PAN

VITAMIN B12

DEFICIENCY IN DISGUISE:

A PHYSICIANS' GUIDE TO VITAMIN B12 IN THE EVOLVING DIETARY LANDSCAPE

Contributed by

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> The doctor of the future will give no medicine but will interest their patients in the care of the human frame, in diet, and in the cause and prevention of disease.
>
> — Thomas Edison

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FOREWORD

In the ever-evolving landscape of health and nutrition, few nutrients have attracted as much scientific interest as Vitamin B12. From its essential role in DNA synthesis and neurological function to its impact on energy metabolism and red blood cell formation, Vitamin B12 is far more than just another micronutrient, it is fundamental to the body's metabolic and physiological balance.

"**A Physicians' Guide to Vitamin B12 in the Evolving Dietary Landscape**" explores the multifaceted role of Vitamin B12, covering its biological importance, dietary sources, absorption pathways, deficiency symptoms, recommended dietary allowances (RDA), diagnostic methods, and treatment options. With the increasing prevalence of dietary restrictions and evolving eating patterns, physicians play a vital role in diagnosing, managing, and preventing B12-related health issues. This guide equips healthcare providers with the scientific knowledge and clinical strategies essential for preventing Vitamin B12 deficiency, ensuring appropriate B12 nutrition, and delivering effective patient care.

Beyond the clinical setting, the book also serves as a valuable resource for dietitians, nutritionists, educators, nutrition students, and health-conscious individuals seeking a comprehensive understanding of Vitamin B12's role in today's dietary environment.

Of particular importance are the dietary implications of Vitamin B12, which is found naturally only in animal-derived foods such as meat, milk, and eggs. This presents a unique challenge for vegetarians and an even greater concern for vegans, who are at significantly higher risk of B12 deficiency.

It is our hope that this document not only highlights the critical importance of this often-overlooked nutrient but also serves as a valuable resource for deepening understanding and guiding evidence-based decisions. By presenting a thorough and accessible exploration of Vitamin B12, from its biological functions to practical dietary considerations, this guide aspires to bridge the gap between scientific knowledge and everyday health practices. Ultimately, we aim to inspire a more informed, proactive, and responsible approach to B12 nutrition, both at the individual and community levels.

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ACKNOWLEDGMENT

Food systems have the power to nourish human health and sustain the planet, yet today, they are doing the opposite. The current global food system is a major driver of malnutrition, obesity, and chronic diseases, while simultaneously contributing to environmental degradation through resource depletion, climate change, and biodiversity loss. A fundamental shift toward healthier, more sustainable diets, particularly those centered on plant-based foods, is urgently needed.

At PAN India, we are committed to advancing scientific, evidence-based nutrition as a powerful strategy to address diet-related diseases and promote planetary health. Physicians, as trusted voices in healthcare, are uniquely positioned to lead this transformation, empowering patients to make informed dietary choices that can prevent and even reverse disease while also sustaining the health of our planet.

As plant-predominant diets gain popularity for both health and environmental reasons, understanding Vitamin B12 becomes increasingly essential. Since B12 is primarily found in animal-based foods, its adequacy requires careful attention among plant-based populations. This guide equips physicians with practical, evidence-informed insights to ensure nutritional adequacy and support the transition to sustainable, health-promoting dietary patterns.

We are deeply grateful to the PAN International leadership, PAN India Governance Board, PAN INT medical content team, and PAN India leadership for their unwavering support, vision, and guidance. Their collective dedication has been vital in advancing our mission to integrate evidence-based nutrition into healthcare and build a healthier, more sustainable future. Their continued belief in our purpose inspires and empowers us every step of the way.

This document is the outcome of a collaborative effort involving our domain experts, medical content and research teams, communications staff, and the invaluable support of our patrons and ambassadors. Their collective guidance added depth and clarity to this initiative. We extend special thanks to the subject matter experts who rigorously reviewed the content, ensuring its scientific accuracy and clinical relevance as a trusted resource for physicians.

We extend heartfelt appreciation to the wider plant-based & lifestyle medicine community especially the pioneering researchers, clinicians, and educators whose tireless advocacy and scientific contributions have laid the foundation for this guide. In the spirit of thanksgiving and gratitude, we honour every individual and organisation working towards a healthier, more compassionate, and sustainable world.

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WITH GRATITUDE TO OUR PATRONS & AMBASSADORS

This guide was developed by the PAN India Medical Content and Research Team, a group of dedicated young physicians committed to advancing evidence-based nutrition in clinical care. Their efforts were enriched by the guidance and support of senior physicians, esteemed patrons, and ambassadors whose insights brought depth and credibility to this resource.

We extend our sincere thanks to Dr. Roberta Alessandrini and Dr. Nanine Wyna for their valuable contributions and to our broader medical network across PAN India city chapters for their continued support and shared commitment to our mission.

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Together, we are not just creating a guide - we are shaping the future of medicine, where nutrition is foundational, prevention is prioritized, and healthcare becomes a force for healing both people and the planet.

WHAT IS THE SCOPE OF THIS DOCUMENT?

This comprehensive guide on Vitamin B12 has been developed with scientific rigor to support healthcare professionals—primarily physicians, family physicians, lifestyle physicians, and specialists—in understanding the critical role of B12 in human health. With a special focus on plant-based diets, it offers an evidence-based framework to identify, prevent, and manage B12 deficiency across diverse dietary patterns. While the guide is designed chiefly for clinical application, it may also serve as a valuable reference for dietitians, nutritionists, and other professionals engaged in nutrition education and patient care.

The guide covers key aspects of Vitamin B12, including its absorption, physiological functions, recommended dietary intakes, and food sources. It details the clinical manifestations of deficiency, timelines for progression, and the role of functional biomarkers in diagnosis. Emphasis is placed on identifying high-risk groups and understanding the global and Indian prevalence of B12 deficiency in the context of dietary diversity.

Importantly, the document explores recent advances in non-traditional sources of B12—including algae, fungi, edible plants, and fortified foods—which show promising potential in contributing to B12 adequacy, particularly in plant-based populations.

By offering practical, evidence-informed strategies for the evaluation, prevention, and management of deficiencies across age groups and physiological conditions, this guide aims to equip healthcare providers to deliver proactive, effective, and nutritionally sound care—especially in support of those embracing plant-forward lifestyles.

VITAMIN B12: THE BASICS

INTRODUCTION

Vitamin B12, or cobalamin, is a water-soluble Vitamin essential for red blood cell formation, DNA synthesis, and the maintenance of a healthy nervous system. It supports the production of myelin, the protective sheath around nerves, and helps prevent neurological impairments and megaloblastic anemia.

Unlike many nutrients, Vitamin B12 is not produced directly by plants or animals but is synthesized by specific bacteria. Animal-based foods such as meat, eggs, and dairy serve as primary dietary sources because they accumulate B12 through microbial synthesis within the food chain. Individuals adhering to vegetarian or vegan diets, particularly in regions like India, are at an increased risk of deficiency without adequate intake from fortified foods or supplements.

However, the long-standing assumption that B12 deficiency in India is predominantly due to vegetarianism needs to be reconsidered. Although only about 30% of the Indian population identifies as vegetarian, studies show that over 70% may be deficient in B12. This highlights B12 as a widespread shortfall nutrient across all dietary patterns, including among non-vegetarians. Contributing factors include the low frequency of animal product consumption, degradation of B12 during cooking, poor dietary diversity, and impaired absorption due to gastrointestinal conditions.
Absorption challenges may be exacerbated by conditions such as atrophic gastritis, gastrointestinal surgeries, and the use of medications like metformin and proton pump inhibitors. Additional factors, including Helicobacter pylori infection, age-related decline in intrinsic factor production, and chronic alcohol consumption, further compromise B12 bioavailability.

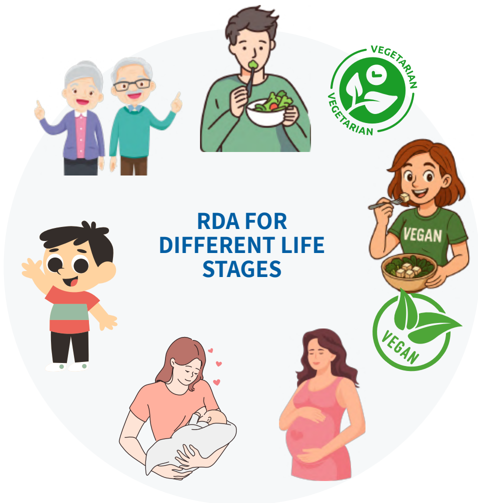
Public awareness regarding the necessity of B12 supplementation in plant-based diets remains limited, compounding the problem. If left unaddressed, B12 deficiency can lead to megaloblastic anemia, neurological impairments, and elevated homocysteine levels, a known cardiovascular risk factor. Symptoms often appear late and may become irreversible if not treated promptly. Given B12's vital role in mitochondrial function, antioxidant defense, and genomic stability, maintaining adequate levels is essential—especially in populations transitioning to or maintaining plant-predominant diets.

RECOMMENDED DIETARY ALLOWANCE

Vitamin B12 is essential in small amounts for maintaining health, with recommended intakes varying by age, gender, and physiological status. The Recommended Dietary Allowance (RDA) for adults is 2.2 micrograms (mcg) (79). Infants and preschool children require about 1.2 mcg of Vitamin B12 daily, while school-aged children and adolescents require around 2.2 mcg, similar to adults (79). Individuals following plant-based diets may need fortified foods or supplements, as B12 is primarily found in animal-based sources. While Vitamin B12 deficiency is more commonly associated with vegetarian and vegan diets, it is not uncommon among non-vegetarians. Factors such as inadequate intake, malabsorption issues, and certain medications can contribute to deficiency even in those who consume animal products. Populations with impaired intrinsic factor production or chronic digestive conditions are also at increased risk, regardless of dietary patterns (32, 74).

The Recommended Dietary Allowance(RDA) for men and women aged 14 years and older is **2.2 mcg per day** (79). The RDA increases to 2.45 mcg per day during pregnancy and 3.2 mcg per day during lactation (79).

Life Stage	RDA (µg/day)
Adolescents & Adults (14+)	2.2 µg
Pregnancy	2.45 µg
Lactation	3.2 µg



EAR (Estimated Average Requirement)

EAR for Vitamin B12 in adults aged 19–50 years is **2.0 mcg per day** (79).
Studies involving individuals with low Vitamin B12 intake, such as vegetarians and vegans, have shown that a daily intake of 1.5 mcg often does not maintain adequate B12 status, further supporting the 2.0 mcg/day EAR estimate. (49)

Other important factors to consider

The Recommended Dietary Allowance (RDA) and Estimated Average Requirement (EAR) for Vitamin B12 are based on maintaining adequate hematologic and neurologic function in healthy individuals, assuming normal absorption and metabolic conditions.

Older adults, vegetarians/vegans, and individuals with conditions such as **pernicious anemia** may require higher doses of B12, as fortified foods or supplements, due to impaired absorption or limited dietary sources.

B12 SOURCES:
EXPLORING KNOWN AND NOVEL SOURCES

SOURCES OF VITAMIN B12- ANIMAL BASED

Vitamin B12 is found primarily in animal-based foods such as meat, poultry, fish, eggs, and dairy products. Understanding both animal and fortified plant-based sources is essential to ensure adequate B12 intake across different dietary patterns. The meat and liver of ruminant animals contain higher amounts of B12 compared to those of omnivorous animals. Significant losses of B12 have been reported after cooking beef, pork, and chicken (43,44, 46).

Meat, Egg, Poultry, Milk, Cheese, Yogurt, Fish, Shellfish (39, 122)

Per 100gm :


Cooked beef liver
~70–83 µg


Cooked pork liver
~18.6 µg


Goat liver
~90.4 µg


Cooked chicken liver
~23 µg


Sardines (canned in oil, drained) **~8.9 µg**


Tuna (light, canned in water, drained) **~9.3 µg**


Salmon (atlantic) **~4.8 µg**


Beef meat
~1.7 µg


Mutton
~2.6 µg


Pork meat (cooked)
~0.3 µg


Chicken breast (cooked)
~0.3 µg


Whole fat milk (buffalo)
~0.14 µg


Curd per 100 g:
~0.10-0.13 µg


Swiss cheese 1oz (28g) **~0.9 µg**


1 Large egg:
~1.8 µg

Potential downsides of consuming large quantities of animal-based Vitamin B12 sources

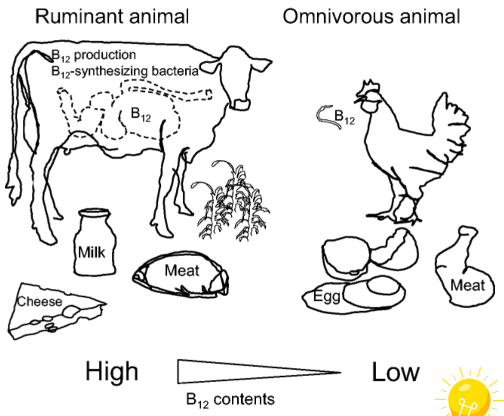
Animal-based foods are natural sources of Vitamin B12; however, frequent consumption of foods high in saturated fats, trans fats, sodium, and added preservatives-such as red and processed meats or full-fat dairy has been linked to increased risks of chronic diseases, including cardiovascular disease and colorectal cancer. These foods may also crowd out fiber and phytonutrient-rich plant foods that are essential for overall health. To meet B12 needs without compromising long-term health, it is advisable to emphasize nutrient-dense, minimally processed foods alongside B12 supplementation or fortified sources (3, 8, 47).

