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**Title** Just Vitamin B12 Deficiency?

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### **CLINICAL VIGNETTE**

## Just Vitamin B12 Deficiency?

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A 46-year-old female presented for urgent follow-up with a specific request for early vitamin B12 injection. She was diagnosed with vitamin B12 deficiency 3 years ago after years of chronic fatigue, breathlessness, bilateral lower extremity paresthesia, and inability to gain weight which she attributed to chronic dyspepsia.

She underwent extensive gastrological work-up including endoscopy and colonoscopy by an outside gastroenterologist 5 years ago and diagnosed with dyspepsia and gastritis. She has been on daily PPI and was told "everything is fine and she has no cancer." She still complained of constant stomach upset with diarrhea despite the PPI and did not gain weight.

She was ordered for vitamin B12 injections in the office every three months, but was not compliant because of hectic daily activities with her pre-teenage children. She feels wonderful and energized after each injection, but reports the fatigue returning in less than 4 weeks.

Her diet includes meats, including beef, chicken, fish, and all dairy products. She has no family history of vitamin B12 deficiency or other autoimmune conditions.

#### Physical Exam

Overall, vitals are stable, with stable BMI of 20. Her exam was unremarkable, including a benign abdominal exam.

#### Laboratory Data

CBC remarkable for mildly macrocytic anemic, with hemoglobin 11 (normal 11.6 - 15.2), and MCV of 110 (79-98). Vitamin B12 was low at 150 (normal range 254-1060), taken 3 weeks from last injection. Iron, ferritin, folate and chemistries are normal. Intrinsic Factor Antibody was positive.

Pernicious Anemia is a form of anemia which was first described in the mid-19th century and known to cause jaundice, severe fatigue, weight loss, muscle spasms and pallor. Symptoms are initially very subtle but progressive, and can lead to death. Initial treatments were devised by an American physician George Whipple, who noted in experiments with anemic dogs that feeding large amounts of liver to these dogs improved their symptoms. Dr. Whipple's work suggested that in certain types of anemia there may be a decreased amount of "material" from which red blood cells are formed. Two other physicians, William Murphy and George Minot, observed that upon consumption of liver extract, patients with pernicious anemia could recover for extended periods. Dr. Minot also noted that achlorhydia consistently preceded pernicious anemia. Ultimately the liver extract was found to contain a "gastric factor" that promoted a reaction in the stomach which enabled the absorption of vitamin B12, the material missing in red blood cell formation which Dr. Whipple had alluded to many years before.

Pernicious Anemia is an autoimmune disease involving decreased production of intrinsic factor secondary to gastric mucosa atrophy, although antibodies directed against binding of Intrinsic Factor to Vitamin B12 and ileal mucosa have also been identified. The incidence is approximately 120/100,000.<sup>1</sup> Pernicious Anemia is a disease which can occur in all ethnic groups and ages but generally affects people older than 60 of European descent. It can occur earlier in life, particularly in patients who are not of European descent. It is also common for diagnosis to be delayed for years due to its subtle clinical presentation.

Evaluation for Pernicious Anemia usually begins after identification of Anemia with a mean corpuscular volume above 100 and a low reticulocyte count. Folic acid deficiency should also be screened for at this stage. Hyperpigmentation of skin, psychiatric symptoms or neurologic symptoms can be early clues. The more common neurologic findings include symmetric extremity paresthesias, gait issues and numbness. Neuropathy usually affects lower bilateral extremities more often than upper extremities.<sup>1</sup> Psychiatric findings include depression, increased irritability, and occasionally psychosis. Neuropsychiatric symptoms have been observed to precede macrocytosis. Suspicion for Pernicious Anemia based on Macrocytic Anemia or clinical findings should prompt measurement of Vitamin B12. If levels of Vitamin B12 are low or borderline, Intrinsic Factor Antibody can then confirm the diagnosis of Pernicious Anemia.

Pernicious Anemia is a prevalent autoimmune blood disorder which can be identified in the primary care clinic setting. In our patient, use of a proton pump inhibitor for Gastroesophageal Reflux Disease was an initial confounding variable due to the known side effect of diminished B12 absorption. Worsening abdominal discomfort despite PPI therapy prompted gastroenterology evaluation which confirmed Atrophic Gastritis on endoscopy. The diagnosis of Pernicious Anemia via positive Intrinsic Factor antibody testing was conducted afterwards. This patient visited our office after diagnosis of Atrophic Gastritis. She had been tolerating B12 injections well but was confused about her actual diagnosis. She was relieved to have an answer after Pernicious Anemia was confirmed. Surveillance endoscopy will be scheduled due to a slightly increased risk of Gastric Cancer.

#### REFERENCES

1. **Hoffbrand AV**. Megaloblastic Anemias.In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, editors. *Harrison's Principles of Internal Medicine 19e*. New York: McGraw-Hill; 2014.

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