An explanation on the importance of folate and ferritin levels and why you must always get copies of test results

1. Question your doctor about blood tests or any test result. Never accept your doctor's answer that everything is normal or all is fine. What may mean normal to your doctor may not be helping you at all. You could be on the low end of normal and getting worse. Ask your doctor, never the nurse or receptionist, for copies of all of your test results. You are entitled to them. Some doctors may request that you put it in writing, if so, just write a letter. You may or may not be charged a fee for photocopies.

Once you get a copy of your blood tests, keep them for comparison purposes, you will learn how to interpret them and be able to see for yourself if you are improving. You will know exactly what your B12 level is and what tests may or may not have been done. Ask for copies of any letter or report that a specialist may have sent to your GP regarding your illness..the specialist may have made certain recommendations as to frequency of injections. This kind of letter is important should you change doctors.

2.(a) Always have your doctor check your folate (folic acid) and ferritin (iron stores) levels as often as the B12 level. When you get your test result for ferritin, look at the reference range. If the upper range is 300, then you need to have a ferritin level of at least 80. Folate levels need to be in the high upper end of the reference range, about ¾ of the range. If the upper range for serum folate is 30, then you need to be at least 15.

(b) It is quite common for PA/B12D patients to develop another co-existing anaemia, either folate or iron. If you are low in folate, it affects the uptake of B12, meaning the B12 is not properly utilised. . Further, research states that a low serum folate causes more B12 to be excreted. B12 needs folate as much as folate needs B12, they really do work hand in hand. Read more at the link below.

https://link.springer.com/article/10.1007%2FBF00256639

If you are low in iron then frequent B12 injections will increase the risk of developing iron anaemia. B12 increases red blood cell production and in so doing, places a greater demand on iron as iron, as well as folate, form part of the red blood cell.

Once vitamin B12 has been administered, the increase in red cell production will increase the demand on iron stores and, therefore, it is important to monitor – and correct – any signs of iron deficiency.

http://www.haematologica.org/content/91/11/1506.full.pdf+html

3. The importance of folate to B12 and B12 to folate. The interrelationship between the two.
INTERRELATIONS OF VITAMIN B12 AND FOLIC ACID METABOLISM:

FOLIC ACID CLEARANCE STUDIES
These findings suggest that in the vitamin B12-deficient subject, PGA is rapidly converted to an L. casei-active and presumably metabolically useful form (probably N5-methyl-tetrahydrofolic acid) which then "piles up" in the serum because vitamin B12 is required for its normal utilization. This "piled up" folate activity would tend to reduce the amount of folic acid available for other 1-carbon unit transfers. These studies, by providing evidence for the concept that vitamin B12 is required for normal folic acid metabolism, support the possibility that the apparent folic acid deficiency in many patients with vitamin B12 deficiency may be in large measure due to secondarily deranged folic acid metabolism.

Two minor observations of the present study were:

1. The intravenous injection of 15 Mtg of PGA per kg of body weight did not appear to affect significantly either the serum vitamin B12 level or the folic acid activity of the red cell for L. casei. The latter finding suggests that the mature erythrocyte is relatively impermeable to folic acid.

2. Folic acid activity for L. casei and vitamin B12 activity for E. gracilis both may be much higher in reticulocyte-rich than in reticulocyte-poor erythrocytes after vitamin B12 therapy. This suggests that the reticulocyte or its precursors, or both are relatively permeable to folic acid and vitamin B12.
NOTE – PGA is short for pteroylglutamic acid which is folic acid.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC291041/pdf/jcinvest00315-0081.pdf

4. The Folate Trap – Vitamin B12 and Folic deficiencies always co-exist. Deficiency of one vitamin can precipitate the deficiency of the other vitamin also.
http://www.namrata.co/folate-trap/

5. A good description of Folate deficiency and its causes:
http://www.namrata.co/case-study-folic-acid-deficiency/

6. A research article by Scand J Haematol(l980) Sheppard K, Ryrie D. states that B12 levels are dependent on folate status. This means that a person could be folate deficient which causes the B12

level to go low. Once the person is treated with folic acid this also returns the B12 level to normal. However, if you are already deficient in B12 and getting B12 injections the artiicle may explain why it seems the injections are not working the way they should. When your folate level is low, it causes the B12 analogues (inactive B12) to increase and the cobalamin (active B12) to decrease. Inactive B12 or B12 analogues is the B12 your body cannot convert. Active B12 is the B12 your body needs and can use...Methylcobalamin and Adenosylcobalamin are the two active forms of B12 and are what your body converts cyanocobalamin and hydroxocobalamin injections to. The link to the research article is below:

http://www.ncbi.nlm.nih.gov/pubmed/7221475

7. (a) Low folate impairs glucose tolerance and can elevate cholesterol levels..

