Peripheral Neuropathy and Other Consequences of Vitamin B$_{12}$ Deficiency

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WHO ARE WE?

• The only Patient Support Group in the world for patients and their families and friends

• Original remit – provide a plain English explanation of the condition to newly diagnosed patients

• It soon became clear there were serious issues with the diagnosis and treatment of the disease
How Widespread is the $\text{B}_{12}$ Deficiency?

- Impossible to Say – misdiagnosis is common
- The current threshold may be far too low
  \cite{Smith & Refsum; Do We Need To Reconsider Blood Level of Vitamin B12?; Journal of Internal Medicine, 2012;271(2): 179-182}
- Current RDI of Vitamin $\text{B}_{12}$ was established in 1948 based on 7 people with PA
  \cite{A Statistical Method to Base Nutrient Recommendations on Meta-Analysis of Intake and Health-Related Status Biomarkers; Hilko van der Voe et al: Plos One DOI: 10.1371/journal.pone.009317}
- It is estimated that between 40 – 50% of the population in the developed world is deficient

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SYMPTOMS

• Very Wide-ranging and Vague:

• Original Symptoms used to Diagnose PA are only now making a comeback following the survey of PA Society members

• Doctors are not’ looking’ for any possible deficiency
Our Survey

• Based on Survey Monkey
• Designed & Analysed by three doctors
• Over 1,200 Responded
• 889 responses were analysed
• 38 Questions Asked
• Published as: *Patient Journeys: diagnosis and treatment of Pernicious Anaemia: Hooper et al; British Journal of Nursing, 2014, Vol. 23, No 7*
Time Taken For Diagnosis

- 44% were wrongly diagnosed
- 22% had to wait 2 years,
- 19% for 5 years
- 4% for 10 years.
- 14% waited 10 years or more
Untreated $B_{12}$ Deficiency leads to:

- Psychosis
- Sub-Acute Combined Degeneration of the Cord Secondary to Pernicious Anaemia
- Death
Why So Long?

• There Are Serious Failings with the Current Test
• Combined Binding Luminescence Assay give false high results in between 22-35% of patients who are $B_{12}$ Deficient
• Gives False Negatives in 33-53% for Intrinsic Factor Antibodies
References

• Carmel & Agrawal; Failures of Cobalamin Assays and Pernicious Anaemia, 2012, New England Journal of Medicine
• Yang & Cook; Spurious Elevations of Vitamin B$_{12}$ with Pernicious Anemia, New England Journal of Medicine, 366;18
• Van Rossum et al; False Elevations of Vitamin B$_{12}$ in patients with Pernicious Anaemia Clinical Chemistry and Laboratory Medicine; 2013;0131
• The clinical picture is the most important factor in assessing the significance of test results assessing cobalamin status since there is no ‘gold standard’ test to define deficiency.

• Definitive cut-off points to define clinical and subclinical deficiency states are not possible, given the variety of methodologies used and technical issues, and local reference ranges should be established.

• In the presence of discordance between the test result and strong clinical features of deficiency, treatment should not be delayed to avoid neurological impairment.
Causes of $B_{12}$ Deficiency

- Pernicious Anaemia
- Gastrointestinal Surgery
- Non-specific gastritis (associated with *Helicobacter pylori* & Ageing)
- Medicines: PPI, Antacids, Metformin, Colchicine, Questram, Oral Contraceptive &
- Nitrous Oxide
Whippits
General Symptoms

- Tiredness (96%)
- ‘Waking up tired’ (87%)
- Dry skin (58%)
- Brittle nails with (47%) or without (37%) ridging
- Flushes or fever (43%)
- Glossitis (34%)
- Hair loss or greying (30%),
Gastrointestinal problems were commonly reported (82%). These included: Sudden Unaccountable Diarrhoea (58%), Indigestion (42%), Diarrhoea following constipation (40%), Stomach cramps (39%), Loss of appetite (27%), Loss of taste (26%).
Emotional Symptoms

- Emotional symptoms were also commonly reported (86%), including:
  - Irritability (75%),
  - Impatience (64%),
  - Mood swings (58%),
  - Suicidal thoughts (22%).
Neurological Symptoms 1.

- Memory loss (78%)
- Poor concentration (75%)
- Clumsiness (66%)
- Pins and needles (66%)
- Poor sleep (64%)
- Confusion (62%)
- Dizziness (59%),
Neurological Symptoms 2

- Headaches (52%)
- Nominal aphasia (word-finding difficulties) (50%)
- ‘Shoulder bumps’ (frequently bumping into things as a result of balance problems) (48%)
- Unable to stand with eyes closed (34%)
- Grierson-Gopalan syndrome (burning feet syndrome) (33%)
- Vertigo (33%)
Problems With Treatment

- When asked if they were satisfied with their treatment,
- 64% said ‘No’, 28% said ‘Yes’
- Respondents were asked which word best described how they rated their medical care. The results were:
  - Very Poor (20%),
  - Inadequate (18%),
  - Good (10%),
  - Poor (10%),
  - Undecided (9%),
  - Reasonable (8%),
  - Adequate (8%),
  - Very Good (7%),
  - Excellent (3%)
  - Unreasonable (2%).
What Next

• A Thorough Review of the way in which \( B_{12} \) Deficiency in general, and Pernicious Anaemia in particular is diagnosed and treated

• Patients to choose their method of treatment