

## B12 Deficiency - The Need for a Protocol



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### INTRODUCTION

In Ireland, a diagnosis of vitamin B12 deficiency is typically contingent on the results of a total serum B12 test. However, emerging evidence indicates that the total serum B12 assay is inaccurate<sup>1</sup> and that total serum B12 is an insensitive and unspecific biomarker for B12 deficiency<sup>2</sup> suggesting that B12 deficiency may be considerably under diagnosed in Ireland. Dr. Joseph Chandy, a General Practitioner (GP), in the UK National Health Service (NHS), devised a protocol for diagnosing B12 deficiency that emphasises the need to interpret total serum B12 results in light of the clinical symptoms of the patient along with the presence of a strong family history of Pernicious Anaemia and or other autoimmune conditions. Using this protocol he has successfully treated B12 deficiency in patients who would not have received a diagnosis previously. The prevalence of B12 deficiency in his practice population is 18% as opposed to 0.01% nationally.<sup>3</sup>

### METHODOLOGY

A literature review was conducted to critically examine the extent to which Dr. Chandy's protocol is supported by scientific literature.

### RESULTS

It is suggested that Holotranscobalamin (holoTC), also known as active B12, is the earliest laboratory index for B12 deficiency and that it is a much more sensitive biomarker of B12 status than total B12.<sup>2</sup> However direct empirical evidence to substantiate this claim is still lacking. It has additionally been argued that the total serum B12 may not drop significantly until late in the disease process when neurological symptoms can be irreversible.<sup>2</sup> Further evidence of the insensitivity of serum B12 has been demonstrated in a recent study wherein it was identified that when levels of serum B12 drop below 500ng/ml that neurological damage can occur and may cause neuropsychiatric symptoms including dementia.<sup>4</sup> This is particularly significant considering conventional guidelines indicate that 200-1100ng/ml is the normal range<sup>5,6</sup> for serum B12. On a related note, in an investigation of B12 deficiency in alcoholics it was found that the subjects were presenting with severe symptomatic evidence of B12 deficiency despite their serum vitamin B12 results falling within the normal range. It has furthermore been demonstrated that three widely implemented Competitive-Binding Luminescence Assays (CBLA) of serum B12 gave false positive results for individuals with Pernicious Anaemia at rates ranging from 22% to 35%, indicative of serious diagnostic failure.<sup>1</sup> Interestingly, a formerly implemented, older, test termed Radioisotope-Dilution Assay, demonstrated sensitivity of approximately 95% match of serum B12 to symptoms.<sup>1</sup> This indicates that CBLA's are being implemented as diagnostic tools without empirical evidence to support their relative accuracy. A holoTC (active B12) test is not currently available in Ireland.

### CONCLUSIONS

There are no up-to-date national guidelines for the diagnosis and treatment of B12 deficiency, and no single test to definitively identify it. Consequently, the exact prevalence of B12 deficiency in the general population is not known. Interpretation of the threshold of total B12 for treating deficiency is controversial and this is probably the crucial issue. It is likely that general population screening using some diagnostic test will be cost effective sometime in the future. In the meantime, patients are likely to continue to manifest symptoms of B12 deficiency, in the absence of 'abnormal' serum total B12. The viability of diagnosis by signs and symptoms, strong family history and the presence of other autoimmune conditions, as inherent in Dr. Chandy's protocol has been demonstrated over the past 32 years whereby remission of signs and symptoms has consistently been observed following treatment. The cost benefit effect of using the protocol would be high when the low cost of treating with B12 injections is offset against the cost of treating for diseases that can stem from untreated B12 deficiency. In summary implementing the protocol Dr. Chandy has developed would ensure that patients who are manifesting symptoms, but whose serum B12 is in the 'normal' or 'sub normal' range could be effectively diagnosed, relieved of their symptoms, and protected against potentially irreversible neurological damage. Furthermore, the health services would also likely gain from a reduction in expenditure through reduced in-patient services.

### REFERENCES

Available on request.

### PRESENTED

As 'A Protocol for B12 Diagnosis and Treatment by Primary Care Clinicians' by Dr. J. Chandy at the Pernicious Anaemia Society Annual Conference, Bridgend, South Wales on March 31st, 2012. It can be viewed along with an interactive signs and symptoms score sheet at [www.B12d.org](http://www.B12d.org)