VITAMIN B12 SOURCES AND MICROBIAL INTERACTION

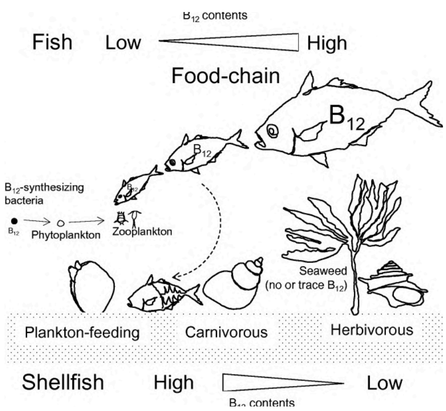
Vitamin B12 is produced solely by specific bacteria and archaea, not by plants or animals (21). However, it can accumulate in animal tissues, and in rare cases, in certain plants and mushrooms through microbial interactions. Herbivorous ruminants such as cows and sheep serve as major dietary sources of B12 for humans, thanks to their symbiotic gut bacteria that synthesize the Vitamin (128). In aquatic ecosystems, B12 is first acquired by phytoplankton from bacteria and then transferred up the food chain to fish and shellfish, which also contributes significantly to human B12 intake.

How ruminants and omnivores become natural B12 reservoirs

Vitamin B12 found in meat, eggs, milk, and dairy products originates from microbial synthesis within animals (132). In cattle, B12-producing bacteria in the stomach generate the Vitamin, which is later absorbed in the intestines, enters the bloodstream, and is **stored in the liver and muscles** or secreted into the milk. As a result, bovine milk and fermented dairy products such as yogurt and cheese serve as valuable dietary sources of B12 (128). Chickens, being omnivores, consume both plant and animal matter containing B12; however, their meat typically has lower levels of B12 compared to that of cattle (98).



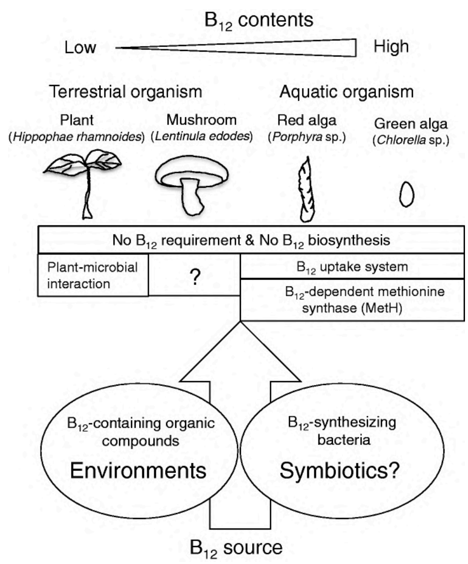
Microbial interactions in animals play a key role in enriching human food sources with bioavailable Vitamin B12.



Marine microbial pathways: How B12 accumulates in the ocean food chain

In aquatic environments, Vitamin B12 produced by bacteria and archaea is absorbed by B12-requiring bacteria and phytoplankton, which are then consumed by zooplankton and small fish. The upward movement of B12 through the marine food chain leads to its accumulation in larger predatory fish.
Thus, fish and especially bivalves serve as rich dietary sources of Vitamin B12 through microbial interactions within the marine ecosystem (6, 13).

Most plants and mushrooms do not produce or require Vitamin B12 but can acquire it through interactions with B12-producing bacteria. In soil and aquatic environments, plant–bacterial and phytoplankton–bacterial interactions support growth and B12 availability. (132). Mushrooms accumulate B12 from external bacterial sources, while many algae rely on B12 for growth or use it as a cofactor in metabolic processes (21).



SOURCES OF VITAMIN B12- PLANT BASED [ALGAE]

Emerging Plant-based sources of Vitamin B12

Traditionally, plant-based sources of Vitamin B12 have been considered unreliable due to inconsistent content and the presence of inactive analogues. Recent research, however, suggests that certain algae, such as nori and Chlorella, may provide bioavailable B12 in sufficient amounts per serving. Yet, their nutrient content varies widely based on species, cultivation conditions, and processing methods, posing challenges to consistency. While these sources show promise, further standardization and validation are needed before they can be considered reliable alternatives (133).

Red algae as a B12 source: Nori

(Dried purple laver, Porphyra sp.)

Emerging evidence suggests that nori (dried purple laver) contains bioavailable Vitamin B12, with approximately 5 grams per day potentially supporting adequate intake in vegetarians and vegans, though individual absorption may vary (48, 96). Seaweed B12 content is highly variable ranging up to 133.8 µg/100g dry weight, with sea lettuce reported at 84.74 µg/100g. In addition to B12, nori is also a source of iron and omega-3 polyunsaturated fatty acids. A nutritional analysis of six vegan children who consumed brown rice and nori for 4–10 years indicated that regular nori intake may help prevent B12 deficiency in long-term vegan diets (23, 113, 129).

Microalgae as a B12 source: Chlorella

Chlorella, a nutrient-rich microalga, is a promising plant-based source of bioavailable Vitamin B12. It accumulates **active cobalamin** through symbiosis with B12-producing bacteria. An analysis of 57 commercial algae supplements, Chlorella products showed predominantly active B12, ranging from **undetectable to 445.9 µg/100g**. Clinical and animal studies indicate its efficacy in restoring B12 levels and reducing serum methylmalonic acid in vegans and vegetarians (72, 89, 124).

Spirulina and Vitamin B12: A misleading source

Spirulina or blue-green algae is often touted as a good source of Vitamin B12, but this claim is inaccurate. While it contains Vitamin B12 analogues and pseudo-Vitamin B12, these are not biologically active for humans and don't contribute to your Vitamin B12 needs. These analogues can interfere with the absorption of genuine Vitamin B12, potentially worsening B12 status (121, 123, 124, 129).

Spirulina is often overstated as a good source of Vitamin B12, but its inactive analogues do not fulfill human B12 needs and may hinder the absorption of the active form.

SOURCES OF VITAMIN B12- PLANT BASED [FUNGI]

Fungi as a B12 source:

Fungi were once thought to lack B12, but early diverging groups like Glomeromycotina and Blastocladiomycota possess B12-dependent enzymes, suggesting ancestral use lost in later lineages like Dikarya. While fungi can't produce B12, some mushroom fruiting bodies accumulate it via symbiosis with B12-producing soil bacteria or through fermentation (65, 72, 130,131,133).

Shiitake mushrooms

Shiitake mushrooms can contain modest amounts of Vitamin B12, with levels varying up to **5.6 µg of B12 per 100 g dry weight** based on cultivation methods. B12 in shiitake mushrooms comes from B12-producing bacteria in the growing medium, not the mushroom itself. While they may contain some inactive B12 analogues, research indicates they still provide a significant amount of bioavailable B12, especially when dried (115, 130).

Dried shiitake mushrooms are among the few fungi that can naturally accumulate bioavailable Vitamin B12—thanks to their interaction with B12-producing microbes in their growing environment.

Golden chanterelle

Golden chanterelle mushrooms (Cantharellus cibarius) have been found to contain small but measurable amounts of naturally occurring, bioactive Vitamin B12 approximately **1.09 to 2.65 mcg per 100g dry weight**. However, typical serving sizes are small, and B12 content can vary depending on soil, environment, and harvesting methods. While promising, they cannot be relied on as a sole source of B12 for those on a 100% plant-based diet (130).

Black truffles

Black truffles (Tuber melanosporum) contain approximately 0.08 µg of Vitamin B12 per 13 gram serving, equating to about **0.62 µg per 100 g** (26% of RDA), While they can contribute to the dietary intake of this essential Vitamin, especially for those following plant-based diets, they should complement rather than replace other reliable sources (131).

SOURCES OF VITAMIN B12- PLANT BASED [FUNGI]

Black trumpet mushrooms

Black trumpet mushrooms (Craterellus cornucopioides) have been reported to contain modest amounts of Vitamin B12, ranging from **1.09 to 2.65 µg per 100 g dry weight.** Although incapable of endogenous synthesis, their B12 is acquired from symbiotic bacteria living in the same substrate (131).

Black trumpets can thus serve as a minor, complementary source of bioavailable B12 within a varied, plant-forward diet.

(Outer peel ≫ Inner flesh)

White Button Mushroom

White button mushrooms (Agaricus bisporus) contain only trace amounts of biologically active Vitamin B12 . Studies report **0.04–0.36 mcg per 100 g dry weight.** Studies show this B12 is surface- or substrate-derived rather than produced by the fungus itself (56, 94).

This minimal B12 load reflects external bacterial colonization and offers little practical contribution to daily requirements.

Oyster Mushroom

Oyster mushrooms (Pleurotus ostreatus) have been found to contain **trace amounts** of Vitamin B12, sourced from environmental bacteria rather than fungal biosynthesis. Their limited B12 content underscores that oysters play a negligible role in addressing dietary B12 needs (131).

Black morels

Black morels contain **trace amounts** of Vitamin B12, likely acquired from B12-producing soil bacteria, However, their modest B12 levels remain insufficient to meet nutritional requirements for those depending on plant-based sources reliably (131).

Porcini mushrooms

Porcini mushrooms harbor **trace** B12, again acquired from B12 -producing soil microbes. (131). These residual amounts are far too low to serve as a dependable supply for individuals at risk of deficiency.

Parasol mushrooms

Parasoi mushrooms also known as Termitomyces species, contain **0.1–1.5 µg B12 per 100g dry weight**. Despite slightly higher levels than some other fungi, variability in bacterial association limits their usefulness for meeting B12 requirements (131).

SOURCES OF VITAMIN B12- PLANT BASED [EDIBLE PLANTS]

Edible plant as B12 source

Sea buckthorn (Hippophae rhamnoides) berries and granulate products, sidea couch grass (Elymus repens) products (dry extract and ground), and elecampane (Inula helenium) reportedly contain considerable amounts of Vitamin B12 (approximately 11–37 μg/100 g of dry weight). This suggests that the B12 found in these plants and plant products is due to symbiosis with B12 -synthesizing bacteria (140).

Sea buckthorn

Sea buckthorn (Hippophae rhamnoides) has shown potential as a natural plant-based source of Vitamin B12, with studies reporting up to **37 μg/100 g dry weight over 98% in active form** (140). Preliminary data indicate this B12 originates from plant-microbe interactions rather than true plant synthesis. While promising, more research is needed to confirm its consistent bioavailability, so fortified foods or supplements remain recommended for those on plant-based diets.

Elecampane

Elecampane (Inula helenium) is occasionally cited as a potential B12 source, but there is no scientific evidence confirming it contains active, bioavailable B12 (132). For reliable intake, fortified foods and supplements remain the preferred sources, especially for plant-based diets.

Sidea couch grass

Couch grass (Elymus repens), also known as Sidea couch grass, has been reported to contain **23.1–28.5 μg of Vitamin B12 per 100 g of dried root,** likely due to symbiotic soil bacteria (88, 131). While promising, more research is needed to confirm its B12 bioavailability and consistency across preparations.

B12-enriched vegetables

Organic fertilizers like cow manure can modestly raise B12 levels in spinach (about **0.14 μg/100 g** fresh weight) (131). Additionally, treating vegetables with B12 solutions has produced B12-enriched produce, which may benefit the elderly, who often struggle to absorb protein-bound B12.

While these findings are promising, it's important to note that further research is needed to confirm the bioavailability and consistency of B12 in couch grass across different preparations. As such, individuals relying on plant-based diets should continue to monitor their B12 intake and consider fortified foods or supplements.

SOURCES OF VITAMIN B12- PLANT BASED [FERMENTED FOODS]

Fermented foods as B12 source

The notion that fermented foods such as tempeh, kimchi, miso, and kombucha may contain Vitamin B12 originates from their microbial content. Certain bacteria involved in fermentation, such as Propionibacterium freudenreichii and some strains of Lactobacillus, can produce cobalamin (B12) analogues under specific conditions (76). This method has emerged as a sustainable method for producing bioactive Vitamin B12.

Fermented foods (tempeh, miso)

Fermented plant foods like tempeh and miso may have trace amounts of B12, but these are often inactive and not bioavailable. Studies show that B12 in fermented foods is either too low or in non-metabolizable forms. Tempeh contains **0.18 to 4.14 mcg of B12 per 100 g** (119), with some brands, like Hello Tempayy, claiming to provide 49% of the RDA (about 1.2 mcg per 100 g). Other fermented soy products like miso also vary in B12 content.

Fermented vegetables (e.g., sauerkraut, kimchi)

In contrast, other fermented products such as kimchi and miso contain trace amounts of Vitamin B12 due to the activity of certain bacteria during fermentation. However, the B12 content is highly variable and often negligible, making them unreliable sources for meeting daily requirements, especially in plant-based diets. The amount of B12 in kimchi is generally low, ranging from **0.013 to 0.03 mcg per 100 g** (58, 132).

Microbial fortification: A promising frontier?

Laboratory studies involving co-fermentation - such as Rhizopus oryzae with Propionibacterium freudenreichii, have shown promise in boosting bioactive Vitamin B12 content in plant foods, producing up to **0.97 mcg/100 g** in lupin tempeh. However, further human trials are needed to confirm its bioavailability and safety. Advanced tools like HPLC and UHPLC-MS/MS are essential to differentiate active B12 from analogues (16, 50, 134).

Traditional fermented foods like tempeh, miso, kimchi, and kombucha may contain trace amounts of B12 due to microbial fermentation, but the levels are highly variable and often too low to meet daily needs. Many microbes produce inactive forms of Vitamin B12 that are not bioavailable and may even hinder the absorption of active B12.

