

## Response to Submissions to PE 1408

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The Pernicious Anaemia Society

We would, first of all, like to thank the Petitions Committee for the opportunity to respond to the submissions from the various health organisations that were asked their opinions regarding the above petition. We would also like to thank the committee's secretariat for the excellent support and guidance in relation to the above.

The submissions further our case that there needs to be a thorough review of the way in which B<sub>12</sub> Deficiency in general, and Pernicious Anaemia in particular is diagnosed and treated. As the committee can see from the submissions, the various responders are divided over the issues raised by the petition:

*"We would agree that Doctors (and medical students) require education on the symptoms of B12 deficiency" . . . "We accept that the diagnosis of B12 deficiency is not foolproof at the present time" (NHS Highland)*

This contrasts with:

*"The current diagnostic tests and treatment are considered by the medical profession to be up to date, accurate and evidence based. There is no question that the current diagnostic methods are 'outdated or unreliable" (NHS GG&C) –*

And again:

*"Whilst we cannot support an 'automatic trial' of B12 injections in patients with no laboratory evidence of B12 deficiency" (NHS Highland) - contrasts with:*

*"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." (NHS Lanarkshire)*

These inconsistencies are enough to support our claim that there is a need for a thorough review to be conducted to answer some fundamental questions relating to the way in which Pernicious Anaemia is diagnosed and treated. There are further inconsistencies but to point these out would be at the expense of providing the committee with what we, as a patient support group, have discovered. We would like to take this opportunity to make the following statements:

### DIAGNOSING B<sub>12</sub> DEFICIENCY

1. The test that was used for many years to give a more or less accurate diagnosis of Pernicious Anaemia is no longer used – the Schilling Test. This is because the radioactive B<sub>12</sub> that was used in the test is no longer produced (it became expensive and not profitable to manufacture). Whilst this test has been withdrawn no other equally dependable or trustworthy test has replaced it.
2. The test mentioned in the submissions that is sometimes, but not always, used to determine whether the patient has antibodies to the Intrinsic Factor that could indicate Pernicious Anaemia – the Intrinsic Factor Antibody Test - is only around 60% reliable:

“A negative Intrinsic Factor antibody result does not exclude the diagnosis of PA as only 60% of patients with PA will have this antibody.”<sup>1</sup> Mr Hooper tested negative for IF antibodies twice before finally testing positive.

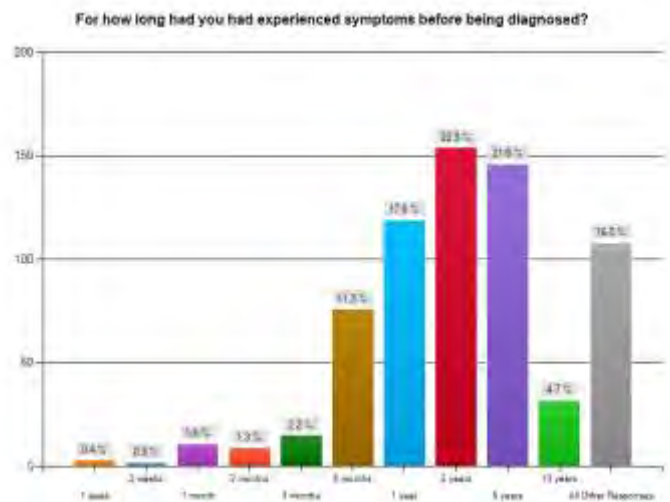
The other test that is sometimes used to determine the cause of the patient’s low serum B<sub>12</sub> – the Parietal Cell Antibody Test - is similarly flawed the full citation is to be found in the same paper as that referenced above.

3. Neither of these tests takes into consideration patients, many of whom tend to be elderly, who produce no Intrinsic Factor for one of a number of reasons. The tests check for *antibodies* and not the intrinsic factor. A patient can test *negative* for IF antibodies and therefore be considered *not* to have Pernicious Anaemia – but might not be producing any IF so *would* be suffering from Pernicious Anaemia. As we have said previously, these anomalies need to be thoroughly investigated – especially as gastric atrophy, which can and does lead to Pernicious Anaemia, is more prominent among the elderly and Scotland’s population, along with other developed countries is ageing.
4. No mention was made in the submissions of the need to check the patient’s Folic Acid. Failure to do so would mean that any folic acid deficiency would go unnoticed. Without high levels of folic acid the B<sub>12</sub> would not do what it was supposed to do – help produce healthy red blood cells. Instead, much of the B<sub>12</sub> would become analogues which are not functional in the body nor are they detected by modern assay methods for B<sub>12</sub>.<sup>2</sup>

The society has, over the last twelve months, been conducting a survey of the experiences of its members in getting their symptoms investigated and diagnosed. The survey, devised by two of our members who are doctors, has now been undertaken by over seven hundred and fifty of our members and the fully analysed results will be published in the spring of 2012. A preliminary report of the findings contained the following information relating to diagnosing Pernicious Anaemia: the results are a reflection of what the PA Society knows from the letters and telephone enquiries we get on a daily basis – that there are serious

issues with the way in which Vitamin B<sub>12</sub> Deficiency in general, and Pernicious Anaemia in particular is diagnosed with 47% of respondents waiting two years or more for an eventual diagnosis. And during this time they were making repeated visits to their doctor’s surgery, being prescribed medicines that didn’t help them and all the while the disease was having an impact on their work and their home-life. What happens is that if the patient has serum B<sub>12</sub> levels above the laboratory threshold for determining B<sub>12</sub> Deficiency then the patient’s symptoms are usually attributed to another condition. By far the most common misdiagnosis is Depression with many of our members being prescribed anti-depressants in some form, but other misdiagnoses include Myalgic Encephalopathy (or Chronic Fatigue Syndrome), Anxiety and Perimenopausal with a wide range of other conditions being blamed on the patient’s malaise.

