Vitamin B-12 deficiency is common in older adults, and is becoming more common in younger adults, primarily due to the use of stomach acid suppressing medications more commonly known as proton-pump inhibitors (PPI's). The most common cause of vitamin B-12 is protein-bound malabsorption due to hypochlorhydria (lack of stomach acid). Recognition of this deficiency is often difficult, however, due to the subtlety of symptoms, slow onset, and absence of a standard diagnostic marker. The clinical presentation of B-12 deficiency varies considerably and includes neuro-psychiatric symptoms, hematologic changes, or both. Additionally, a deficiency can be present in the absence of any signs or symptoms. Early diagnosis is vital because of the potential for irreversible neurologic damage without timely intervention.

There are two primary causes of B-12 deficiency in the older population: protein-bound malabsorption and pernicious anemia, with the former being the most common cause. High-dose oral therapy has been used to treat B-12 deficiency for years, but it remains a highly underutilized therapy.

There are many potential causes of B-12 deficiency. The mechanisms range from inadequate digestion (chronic malnutrition) and inadequate absorption to inadequate stores due to chronic liver disease. Drug-induced nutrient deficiency from biguanides (metformin) and PPI’s is also of concern. However, the primary cause of the deficiency is malabsorption of protein-bound sources. The exact incidence of B-12 deficiency is unknown, but some estimates are fairly high, noting that incidence may be greater than 20% in those 60 years of age and older. B-12 occurs naturally in protein of animal origin, but absorption requires an acidic environment in the stomach for cleavage of B-12 from protein. In the presence of hypochlorhydria, protein-bound B-12 passes through the body unabsorbed. Synthetic sources of B-12 (supplements or fortified food) are not affected by hypochlorhydria.

The most promising early marker of B-12 deficiency is serum Holo-TC, but this assay is not readily available to most clinicians. Consequently, measurement of serum B-12 is used most frequently to diagnose a B-12 deficiency, although it lacks sensitivity and specificity. Although deficiency is clinically defined at levels below 150 pmol/L, individuals can exhibit a deficiency at the tissue level, and symptoms can occur with values as high as 350 pmol/L. B-12 insufficiency is often defined by serum values between 148 and 221 pmol/L.

Increased mean corpuscular volume (MCV) has been used to identify megaloblastic anemia, but it is an insensitive marker because macrocytosis can be caused by many other conditions such as folate deficiency, liver disease, hypothyroidism, or bone disease. It has been estimated that 60% of individuals with macrocytosis do not have anemia. Homocysteine (a B-12 dependent metabolite) has also been used to evaluate B-12 status, but using it for diagnostic purposes is problematic because it is nonspecific for B-12; that is, a deficiency of folate and vitamin B-6 can also raise serum concentrations. Serum methylmalonic acid is highly specific for B-12 deficiency but is expensive, not readily available, and is affected by renal dysfunction.

B-12 deficiency may present asymptptomatically in the absence of hematologic changes or with a variety of neuropsychiatric symptoms. Two of the most common psychiatric symptoms are depression and cognitive impairment. It is important to recognize that treatment of a deficiency must be applied early to avoid permanent neurologic damage such as peripheral neuropathy.
Unfortunately, neurologic dysfunction does not always respond to B-12 treatment. Indeed, there appears to be an inverse relationship between time to diagnose and neurologic recovery.

Regardless of the cause of deficiency, oral treatment is effective. The typical dose is 1,000-2,000 micrograms (µ) per day. In the absence of intrinsic factor in the stomach, high-dose oral B-12 is absorbed via passive diffusion throughout the gastrointestinal tract at a rate of approximately 1%-5%. The efficacy and safety of oral therapy has been demonstrated in recent trials.

Because of slow onset, vitamin B-12 deficiency can be unrecognized for long periods of time. Timely recognition and intervention is imperative. If a deficiency is not recognized early, permanent neurological damage can occur. High dose oral B-12 therapy is an effective and safe treatment for deficiency but it is rarely prescribed, despite lower cost and patient preference, primarily due to poor awareness of this as a treatment option. Dietitians can play pivotal roles in increasing general awareness of the need for synthetic sources of B-12 for adults older than 50 years. RD’s are also in a key position to inform medical staff of the risk of permanent injury if a B-12 deficiency is not identified and treated in a timely manner. If you have symptoms or questions, or think you may be deficient, check with your doctor or dietitian for additional information.

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