IMPORTANCE OF CULTIVATION AND PROCESSING METHODS TO RETAIN B12 CONTENT

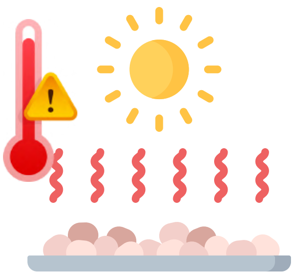
Cultivation and processing methods significantly affect Vitamin B12 content in plant-based foods. Since B12 originates from bacteria, not plants or fungi, its presence depends on factors like soil quality, organic fertilization, minimal washing, and symbiosis with bacteria. Importantly, active B12 cannot be obtained directly from soil; plants may only accumulate it through interactions with soil bacteria. Processing methods such as drying and fermentation can either preserve or degrade B12, making optimization essential to retain it in enriched or fortified foods.

Cultivation practices: Cultivation practices significantly influence B12 content in plant-based foods. Factors like soil microbial richness, use of organic fertilizers, and co-cultivation with B12-producing bacteria can enhance B12 uptake in fungi and leafy greens. However, absorption varies by strain and microbial compatibility in the substrate (50, 75, 114).

Processing methods: Processing methods affect B12 retention in plant-based foods. Fermentation can introduce B12 via bacterial activity, while gentle drying preserves it better than high heat. Excessive washing or sterilization may remove B12-producing surface bacteria, and exposure to light, heat, or air can degrade B12, making proper packaging essential.

Soil to shelf: The impact of growing conditions

Fungi grown in B12-enriched media or alongside B12-producing bacteria like Propionibacterium freudenreichii can absorb bioavailable B12. Watanabe et al. (2012) showed shiitake mushrooms cultivated this way contained usable methylcobalamin, though accumulation varies by strain and growing conditions (130, 114).



Post-harvest processing pitfalls

Vitamin B12 is sensitive to heat, light, and oxygen; high-heat drying can degrade it or form inactive analogues, while low-temperature or vacuum-drying better preserves its active form. Traditional fermented foods like Doenjang and Chungkookjang have higher B12 levels than factory-made versions, underscoring the importance of processing methods.

The bioavailability puzzle: Not all B12 is equal

Fungi may contain B12 analogues (corrinoids) that are structurally similar but biologically inactive in humans. Only specific analogues such as methylcobalamin and adenosylcobalamin, have known physiological benefits. HPLC and bioassays have revealed that many wild or non-enriched mushrooms contain predominantly inactive analogues unless fortified or specially cultivated. Without proper cultivation and testing, these fungi may give a false sense of B12 sufficiency (130).

VITAMIN B12 FORTIFICATION

What is fortification?

Food fortification is the deliberate addition of one or more essential nutrients to commonly consumed foods to prevent or correct nutrient deficiencies in the population. For Vitamin B12, this strategy has gained global importance due to widespread deficiency, affecting an estimated 6-40% of the general population, with significantly higher rates among the elderly, vegetarians, vegans, and individuals with malabsorption disorders (135).

Why is fortification important?

Fortifying plant-based staples like cereals, nutritional yeast, and plant-based milk has effectively reduced B12 deficiency in countries like the U.S and Canada. In India, where over 30% of the population is vegetarian and many others consume little animal food, deficiency rates range from 30% to 70% (135). To address this, FSSAI has issued voluntary guidelines to fortify staples such as wheat flour, rice, oils, and dairy with B12, but adoption remains low due to limited awareness (36). Nonetheless, fortification remains a scalable and equitable solution, especially for those with limited access to supplements or diverse diets. However, B12 fortification can mask the onset of other deficiencies, such as iron or folate, potentially delaying the identification and treatment of these conditions. This concern may contribute to the cautious approach to widespread fortification in some regions.

Western practices

- In the U.S. and in Western markets, many ready-to-eat breakfast cereals deliver **0.6-8 µg of Vitamin B12 per 100g** (25–100 % of the RDA). While soy, almond, and oat milk are routinely fortified to provide **~1 µg per 100 mL**, similar to cow's-milk B12 levels.
- **Regulatory framework:** In the U.S., fortification is largely voluntary except for standards of identity (e.g., enriched flour must include certain B Vitamins), per FDA policy (33).

Indian context

- FSSAI regulations permit but do not mandate the fortification of staples with Vitamin B12.
- **State Initiatives:** Haryana's atta fortification (B12, iron, and folic acid) program reaches millions, aligning with WHO recommendations (34).
- **"+F" Logo:** A standardized symbol to identify compliant fortified foods, aiding consumer choice (36).

Vitamin B12 fortification is a cost-effective public health intervention that helps prevent deficiency-related conditions such as fatigue, cognitive decline, and developmental delays, while supporting maternal and child health. When integrated into existing nutrition and food security programs, it can significantly improve population health and contribute to India's progress toward the Sustainable Development Goals.

FORTIFIED FOODS WITH VITAMIN B12

Available in India: (1, 81, 118, 152, 153, 154, 155, 156, 157)

Fortified plant-based milks:

Oat Milk (e.g., Oatly, Oatopia): fortified with **0.5 to 1 µg of Vitamin B12 per 100 ml.**

Soymilk (Alpro, Soy Life): **0.5 to 1.5 µg of Vitamin B12 per 100 ml**

Almond Milk (e.g., Urban Platter So Good): Around **0.4 to 1 µg of Vitamin B12 per 100 ml.**

Fortified breakfast cereals

Kellogg's cornflakes: Contains **0.6 to 1.5 µg of Vitamin B12 per 30 g serving.**

Quaker oats: Fortified varieties provide **0.5 to 1 µg of Vitamin B12 per serving (30-40 g).**

Fortified nutritional yeast

Urban platter: **2.4 µg per 10g**

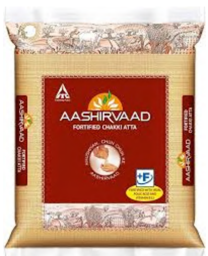
The Health Shop: **1 - 2 µg / 10 g**

Fortified fruit juice & vegan butters

Fortified orange juice: **0.5 to 1 µg of Vitamin B12 per 200 ml serving**

Vegan butters (e.g., Earth Balance): **0.5 to 1 µg per tablespoon**

Fortified flour



Fortified wheat chakki atta **0.09 µg of Vitamin B12 per 100 g serving**

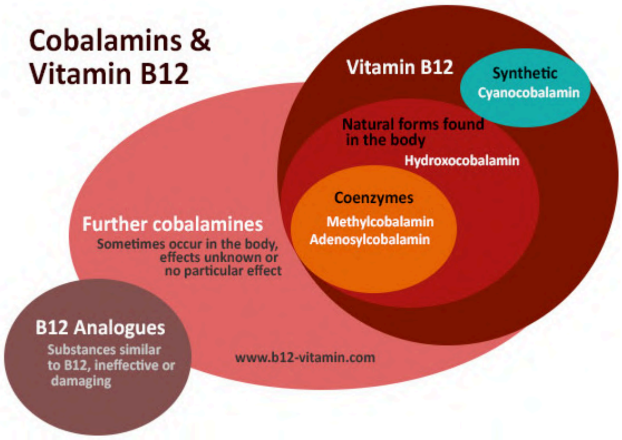
India must prioritize vtamin B12 food fortification to address its silent epidemic—affecting over 70% of the population. Fortified staples offer a practical, scalable solution to bridge the nutritional gap (135).

VITAMIN B12 SUPPLEMENTATION

Vitamin B12 supplementation is essential for those at risk of deficiency, including vegans, vegetarians, older adults, and individuals with absorption issues. As B12 is primarily found in animal products, supplementation with forms like cyanocobalamin or methylcobalamin is often needed. Typical doses range from 250 μg to 1000 μg daily, with injections recommended in some cases. Regular monitoring of B12 levels is advised.

Forms Available:

- Cyanocobalamin (synthetic, stable, inexpensive; converted in the body to active forms)
- Methylcobalamin (bioactive form; directly utilized by the body)
- Hydroxocobalamin (natural form; longer lasting; used in injections)
- Adenosylcobalamin (another active form found in mitochondria)



Both cyanocobalamin and methylcobalamin are effective sources of Vitamin B12, but they differ in form, stability, and how the body uses them.

Cyanacobalamin

VS

- The most commonly used form of Vitamin B12 in supplements
- Stable and cost-effective.
- It contains a cyanide molecule, which the body converts to active Vitamin B12 in the liver, which can be slower for some individuals.
- Often recommended for general B12 supplementation for those with no absorption issues.
- Form: Available in oral tablets, injections, and nasal sprays.

Methylcobalamin

- The active, coenzyme form
- Directly utilised by the body without needing conversion.
- Often preferred for conditions that impair the conversion process (e.g., low levels of intrinsic factor or absorption issues) (137)
- Commonly used for people with neurological symptoms, as it supports nerve health and can help in conditions like neuropathy. (25)
- Form: Available in sublingual tablets, soft gels, and injections.

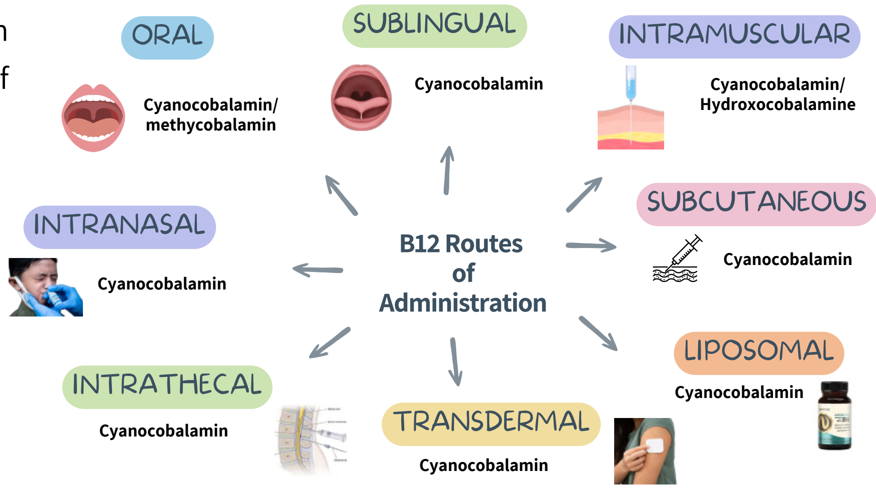
Cyanocobalamin is a safe, effective, and cost-efficient option for most healthy individuals (137). However, methylcobalamin may be preferable for those with absorption difficulties, neurological conditions, or genetic variations affecting B12 metabolism.

It's a myth that methylcobalamin is inherently more "natural" than cyanocobalamin due to the absence of a cyanide molecule.

VITAMIN B12 SUPPLEMENTATION
FROM PILL TO INJECTION: DELIVERING B12

Vitamin B12 is available in various forms and routes of administration.

- Oral
- Sublingual
- Intramuscular (IM)
- Transdermal
- Liposomal
- Subcutaneous
- Intranasal and intrathecal



Administration form	Available doses	Recommended B12 dose	Advantages
Oral Tablets/ Capsules	Cyanocobalamine: 100, 250, 500, 1000, 2500, 5000 mcg (Medscape, 2010) Methylcobalamine: 1000, 2500, 5000 mcg	Adults: 500-2000 mcg/day Perinicious anemia: 1000 mcg/day (11, 20,40)	• 1-5 % of dose absorbed by passive diffusion • Non invasive
Sublingual Tablets	500, 1000, 2500, 5000 mcg (Medscape, 2010)	Adults: 500–2000 mcg/day (20,40)	• Avoids first pass metabolism
Intramuscular (IM)	1000 mcg/mL (cyanocobalamin/hydroxocobalamin) (Medscape, 2010)	Adults: Initial: 1000 mcg x 7 days Maintenance: 1000 mcg X monthly (20,40)	• Bypasses gastrointestinal malabsorption

Other routes of administration:

Transdermal, liposomal, subcutaneous, intranasal, and intrathecal routes are used in specialized cases, typically for chronic deficiencies or when patients experience adverse reactions to oral or injectable forms. These methods offer targeted therapy for those who need alternative administration options (2).

WHY CHOOSE SUBLINGUAL B12?

Clinical highlight:

Oral supplements are convenient and effective for individuals with normal absorption, while sublingual B12 is absorbed directly through the oral mucosa, bypassing the need for stomach acid and intrinsic factor, making it ideal for those with absorption issues. Injectable B12 (IM) is used in severe deficiencies or when rapid correction is needed, especially in cases of pernicious anemia or after gastrointestinal surgery.

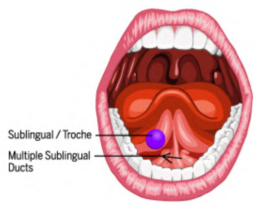
DID YOU KNOW?

The body absorbs only about **1% of a high-dose oral B12 supplement** through passive diffusion- which is why high doses (500–1000 mcg) are often prescribed (77).

INTERESTING FACT

Sublingual supplementation

Sublingual Vitamin B12 supplementation is a convenient and effective option, especially for individuals with impaired absorption due to low stomach acid, intrinsic factor deficiency, or gastrointestinal disorders. By bypassing the digestive tract and absorbing directly through the oral mucosa, sublingual B12 ensures more reliable uptake, making it particularly beneficial for the elderly, those on proton pump inhibitors, or individuals with pernicious anemia (12).



Studies have shown that sublingual B12 is as effective as intramuscular injections in restoring B12 levels in deficient individuals (22).

Co-supplementation with folate

Co-supplementation with folate (Vitamin B9) is often recommended, as both B12 and folate work together in one-carbon metabolism, essential for DNA synthesis, red blood cell production, and nervous system function.