It would not be proper for the Pernicious Anaemia Society to tell medical professionals how to do their job, but there seems to be two ways in which this problem with not identifying B<sub>12</sub> Deficiency in patients quickly and accurately could be solved. One way would be to raise the lower threshold for determining deficiency from the current level of around 140pmol/L to 300pmol/L. This is advocated by Professor David Smith and Professor Helga Refsum<sup>3</sup> along with a number of other medical professionals. The alternative way in which people who are deficient in B<sub>12</sub> might lie in the newly



developed 'Active B<sub>12</sub>' Test that differentiates between Active and Inactive B<sub>12</sub>. The current test does not differentiate between these two types of B<sub>12</sub> and a patient might have up to 90% of their B<sub>12</sub> in the inactive form. Again, the PA Society does not advocate or endorse this test but the fact that it has been developed at all indicates that some scientists are aware of the shortcomings of the current method of diagnosing B<sub>12</sub> Deficiency, and it does seem to provide the answers to the many questions surrounding the current test. Further information about this test can be had by contacting Axis-Shield Diagnostics based in Dundee.

## TREATMENT

The treatment regime to rectify vitamin B<sub>12</sub> Deficiency in the U.K. along with Australia and New Zealand is for administering 1mg of Hydroxocobalamin every three months by intra muscular injections given by a nurse. In North America and on the Continent the treatment is 1mg of Cyanocobalamin every month. It is believed that Hydroxocobalamin is retained by the body longer than Cyanocobalamin but the evidence for this is very weak. By far the most common cause of concern among the society's four thousand plus members is the frequency of injections. Most, though not all, doctors will not deviate from the treatment guidelines set out in the British National Formulary. Interestingly, in the 1960s the BNF stated that injections should be given monthly, then it changed to two monthly in the mid 1970s and to every three months in the 1980s. This is far too long for most of the society's members, however some members manage perfectly well on an injection every three months – though these are a tiny minority. When GPs refuse to prescribe more frequent injections the patient/doctor relationship often breaks down, but only after the patient has made frequent visits to the GP's surgery and taken up numerous appointments with the doctor. Then, the patient will often do one or more of the following:

Resort to buying the injection from pharmacies in mainland Europe where it is available without a prescription and then either inject themselves or get a family member or friend to inject them – usually without receiving any training, using the same needle a number of times and with no sharps bin. This is being done without the knowledge or permission of their doctor. This is becoming increasingly popular as the various Facebook pages relating to B<sub>12</sub> Deficiency inform an increasingly wider audience of this treatment regime.

More worrying is that many members are turning to internet stores to source the injections – they can even be bought from ebay.

Patients will also supplement their treatment by paying doctors in the private sector for the injections – one member is charged £110 for one injection where the cost of the vial is around 60p. Others follow celebrities and receive massive doses of B<sub>12</sub> via an intravenous drip (Simon Cowell receives one of these every week), and then give themselves small regular injections under their skin using diabetes needles. The type of B<sub>12</sub> used in the infusion is Methylcobalamin which is not licensed for use in the UK but can be bought as brands in Malaysia and Japan. In the best case scenarios the patient's doctor will have referred him or her to one of the many doctors who provide this alternative treatment. The society is aware that beauticians and hairdressers are providing this form of treatment.

Other patients will try the wide range of alternative treatments now available including sub-lingual drops (the B<sub>12</sub> gets into the bloodstream via a membrane under the tongue), sub-lingual lozenges, nasal sprays, behind the ear skin patches and even ointment. None of these treatments has, as far as the society has been able to determine, been tested as to their efficacy or had any long term use implications evaluated. And patients do not inform their doctor of their supplementation more often than not.

There are major problems with the way in which B<sub>12</sub> Deficiency in general, and Pernicious Anaemia in particular is diagnosed and treated. The cost of providing medicines alone for misdiagnosed illnesses

has been conservatively estimated as costing the NHS £854 Million every year. Then there is the question of the doctor's time being taken up with patients pleading for more frequent injections, the implications on careers and jobs by being under-treated and consequently still symptomatic and the impact that the condition has on family life by the patient struggling to deal with the disease.

The time has come for a review to be undertaken into the consequences of all of this. The Pernicious Anaemia Society will gladly provide any reviewer with our findings and the contact details of medical professionals including those who are highly respected internationally renowned Professors, and who have agreed for their details to be given to any interested party.

Thank you for taking the time to read this information sheet.

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<sup>1</sup> Consensus Guidelines on Anti-Intrinsic Factor Antibody Testing: Australasian Society of Clinical Immunology and Allergy in conjunction with the Royal Australasian College of Pathologists. 1 Nov. 2004.

[http://www.allergy.org.au/images/stories/pospapers/ASCIA\\_Guidelines\\_IFA\\_1-%20Nov04.pdf](http://www.allergy.org.au/images/stories/pospapers/ASCIA_Guidelines_IFA_1-%20Nov04.pdf)

<sup>2</sup> Changes in Serum Levels of Cobalamin and Cobalamin Analogues in Folate Deficiency, Kelvin Sheppard & David Ryrle. *Scan J Haematol*: (1980) **25**, 401-406.

<sup>3</sup> *Do We Need To Reconsider The Desirable Blood Level of Vitamin B<sub>12</sub>?* D. Smith, H. Refsum. *Journal of Internal Medicine*, Manuscript 2485. Nov. 30<sup>th</sup>, 2011.