pas Pernicious Anaemia Society

Cobalamin News

AUTUMN 2022

PAS ONLINE SEMINAR

15 October

10:00 BST

Speakers:
Dr Heidi Seage
Dr Kourosh Ahmadi
Martyn Hooper MBE

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James Lind Alliance - PSP - Findings Published!

As members will be aware, we spent nearly 18 months working with the James Lind Alliance on a Priority Setting Partnership, which culminated in the Top Ten questions for research.

Following on from this, we have been working for many months to complete an article that would be considered by and acceptable to medical journals, so that we could get the evidence from this process published and believe me, it is not easy to get articles published!

We are pleased to confirm that our article has been accepted and published online in BMJ Open. Needless to say, we are over the moon with this outcome. We are sure you will find the article interesting and urge you to share it with your contacts/medical professionals/GP's.

Thank you to every single person that was part of this process. It has been a lot of work but extremely worthwhile. Link below:

Research priorities in pernicious anaemia: James Lind Alliance Priority Setting Partnership

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Our warmest congratulations go to Dr Nicola Ward, and our very own Martyn Hooper for their excellent article which has recently been published in the Pharmaceutical Journal:

Pernicious anaemia: recognition, diagnosis and management

How to spot the signs and symptoms of pernicious anaemia, the difficulties in gaining an accurate diagnosis and the importance of individualised, long-term management for patients.

The amount of work and the length of time it takes to produce an article is enormous, so we offer our heartfelt thanks to those who worked so hard to produce the articles and to keep PA and the problems experineced by our Members in the public eye.

PAS Online Seminar

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Speakers:
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The PAS Management Committee have taken on board members' comments about being able to attend our bi-annual conferences and appreciate that travel costs could preclude members from being able to attend.

For this reason, we decided to replace this years conference with a half-day online Seminar and this will take place on Saturday October 15th 2022. Our guest speakers are Dr Heidi Seage and Dr Kourosh Ahmadi and, of course, Martyn Hooper will update everyone on the fantastic work being carried out by PAS.

Attendance is open to members of The Pernicious Anaemia Society. This event requires registration so please click on the link below to register and you'll receive the details via email.

https://us02web.zoom.us/meeting/register/tZEsf-yqqjgqG9X7dQR02QuKdn4sqHGS_64O

CluB-12 Symposium

by Katrina Burchell

CluB-12 was formed in January 2020 to facilitate the sharing of knowledge and to co-ordinate research into Vitamin B12 between Scientists and Healthcare Professionals. After being delayed due to the pandemic, CluB-12 held their 1st Symposium in Cambridge on 7th and 8th September which was well attended by eminent physicians and researchers. The Pernicious Anaemia Society sponsored the symposium and Martyn Hooper, Katrina Burchell and Karyl Carter attended representing the Society. Many of our long time supporters and friends were there as speakers or attendees.

The Symposium took place in Trinity Hall Conference Facility and thanks to other generous donations lunch was provided at the Maypole and dinner at Emmanuel College. The event was a resounding success and everyone left feeling inspired and enthusiastic about B12 and for me, in particular, hopeful for the future for the Pernicious Anaemia patient.

Day 1 started with a session focusing on the Patient and first to the podium to speak was our own Martyn Hooper MBE who talked about the Achievements and Future Challenges for the Pernicious Anaemia Society. Questions and comments from the audience were encouraging in terms of more international collaboration and the importance of patient representation to understand the experience of living with PA and B12 deficiency and finding a strong cohort of people for conducting research.

Next up was Cindy Stirrat, chair of The B12 Society a Scottish registered charity with aims to create and deliver teaching material to healthcare professionals about B12 deficiency. They also run a Facebook support group with a large number of active followers. Recent polls conducted on FB suggested that amongst their followers 29% had B12 injections stopped during Covid and not re-instated. Cindy described her own journey and talked about the difference in the EU of being able to obtain B12 over the counter and pointing out that the World Health Organisation had set no upper safety limits for B12 which made it difficult to understand why patients were often refused effective treatment based upon a blood test showed high B12 levels. Their plan is to start to re-focus on their education programme and they are hoping to get RCGP accreditation for their materials to disseminate to the medical profession. Comments from the audience underlined the poor level of education of medical students on B12 and nutrition generally.

Tracey Witty from B12deficiency.info then spoke about her petition to get B12 injections available over the counter and referred to her commercial applications for risk diagnosis and monitoring.

The final patient speaker was Bettina Borre Buhl who took us through her 6 year journey to diagnosis. As a scientist herself her clear description of the symptoms, tests and economics of the waste due to poor diagnostic tools resounded well with the audience. She concluded with her wish list of “better diagnostic tools’ for B12 deficiency and more studies on frequency of injections and into oral or other supplementation as well as education being key for doctors and patients. Her wishes are all key uncertainties that came out in the Top Ten list from the James Lind Alliance Priority Setting Partnership.

