19 000 suggested that substantial savings could be made with an oral preparation. An oral preparation of vitamin B12 (Cytacor 50 μg) is available in the UK but the NHS licence restricts its use to vitamin B12 deficiency of dietary origin and for vegans.

PATIENTS AND METHODS
This was a prospective case series of 50 of the 108 eligible patients with vitamin B12 deficiency within the combined practice populations of 19 000 patients. Ten patients had pernicious anaemia as confirmed by a positive Schilling test and/or raised intrinsic factor antibody (as confirmed by the antibody test for anti-intrinsic factor antibody). Nine of the patients had gastrointestinal surgery related vitamin B12 deficiency and the remainder were intrinsic factor negative. Exclusions were because of refusal, cognitive impairment, or acute illness. Patients were recruited to the study at the rate of two or three per week but the study ended on a specific date such that patients took study medication for variable periods of time. There were 17 males and 33 females with an age range of 31 to 90. Ethical approval was obtained from the East Birmingham Local Research and Ethics Committee. At study entry patients completed a medical history and received a physical examination with emphasis on cognition and the nervous system. Repeat medical histories were taken every six months. Physical examination was repeated in all patients at the end of the study and if the serum vitamin B12 level fell into the lower 25% of the reference range (vitamin B12 reference range 180–1132 pg/ml) or new neurological symptoms developed. The Abbreviated Mental Test score was used to assess cognitive impairment and neurological examinations were standardised by one of the authors, DS, who had recognised expertise in such assessments. Patients received a loading dose of intramuscular 1000 μg hydroxocobalamin at study entry and then followed the patient pathway as outlined (fig 1). Thus all patients started the oral stage of the study with a similar baseline, receiving the oral study tablet medication of 1000 μg of cyanocobalamin daily. Extra serum B12 levels were measured monthly if serum vitamin B12 levels were approaching the lower limits of the acceptable study ranges.

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**ORIGINAL ARTICLE**

**Oral vitamin B12 can change our practice**

E Nyholm, P Turpin, D Swain, B Cunningham, S Daly, P Nightingale, C Fegan

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Oral vitamin B12 can provide an effective alternative to intramuscular injections, so giving patients a choice and reducing costs in primary care. This study investigated the effectiveness, safety, and acceptability of oral vitamin B12 as replacement therapy in patients with vitamin B12 deficiency in a city general practice population. Forty patients previously maintained on vitamin B12 injections were given 1000 μg of oral cyanocobalamin daily for up to 18 months. All the patients maintained satisfactory serum B12 levels and showed normal haematology and neurology. Compliance and acceptability was excellent. The time for a change in practice has indeed arrived.
RESULTS

Of the 50 patients who entered the study and received the intramuscular dose of 1000 µg hydroxocobalamin, three patients were withdrawn before starting oral vitamin B12 for social reasons. Two patients whose serum B12 level did not fall sufficiently to reach the lower quartile did not enter the oral phase of the study. Five patients were withdrawn from the oral stage of the study: death (2), protocol violation (2), leaving the area (1). Forty patients were then analysed from the oral treatment group. Patients were recruited to the study at a rate of eight to 10 per month and the study ended on a fixed date over two years later. Thus, patients took the treatments for variable periods of time. Eleven patients took the preparation for 18 months, 19 patients for 15 months, 34 patients took Cytacon for nine months, 38 for six months, and 39 for three months. The values of continuous variables at different time points were compared using Friedman’s test (fig 2).

Cyanocobalamin was effective in 100% of the patients in all the diagnostic groups—that is, no patients had to restart vitamin B12 injections.

There was a plateau in serum vitamin B12 levels at three months on oral treatment with a median value of 1164 pg/ml (interquartile range 854–1578 pg/ml). This compared with a median at the start of oral therapy of 410 pg/ml (interquartile range 356–473 pg/ml). There is no significant fall in haemoglobin (p = 0.4) or mean corpuscular volume (p = 0.42) over time. Physical examinations undertaken when the serum level of vitamin B12 entered the lower 25% of the reference range and at the end of the study showed that the treatment did not result in any new neurological complications. Homocysteine levels monitored after the start of oral therapy showed no rise (p = 0.32) demonstrating that tissue vitamin B12 deficiency did not occur (table 1).

DISCUSSION

This study confirms that oral 1000 µg cyanocobalamin provides effective maintenance therapy for vitamin B12 deficiency of all causes. General practitioners can be confident that this alternative treatment is both safe and effective in the long term—ongoing monitoring of our patients has substantiated that belief.

An oral treatment can produce substantial savings by removing the necessity for nurse involvement either at home or at the surgery for injection therapy. Patients much prefer oral medication and given the opportunity to choose between an injection and a tablet of vitamin B12, clearly demonstrated this preference. Vitamin B12 replacement therapy is ideally suited to a standard monitoring protocol and this should become a regular part of our care.

Patients with the very rare condition of tobacco amblyopia should remain on hydroxocobalamin as there is a theoretical possibility of cyanocobalamin (rather than hydroxocobalamin) increasing the risks of this condition.

There is now an oral alternative to a parenteral treatment and oral vitamin B12 is now a therapy option. The study confirms oral vitamin B12 is effective and acceptable as...
A 58 year old woman with rheumatoid arthritis suffered from pain and swelling in the right buttock. The pain was greatly aggravated by sitting. Computed tomography and magnetic resonance imaging (MRI) revealed a cystic mass lesion with thick wall, adjacent to the right ischial tuberosity and gluteus maximus muscle. On T2-weighted MRI, the mass contained multiple hypointense small nodules, indicating rice bodies (Fig 1). Total resection was performed and histopathological findings were compatible with chronic bursitis; rice bodies consisted of dense fibrinous material.


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All the authors contributed to the design and the clinical work. EN and PT organised the study. BC and SD ran the study and PN undertook statistical analysis. We are grateful to our colleagues at Yardley Green Medical Centre and to laboratory staff at Birmingham Heartlands Hospital for their help and support in running the study.

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## IMAGES IN MEDICINE

Rice bodies in ischiogluteal bursitis

[Figure 1] T2-weighted MRI scan.
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