The B12-Folate interdependence

- Methylation Cycle Dependency: B12 deficiency traps folate as 5-methyltetrahydrofolate (5-MTHF), causing a functional folate deficiency despite normal serum levels (37).
- Folic acid supplementation can mask B12 deficiency, correcting anemia but allowing neurological damage (subacute combined degeneration).
- Megaloblastic Anemia: Both deficiencies cause macrocytic anemia, but only B12 deficiency leads to neuropathy.

Clinical recommendation

- Pregnant women- 400-800 mcg/day (L-methyl folate preferred for MTHFR-Methylenetetrahydrofolate Reductase variants).
- High homocysteine - Combined B12 + L-methyl folate + B6 reduces cardiovascular risk.
- MTHFR mutation carriers- L-methyl folate (5-MTHF) bypasses the defective enzyme (37).

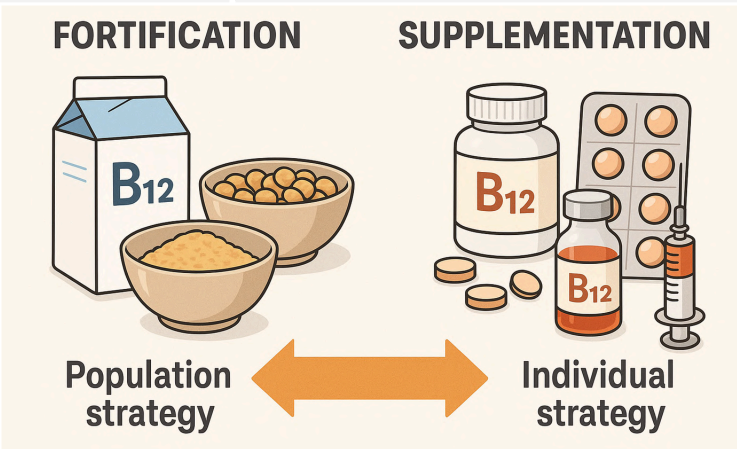
Prefer L-methyl folate (5-MTHF) over folic acid for better bioavailability, especially in individuals with MTHFR gene variants. Always assess Vitamin B12 status before initiating high-dose folate to avoid masking a B12 deficiency. During pregnancy, ensure adequate B12 alongside folate to reduce the risk of neural tube defects.

FORTIFICATION VS SUPPLEMENTATION – WHAT'S MORE EFFECTIVE

Both food fortification and supplementation are effective strategies for preventing Vitamin B12 deficiency, and it is important to recognize that they can complement each other rather than be viewed as alternatives. Fortification offers a population-wide, low-cost approach through commonly consumed foods, while supplementation provides targeted support for individuals at higher risk. The choice depends on factors like accessibility, risk level, and adherence.

Aspect	Fortification	Supplementation
Definition	Adding B12 to foods (e.g., cereals, plant milks).	Direct intake via pills, tablets, or injections.
Pros	Broad reach, effective for general populations.	Reliable source, essential for high-risk groups.
Cons	Limited if intake is inconsistent. Less access to rural populations, not a classic staple in India.	Requires adherence and monitoring. Requires adherence and monitoring. Lack of awareness and high cost.
Best for	General populations with easy access to fortified foods.	High-risk individuals (e.g., vegans, elderly, malabsorption).
Notes	Needs daily fortified food intake.	Daily low-dose or weekly high-dose is effective.

The EPIC-Oxford and Adventist Health Studies highlighted that vegans without supplementation or fortification had the highest risk of B12 deficiency.



VITAMIN B12 SUPPLEMENTATION- INDIAN CONTEXT

In India, where Vitamin B12 deficiency is widespread due to predominantly vegetarian diets, oral supplementation plays a crucial role. Commonly available as methylcobalamin or cyanocobalamin, these supplements are accessible, affordable, and effective, with doses tailored to the severity of deficiency.

- **General population (especially vegetarians and vegans):** Cyanocobalamin 250–500 mcg/day is effective for prevention (125).
- **High-risk groups (pregnant women, elderly, patients with malabsorption):** Methylcobalamin 500–1000 mcg/day is preferred for better absorption (77).

While many multiVitamins toss in a sprinkle of B12, it's often too little to meet the needs of strict vegans or those battling a deficiency. For true efficacy, choose a dedicated B12 supplement formulated to support both therapeutic recovery and long-term maintenance. Whereas sublingual forms offer better absorption compared to regular tablets.

Vitamin B12 commonly prescribed	
Nurokind	Methylcobalamin (500–1500 mcg)
Methycobal	Methylcobalamin (500 mcg/tablet)
Renerve Plus	Methylcobalamin (1500 mcg/tablet)
C. Matilda Forte	Methylcobalamin (1500 mcg) + Folate + Pyridoxine (B6)
Neurobion Forte	Cyanocobalamin (15 mcg) + B1 + B6

Combined B12 + folate formulations		
Neurobion Forte	Methylcobalamin (1500 mcg) + Folic Acid (500 mcg) + B6	Neuropathy, high homocysteine
Folvite-M	Folic Acid (5 mg) + Methylcobalamin (1500 mcg)	Megaloblastic anemia
Bifolate Plus	L-methylfolate (1 mg) + Methylcobalamin (1500 mcg)	MTHFR mutation + B12 deficiency
Homocysteine-X	B12 (500 mcg) + 5-MTHF (400 mcg) + B6 (25 mg)	Cardiovascular support

NAVIGATING B12: SYNTHESIS, TRANSFER & BIOAVAILABILITY

SYNTHESIS, TRANSFER & BIOAVAILABILITY

Vitamin B12 (cobalamin) is exclusively synthesized by certain bacteria and archaea through a complex, multi-step enzymatic process. Neither plants nor animals can produce B12 on their own. In nature, these microbes are commonly found in soil, water, and the gastrointestinal tracts of animals, where they contribute to the ecological B12 cycle.

Microbial synthesis

The biosynthesis of Vitamin B12 is a complex process involving nearly 30 enzyme-catalyzed reactions, making it one of the most structurally and biochemically intricate Vitamins. Two main pathways exist for its production.

- Aerobic pathway (e.g., Pseudomonas denitrificans)
- Anaerobic pathway (e.g., Propionibacterium shermanii)

Both pathways ultimately lead to the formation of active cobalamin, but each requires distinct enzymes and environmental conditions. These processes are limited to certain microorganisms, making B12 naturally scarce in the human food chain.

Transfer

Herbivorous animals obtain Vitamin B12 from bacteria in soil or through gut microbes that synthesize it. Humans typically get B12 from animal-based foods, as these animals accumulate the Vitamin. Although B12 is produced by bacteria in the human colon, it is generally not absorbed due to its location beyond the terminal ileum (site of absorption). However, a study by Dr. Kurpad et al suggests that some B12 may be absorbed in the colon, potentially contributing to daily intake and implying a lower dietary requirement (57).

Bioavailability

Vitamin B12 bioavailability depends on its form, the food matrix, and individual absorption. Animal foods provide active forms like methylcobalamin and adenosylcobalamin, traditionally considered more bioavailable. However, current evidence shows that B12 from fortified foods and supplements, often in free form, is equally or even more easily absorbed (54).

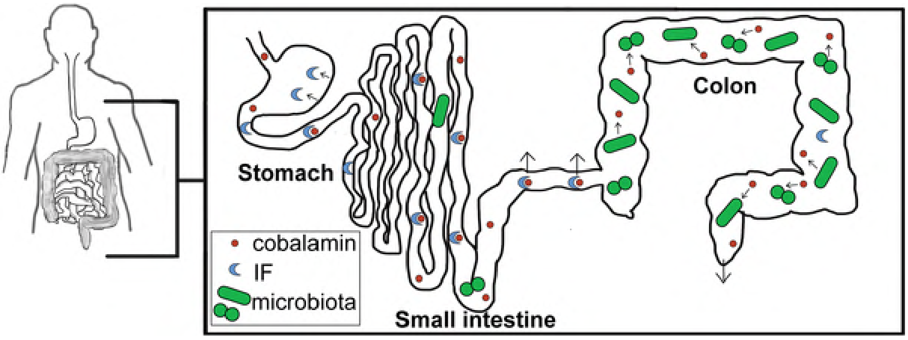
B12 stores in the liver can last for several years, so deficiency symptoms may appear after prolonged inadequate intake.

INTERESTING FACT

COLONIC B12 SYNTHESIS: NOT BIOAVAILABLE TO HUMANS

Although certain bacteria in the human colon can synthesize Vitamin B12, this B12 is not bioavailable because absorption occurs in the ileum of the small intestine, where intrinsic factor-mediated uptake takes place. Since colonic B12 production happens downstream of the absorption site, it is excreted in feces and does not contribute to systemic B12 levels. Therefore, despite microbial synthesis, humans cannot rely on gut bacteria to meet their B12 needs; dietary intake or supplementation remains essential, especially for those following plant-based diets.

Colonic B12 synthesis exists but it's beyond reach. Absorption happens upstream in the ileum, making gut-derived B12 nutritionally irrelevant.



Cobalamin in the healthy human intestinal tract
Source: Rowley, 2019

Cobalamin from food is absorbed in the terminal ileum, where it binds to intrinsic factor (IF) and is taken up by enterocytes. While certain gut bacteria do produce Vitamin B12, it is generally not available to the host because the colon lacks efficient absorption mechanisms. However, some studies suggest that limited absorption may occur in the colon, indicating a need for further research to clarify this potential pathway.

Although corrinoids are abundant in the **large intestine** due to the activity of the **gut microbiota**, multiple factors prevent humans from acquiring significant levels of cobalamin from this source.

1. First, cobalamin produced by gut microbes represents less than 2% of the total corrinoid content in feces (21).
2. Further, cobalamin produced in the colon, where microbial numbers are highest, is not bioavailable because the receptors necessary for absorbing the Vitamin are found in the small intestine, upstream of the site of corrinoid production (21).

Can B12 be absorbed through gardening?

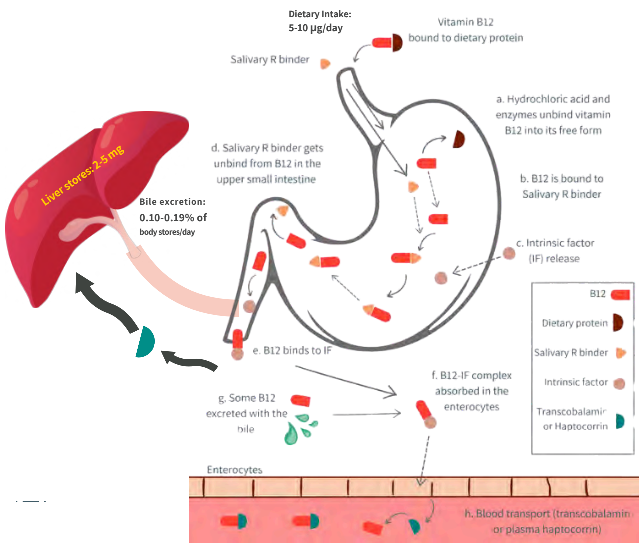
No, Vitamin B12 cannot be absorbed through the skin by touching soil or plants. While soil microbes produce B12 and some plants can absorb it if present in the growth medium, humans must consume B12 orally through food or supplements. Absorption occurs in the small intestine and requires specific proteins like intrinsic factor. Gardening, though beneficial in many ways, does not provide a significant source of B12.

HOW IS VITAMIN B12 ABSORBED?

Vitamin B12 is absorbed through two processes: passive diffusion and an active physiological process. Vitamin B12 is assimilated and transported by complex mechanisms that involve three transport proteins, intrinsic factor (IF), haptocorrin (HC), and transcobalamin (TC), and their respective membrane receptors (49).

Passive diffusion: This process, accounting for only **1-2% of B12 absorption**, happens across the digestive tract and mucous membranes. µg). Absorption by passive diffusion can occur without the intrinsic factor.

Active absorption: This process starts in the mouth, where B12 binds to R-binders, and then in the stomach, intrinsic factor (IF) is produced, facilitating absorption in the small intestine. The Vitamin B12-intrinsic factor is absorbed through specific receptors located on the enterocytes. Maximum B12 absorbed through active absorption is **~2 mcg** (IF saturation).



SOURCE:
1. HTTPS://WWW.SCIENCEDIRECT.COM/SCIENCE/ARTICLE/ABS/PII/S0083672922000164
2. HTTPS://PANCO.MN.CO/POSTS/FREE-DOWNLOADS-VITAMIN-B12

Plasma transport: After absorption, B12 is transported in the bloodstream by haptocorrin and transcobalamin, with the latter delivering it to cells for DNA synthesis (49).

It's estimated that approximately 3–5 µg of B12 is secreted into the bile daily, and most of it is efficiently reabsorbed, helping conserve the body's limited B12 stores (2–5 mg), especially given the low daily requirement of around 2.4 µg in adults.

Enterohepatic: circulation Enterohepatic circulation plays a crucial role in maintaining Vitamin B12 homeostasis. Vitamin B12 is secreted into the bile by the liver and released into the small intestine, where it binds to intrinsic factor (IF) and is reabsorbed in the terminal ileum. However, if the reabsorption step is disrupted due to pernicious anemia, inflammatory bowel disease, or certain infections, the enterohepatic circulation breaks down. In such cases, even if bile contains adequate B12, it cannot be reabsorbed, leading to gradual depletion of body stores. Because the body loses a small amount of B12 daily through urine and skin and can't reabsorb it via bile in these conditions, deficiency symptoms may appear relatively quickly (within months to a year), despite normal dietary intake (49).