The best slide of day 1 was at the end of Bettina's talk which drew much laughter from the audience when she presented the saying "Be nice to Pernicious Anaemia Survivors, we deal with enough pricks already" accompanied by an image of a hypodermic needle. Julian Owen, a co-founder of CluB-12, Consultant Trauma & Orthopaedic Surgeon at Addenbrooke's Hospital in Cambridge, and our Chair for the Symposium, pointed out that with these patient stories, CluB-12 and the research and discussions in this event was "something that we couldn't not do!"

The Second session was the Perspective of the Clinic with Clara Plattel of the B12 Institute, recounting her experiences and research from treating B12 deficiency in the Netherlands. Clara was keen to encourage collaboration and make their Spring 2023 conference in Rotterdam a truly global one so we can all draw on the best worldwide expertise. Collaboration was a key theme throughout the Symposium with many networking opportunities for researchers to talk to each other about new and existing questions to answer.

Andrew Klein from the Cambridge Iron Clinic talked about Long Covid, B12 and Iron Deficiency. He gave his view on the frustration of the word Anaemia as both PA and Iron deficiency patients do not always have anaemia. 2.1 million people in the UK are estimated to have long covid and Andrew presented a slide comparing the overlapping symptoms of this with PA and Iron deficiency namely fatigue, shortness of breath, palpitations, faint/dizziness, brain fog and countless others. He pointed out that Long Covid clinics have lots of data which are ripe for research although no studies have yet taken place about giving B12 to long covid patients.

Agata Malefora from Viapath outlined her research into laboratory tests and reference intervals and pointed out the vast discrepancies which leads to an under-diagnosis of B12 deficiency. An over-riding theme of the Symposium was the very real need for harmonization of Lab results and consistency in best practice.

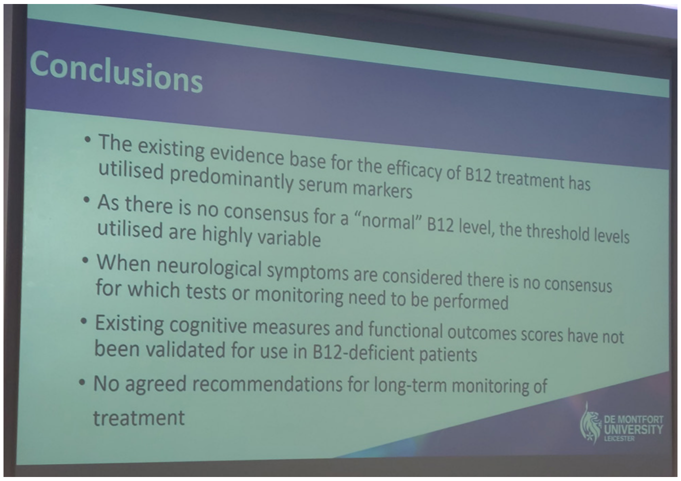
Luciana Hannibal and Jean Louis Gueant respectively from the Universities of Freiburg and Lorraine then covered The Science with numerous complex slides on the chemistry of Cobalamin and B12 analogues. Jean-Louis provided details about tests on animals and what we might then see in humans and it was generally agreed that more questions were raised than answers available about the various assays for Cobalamin. During the Symposium several speakers referred to the rise in veganism contributing to a major risk for increased B12 deficiency in the population. The conclusion however from the Science section of the day, was that our knowledge about B12 in humans is still very limited and there is much work to do.

Day 2 and the first session was entitled "Improvement" and started with Catherine Hughes outlining the TUDA (Trinity and Ulster Department of Agriculture) Study. Catherine pointed out that there is a 23% increase in the global burden during to an aging population and the aim of the study is to understand how nutrition, lifestyle and genetic factors impact on aging. Catherine's and the teams in-depth study on a significant and engaged cohort will provide valuable data around B vitamins being important to help prevent cognitive decline and supplementation improving visual and spatial skills. Catherine also spoke about Atrophic Gastritis, Vitamin B12 and PPI drugs, referring to Michelle Clements research in this area and explained about Fortified Food consumption improving Biomarker status. According to research, the impact of Atrophic Gastritis on bone health suggested a slight risk of osteoporosis but that B vitamin supplements had a slight benefit on bone health. There was a need for more studies in this area to confirm these findings and for the future of further research into nutrition, genetics and aging cognitive decline.

