PE1408/JJ

Petitioner Letter of 14 November 2016

I am greatly disappointed that the Scottish Government has given up trying to have the summary document finalised for clinical use. I feel it is totally unreasonable to expect GPs to read through the full BSH Guideline, which is a very lengthy article, and in reality it is not going to happen.

There are at least three separate sources of guidance on B12 Deficiency:

1. British National Formulary – Section 9.1.2 (bnf.org)
2. BSH – Full 2014 Guideline
(http://onlinelibrary.wiley.com/doi/10.1111/bjh.12959/full)
3. Patient Info (http://patient.info/doctor/pernicious-anaemia-and-b12-deficiency)

From experience, the one that GPs mostly refer to is almost certainly the BNF. The guidance there presently contains what has been the established treatment regime for many years, i.e., an initial 6 injections over the course of a fortnight, followed by either 2 or 3-monthly maintenance injections thereafter. This has been the whole focus of my petition, which was to highlight the fact that many patients do not do at all well on this treatment regime. As stated at the start of my petition, I was one such person who required thrice-weekly injections to keep my head above water. This continued at that level for a period of five years, after which I finally discovered the underlying reason for my extreme deficiency and was able to have it treated and resolved, although not until well after I had developed major, serious and permanent disability. However, without the excellent cooperation I had from my GP during that time, I know that death would have been the inevitable outcome for me. I am also proof that such frequent B12 injections are not harmful so why is there such resistance to a symptomatic level of treatment?

There is no known evidence of toxicity from such frequent injections yet the following extracts from actual NHS Consultant letters[1] display the reactions patients frequently experience:

1. '*Thank you for writing about this patient with a strong family history of PA and known B12 deficiency herself. You mention that she has now increased her B12 injections initially to monthly and now to every week. This is because she feels her symptoms . . . improved following B12 injection. This is of course a well recognised effect . . . B12 has a non-specific mood lifting effect but it is not actually necessary to replace her B12 this often. I think you would be much better placed to consider treating her for her mood changes along standard lines (psychotherapy and/or antidepressants).'*

   So, even although this patient's symptoms are relieved by her frequent injections, this consultant prefers to recommend her instead for other far more serious and addictive medicines!

2. Neurologist: *'Today's consultation was initially challenging because of the patient's strong belief that her symptoms must be something to do with the*

previous B12 deficiency and its subsequent treatment . . . I explained that, in my opinion, once long term replacement has begun with 3-monthly injections it is extremely unlikely B12 deficiency can still be responsible. Although she feels that her symptoms worsen as the time her B12 injection approaches and improve straight afterwards this is, in my opinion, likely to be the placebo effect . . . '

3. Letter signed by every GP at a patient's surgery: *'We have discussed your current treatment plan with a neurologist and have been advised that after the initial "loading" doses . . . it is recommended that continuing injections for three times per week are more likely to do more harm than good.'*

4. Consultant Haematologist: *'I note that she developed symptoms which occur pre-injection are relieved post-injection and is receiving B12 injections every four weeks. I would like to suggest that a B12 level is checked and should this be normal there is no value in increasing the frequency of the B12 injections. In fact, these are recommended to be given every three months and I would strongly suggest that this is pursued as at the minute she is being significantly overdosed.'*

This consultant clearly doesn't read the BSH Guideline either as it specifically says: *'No further testing for cobalamin levels is required.'* This is because once treatment has commenced, the serum level will invariably be considerably higher than before treatment, regardless of whether or not the treatment regime is sufficient for these patients. In my own case, my serum level was still above range after a year without any B12 supplementation.

5. GP Practice letter: *'I write to you on behalf of the practice about your B12 injections. Evidence has come to light that, in many cases, B12 injections are given too easily. To continue having B12 injections we need to prove that people cannot absorb the carrier across the stomach membrane. You are one of the cohort of patients who have been tested and should be able to absorb B12.'*

There is so much wrong with this letter that I can't even bring myself to address it. The patient was then informed that the appointments she had already made for further injections had been cancelled.

There is though the occasional consultant who takes the time to check out the safety of increased B12 dosage in order to enable their patient to be effectively treated, as seen here:

'I have consulted the SPC, i.e. summary of product characteristics of Hydroxocobalamin, and indeed some conditions . . . require daily administration . . . for a limited period of time but this is not described in the treatment of PA. However, ___ is very symptomatic . . . and as per SPC there is no evidence that she will come to any harm by continuing on this dose.'

The BSH Guideline states the following:

> *Gastric parietal cell (GPC) antibodies have a low specificity for the presence of pernicious anaemia as, despite being positive in 80% of pernicious anaemia subjects, they are also positive in 10% of normal individuals. Positive GPC antibodies may cause gastric acid achlorhydria and progression to pernicious anaemia may occur. However, a positive GPC antibody test is not definitive for pernicious anaemia.*
>
> *Recommendation: Anti-GPC antibody testing for diagnosing pernicious anaemia is not recommended*

Yet, the following article[2] from the Food & Agriculture Organisation of the UN (FAO) has this to say:

Malabsorption of vitamin B_{12} can occur at several points during digestion. By far the most important condition resulting in vitamin B_{12} malabsorption is the auto-immune disease called pernicious anaemia (PA). In most cases of PA, antibodies are produced against the parietal cells causing them to atrophy, lose their ability to produce intrinsic factor, and secrete hydrochloric acid.

Now, by comparing these two statements alone, it is not necessary to have any medical knowledge to understand that the presence of Parietal Cell antibodies (PCAbs) will lead to the loss of Intrinsic Factor, and therefore inevitably result in permanent PA. What about this reported 10% of 'normal' patients who test positive for PCAbs? Could the reason be that they already have the symptoms which prompted the test to be carried out, but do not yet have a deficient serum B12 level? Why should that be a surprise when the same BSH Guideline also says:

A serum cobalamin assay is currently the standard initial routine diagnostic test . . . However, it lacks the specificity and sensitivity required of a robust diagnostic test.

. . . Establishment of reference ranges by individual laboratories can be challenging because the serum cobalamin level can be affected by many variables i.e. diet, pregnancy, vitamin supplements, contraceptive pill, metformin etc.

Finally, I am asking, yet again, that my question about the presence of Gastric Parietal Cell Autoimmune Antibodies be answered by the medical profession. This issue affects up to 80% of patients with PA, regardless of whether or not they are recognised as such due to the failure to accept the result of this particular test. It is also one of the two main reasons why I cannot accept the BSH Guideline in its present form. The other reason is that no recognition is given to the many patients who require more frequent treatment than the present recommendation. Their plight is simply ignored as no one can agree about how they should be treated, or that their need is genuine! At the very least, and given the lack of evidence of B12 toxicity,

there is no reason why these patients cannot be given access to whatever amount of B12 keeps them stable. I am an example of the benefit of this approach and owe the last eight years of my life to being permitted an adequate level of treatment. It also brought me back from the brink of dementia, the early symptoms of which I was already displaying.

Yours faithfully,

Andrea MacArthur

[2] http://www.fao.org/docrep/004/y2809e/y2809e0b.htm