Soluble fiber, alcohol, and substances like tannins in coffee and tea can hinder Vitamin B12 absorption. Additionally, excess calcium from dairy or fortified plant-based milks may also reduce its uptake.

WHERE IS VITAMIN B12 STORED?

The body stores about 2–5 mg of Vitamin B12, with around 50% stored in the liver. Daily losses are minimal (approximately 0.1%), occurring mainly through bile and intestinal cell turnover. Due to these small losses, if B12 intake stops (e.g., in strict vegans without supplementation), existing stores can sustain normal blood levels for 3–5 years before deficiency symptoms typically develop. Efficient conservation mechanisms help slow the depletion process (77).

Primary storage site: liver (**50-60%** of total body B12)

These liver stores play a crucial role in maintaining sufficient circulating levels even if dietary intake temporarily drops. The body loses only about 0.1% of its total B12 content daily, primarily through bile secretion into the intestine and loss of intestinal cells.

Secondary storage: muscles, brain, kidneys

Beyond the liver, smaller amounts of B12 are also stored in other tissues such as the muscles, brain, kidneys, and bone marrow. These secondary stores contribute to maintaining overall metabolic functions but are comparatively less significant than hepatic stores.

A 2002 study in the American Journal of Clinical Nutrition found that among 49 individuals on a raw vegan diet for 23–49 months, many had low serum B12 and elevated methylmalonic acid (MMA) levels, indicating deficiency. Supplementation with sublingual cyanocobalamin and nutritional yeast significantly improved B12 status (24).

How long do B12 stores last in the body?

The body stores about **2 to 5 milligrams** of Vitamin B12, with nearly half of it kept in the liver. Since daily losses are very small, about 0.1% through bile and shedding of intestinal cells, these stores can last a long time. In situations where dietary intake of Vitamin B12 stops, such as in individuals following a strict vegan diet without appropriate supplementation, the body's existing stores are typically sufficient to maintain adequate plasma levels for an extended period. It is generally estimated that these reserves can support bodily needs for about 3 to 5 years before clinical signs of deficiency begin to manifest.

WILL EXCESS B12 CAUSE DAMAGE?

Safety of Vitamin B12 in healthy individuals

- **Water-Soluble Nature:** Vitamin B12 is water-soluble, meaning excess amounts are typically excreted through urine, reducing the risk of toxicity.
- **No Established Upper Limit:** Due to its low toxicity, no tolerable upper intake level (UL) has been set for Vitamin B12.
- **Long-Term Supplementation:** Studies have shown that long-term supplementation of Vitamin B12 does not have adverse effects on fracture risk or cardiovascular disease in older individuals (150).

In healthy individuals, Vitamin B12 is safe even at high doses, with excess excreted in urine. Higher doses are typically used for deficiency; it's best to avoid excessive amounts, particularly when not needed.

Considerations for specific populations

- **Chronic Kidney Disease (CKD):** Individuals with CKD may have impaired Vitamin B12 metabolism, and high doses, especially of cyanocobalamin, could lead to accumulation and potential toxicity.
- **High serum B12 levels and mortality:** Some studies have found associations between elevated serum Vitamin B12 levels and increased all-cause mortality, particularly in older adults.
- **Cancer risk**: Observational studies have suggested a potential link between high Vitamin B12 intake and increased cancer risk, such as lung cancer in men taking high doses over extended periods.

A comprehensive meta-analysis encompassing 22 cohort studies with over 92,000 participants found that each 100 pmol/L increase in serum Vitamin B12 concentration was associated with a 4% higher risk of all-cause mortality in the general population and a 6% higher risk among older adults. The analysis revealed a linear relationship between elevated Vitamin B12 levels and increased mortality risk, particularly in older individuals. These findings underscore the importance of identifying and managing the underlying causes of elevated serum Vitamin B12 concentrations in clinical practice (70).

B-PROOF Trial: This randomized controlled trial investigated the effects of folic acid and Vitamin B12 supplementation on fracture risk and cardiovascular disease over a median follow-up of 54 months. The study found no significant effects on fracture risk or cardiovascular disease in older individuals (150).

Interestingly, studies reveal that CKD patients often have elevated homocysteine levels a red flag for cardiovascular risk. The silver lining? Vitamin B12, especially when combined with folic acid, has been shown to lower these levels, particularly in those undergoing hemodialysis. Despite this promise, there's still need for more research (149).

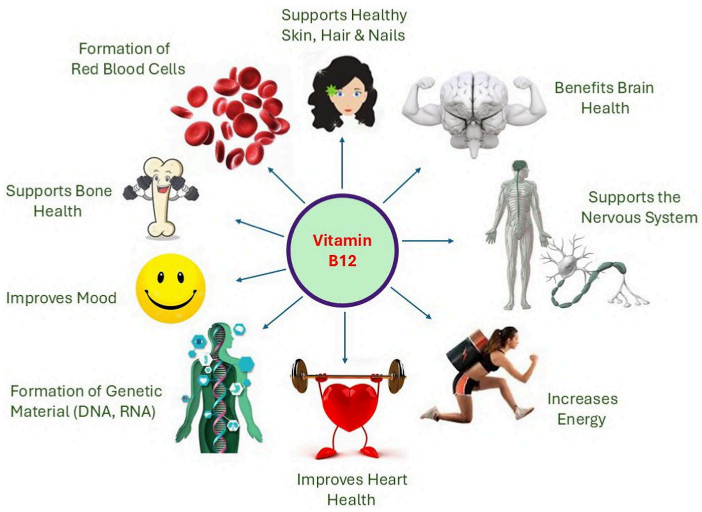
VITAMIN B12 SPECTRUM: FROM VITAL FUNCTIONS TO DEFICIENCY AND BEYOND

PHYSIOLOGICAL ROLES OF VITAMIN B12

Vitamin B12 is a vital micronutrient that supports several essential physiological processes. It acts as a coenzyme in important metabolic reactions and plays a key role in maintaining healthy blood, nerve function, and DNA integrity. Its deficiency can lead to hematological and neurological complications, making its adequate intake crucial for long-term health (66, 73, 80).

Functions of Vitamin B12

B12 IN ACTION: FROM RED BLOOD CELLS TO NERVOUS SYSTEM SUPPORT



Source: https://www.frontiersin.org/journals/nutrition/articles/10.3389/fnut.2024.1493593/full

DNA synthesis

- Acts as a cofactor for methionine synthase, facilitating the conversion of homocysteine to methionine, which is vital for DNA methylation and synthesis.

Neurological function

- Essential for the maintenance of myelin sheaths around nerves.
- Deficiency can lead to neurological impairments such as numbness, tingling, and cognitive disturbances.

Red blood cell formation

- Necessary for the production of healthy red blood cells; deficiency can result in megaloblastic anemia.

Energy production

- Involved in the metabolism of fatty acids and amino acids, contributing to energy production.

Enzymatic cofactor

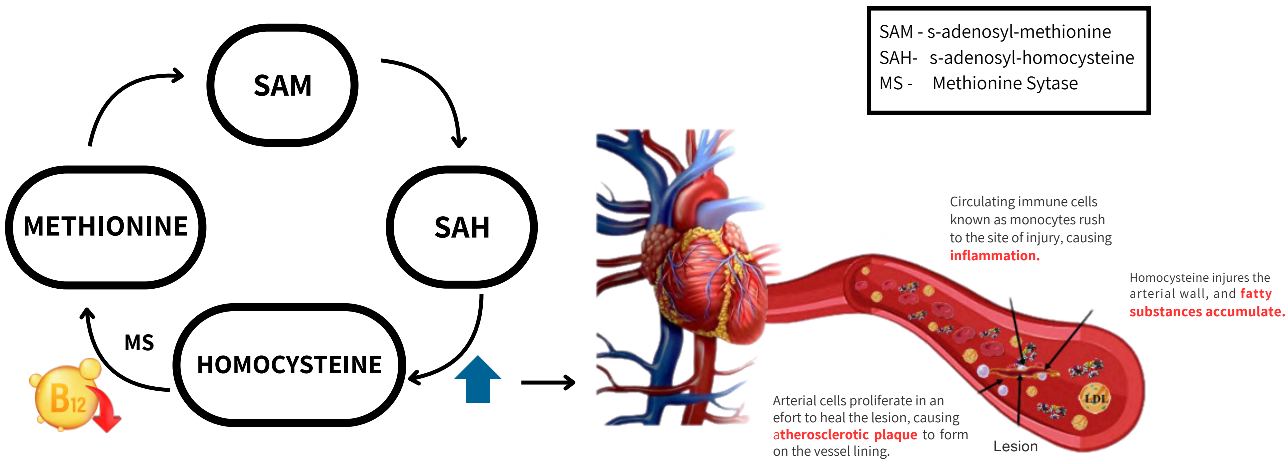
- Methionine synthase (converts homocysteine to methionine).
- Methylmalonyl-CoA mutase (converts methylmalonyl-CoA to succinyl-CoA).

WHY HOMOCYSTEINE LEVELS RISE IN VITAMIN B12 DEFICIENCY AND ITS SIGNIFICANCE IN CARDIOVASCULAR DISEASE (CVD)

Vitamin B12 is crucial for the proper function of two key enzymes involved in amino acid and fatty acid metabolism: **methionine synthase** and **L-methylmalonyl-CoA mutase.** The disruption of these enzymatic processes due to Vitamin B12 deficiency results in an imbalance of homocysteine and methylmalonic acid, both of which can contribute to adverse health effects if left untreated.

Methionine synthase and homocysteine: Vitamin B12 is a cofactor for methionine synthase, an enzyme that converts homocysteine into methionine, crucial for protein and nucleic acid synthesis, as well as the formation of S-adenosylmethionine (SAMe), a key methyl donor that affects DNA, RNA, proteins, and lipids. In B12 deficiency, the activity of the enzyme methionine synthase is impaired, disrupting the conversion of homocysteine to methionine, a process vital for methylation reactions and overall cellular function. This leads to elevated homocysteine levels, a known risk factor for cardiovascular disease (CVD), as it can damage blood vessels, promote inflammation, and accelerate atherosclerosis (35, 103).

Vitamin B12 is also a cofactor for L-methylmalonyl-CoA mutase, which plays a key role in converting L-methylmalonyl-CoA to succinyl-CoA for energy production. In B12 deficiency, impaired enzyme activity causes a buildup of methylmalonic acid (MMA) in the blood and urine, which serves as a diagnostic marker for the deficiency (93).



Elevated homocysteine levels increase risk of CVD (93)

Vitamin B12 keeps homocysteine in check.
A key to cardiovascular and cognitive health.

DEFICIENCY OF VITAMIN B12

Vitamin B12 deficiency is a widespread yet underdiagnosed concern globally, including in India. It occurs when the body lacks adequate levels of cobalamin to meet its metabolic needs, often leading to a range of hematologic, neurological, or psychiatric symptoms if left unaddressed.

Actual (biochemical) deficiency:

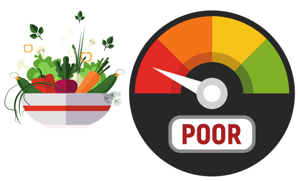
Refers to low levels of Vitamin B12 in the blood, typically detected through serum B12 testing. Levels are below the clinical cutoff (usually <200 pg/mL), clearly indicating insufficient intake or absorption. Often associated with overt symptoms like anemia, fatigue, neurological issues, etc.

World Health Organization (WHO): Serum Vitamin B12 **<150 pmol/L (≈203 pg/mL)**

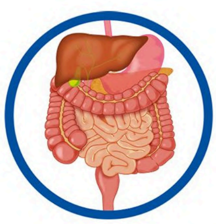
National Institutes of Health (NIH): (77) Serum B12 **< 200 pg/mL** (**deficiency**) **200–300 pg/mL (borderline)**

Indian Council of Medical Research: (79) Serum B12 **< 200 pg/mL (148 pmol/L).**

What causes Vitamin B12 deficiency?



Inadequate dietary intake



Impaired absorption

Increased requirement or loss

Functional deficiency:

While serum B12 is a primary indicator, it may not detect cases of functional deficiency where B12 levels appear normal, but the body cannot effectively utilize the Vitamin. This can be identified through elevated levels of metabolites such as methylmalonic acid (MMA) and homocysteine, which signal tissue-level insufficiency (55, 78, 82).

UNMASKING THE IMPACT OF VITAMIN B12 DEFICIENCY

Vitamin B12 deficiency **does not develop overnight**. Symptoms of Vitamin B12 deficiency may not appear for several years after dietary intake ceases due to the body's substantial liver stores. However, once these reserves are exhausted, the effects can be severe and often irreversible. Deficiency may result in megaloblastic anemia, permanent nerve damage, cognitive impairment, depression, infertility, and complications during pregnancy.

Importantly, **"subclinical or mild deficiency",** in which neurological symptoms begin even without overt anemia, is more prevalent than fully developed deficiency. This underscores the critical need for early detection, well before advanced clinical signs emerge.

SUBCLINICAL DEFICIENCY: THE HIDDEN BURDEN

Subclinical (mild) B12 deficiency, whereby rising MMA or homocysteine heralds neuronal injury before anemia develops, is more prevalent than overt deficiency. Studies estimate up to 15 % of adults worldwide exhibit biochemical B12 depletion, with rates higher among:

- Older adults (> 60 years)
- Strict vegetarians/vegans
- Post–gastric surgery or ileal resection
- Long-term metformin or PPI users

Early detection in these groups can prevent progression to irreversible nerve damage (42, 84, 107).