Martin Myers from NHS England then spoke about GIRFT – Getting It Right First Time, a project to look into service delivery in the NHS with the objective to review available evidence to see why there were such discrepancies across the regions and ICS (formerly the CCGs) as "we cant all be right and yet so different". Martin and his team's principles are to focus on the patient, on quality, and to support best practice. Data shows significant differences, for example, in the requests by region for tests for potassium, Hb etc. across the country, and not surprisingly to any of the Patient support group, presents a significant difference across England on the number of B12 tests requested and why.

With regard to B12, Martin's slide sets out the purpose of the group in the area of B12 with results due back next year. Martin said that from the initial findings he was very worried as they had sent the same sample to different laboratories with highly varying results on B12 testing. Martin's comment that "next year is the year of B12" was roundly applauded. Martyn Hooper asked a pertinent question regarding why there was no patient support group member on Martin's work group and Martin promised to look into that. Martyn then pressed him further to bear in mind that PA/AIG is the main cause of B12 deficiency and to recognize that the test for PA needs to be looked into and improved. Martin confirmed that this point was on his radar but that they were not focusing on an IF assay at this stage.

Next Nicola Ward, a long time friend and supporter and ex-trustee of the Pernicious Anaemia Society described how as a result of the JLA Top Ten Uncertainties she had started looking at new formulations and treatment plans. In order to do this, it was first necessary to understand treatment efficacy and how we monitor it so she had conducted a review of papers published which showed lots of gaps in what is being monitored especially around the area of symptoms. Nicola set out the conclusions of this review on her final slide and asked some thought provoking questions including “how do we define effective treatment”. For someone who used to run 10K, does that mean getting close to that again or is it just the ability to get out of bed?!!



Conclusions

- The existing evidence base for the efficacy of B12 treatment has utilised predominantly serum markers
- As there is no consensus for a “normal” B12 level, the threshold levels utilised are highly variable
- When neurological symptoms are considered there is no consensus for which tests or monitoring need to be performed
- Existing cognitive measures and functional outcomes scores have not been validated for use in B12-deficient patients
- No agreed recommendations for long-term monitoring of treatment

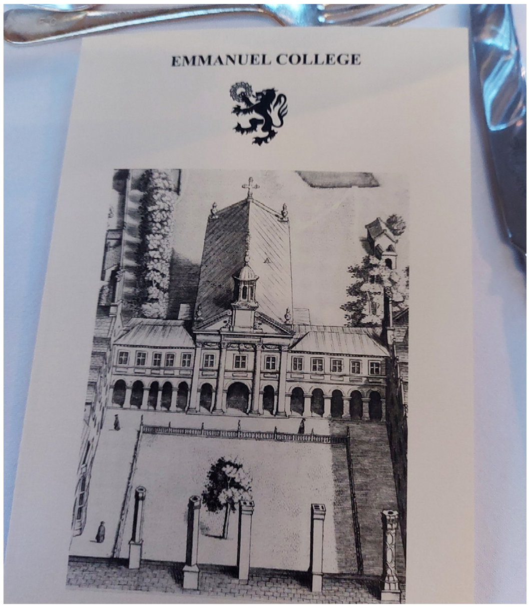
Day 2 continued with a session on Natural Corronoids with Alison Smith from the University of Cambridge Plant Sciences reviewing her study on Algae and B12. This was a fascinating area of study and covered a rapid run through of bio-chemisty and evolution, and finding out that researchers of Algae have pet names for their favourite algae! Ultimately this research again raises so many questions about B12 in algae and in humans. There was also an interesting discussion about Chlorella Vulgaris and Spirulina (the latter not really an algae but often recommended as a supplement to Vegans) and the concerns about pseudo-cobalamin and the effectiveness or otherwise of health care products and their ingredients.

Jonathan Clarke from John Innes Centre (yes the famous potting compost company) then gave a talk about another Novel Cobalamin source namely fortification or bio-fortification of plants with B12. Again referring to the vegan diet being the fastest growth level in food, he pointed out that this comes with a consequence that this is going to exacerbate B12 deficiency. He reported that according to their data 6% of the UK adult population is B12 deficient and 44% is at marginal or insufficient levels. Their research was focused on two areas – fortification of foods – i.e. can B12 be taken up in plants such that it could then deliver B12 to humans in consumption. Some research into pea shoots suggests this might be the case. The second is bio-fortification where genetically modifying plants may enable them to release Intrinsic Factor and thereby potentially help humans with no or low IF absorb B12 from meat products. It is clear we are still a long way from finding the solution from plants but it was fascinating hearing about these options and all the work that goes into this research and ultimately regulation and commercialization.

