

Pernicious Anaemia

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INTRODUCTION

The definition of pernicious means “highly injurious, destructive or deadly which accurately depicts the type of anaemia that Thomas Addison, an English physician first described in 1855. But it was Anton Biermer, a German physician who coined the name of “pernicious anaemia” between 1868 and 1872, after noting the progressive destructive course it took. The first step towards controlling the disease was taken by American pathologist, George Whipple who induced anaemia in dogs and experimented with different kinds of diets including liver to see which food would regenerate the dog’s haemoglobin. Liver was obviously the answer. However, it was in 1948, an American group led by Karl Folkers and an English group led by E. Lester-Smith published, within weeks of each other, the isolation of a red crystalline substance termed vitamin B12 and subsequently renamed cobalamin. The disease was now controllable and no longer fatal.

While, it is believed that Pernicious Anaemia (PA) is a disease associated with the process of aging, there are many persons of a younger age from late teens, twenties and thirties who have been diagnosed with PA. PA is not a curable disease, but a controllable condition, managed by the administering of Vitamin B12. PA is the result of the inability of the body to absorb vitamin B12. It is a type of anaemia which causes a fall in the number of red blood cells. The formation of the red blood cells depends on the adequate absorption of vitamin B12, which depends upon the presence of the “intrinsic factor” that is secreted by the stomach lining. If the secretion of this substance stops, it will never restart and the treatment of this condition is injections of vitamin B12, bypassing intestinal absorption, which will be required for the patients’ remaining life span.

Although anaemia is often a symptom, PA is actually the end stage of an autoimmune inflammation of the stomach, resulting in destruction of stomach cells by one's own antibodies. Progressive destruction of the cells that line the stomach cause decreased secretion of acid and enzymes required to release food bound vitamin B12. Antibodies to intrinsic factor (IF) bind to IF preventing formation of the IF-B12 complex, further inhibiting vitamin B12 absorption. Eating large amounts of vitamin B12 enriched liver or taking B12 tablets orally, will not make a difference to a person with PA because the B12 contained in the liver/tablets cannot be absorbed when the IF is absent.

Those with one autoimmune disease like PA may also have other autoimmune diseases such as:

- Autoimmune Thyroiditis (this can result in an underactive or over active thyroid)
- Coeliac Sprue (the inability of the body to deal with gluten)
- Eczema
- Psoriasis etc.

It is important for those with PA to have their bloods checked for all related auto immune diseases on a regular basis e.g. every 6 months. PA often results in the body's inability to absorb iron and folate from food so this should also be monitored to ensure that the affected person does not become iron and/or folate deficient which can compound and worsen the symptoms of PA.

MEDICAL DEFINITIONS:

Intrinsic Factor: A substance that is secreted by the gastric mucous membrane in the stomach and is essential for the absorption of vitamin B12 in the intestines.

Vitamin B12: Vitamin B12 (cobalamin) is an important water-soluble vitamin. In contrast to other water-soluble vitamins it is not excreted quickly in the urine, but rather accumulates and is stored in the liver, kidney and other body tissues. As a result, a vitamin B12 deficiency may not manifest itself until after 5 or 6 years of a diet supplying inadequate amounts or the onset of PA. Vitamin B12 functions as a methyl donor and works with folic acid in the synthesis of DNA and red blood cells and is vitally important in maintaining the health of the insulation sheath (myelin sheath) that surrounds nerve cells.

Autoimmune Disease: A condition in which the body's immune system reacts against its own tissues.

Antibodies: Specialized proteins produced by white blood cells (lymphocytes) that recognize and bind to foreign proteins or pathogens in order to neutralize them or mark them for destruction.

Atrophic Gastritis: A chronic inflammation of the lining of the stomach, which ultimately results in the loss of glands in the stomach (atrophy) and decreased stomach acid production.

Atrophy: A decrease in size or wasting away of a body part or tissue.

Endoscopy: A procedure by which a camera is introduced down to the stomach and the ileum (small intestine) to visually examine the stomach and ileum. A biopsy can be taken to rule out coeliac sprue and determine whether chronic atrophic gastritis exists, which would confirm a diagnosis of PA. This test can be performed using a numbing spray on the throat and takes approximately 10 minutes. Alternatively the patient can request a sedative but must then be accompanied for the following 24 hours and must not drive or operate machinery. Whether with sedative or not this is generally an out patient procedure, however it does differ from country to country. It is important to discuss the above options with your consultant prior to the procedure. Most consultants run appointment clinics and surgery clinics. If you leave it to the day of the procedure your consultant may not have enough time to discuss this with you so you may find it helpful to first get an appointment to discuss the procedure and then book your endoscopy date once you have all the information you need.