B12 deficiency can mimic multiple disorders, from depression to dementia and fatigue to folate deficiency. It is easily preventable and treatable, but only when recognized early.
Regular screening of older adults, individuals on plant-based diets, and patients on long-term medications affecting B12 absorption can facilitate proactive care.

Highly processed diets, urbanisation, and plant-forward eating patterns have made Vitamin B12 deficiency a critical public health priority.

DID YOU KNOW?

30% of individuals with "normal" serum B12 may still have metabolic deficiency (45).

INTERESTING FACT

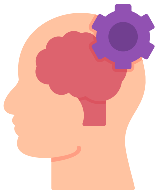
VITAMIN B12 DEFICIENCY: WHAT'S REALLY AT STAKE?

Symptoms of B12 deficiency:

Vitamin B12 deficiency can manifest through a variety of symptoms. Early B12 deficiency can present with neurological symptoms even in the absence of anemia (7, 42, 63).

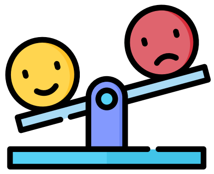
Neurological

Peripheral neuropathy
Numbness, tingling or burning sensations in the hands and feet.



Cognitive impairment
Memory loss confusion, difficulty concentrating.

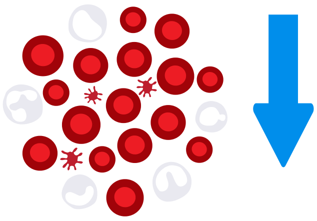
Gait disturbances
Unsteadiness, balance issues, and increased risk of falls.



Mood changes
Depression, irritability, or even psychosis in severe case.

Hematological

Megaloblastic anemia
Characterised by large, immature red blood cells and reduced hemoglobin.

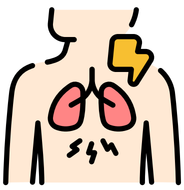


Mild leukopenia & thrombocytopenia
Low white blood cells or platelets in severe or prolonged cases.

Hyper-segmented neutrophils
Neutrophils with ≥6 nuclear lobes seen on blood smear are an early sign of B12 deficiency due to impaired DNA synthesis.

General Symptoms

Fatigue, weakness, pallor



Shortness of breath and dizziness

Muscle weakness and difficulty walking

Glossitis inflamed, smooth, and sore tongue

Clinicians should consider Vitamin B12 deficiency in patients with nonspecific symptoms like fatigue, weakness, or neurological issues. Early diagnosis and testing are crucial to prevent irreversible nerve damage, and timely intervention with supplementation or dietary changes can help avoid long-term complications.

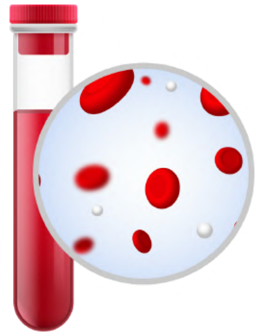
PROGRESSION OF VITAMIN B12 DEFICIENCY: FROM SILENT TO SEVERE

1. Normal status

- Adequate dietary intake.
- No symptoms.
- Normal serum B12, MMA, and homocysteine (77, 112).

2. Subclinical deficiency: Refers to a condition where individuals have low Vitamin B12 levels but no overt clinical symptoms.

- Common in vegetarians & elderly (4,5).
- Decreased B12 stores in tissues.
- Mild ↑ homocysteine or MMA.
- Detected only through lab tests.
- Even in the presence of normal B12, raised MMA/homocysteine is an early flag (80).



3. Early deficiency: Early Vitamin B12 deficiency is a stage where individuals may experience subtle, nonspecific symptoms such as fatigue, weakness, and mild neurological disturbances. At this point, serum B12 levels might still be borderline low, and symptoms may not be severe enough to raise suspicion.

- Serum B12 = 200–300 pg/mL (borderline), ↑ MMA, ↑ Homocysteine (112).
- Subtle symptoms should trigger a dietary history review. Begin supplementation if B12 status is borderline and symptoms are present.
- Educate transitioning WFPB patients to start supplements early (7, 63).

4. Severe deficiency: Severe Vitamin B12 deficiency presents with marked neurological issues (e.g., memory loss, neuropathy, gait disturbances, and depression) and megaloblastic anemia (63, 112).

If untreated, nerve damage can become irreversible.

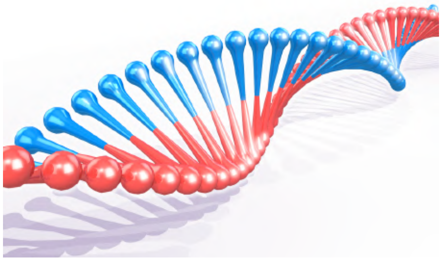
- Very low B12 + highly elevated MMA & homocysteine.
- Avoid reaching this stage via preventive education & routine screening. Especially screen high-risk populations: the elderly, vegans, and pregnant women (77).

WHO IS AT RISK OF B12 DEFICIENCY?

Diet and B12 deficiency:

5% to 52% prevalence of B12 deficiency

Vegan and vegetarian diets, which exclude or minimise animal products, are at a significantly higher risk for Vitamin B12 deficiency. India's predominantly vegetarian dietary habits contribute substantially to the high prevalence of Vitamin B12 deficiency (18).



Genetic factors

Genetic mutations affecting intrinsic factor production or transcobalamin II can lead to impaired B12 absorption and transport, Imerslund-Gräsbeck disease.

Long-term medications: (5.8- 30%)

Metformin: Long-term use (≥5 years) or high doses (≥1,500 mg/day) of metformin in diabetic patients is associated with B12 deficiency.

Proton Pump Inhibitors (PPIs): Prolonged use (≥12 months) of PPIs can reduce stomach acid, leading to decreased B12 absorption.

A study from northern India found that 27.73% of B12-deficient patients had a history of long-term PPI or H2 blocker use (109).

Alcohol abuse: Chronic drinking damages the gut lining and liver, undermining B12 absorption and storage. Moreover, heavy drinkers often follow a nutritionally poor diet, compounding the risk of deficiency, and even when blood levels of B12 appear normal, alcohol's interference with cellular uptake can produce a "functional" deficiency. The fallout from B12 deficiency includes nerve damage, fatigue, and anemia. Treating alcohol abuse is key, along with B12 supplements and a balanced, B12-rich diet to restore levels (41, 91).

Low- and middle-income countries:

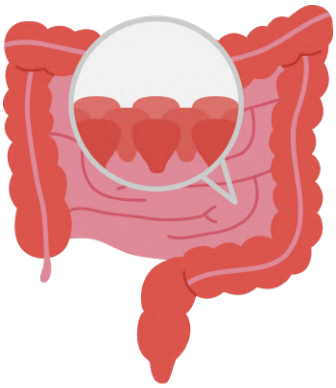
Primarily due to limited intake of animal-source foods, lack of fortification programs, and higher rates of gastrointestinal infections that impair absorption. In 2017, B12 supply averaged 3.21 μg/day in high-income countries versus 2.58 and 1.58 μg in low-middle and low-income countries (91).

WHO IS AT RISK OF B12 DEFICIENCY?

Age-related

Older adults (>60 yrs): 12-20%

Elderly individuals are at increased risk due to malabsorption syndrome (>60%) and decreased stomach acid production (achlorhydria), which impairs B12 absorption (5, 7).



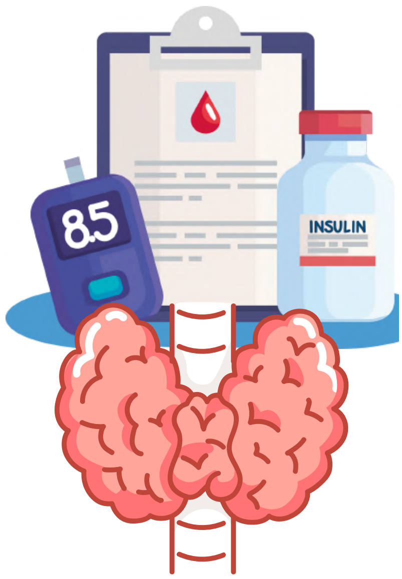
GI disorders (e.g., Crohn's, celiac, atrophic gastritis): 6%- 38%

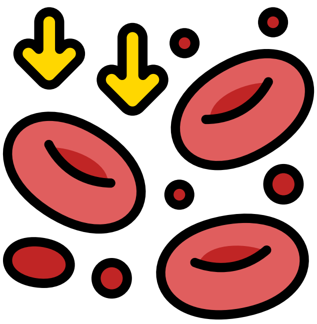
Pancreatic insufficiency, obstructive jaundice, tropical sprue, celiac disease, inflammatory bowel diseases (e.g., Crohn's disease), chronic radiation enteritis of the distal ileum, short bowel syndrome, parasitic infestations (e.g., tapeworm infections), zollinger-ellison syndrome, bariatric & GI surgeries.

Type 1 diabetes and autoimmune thyroid diseases:

Autoimmune targeting of gastric parietal cells and intrinsic factor in both type 1 diabetes and autoimmune thyroid disease causes atrophic gastritis and pernicious anemia, leading to impaired cobalamin binding, malabsorption, and disrupted enterohepatic recycling of Vitamin B12 (53).

Despite normal serum B12 levels, patients often exhibit functional deficiency evidenced by elevated methylmalonic acid and homocysteine manifesting as megaloblastic anemia, neuropathy, and cognitive impairment, which necessitates high-dose supplementation and regular monitoring (55, 104).





Pernicious anaemia:

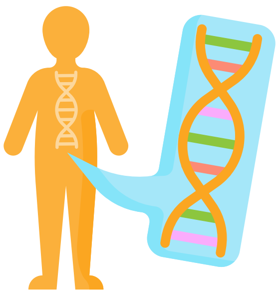
Autoimmune disorder in which loss of gastric parietal cells and intrinsic factor causes malabsorption of Vitamin B12 and depletion of hepatic stores; this results in megaloblastic (macrocytic) anemia, peripheral neuropathy, and cognitive disturbances. Elevated homocysteine concentration in plasma was observed in 66% of the vegans and about 45-50% of the omnivores and vegetarians (64, 67).

IS IT POSSIBLE TO BE VITAMIN B12 DEFICIENT DESPITE FOLLOWING A MEAT-RICH DIET?

While Vitamin B12 deficiency has traditionally been associated with vegetarian diets, despite only about 29.5 % of Indian adults identifying as vegetarian, studies report Vitamin B12 deficiency rates as high as 40–70% (135). If the majority of Indians consume some portion of animal-source foods, why does B12 insufficiency remain so pervasive? This discrepancy raises critical questions about bioavailability, food preparation practices, and non-dietary barriers to B12 uptake in India's diverse communities.

a. Genetic variants:

MTHFR gene mutations (e.g., C677T) can impair B12 metabolism. A study of 105 Italians with B12 deficiency found these variants linked to more severe anemia and thrombocytopenia. However, larger studies are needed to confirm these findings (37).



b. Soil depletion:

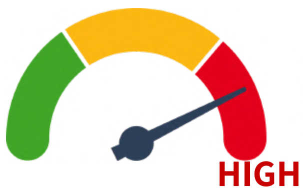
Modern monoculture farming and heavy chemical use reduce soil microbes that naturally produce B12, lowering its content in plants and the animals that feed on them.

c. Factory Farming:

Livestock are often given synthetic B12 due to poor feed quality, which may affect the form and absorption of B12 in meat.

d. Lower B12 in Commonly Consumed Meats:

In Telangana, India, despite 98% being non-vegetarian, B12 deficiency is widespread, likely due to a reliance on chicken, which has lower B12 levels than mutton or seafood (69).



Regardless of dietary pattern, monitoring Vitamin B12 levels and considering supplementation when needed is essential for maintaining long-term health.

PREVALENCE OF VITAMIN B12 DEFICIENCY

PREVALENCE OF B12 DEFICIENCY

GLOBAL CONTEXT

Vitamin B12 deficiency is a significant global public health concern, particularly in regions where diets are predominantly plant-based and access to animal-source foods or fortified products is limited. Surveys indicate widespread deficiency in many low- and middle-income countries, with estimates showing that approximately 40% of people in Latin America, 70% in Africa, and 70–80% in South Asia have subnormal B12 status (60). Despite the known risks, B12 supplementation remains low, with data from NHANES showing that only 24% of men and 29% of women report using B12 supplements.

Adults: 3.6% of adults (≥19 y), ~3.7% in those ≥60 y * (NHANES)

Children and adolescents: Often underreported in children from developing countries, with a varying prevalence of 21–45% (85).

- In Ethiopia, a recent survey found ~34% of schoolchildren to be Vitamin B12 deficient (85).

Pregnant and reproductive-age women: ~1/3rd of pregnant women worldwide are B12 deficient on average, although studies vary by setting and cutoff (87).

- Since pregnancy increases demand and serum B12 naturally falls, women in regions with borderline intakes are at special risk.

Elderly adults: In the US, ~3- 6% of people ≥60 y are deficient (<148 pmol/L) (107).

- NHANES roundtable noted ~21% of Americans ≥60 y have at least one abnormal B12 marker.
- A study of long-term care residents found 14% <156 pmol/L and 38% <300 pmol/L on admission (77).
- In countries like the US, ~20% of elderly show marginal depletion (148–300 pmol/L) (77).

High-income countries: By contrast, deficiency in children is rare in wealthy nations. In US NHANES data (1999–2002) <1% of children/adolescents had B12 <148 pmol/L.