Next up was Martin Warren, President of CluB-12 (and yes, several observed how many people are called Martin in this field!). Professor Warren reminded us that B12 is one of the least abundant molecules in the human body with Cobalt equalling 21billionth of body mass. Martin raised the concern of trade wars affecting B12 where 90% of production is from China and 10% from France. He pointed out that 1Kg of vitamin C costs around £40 whereas 1Kg of B12 cost around £16,000 to the food , supplemental and pharma industries. Kourosh Ahmadi   asked Martin about developing a test for B12 absorption as this would be valuable(there is always harking back to the lack of the Schilling test) and we desperately need something   that is reliable to see if B12 is actually being absorbed.

The final session was about the future and Dr Bruce Wolfenbuttel gave an entertaining but also somewhat worrying presentation of his journey in treating patients with B12 Deficiency in Groningen in the Netherlands. Using Beatles songs he chartered the journey of various patients presenting with neurological and other symptoms and sometimes (although actually rarely) anaemia. References to songs such as Help (patients being misdiagnosed), A Day in the Life (his data group of 82% women aged between 5 and 84), Across the Universe (variation in treatment is huge) was combined with positive stories of success All You Need is Love (and someone who understands B12 deficiency) and She Loves You (because you listened to her!). There was a healthy debate with the audience about autoimmune diseases generally, lack of people in the biobank who have been diagnosed properly and potential problems with Macro vitamin B12 (it was new to me as were anti-vitamins and numerous other words which I have on my note pad to Google later!). The overriding message however was clear, you have to look at the clinical position of the patient.

The last speaker was Ed Quadros who appeared by Zoom from New York, as Covid positive test had stopped him travelling at the last moment. Ed talked about SubAcute Myelination of the Spinal Cord and reviewed research papers on B12 and Intrinsic Factor. To the general agreement of the audience he described Julian Owen as the new Indiana Jones in the quest for the treasure that is the solution to all these B12 questions and many of us finished the day with the image of Julian wearing Indiana's hat accompanied by the theme tune – a slide which I think may appear at future meetings and seminars of this Group!



An Update from Martyn Hooper MBE

For the last three months I have been busy with my two main two tasks. The first is ensuring that as much information as possible is made available to the National Institute for Health and Care Excellence (NICE) as they go about producing a Guideline on Vitamin B12 Deficiency and Pernicious Anaemia. This is because NICE like up-to-date information. This means that I have been encouraging researchers to undertake systematic reviews and rapid reviews of evidence with a view to getting these results published. There are currently three reviews that have either been completed or are in the process of being completed. As well as this I have facilitated meetings between two different students who have completed Masters Degrees on PA and experienced published scientists with a view to getting their findings published.

The second task I have been busy with is putting together a team of clinicians and scientists who will apply for funding to research the questions identified by the James Lind Alliance as being important to both doctors and patients. The questions, can be found here https://www.jla.nihr.ac.uk/priority-setting-partnerships/pernicious-anaemia/top-10-priorities.htm
This is such an important issue and, whilst I now have quite an impressive team who want to help, it is a little more challenging to find someone who has the time and experience to write the bid and lead the programme – but I'm confident that we will find the right person!

As part of my role in getting researchers to take up the challenge of finding the answers to the James Lind Alliance's list of 'uncertainties' I attended a seminar that explained how the National Institute of Health Research funds research projects like ours. Basically, there are eight separate funding streams. I also learned that because our research questions have been through the James Lind Alliance process any research team applying for funds would most likely be 'fast-tracked' through the funding application process.

New Delivery Methods

Some time ago I made a presentation to a panel of medical professionals at ARCH (a regional collaboration in health) – it was a sort of 'dragons' den' (but without the dragons I was assured). Well, they liked my presentation and now I have signed agreements with the Tritech Institute and the Accelerate Healthcare Technology Centre to facilitate looking at a better, more personalised way of delivering B12 to patients with PA. This will, hopefully, lead to us improving the management of the condition and improving our quality of life. This project is, believe it or not, headed by a Professor of Engineering.

Licence Change

In the UK the only licenced treatment for pernicious anaemia is by intramuscular injection. Any new, more personal treatment would involve the use of patches, self-administered injections (maybe by some sort of pen) etc. which would be most likely delivered sub-cutaneously – under the skin rather than into a muscle. So, before any new treatment is developed, it would mean that treating using sub-cutaneous method would have to be licenced. We know that those of us who treat themselves using injections (myself included) usually administer small injections just under the skin rather than into a muscle. So, we know it works. And so I have also been busy trying to get pharmaceutical companies, who produce licenced intra-muscular B12 to apply to the Medicines and Healthcare Regulatory Agency for their product to be licenced for sub-cutaneous use. This is, of course, a big ask as it will involve money but I am hopeful that the next time I write to you I will be able to report some progress.

