Dear Madam

Thanks for giving me the opportunity to respond to the questions arising from the Public Petitions Committee consideration of PE1408.

It is well recognised within the Haematology Service that the vitamin B12 assay does not completely reflect the tissue availability of vitamin B12. More complex and detailed assays are available which will more accurately reflect the body’s vitamin B12 state but these assays are beyond the scope of the general Hospital Laboratory at this time. There are some companies working towards making these more sensitive assays available but this will come at a cost premium. Currently NHSL perform around 114,000 vitamin B12 assays on an annual basis. Clearly in these stringent economic times anything that would increase this cost will have a potential for considerable financial hit given these numbers.

In relation to pernicious anaemia which is a specific autoimmune disorder related to the failure to properly produce intrinsic factor to bind vitamin B12 in the bowel to permit its enhanced absorption. We would currently suggest checking the intrinsic factor and parietal cell antibodies of any patient found to have a low B12 or in whom a diagnosis of pernicious anaemia is being entertained. Further to this, any patient in whom there are neurological signs which may be suggestive of a B12 related problem could also not only have their vitamin B12 level checked but further investigations along these lines with intrinsic factor and parietal cell antibodies. Whilst it would be unusual for a patient to have neurological sequelae with a normal serum B12 on the standard assay, this is a recognised phenomenon and if there is concern that there may be vitamin B12 related symptoms it would be normal practice to advise vitamin B12 to be given and see whether these symptoms improved. Most apparent low vitamin B12 levels are related to the wide spread use of proton pump inhibitors such as Omeprazole. These so significantly reduce acid secretion in the stomach that vitamin B12 absorption is impaired. Whilst B12 malabsorption was considered previously rare, this is now a far more common phenomena. True dietary deficiency of vitamin B12 is unusual as vitamin B12 is a pervasive vitamin but it can occur with some diets particularly when they are of a limited nature. This can also be an issue for vegans. In terms of our Standard Policy with respect to GP advice, we normally advise
vitamin B12 be checked if there are symptoms suggestive of vitamin B12 deficiency or if a peripheral blood picture is suggestive of vitamin B12 deficiency, mainly an anaemia and/or a macrocytosis. Thereafter if there is clinical concern it is entirely appropriate for the Doctor looking after the patients to administer vitamin B12. If there is symptomatic improvement it would seem reasonable to continue with a vitamin B12. For most patients this will require vitamin B12 on a 3 monthly basis. Vitamin B12 is stored very efficiently in the liver and the normal liver will contain some years worth of vitamin B12. Only in exceptional situations where perhaps there is an abnormal handling of vitamin B12 would there be any need for more frequent vitamin B12 administration. As ever of course, each case must be judged on its individual merits. Most patients who are on 3 monthly vitamin B12 will run with higher than population norms of vitamin B12 levels and these can easily be assayed. Were we to see a patient who ran with lower than normal levels despite “a standard vitamin B12 supplementation” and particularly were they symptomatic, it would certainly be our guidance to consider increasing the frequency of B12 administration.

The diagnosis of pernicious anaemia in NHSL is based upon the finding of a positive intrinsic factor antibody which is present in around 50% of cases of pernicious anaemia. Parietal cell antibody is positive in around 90% of cases of pernicious anaemia but is also present in a number of cases at a low level in the population where there is no pernicious anaemia, perhaps 1 to 2% of the population. It is therefore unusual to make a diagnosis of pernicious anaemia without a positive parietal cell antibody but its presence per se does not make the diagnosis. Our usual policy were the patients simply to be found with a borderline low vitamin B12 level and no stigmata of neurological disease would be to suggest oral supplementation. In the context of pernicious anaemia this will not work but in the context of dietary insufficiency or PPI use, oral vitamin B12 will be absorbed if given at a relatively modest dose. As you will be aware, on the Continent high dose vitamin B12 can be given and indeed we have used this for one or two of our patients who are allergic to intramuscular/subcutaneous vitamin B12 injections. Around 1% of a dose of vitamin B12 will be absorbed and as the human body requires only 6-12ug daily a dose of 1mg per day will generally meet the need. These tablets however are not available routinely and need to be specifically sourced.

If a patient is diagnosed with pernicious anaemia generally they will stabilise with the use of 3 monthly vitamin B12 after a short course of more frequent doses to replace body stores. For dietary insufficiency oral medication is usually sufficient to return the vitamin B12 level to within the normal range and this can be continued if there were evidence of symptomatic issues with respect to B12 deficiency, dietary advice is also helpful. If there is no improvement on oral supplements then B12 injections are advised. The main problem with the B12 assay is that for many patients with a slightly low serum B12 there is no clinical consequence to this in terms of symptomatology and returning their B12 levels to the normal range, likewise, has no clinical benefit.

In the context of patients with neurological signs one would check the B12 level but if there is concern that it is B12 related administer vitamin B12 at that time. If there is evidence of clinical improvement regardless of the B12 level one would continue with vitamin B12.

I hope this addresses the concerns raised but if there are any more specific questions please do not hesitate to get back in touch.

Yours faithfully
Dr I O Singer
Consultant Haematologist