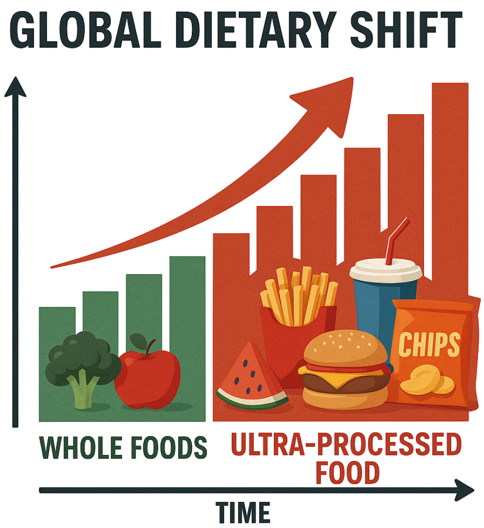
- UK data (NDNS 2008–2011) found only ~3% of adults 19–64 y had <150 pmol/L (141).
- When using serum B12 <148 pmol/L (deficiency), but using a higher cutoff (<221 pmol/L) yields ~12–13% of adults affected.

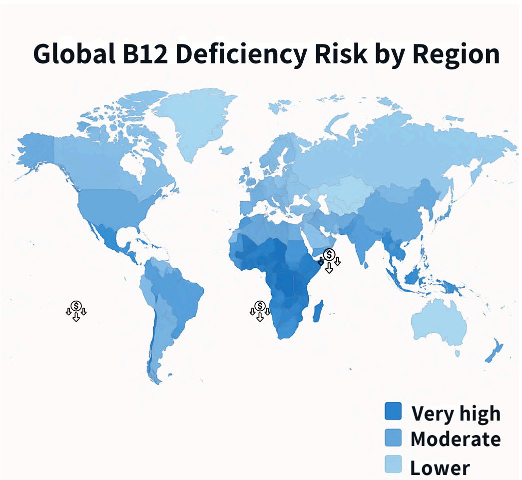
These gaps reflect differences in diet (animal product intake), absorption, and public health programs across regions. In short, developed nations see low prevalence in the general population, whereas many developing regions report rates an order of magnitude higher.

FACTORS IMPACTING THE PREVALENCE OF B12 DEFICIENCY GLOBAL CONTEXT

Global dietary shift:

Increased intake of ultra-processed foods, low in essential nutrients like B12 and high in empty calories, is a major concern. Even ultra-processed animal products may impair B12 absorption due to nitrosamines and gut microbiota changes. Meanwhile, poorly planned plant-based diets without fortified foods or supplements heighten deficiency risk, worsened by misconceptions about inactive B12 analogues in seaweed, mushrooms, and fermented foods. Overall, lack of awareness remains a key driver across dietary patterns (3, 52, 144).





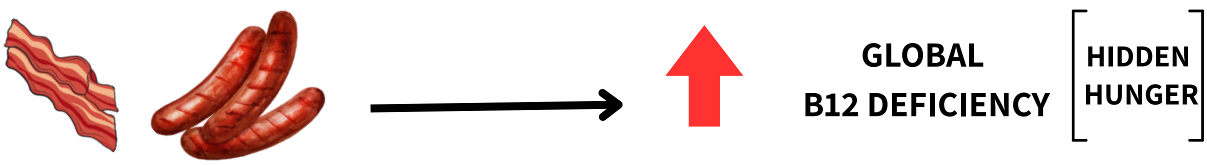
Demographic and socioeconomic factors

Low-income groups often lack access to diverse, nutrient-rich foods, relying instead on staple-based diets low in micronutrients. Rising elderly populations face impaired absorption due to age-related gastric changes, increasing vulnerability. **South Asia, Africa, and Latin America** show some of the highest deficiency rates due to a combination of dietary patterns, low awareness, and poor healthcare access (49, 145).

Medical conditions & medications

Conditions like pernicious anemia, celiac disease, crohn's disease, and H. pylori infection impair absorption. Surgeries (e.g., gastric bypass) that remove/inactivate parts of the stomach or ileum reduce B12 absorption. Proton pump inhibitors, H2 blockers, and metformin interfere with B12 absorption when used long-term.

Moreover, uneven access to fortified products (urban vs. rural) and suboptimal uptake among vulnerable groups further exacerbate deficiency risks despite overall shifts toward plant-forward eating. (86)



A meta-analysis by Green et al. (2017) reviewed data from 68 countries, finding that subclinical B12 deficiency affects up to 2.5% to 26% of the general population, while overt deficiency impacts about 5-15%. Definitions of B12 deficiency vary, with serum levels <148 pmol/L commonly used as a cutoff, though functional deficiency may occur at higher levels (42).

B12 DEFICIENCY ACROSS DIETARY PATTERNS

GLOBAL

Vitamin B12 deficiency is more common in vegans and vegetarians due to the absence of reliable B12 sources in plant-based diets. However, it also occurs in non-vegetarians, often due to poor absorption, aging, medical conditions, or reliance on ultra-processed animal products (90).

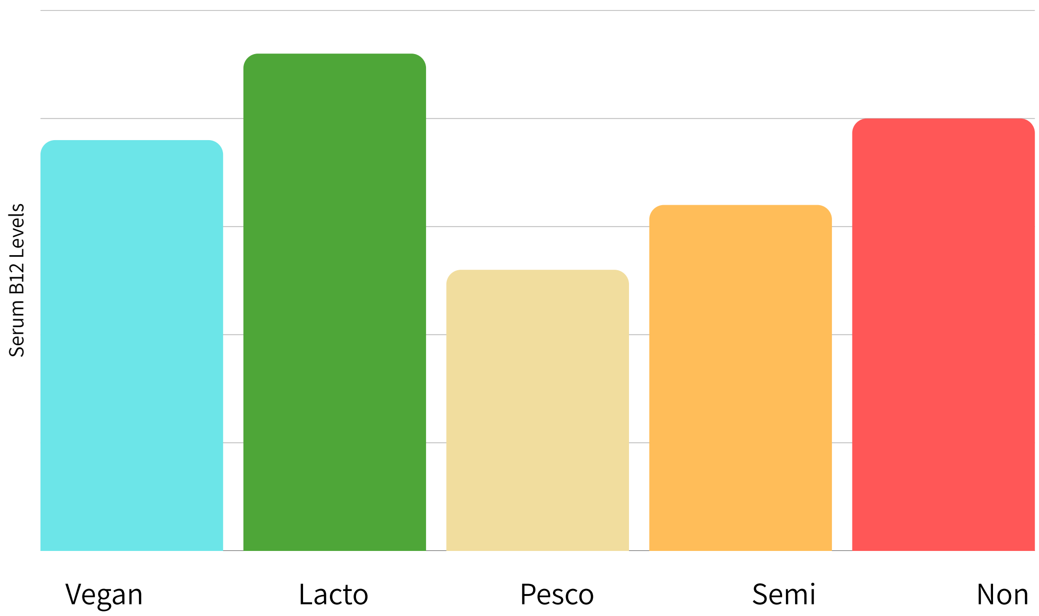
Diet type	B12 deficiency prevalence	Population	Fats and fiber	Note
Omnivore	1%	British males (EPIC- OXFORD) (38)	High saturated fat consumption, least fiber in diet	Lower risk but recently increased deficiency due to absorption issues.
Lacto-ovo vegetarian	40%	Latin Americans (142)	Moderate saturated fats and fiber	Bioavailability of B12 from dairy is variable and not a significant impact from eggs.
Vegetarian (general)	6-14%	British males (EPIC- OXFORD) (38)	Low saturated fats and high fiber	Risk varies with the inclusion of dairy/eggs.
Vegan	5- 52% based on supplementation	British males (EPIC- OXFORD) (38) No B12 supplementation	Least saturated fats and highest fiber	Highest risk due to complete exclusion of animal products. Varies based on supplementation.

- Vegans without supplementation have significantly lower serum Vitamin B12 concentrations than omnivores and vegetarians (64, 83, 146).
- People are at higher risk if relying only on eggs and dairy sources without fortified foods or supplements.

Omnivore diets are NOT immune to B12 deficiency.

B12 INTAKE ACROSS DIETARY PATTERNS (INSIGHT FROM ADVENTIST HEALTH STUDY)

VITAMIN B12 INTAKE [INCLUDING SUPPLEMENTS]



Source: Living Longer: Living Better. The Health Experience of California Seventh-day Adventists. Gary E. Fraser, MB ChB, PhD, FACC, FRACP, Professor of Medicine Professor of Epidemiology, Loma Linda University. The Adventist Health Studies: A contribution to preventive medicine. 1958-2010.

Based on data from the **Adventist Health Study ("Living Longer: Living Better – The Health Experience of California Seventh-day Adventists")**, compare Vitamin B12 intake (including supplements) across different dietary groups:

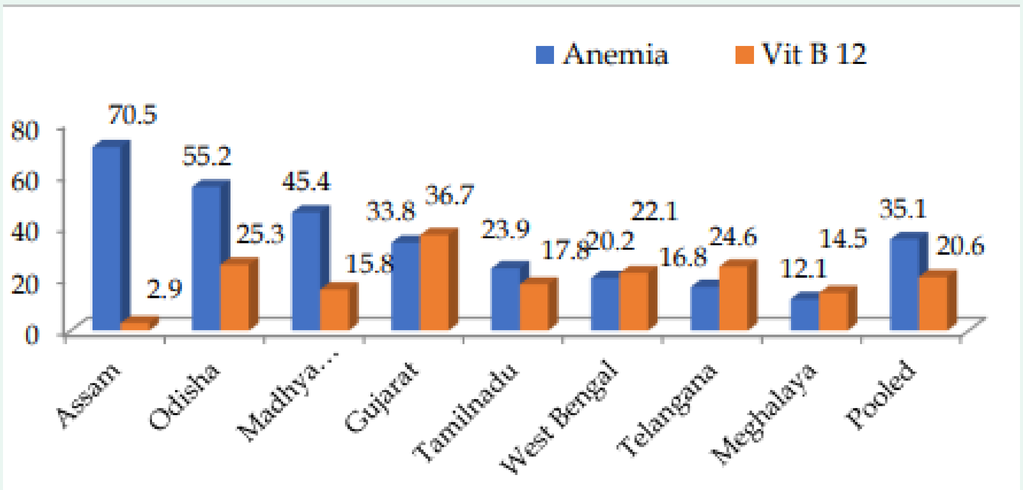
- Lacto-vegetarians had the highest intake **(~23 µg/day)**, likely due to supplementation, as B12 bioavailability is limited from dairy, and eggs contribute minimally.
- Non-vegetarians followed **(~20 µg/day)**, benefiting from regular intake of animal-based foods.
- Vegans consumed around **18 µg/day**, mostly through fortified foods and supplements.
- Semi-vegetarians **(~16 µg/day)** and pescatarians **(~13 µg/day)** showed relatively lower intake.

Despite restrictions, vegans in this study had adequate B12 intake, highlighting the importance of supplementation and fortified foods in plant-based diets (19).

A 2016 Nutrients review highlights the high risk of Vitamin B12 deficiency in vegans and vegetarians, including those consuming dairy and eggs, due to limited intake (96). To prevent neurological and hematological issues, the authors recommend starting B12 supplementation early, with at least 250 µg/day of oral cyanocobalamin (5).

PREVALENCE OF B12 DEFICIENCY

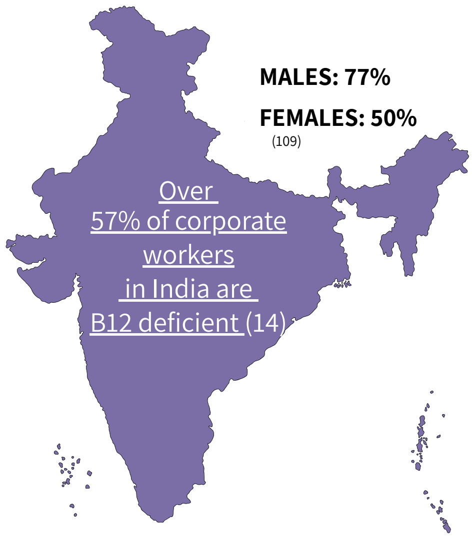
INDIAN CONTEXT



Prevalence of Vitamin B12 deficiency among adult population in India

Source: https://www.nin.res.in/researchhighlights/2020-21.pdf

- **Children:** The Indian CNNS national survey found 13.8% of preschoolers and 17.3% of school-age children deficient; for adolescents it was 31.0% (105).
- **Pregnant women:** Among pregnant women in rural South India, B12 deficiency is notably high, with prevalence rates ranging from 52% to 74% (9).
- A study conducted among the South Indian urban population reported an overall Vitamin B12 deficiency prevalence of 35%, with significantly higher rates among vegetarians (54%) compared to those following a mixed diet (31%) (110).
- The study done by Medibuddy, which analysed data from 4400 people, shows that a significant proportion of corporate workers in India are affected by Vitamin B12 deficiency (14).



"Invisible Epidemic" of B12 deficiency in India.

- Contributing factors include **demanding work schedules, high stress, poor dietary choices, and sedentary lifestyles.** These conditions often lead to erratic eating patterns, increased intake of processed foods and sugary drinks, and impaired B12 absorption and utilisation.

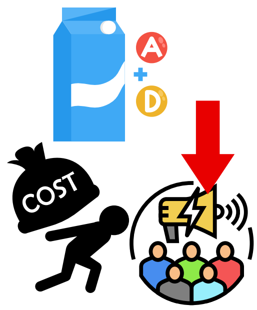
FACTORS IMPACTING THE PREVALENCE OF B12 DEFICIENCY

INDIAN CONTEXT

Dietary Patterns

- >30% of Indians follow a vegetarian diet, and many more consume limited animal products (135).
- Traditional vegetarian diets lack reliable B12 sources unless fortified foods or supplements are consumed.
- Low income & dietary monotony (e.g., reliance on rice or wheat staples) reduces micronutrient intake overall, including B12.
- Animal- source foods are expensive.