Effectiveness of Treatment

Following on from the development of a new, less painful and more tailored treatment there is the problem of finding out just how effective any treatment, including injections, is. This is because once treatment has started it is impossible to use the B12 level in the blood to determine how effective the treatment is. What is needed is a Functional Outcome Score – so that the patient can measure how they feel on a particular treatment regimen. I have been facilitating the development of a team to create such a score and am now involved in helping to write the bid for funding which must include Patient and Public Involvement (PPI).

Visit of the Health Minister for Wales, Eluned Morgan

For many years I have been making politicians aware of the problems with the diagnosis and treatment of pernicious anaemia and I continue to do so. I have written to the four ministers for health in the United Kingdom asking for a meeting. It seems that before this happens the ministers ask their chief medical officers to meet me and during the summer, I met with the deputy chief medical officers for Wales and Northern Ireland. I was able to tell them about what we had achieved with NICE and the James Lind Alliance etc.

Subsequently, the Welsh Minister for Health, Eluned Morgan, attended the society's offices on Thursday 29th September. She was accompanied by Huw Irranca-Davies, AM and Catherine Cody. It was a very good meeting with the Health Minister taking on board the problems with the diagnosis and treatment of PA and asking many pertinent questions. The Health Minister also met some of our Members and listened intently to their PA journey and the problems they have/are facing with the medical blind spot that is PA. The Health Minister will be contacting NICE for an up date and will contact her fellow Health Ministers, urging them to get in touch with PAS.

As you can see, I have been busy using my network of contacts to bring about much needed change, and consequently improvements in the way in which pernicious anaemia is diagnosed and treated. It's a frustratingly slow process that involves working with and through established pathways and institutions. My efforts go largely unnoticed but you can be assured that my 'shoulder is to the wheel' every day in some form. And I am hopeful that we can build on the past successes to bring about the change that will improve the lives of patients with pernicious anaemia along with their families and friends.

Unintended Consequences on B12 of Prescribed Medication

by Dr Simon Chatfield

Dr Chatfield is a recently retired GP formerly practicing in Hertfordshire. He is also a trustee of a local hospice and after a chance meeting with a former patient of his who is also a trustee of the PAS, he was introduced to the challenges that PA patients suffer with diagnosis and treatment and has kindly volunteered some of his time to help us improve communications with our membership, especially on the health care professional side and bring his valuable experience from GP practice to help our members. Dr Chatfield is still actively involved with the NHS in a number of advisory roles and we are very grateful for his membership and support of our organisation.

All Doctors recognise times when their attempts to be helpful backfire. This might be issuing a prescription or another treatment, designed to help one problem, which results in something adverse happening instead. The consequence may be transient, inconvenient or more significant with avoidable harm. Some common medications interfere with B12 absorption, and it is likely that many health care workers do not know or fully understand this potential problem which means an opportunity exists for an unintended outcome.

Let's take Metformin. A 1st line tablet to help type 2 Diabetes and widely used all over the world for many years. NHSE data shows us that 6% of the population are known to have diabetes and about another 1.5% have the disease but are yet to be diagnosed. These are big numbers. Guidance indicates that around 3 or more million people in the UK should be prescribed Metformin. However there in the small print under "rare or very rare" side effects, and 4th on the list, you find vitamin B12 absorption decreased. This has been known for years. Early studies reported an average >20% reduction in B12 levels with long term treatment. If true it is hard to describe that as a rare event. The Pernicious Anaemia Society was writing about this issue in 2016.

Fast-forward to June 2022 and NHS publishes new guidance for Drs about B12 and Metformin in a Drug Safety Update. This tells us that Metformin reduces B12 levels, and the problem is "now considered to be common". 1:10 patients are thought to be affected. It adds that these risks increase with higher Metformin dose, longer treatment duration, and in patients with risk factors for vitamin B12 deficiency. A health care worker reading this update may be learning about the potential problem for the first time or they knew about it but did not know for sure what to do.

But what is it exactly that the clinician should do? The reasonable assumption is that this new safety update will make that clear. However, it is not that straightforward. An easy response, probably the easiest, is to add a test for B12 every time a diabetes blood check is arranged. After all, you can assume that the risk of missing a case of deficiency would be reduced. However, this new guidance suggests that a blood test for B12 should only be taken if the patient has symptoms that suggest deficiency and that a review for these symptoms should happen "periodically". You can interpret this as advising clinicians to wait until someone is unwell and then act. This would not be the most helpful guidance I have ever read. We must remember that we cannot be sure that diabetic clinic staff will reliably pick up the symptoms of low B12. Can we be confident that they will know all the risk factors?

Patients will reasonably expect that their clinician will interpret this guidance in a clear, consistent, and conventional way. There should be no postcode lottery of response. This consistency will only happen if, for example, everyone uses the word "periodically" in the same way and that diabetic clinic staff all know the relevant symptoms to watch for. I may be alone, but I do not know if periodically suggests every few months or once every 3 years.