"These results demonstrate impaired glucose tolerance and disturbed plasma lipid profile induced by oral contraceptive treatment in folic acid deficient rats and suggest that inadequate folic acid intake might contribute to increased cardiovascular risk during oral contraceptive use that could be prevented by proper oral folic acid intake."

http://www.ncbi.nlm.nih.gov/pubmed/18572393

7. (b) Folate deficiency associated with insulin resistance

"CONCLUSION: These findings demonstrate that the SHR model is susceptible to the adverse metabolic and hemodynamic effects of low dietary intake of folate. The results are consistent with the hypothesis that folate deficiency can promote oxidative stress and multiple features of the metabolic syndrome that are associated with increased risk for diabetes and cardiovascular disease.

http://www.ncbi.nlm.nih.gov/pubmed/23382337

8. Folate Anaemia caused by antibodies to Folate Receptors:
The diagnostic utility of folate receptor autoantibodies in blood.

Abstract

Folate supplementation reduces the risk of neural tube defect (NTD) pregnancy, and folinic acid has been used to correct cerebral folate deficiency (CFD) in children with developmental disorders. In the absence of systemic folate deficiency, the discovery of autoantibodies (AuAbs) to folate receptor α (FRα) that block the uptake of folate offers one mechanism to explain the response to folate in these disorders. The association of FRα AuAbs with pregnancy-related complications, CFD syndrome, and autism spectrum disorders and response to folate therapy is highly suggestive of the involvement of these AuAbs in the disruption of brain development and function via folate pathways. The two types of antibodies identified in the serum of patients are blocking antibody and binding antibody. The two antibodies can be measured by the specific assays described and exert their pathological effects either

by functional blocking of folate transport as previously shown or hypothetically by disrupting the FR by an antigen-antibody-mediated inflammatory response. We have identified both IgG and IgM AuAbs in these conditions. The predominant antibodies in women with NTD pregnancy belong to the IgG1 and IgG2 isotype and in CFD children, the IgG1 and IgG4 isotype. This review describes the methods used to measure these AuAbs, their binding characteristics, affinity, cross-reactivity, and potential mechanisms by which folate therapy could work. Because these AuAbs are associated with various pathologies during fetal and neonatal development, early detection and intervention could prevent or reverse the consequences of exposure to these AuAbs.

http://www.ncbi.nlm.nih.gov/pubmed/23314538

9. Chronic conjunctivitis linked to low normal folate levels..patient was not even folate deficient but responded to folic acid supplements.

Chronic conjunctivitis in a patient with folic acid deficiency

"*The patient's level of folic acid was in the lower reference range (9.9 nmol/l, reference 7.0–40 nmol/l). Oral folic acid was prescribed to the patient by her general physician, her level of folic acid increased rapidly and she was relieved from all her symptoms. When serum levels of vitamins are measured, there are sources of error and 'grey zones' of clinical relevance. As always, the clinical picture and laboratory tests must be weighed together – treatment should not rely on a single laboratory test.Because treatment with folic acid normalized the patient's level of folic acid and relieved her from all symptoms, we believe that a clinically significant lack of folic acid did indeed exist*."

http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0420.2007.01017.x/pdf

10**. Folate Deficiency and Cervical Dysplasia**

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JAMA. 1992;267(4):528-533. doi:10.1001/jama.1992.03480040076034

Abstract

Objective. —To test the hypothesis that nutritional deficiency affects the incidence of cervical dysplasia in young women.

Design and Setting. —Case-control study. Participants were derived from community family-planning clinics and referrals to a colposcopy center.

Participants. —A total of 726 subjects were screened, yielding 294 cases of dysplasia and 170 controls defined by coexistent cytologic and colposcopic evidence.

Main Outcome Measures. —Planned prior to data collection. Odds ratios were computed using logistic regression models to evaluate association between cervical dysplasia and sociodemographic, sexual, and reproductive factors; smoking; oral contraceptive use; human papillomavirus (HPV) infection; and 12 nutritional indices determined by blind analysis of nonfasting blood specimens.