GENERAL PA SYMPTOMS

The following general symptoms are common in those with PA:

- Weakness
- Fatigue
- Upset stomach
- Abnormally rapid heartbeat (tachycardia) and/or chest pains
- Abnormal yellow colouration of the skin (jaundice)
- Heightened sensitivity to hearing, smell, and taste
- Vision distortion, e.g. seeing stars, or double vision
- Fog days, where you have difficulty in thinking clearly
- Breathlessness
- Headache.

NEUROLOGICAL SYMPTOMS

The neurological symptoms of vitamin B12 deficiency may include:

- Numbness and tingling of the arms and more commonly the legs
- Difficulty walking
- Loss of balance
- Memory loss
- Disorientation
- Dementia
- Extreme mood changes.

Some experience many of these symptoms and some none of them. It depends on how quickly the PA is treated and on how well managed it is.

GASTROINTESTINAL SYMPTOMS

The gastrointestinal symptoms of vitamin B12 deficiency may include:

- A sore tongue
- Appetite loss
- Diarrhea and constipation - These have been associated with vitamin B12 deficiency. Their origins are unclear, but may be related to the stomach inflammation underlying some cases of B12 deficiency, or the increased vulnerability of the rapidly dividing cells along the gastrointestinal tract to impaired DNA synthesis.

DIAGNOSIS - TESTS

The usual tests performed by your doctor to reach a diagnosis of PA are as follows:

Blood Tests

- Full Blood Count
- B12 Levels
- Intrinsic Factor Antibodies
- Parietal Cell Antibodies

Further Tests

- **Endoscopy** — You may be referred for an endoscopy to rule out other reasons for B12 deficiency
- **Schillings Test** — this test involves ingesting radioactive B12 to determine the bodies ability to absorb B12. 2 tests are usually performed, 1 without intrinsic factor and one with added intrinsic factor. This test can be inconclusive for many people, while it can give a definitive diagnosis this is not always achieved and the risk involved needs to be taken into consideration.
- **MRI:** Magnetic Resonance Imaging is an imaging technique used primarily in medical settings to produce high quality images of the inside of the human body --
- to look for subacute combined degeneration of the spinal cord, a definite diagnosis of PA.

TREATMENTS:

B12 - Injections

Loading — on first diagnosis with PA it is essential to get what are called “Loading Doses”. These are injections of B12 at short intervals in order to quickly build up your levels of B12. An example of a loading regime is:

1. Daily injections x 2 weeks
2. Weekly injections x 4-8 weeks

Then the prescription changes to monthly or tri-monthly depending on where you live. The treatment for PA is very fragmented world-wide.

The majority of countries use Hydroxocobalamin as their preferred choice of injectable B12 serum. Other countries, such as Spain, France, Belgium and Canada use Cyanocobalamin. The United States uses both Hydroxocobalamin and Cyanocobalamin. After initial loading doses, Hydroxocobalamin users usually begin a regime of injections, monthly, once every 2 months or once every 3 months depending on what is recommended by their doctor. Cyanocobalamin users generally begin a regime of monthly injections once the loading doses have been given.

B12 - Lozenges

Many of those diagnosed with PA benefit from the use of Methylcobalamin sublingual lozenges in addition to their injections. Methylcobalamin differs from Hydroxocobalamin and Cyanocobalamin, it is considered “bioactive”, which means that it doesn’t have to undergo any chemical reactions in the body before it starts working. It is best to use the lozenges that contain the added supplements of Vitamin C and Folate which ensures maximum absorption of B12. However, if you are already taking a prescribed folate supplement, you should just use the methylcobalamin without the added supplements.

Iron

Those diagnosed with PA may have no stomach acid which seriously inhibits the body’s ability to absorb iron from foodstuffs. Therefore iron supplementation may be required. If this is required it is lifelong and should be taken along with the prescribed B12 treatment to ensure one’s wellbeing.

Folate

Folic acid anaemia can co-exist with PA and as such means taking a prescribed amount of 5 mcg daily for life-time. B12 levels should always be checked before supplementing with folate as folate supplements can improve the well-being so much that they can mask an underlying B12 deficiency. This can result in nerve damage over a long time. It is perfectly ok to take folate supplements while on a regime of B12 injections.

ONGOING TESTS:

The following tests should be performed on those with PA at regular intervals once stabilised:

Blood Tests

- Full Blood Count (~every 6mths)
- B12 Levels (~every 6mths)
- Folate Levels (~every 6mths)
- Ferritin Levels (~every 6mths)
- Thyroid Function Tests (TFT) (~every 6mths)
- Thyroid Antibody Tests (~every 6mths)

Further Tests

- **Endoscopy** (~every 2yrs)