You will already likely know that testing blood for B12 levels reliably is not easy and now this adds an uncertainty as to how often we should check. Additionally, patients presenting symptoms of B12 deficiency are yet to be offered reliable tests for Pernicious Anaemia and supplementing B12 can have an impact on these tests.The most reliable methods to test for B12 deficiency, especially active B12, are not widely available in GP's surgeries. There remains a lack of consensus about which tests should be there for a Dr, who does not have specialist status, to order on the blood form.
A real problem in the GP world currently is the over-

whelming levels of demand for their services from the post pandemic public. Consultations are inevitably shorter than ideal and that may mean, at times, there is too much to do and too little time and the clinicians do not “think B12” often enough as it were. This is not written or intended as an excuse for something being overlooked, another unintended consequence, but as an explanation as to why things are as they are.
The main effect of this guidance, time will tell, may be to raise awareness that commonly used medicines can lower B12. This must be a good thing.
The story can get more complicated. The lists of medications which are known to lower B12 are long - Anaemia - B12 and folate deficiency | Health topics A to Z | CKS | NICE - and contain drugs that are commonly used.

How to test for this deficiency, and this deserves repetition, is not yet at consensus and experts disagree as to how much this lowering of B12 is a significant problem. Here is another example. Indigestion and acid reflux symptoms are common. Annually NICE reports 40% of the UK population will experience some dyspeptic symptoms which are usually annoying and rarely sinister symptoms. A challenge for health-care workers is spotting this small minority who have what we call “red flag” symptoms. Many of these people will take simple remedies but others go for more powerful stomach acid reducing medicines, that are available off prescription. Broadly these drugs are the H2 blockers, ranitidine and cimetidine are well known, and PPIs like Omeprazole and Lansoprazole. PPIs generate 58 million prescriptions per annum in the UK in addition to large over the counter sales. I doubt that many pharmacists think B12 when they are talking to their customers or dispensing these prescriptions. Should there be a similar safety alert circulated across the NHS to cover this?

You can also find concerns about Nitrous Oxide, chemical formula N2O, which is a commonly used inhaled medicine that quickly eases pain. Examples of use include dentistry, women in labour and trauma. Colloquially it has many names that refer to the non-medical recreational use including laughing gas and hippy crack. It is not illegal to possess N2O and not uncommon to find empty small cylinders littering spots where users have congregated to inhale together for the euphoric effects. It has long been known that high exposure to nitrous oxide can effectively reduce B12 levels and we know that prolonged use may lead to anaemia and neurological toxicity. The guidelines state that N2O should not be given continuously for more than 24 hours, or more frequently than every 4 days, unless closely monitored. So, what should someone who is concerned about this do? My first answer is to not assume that your clinician will know about N2O and B12. If you are worried about this issue speak up and ask the anaesthetist, dentist, midwife, or paramedic. Reports exist of people with pre-existing but unknown low B12 running into trouble after a single exposure to nitrous oxide during an anaesthetic.

NICE has formed a committee to publish clear UK guidance on B12 deficiency and the guidance is listed as “in development”. The publication date, currently, is Nov 2023. It may not be until then, if they meet their deadline, that we can start to reduce the uncertainties here. Until then we can and should trust our GPs and their teams in primary care to make sensible, pragmatic decisions on how to manage their patients following the recent publication from the NHS, doing their best with what they have available. However, if you are worried then ask as staying quiet may, just may, turn out to run into a problem that was avoidable.

The Coalition for Personalised Care

This coalition is an organisation the PAS are a member of and our Acting Chair of Trustees Katrina Burchell attended their first meeting where the role of the C4PC, ambassadors and future contributors were subjects of discussion alongside “what makes good personalised care”. The outcome in a nutshell was that people felt being listened to and being seen as a human and holistically were key factors. The C4PC is part of NHS England and is looking to answer questions and provide information on improving health and social care. If you are interested in finding out more you can visit their website at Coalition for Personalised Care https://coalitionforpersonalisedcare.org.uk
This organisation is looking for a more diverse range of contributors in terms of age, health issues, race and sex so if you know anyone who might be interested as an individual in contributing please pass on the website address.

Personal Stories

Whether you are newly diagnosed, still struggling for an answer, or a long-time member with PA, we would love to hear from you to contribute to our new series of Personal Stories. We know that these stories resonate loudly with our members and provide comfort in what is often a challenging journey to getting appropriate treatment and support. If you are willing to share your story with our members, either here in our newsletter or on our website (or both) please contact katrina@pasoc.org.uk who will provide our outline template and requirements for what is required. By sharing your story, wherever you are in the journey you will really help your fellow members and support our ongoing drive to raise awareness to the wider community.