Results. —The number of sexual partners, parity, oral contraceptive use, and HPV-16 infection were significantly associated with cervical dysplasia. Plasma nutrient levels were generally not associated with risk. However, red blood cell folate levels at or below 660 nmol/L interacted with HPV-16 infection. The adjusted odds ratio for HPV-16 was 1.1 among women with folate levels above 660 nmol/L but 5.1 (95% confidence interval, 2.3 to 11) among women with lower levels. Interactions of red blood cell folate levels with cigarette smoking and parity were also present but were not statistically significant.

Conclusion. —Low red blood cell folate levels enhance the effect of other risk factors for cervical dysplasia and, in particular, that of HPV-16 infection.(JAMA. 1992;267:528-533)

http://jamanetwork.com/journals/jama/article-abstract/394723

11**. Public health failure in the prevention of neural tube defects: time to abandon the tolerable upper intake level of folate**

Taking folic acid will mask a B12 Deficiency – this phrase is outdated and applied to that time in the history of B12 deficiency when there was not a serum B12 test. This article places the emphasis on the doctors to know enough to check both B12 and folate levels.

For folate, the IOM attempted to determine an LOAEL from a review of 23 studies of patients with a B12 macrocytic anaemia (pernicious anaemia), mainly conducted in the 1950s, 11 of which were single-patient case reports [15]. At that time, the distinction between folate deficiency and B12 deficiency was not recognised and assays for the two vitamins had not been developed. A deficiency in either vitamin causes the same type of anaemia— a macrocytic anaemia with a megaloblastic bone marrow. A patient with B12 deficiency may superficially appear to be treated successfully with folic acid because the macrocytic anaemia can resolve, but not the neurological disease. Only B12 administration will stop the subacute combined degeneration of the spinal cord and peripheral neuropathy. Intake of folic acid was, then, said to "mask" the diagnosis of B12 deficiency because folic acid resolves the anaemia. However, masking is now a misleading term to describe the clinical situation, because it reflects a historical period when folate deficiency could not be distinguished from B12 deficiency. Folic acid was used as treatment, and the macrocytic anaemia due to B12 deficiency remitted; the subsequent occurrence of a neurological

deficit was wrongly interpreted as an adverse effect of folic acid instead of an inability to make the correct diagnosis and provide the necessary B12 treatment. Dickinson [17], who considered these reports, concluded that making an error of diagnosis should not be confused with possible folic acid toxicity. The likelihood of masking an incorrect diagnosis disappeared during the latter half of the last century, with the introduction of specific assays for folate and B12 deficiency, and with the ready availability and common use of B12 therapy.
https://publichealthreviews.biomedcentral.com/articles/10.1186/s40985-018-0079-6

12. **Ferritin levels** must be monitored for the following reason:

" *Once vitamin B12 has been administered, the increase in red cell production will increase the demand on iron stores and, therefore, it is important to monitor – and correct – any signs of iron deficiency*." Page 5 of the article, 2nd paragraph from bottom on right side.

http://www.haematologica.org/content/haematol/91/11/1506.full.pdf

Low iron can also cause problems with swallowing. Thanks to Nichola Watson for finding the article below:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1440161/?page=1

13. **Cobalamin deficiency can mask depleted body iron reserves**.

Solmaz S, et al. Indian J Hematol Blood Transfus. 2015.

Show full citation

Abstract

Vitamin B12 deficiency impairs DNA synthesis and causes erythroblast apoptosis, resulting in anaemia from ineffective erythropoiesis. Iron and cobalamin deficiency are found together in patients for various reasons. We have observed that cobalamin deficiency masks iron deficiency in some patients. We hypothesised that iron is not used by erythroblasts because of ineffective erythropoiesis due to cobalamin deficiency. Therefore, we aimed to demonstrate that depleted iron body reserves are masked by cobalamin deficiency. Seventy-five patients who were diagnosed with cobalamin deficiency were enrolled in this study. Complete blood counts and serum levels of iron, unsaturated iron binding capacity (UIBC), ferritin, vitamin B12, and thyroid stimulant hormone were determined at diagnosis and after cobalamin therapy. Patients who had a combined deficiency at diagnosis and after cobalamin therapy were recorded. Before cobalamin therapy, we found increased serum iron levels (126.4 ± 63.4 µg/dL), decreased serum UIBC levels (143.7 ± 70.8 µg/dL), increased serum ferritin levels (192.5 ± 116.4