Personal Story: Dr. John Warren

I'm a doctor, now 79 years old. There is no family history of pernicious anaemia. My sister and maternal grandfather both had type 1 diabetes, adult onset, a condition which nowadays is considered to have an autoimmune basis. In my 30's I was having a haircut, and the barber commented on a circular bald patch on my scalp. I recalled having noticed a bald patch on my leg a couple of years earlier, but the hair had regrown. I consulted a dermatologist colleague, who confirmed that I had alopecia areata, an autoimmune disease. I wasn't too bothered about this and life went on.

Around the age of 50, I started to get very tired, and my memory seemed strangely unreliable. I would see a patient whom I had seen a month or two before, and there was my handwriting in the notes, but I had no recollection of the previous consultation. This was scary. At the same time I developed chronic diarrhoea, 8-10 times a day. And my mouth was full of aphthous ulcers, and the tip of my tongue was sore. I began to think I might have some serious condition, but had no idea what it was. Once, after I had climbed four flights of stairs in the hospital one of the junior doctors I worked with asked if I had checked my haemoglobin recently, and, stupidly, I took no notice. Every day when I got home from the hospital I just went to bed and slept most of the evening.

I was reluctant to consult a colleague and say 'I feel tired all the time', as I know this is a symptom most of my colleagues dread to hear from a patient. Likewise, I wasn't keen on seeing a gastroenterologist, as I knew this would inevitably result in unpleasant endoscopic examination of my guts, particularly not a nice prospect in the department where I myself worked. I began to think I must have some fatal illness, and I just would struggle on until I couldn't go on anymore. In retrospect, I think I was depressed, and my judgement must have been impaired. I went on a skiing holiday in the Alps, thinking a holiday would do me good, but felt even worse at the high altitude and spent most of the week in bed.

I had been a blood donor, and was called to give blood every 6 months. The call came, and even though I felt so ill, I went along. They carried out the customary finger prick blood test, and then, to my surprise, refused to take my blood, as the haemoglobin was low. That galvanised me, and I immediately wrote out a request for a full blood count for myself, and went round to the pathology laboratory. Within 3 hours I had the haematologist on the phone to me, to say that there was something very wrong with my blood. I was anaemic, and the red cells were all funny shapes and sizes, some big and some small. The haematologist arranged a check of my iron, B12 and folate. The results showed a very low B12, and very low iron, with normal folate. I immediately prescribed B12 injections and iron tablets for myself.

Following this I contacted a gastroenterologist at a neighbouring hospital and asked if he would investigate my problem. I had my autoantibodies done, and I had antibodies to intrinsic factor, gastric parietal cells and thyroid. Thyroid function showed an abnormal result indicating subclinical hypothyroidism. I had a gastroscopy, and this showed gastric atrophy. I also had a colonoscopy, and this showed no source of bleeding to account for the iron deficiency. Biopsies of the terminal ileum showed a non-specific ileitis, insufficient to support a diagnosis of Crohn's disease. Tests for coeliac disease were negative.

With B12 treatment my memory and fatigue gradually recovered. I reckoned it took 2 years for me to regain my full strength and joie de vivre, but my wife insists it took 3 years. I reckon now, as I approach 80, my cognitive function is as good as anyone could expect.

So it became clear that I had pernicious anaemia, associated with autoimmune thyroid disease and alopecia. Initially, oral iron supplements made the diarrhoea even worse, but after 2 or 3 months I was able to stop them, once the blood count and iron levels had normalised. Naturally I carried on injecting myself with intramuscular hydroxocobalamin 1000 microgrammes. I tried to reduce the frequency of the injections to 3 monthly, as recommended. But I found this was impossible without recurrence of symptoms. About 4-6 weeks after the dose, mouth ulcers, sore tongue and diarrhoea would return, and so I settled on monthly dosage, which I have maintained for the last 30 years since diagnosis. Since I have been on B12 my iron levels have remained in the normal range.

The alopecia has become universal and irreversible now. I continued checking my thyroid function from time to time and the tests remained slightly abnormal, so after 2 or 3 years, and discussion with an endocrinologist, I started taking thyroxine tablets, adjusting the dose to achieve normal thyroid blood tests.

There are some interesting lessons arising from my history. Prior to diagnosis I had not been aware of the impact B12 deficiency may have on the gut. It is mentioned in small print in some textbooks, but I suspect most doctors would not be aware of it. It seems that either the B12 deficiency caused a failure of iron absorption, or it resulted from lack of acid secretion in the stomach, which aids iron absorption. In my case, it seems that a direct effect of B12 deficiency was mainly responsible, since B12 replacement treatment has prevented further episodes of iron deficiency.

The fact that some patients with PA need much more frequent B12 dosage than others remains unexplained, and some of my colleagues believe that patients who request more frequent dosage are making a nuisance of themselves. But who would demand more frequent intramuscular injections than their doctor advised, unless there was a massive benefit from it? One might have expected patients on regular IM injections to abscond.

The clustering of autoimmune diseases has been noticed for many years. In the 1960's the term 'thyrogastric syndrome' was given to the association of autoimmune thyroid disease and chronic autoimmune gastritis (which leads to malabsorption of vitamin B12, and failure of hydrochloric acid secretion by the stomach). More recently this association has been included in 'polyglandular autoimmune syndrome type IIIb'. The thyroid disorder is the most frequent autoimmune disease, and has been found to be associated with gastric disorders in 10-40% of patients. The other way on, some 40% of patients with autoimmune gastritis are found to have thyroid disorder. So far as I know no one has explained what triggers the onset of these autoimmune diseases. Clearly some patients inherit a genetic tendency to get them. But not all patients with such a tendency develop disease. My mother (whose father and daughter both developed type I diabetes) lived to 96, and had thyroid and gastric parietal cell antibodies, but she never developed clinical pernicious anaemia, thyroid disorder, or any other autoimmune disease.

Report of the AGM

The Pernicious Anaemia Society's Annual General Meeting took place on Saturday 10th September 2022.
Including Trustees, 24 people attended. A minutes silence was held prior to the start of the meeting as a mark of respect to HM Majesty, Queen Elizabeth II.
With the resignation of Martyn as Chair of the Trustees in June 2022, the acting Chair, Katrina Burchell chaired the meeting.
It is confirmed that Mr Norman Thomas, Mr Mike Stevenson and Mrs Elise Dyer have now resigned as Trustees whilst Dr John Warren and Mrs LIz Smart have accepted roles as Trustees. Katrina thanked the outgoing and the new Trustees for their support.
Quarterly Trustee meetings are now going to be held and the proposed date for the 2023 AGM is 9th September.

Participants needed for Research Project

Exploring patient experiences of Pernicious Anaemia symptoms and their effects on functioning and well-being.

Whilst research is growing around the symptoms of Pernicious Anaemia, the effect these symptoms have on patients functioning and well-being, needs to be investigated and highlighted further.
For this reason, a research project exploring patient experiences of Pernicious Anaemia symptoms, and their effects on functioning and well-being, is going to be carried and we need your support please.

To find out more about this study and to offer your help, please contact Hannah Marshall at Cardiff Metropolitan University, to see if you are eligible to take part in this important and growing area of research:
To contact Hannah, please email: st20105513@outlook.cardiffmet.ac.uk

Please note, you will need to have a formal diagnosis of Pernicious Anaemia from a medical professional to participate in the study.

Supporting Alzheimer's is Preventable Campaign

We were recently contacted by Foodforthebrain.org, a charity that aims to raise awareness of the importance of optimum nutrition in mental health. This organisation aims to inform organisations and empower individuals to change their diet and lifestyle and take greater control over their own mental health. Knowing that B12 is fundamental to cognitive function we were happy to support their latest campaign entitled Alzheimer's is Preventable by allowing them to use the PAS logo in their marketing materials and to provide a link to their campaign here in our newsletter.
https://foodforthebrain.org/
At their website they are encouraging visitors to take the Cognitive Function Test which will help them research what prevents cognitive decline.
On their website you can read various articles about diet and mental health including ones specifically on B12. Details of their current campaign are here : Alzheimer's Is Preventable - Food for the Brain

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New US PAS Support Group

We are very fortunate to have a lovely member who has carried out our volunteer training in order to take on the role of Support Group Coodinator - in Chicago!!
Julie's first meeting will take place online on 12th November - if you live in the US, keep an eye on your mailbox for further details!

Currently, we have Support Groups in Wiltshire, Somerset, West Sussex, West Wales, South Wales and Greater London East & West and we send our thanks to the wonderful Coordinators that hold the reins in these areas.
Contact details for our groups can be found on our [Support Group website-page](#).

If you are interested in becoming a Support Group Coordinator, please get in touch. We would love to hear from you and it is very rewarding knowing you are making a difference. We are able to offer a training course and a 'coordinators toolkit' which gives you all the information you would need to manage a successful support group. Want to know more? Get in touch! You will be given an informal introductory meeting with the PAS team, training and support.
Email to: info@pasoc.org.uk or call +44 (0)7783 318525

PAS Support

Call the Helpline

01656 817085

Monday-Friday between 8.30am and 12.30pm.

Volunteers: Alex, Kathy, Jane, Alex, Liz & Karyl

Send us an email

For members who live overseas or prefer email:
support@pasoc.org.uk
Questions about your membership:
membership@pasoc.org.uk.
For general questions:
info@pasoc.org.uk