ng/mL), and increased transferrin saturation values (47.2 ± 23.5 %). After cobalamin therapy, serum iron levels (59.1 ± 30 µg/dL), serum ferritin levels (44.9 ± 38.9 ng/mL) and transferrin saturation values (17.5 ± 9.6 %) decreased, and serum UIBC levels (295.9 ± 80.6 µg/dL) increased. Significant differences were observed in all values ($p < 0.0001$). Seven patients (9.3 %) had iron deficiency before cobalamin therapy, 37 (49.3 %) had iron deficiency after cobalamin therapy, and a significant difference was detected between the proportions of patients who had iron deficiency ($p < 0.0001$). This study is important because insufficient data are available on this condition. **Our results indicate that iron deficiency is common in patients with cobalamin deficiency, and that cobalamin deficiency can mask iron deficiency. Therefore, we suggest that all patients diagnosed with cobalamin deficiency should be screened for iron deficiency, particularly after cobalamin therapy.**

PMID 25825568 [PubMed]

PMC4375157 [Available on 2016/6/1])

http://www.ncbi.nlm.nih.gov/m/pubmed/25825568/?i=7&from=b12&sort=PublicationDate

14. Learn as much as you can about PA/B12 Deficiency because most doctors are not forthcoming with information regarding PA/B12 Deficiency. You can read more on PA/B12D at the following links below:

http://www.nhlbi.nih.gov/health/health-topics/topics/prnanmia/

http://emedicine.medscape.com/article/204930-overview

http://www.patient.co.uk/doctor/Pernicious-Anaemia-and-B12-Deficiency.htm

An up to date website providing information on all things related to B12 Deficiency, including signs and symptoms, please visit
http://www.b12deficiency.info/

15. Cyanocobalamin is the B12 serum that is used in the United States and Canada and some European countries. The UK, Australia, New Zealand and other countries use hydroxocobalamin. If you are not sure what serum is being used, ask your doctor. Anyone who smokes should not use cyanocobalamin in any form, be it injections or oral tabs. "*Cobalamin has a strong attraction to cyanide. Heavy smokers can build up too much cyanide in their bodies which can overwhelm the pathway that converts cyanide to thiocyanate in order to detoxify the cyanide. If that happens then the body may detoxify the cyanide by attaching it to cobalamin and then excreting the cyanocobalamin*."

Which means that most of the injection is wasted.

Linnell JC, Matthews DM. Cobalamin metabolism and its clinical aspects. Clin Sci (Lond). 1984 Feb;66(2):113-21.

16. Anyone who carries the Lebers Optic Neuropathy Disease gene should not use cyanocobalamin because the cyanocobalamin can make the disease worse and could cause blindness.

Leber hereditary optic neuropathy (LHON) is an inherited form of vision loss. Although this condition usually begins in a person's teens or twenties, rare cases may appear in early childhood or later in adulthood. For unknown reasons, males are affected much more often than females.

Blurring and clouding of vision are usually the first symptoms of LHON.

http://ghr.nlm.nih.gov/condition/leber-hereditary-optic-neuropathy

HYDROXOCOBALAMIN IN THE TREATMENT OF LEBER'S HEREDITARY OPTIC ATROPHY

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Abstract

Two patients with Leber's hereditary optic atrophy had been treated unsuccessfully with cyanocobalamin. The discovery that hydroxocobalamin is superior to cyanocobalamin in the treatment of tobacco amblyopia prompted a trial of this compound in the two patients. The dose was 1 mg. twice weekly in one, and 1 mg. weekly in the other. Visual acuity in both eyes improved, though in one case this improvement might have been fortuitous.

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(68)90243-2/abstract

17. Taking a Vitamin B complex also assists in recovery from B12 Deficiency. It is suggested by the University of Maryland Medical Centre that taking a single B vitamin such as B12 for a period of time can cause an imbalance in the rest of the B vitamins. Do not exceed 10 mg of B6 daily. B6 is the only B vitamin that can cause toxicity if too much is taken. Please read the protocol file, Section, Other Supplements – B complex for the link to the research that supports 10 mg daily. We also recommend that you take a B complex for 4 months and then stop for 2 months.
" According to the University of Maryland University Medical Centre, "Taking any one of the B complex vitamins by itself for a long period of time can result in an imbalance of other important B vitamins. For this reason, it is generally important to take a B complex vitamin with any single B vitamin."

http://www.umm.edu/altmed/articles/vitamin-b12-000332.htm