Fortification & Supplementation Issues

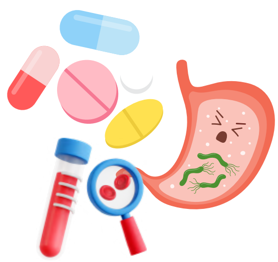


- Limited mandatory fortification policies compared to the West.
- Low availability and high cost of fortified foods.
- Awareness and labeling of B12 fortification in foods is also limited.
- Routine B12 supplementation is not common practice in India, even among vegans or vegetarians.

Lack of awareness about evidence based nutrition

- Complete reliance on unreliable or inactive B12 sources (e.g., spirulina, tempeh, fermented foods) persists in some populations contributing to deficiency.
- B12 is heat-sensitive and may degrade with traditional prolonged cooking methods.

Medical and Drug-Related Factors



- High prevalence of Helicobacter pylori infection (40-70% of the population); 4 out of 5 Indian adults harbor H. pylori (108).
- Widespread use of PPIs, and metformin.
- Limited screening programs and healthcare access.
- Conditions like Crohn's disease, celiac disease, or gastric surgeries affect B12 uptake.

A landmark study -a multicentric Indian study found B12 deficiency in 46% of adults, 62% among vegetarians and 38% among non-vegetarians, highlighting widespread deficiency and low awareness among both the public and healthcare providers (110).

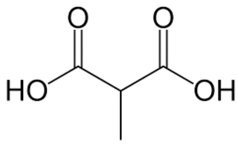
A cross-sectional study of 2,403 healthy Indian school-going adolescents (11–17 years) found an overall Vitamin B12 deficiency prevalence of **32.4%,** with rural participants showing a significantly higher **rate (43.9%) than urban participants (30.1%)** (17).

B12 DIAGNOSTIC JOURNEY: TESTS, THRESHOLDS & INTERPRETATIONS

HOW TO EVALUATE VITAMIN B12 DEFICIENCY?

Initial screening measures serum B12, but because levels often sit in a **"grey zone,"** functional markers methylmalonic acid and homocysteine are needed to confirm deficiency. When pernicious anemia is suspected, intrinsic factor and parietal cell antibody tests clarify the cause. Combining clinical evaluation with these targeted biochemical assays ensures accurate diagnosis and individualized supplementation.

Serum Vitamin B12
Traditional but limited



Methylmalonic Acid (MMA) specific, early marker

Homocysteine rises in B12, folate, and B6 deficiency

CB12 index combined biomarker score

Holotranscobalamin (holo-TC)
Active B12; more sensitive

Assess Clinical Context

- Nonspecific symptoms
- Suspected or high risk: (vegan, GI surgery, pernicious anemia, elderly, metformin/PPI use, etc.)

↓

ORDER CBC + SERUM B12 LEVEL

B12 < 200 PG/ML
DIAGNOSE DEFICIENCY
↓
START B12 THERAPY
+
INVESTIGATE CAUSE (e.g., IF Ab test)

200–300 PG/ML
↓
ORDER MMA, HCY ± HOLOTC

> 300 PG/ML
DEFICIENCY UNLIKELY
↓
CONSIDER OTHER CAUSES

MMA OR HOMOCYSTEINE ELEVATED?

YES
↓
CONFIRM METABOLIC B12 DEFICIENCY

NO
↓
HIGH CLINICAL SUSPICION?
↓
THERAPEUTIC TRIAL + REPEAT LABS

*Always rule out underlying causes, and if B12 deficiency is excluded, consider alternative diagnoses like folate deficiency, thyroid dysfunction, or neurological disorders.

DIAGNOSTIC TESTS FOR VITAMIN B12 - Part 1

Total serum/plasma B12:

Vitamin B12 deficiency is often evaluated through blood tests, but interpreting results accurately requires a combination of markers. The serum B12 test is the most commonly used, yet it may not always reflect true cellular deficiency. Some individuals may have normal serum B12 levels but still exhibit signs of functional deficiency, where the Vitamin is not effectively utilised by the body.

Interpretation guidelines– Serum Vitamin B12 levels (in pg/mL)

Category	Serum B12	Interpretation	Recommended action
Deficient	< 200 pg/mL	Likely true deficiency; may show anemia or nerve symptoms.	Start B12 treatment (oral/IM). Identify underlying cause.
Borderline / Indeterminate	200–300 pg/mL	Possible functional deficiency; check MMA or homocysteine.	Order MMA and homocysteine.
Generally Adequate	300–450 pg/mL	Generally sufficient; monitor if symptoms or risks present.	Monitor if high-risk; test MMA/homocysteine if symptoms persist.
Optimal	> 450 pg/mL	Strong B12 status; low risk of deficiency issues.	No action unless symptoms suggest deficiency.

Limitations of serum B12 testing

Serum Vitamin B12 alone is not a reliable indicator of deficiency, as it measures total cobalamin, most of which is inactive. Only 20–25% (holo-transcobalamin) is bioavailable, so normal levels may mask functional deficiency. More sensitive markers like methylmalonic acid (MMA) and homocysteine rise when B12 is insufficient at the cellular level. Levels below 200 pg/mL are considered deficient, while 200–300 pg/mL is borderline and warrants further testing. Up to 15% of people may be deficient, often without clear symptoms (29, 82).

In borderline serum B12 (200–300 pg/mL), always follow up with MMA or homocysteine to avoid missed diagnoses.

Methylmalonic Acid (MMA): MMA is a highly specific functional marker of B12 status. Vitamin B12 is a required cofactor to convert methylmalonyl-CoA to succinyl-CoA; without adequate B12, methylmalonic acid accumulates. Serum or plasma MMA rises early in deficiency, often before hematologic changes appear. MMA is highly specific for B12, it is not elevated in folate deficiency, but it is also **increased in renal failure and with aging.** (82)

Elevated MMA + low/normal B12 → **True deficiency (strongly indicative)**

DIAGNOSTIC TESTS FOR VITAMIN B12 - Part 2

Total Homocysteine (tHcy): Homocysteine rises in B12 deficiency because B12 is required (along with folate and B6) to remethylate homocysteine to methionine. **Increases with folate or B6 deficiency, hypothyroidism, and chronic renal disease** (27, 29).

tHcy > 15 µmol/L	→	**B12 deficiency (less specific)**

Holotranscobalamin (holo-TC): This newer marker measures the transcobalamin-bound (active) B12 fraction. Holo-TC often declines earlier than total B12 in deficiency. Studies show holo-TC is more sensitive than total B12. **Not yet universally available.**

Combined Indicator (cB_{12}): Fedosov et al. (2015) introduced cB_{12}, a composite score combining total B12, holo-TC, MMA, and tHcy (with an age adjustment) (29).

$$cB_{12} = \log10[(\text{holo-TC} \times B_{12})/(\text{MMA} \times \text{tHcy})] - (\text{age factor})$$

$CB_{12} < -0.5$ → **B12 DEFICIENCY**

Other tests:

- **Intrinsic factor or parietal cell antibodies:** To diagnose pernicious anemia
- **Serum MMA in urine**
- **Genetic tests** (for inborn cobalamin disorders)

Vitamin B12 insufficiency may include one or more of the following:

- ↓ serum holoTC (transcobalamin) and serum B12
- ↑ plasma methylmalonic acid (MMA) and urinary MMA excretion
- ↑ plasma homocysteine (tHcy)
- Hypersegmentation of nuclei in neutrophils
- Megaloblastic anemia (MCV, Hg, large RBC)

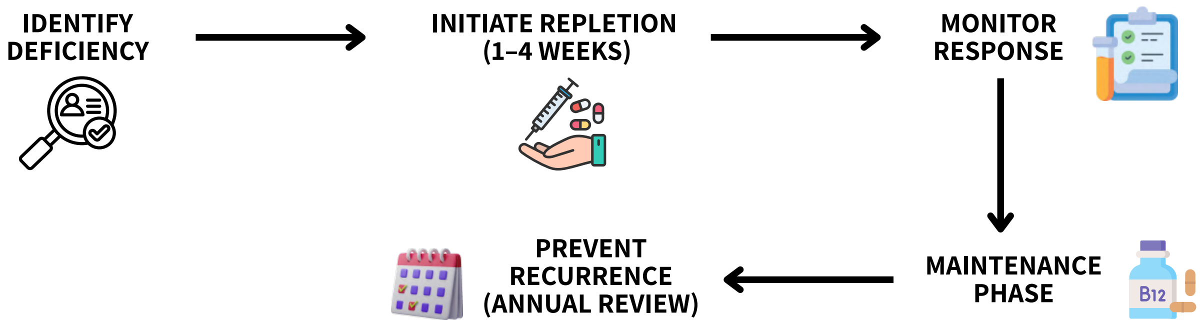
At-a-glance: B12 diagnostic markers

Test	Marker	Cost (in rupees)	Specificity	Use
Serum B12	Total circulating B12	490-1200	Low–Moderate	First-line screen
MMA	Functional marker	800-1500	High	Early/B12-specific
Homocysteine	Metabolic marker	950-1200	Moderate	Supports diagnosis
Holo-TC	Active B12	829-1800	High	Early indicator
cB12 Index	Composite of all	420-1250	Very High	Research/Advanced

MANAGING VITAMIN B12 DEFICIENCY

MANAGEMENT OF B12 DEFICIENCY

Vitamin B12 deficiency in India is often due to low dietary intake (especially in vegetarians) or malabsorption (pernicious anemia, gastric surgery, ileal disease). Treatment must address the cause; malabsorptive deficiencies generally require parenteral therapy, whereas dietary deficiencies can often be corrected with high-dose oral supplements. Vitamin B12 deficiency is one of the few nutritional deficiencies that is fully reversible with timely intervention.



Malabsorption (pernicious anemia, gastric/ileal pathology)

- **1000 µg** hydroxocobalamin or cyanocobalamin (102). This reliably replenishes stores and raises hematologic parameters.

IM daily for 5–7 days → Weekly for 4–6 weeks → Every 1-3 months (maintenance)

NIH recommendation for B12 deficiency (147):

- **Serum B12 < 150 +/- anemia:** 1000 µg intramuscularly (oral) 3 months.
- **Anemia + Malabsorption:**

1000mcg IM Daily or 3 times/week for 2 weeks → **Oral 1000 mcg/day** (maintenance)

Pernicious Anemia Society recommendation (Pernicious Anemia) (87)

- Hydroxocobalamin 1 mg intramuscularly three times a week for 2 weeks.
- Followed by 1 mg intramuscularly every 2–3 months for life.

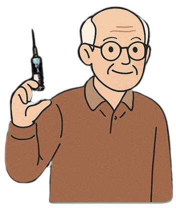
Dietary deficiency (strict vegetarians, vegans low intake):

- High-dose oral B12 is effective because a small fraction (~1–2%) is absorbed passively.
- **1000–2000 µg** oral cyanocobalamin daily (102, 147).

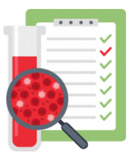
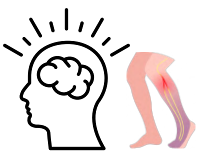
1000 µg/day until blood indices normalize → 1000 µg weekly or monthly maintenance

LONG-TERM MAINTENANCE AND MONITORING IN HIGH-RISK GROUPS

- **Elderly:** Prophylactic supplementation in the elderly, for example, 1000 µg IM every 1–3 months or 1000 µg orally weekly if levels are borderline (82). High-dose oral supplementation (e.g., 1000 µg/day) is as effective as IM injections in correcting B12 deficiency in elderly individuals.
- **Vegans and vegetarians:** **All vegans should take a supplement or consume fortified foods,** >10 µg oral B12 daily or 2000 µg weekly + fortified foods (116).
- **Pregnant and lactating women:** A cochrane review found that orally supplementing ~5-250 µg/day of B12 during pregnancy significantly improved maternal B_{12} status (31).



From deficiency to recovery: How quickly do B12-related symptoms improve? (59, 87)

	Abnormality	Expected time until improvement
	Homocysteine or methylmalonic acid level, or reticulocyte count	One week
	Neurological symptoms	Six weeks to three months
	Anemia, leukopenia, thrombocytopenia Increased mean corpuscular volume (MCV)	Eight weeks

Avoid delays in treatment; if neurological symptoms are present, early repletion is critical.

WHY IS 1000 MCG OF B12 RECOMMENDED DURING DEFICIENCY WHEN THE RDA IS ONLY 2.4 MCG?

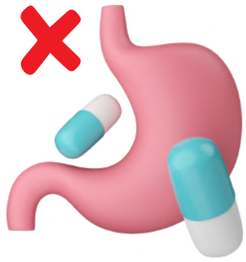
The Recommended Dietary Allowance (RDA) for Vitamin B12 is 2.4 mcg per day, assuming normal absorption via intrinsic factor in the ileum. However, in cases of deficiency, whether due to poor intake, aging, gastrointestinal issues, or medications, this active absorption pathway is often impaired. High-dose oral supplementation (e.g., 1000 mcg/day) is then used to bypass this limitation by leveraging passive diffusion, which absorbs 1–2% of the dose independently of intrinsic factor. This yields 10–20 mcg daily, well above the RDA, making it a safe, effective strategy that often negates the need for injections.

1000 mcg

Recommended oral dose for deficiency

Active pathway

In cases of deficiency: due to poor intake, aging, gastrointestinal issues, or medications, active absorption pathway is impaired.



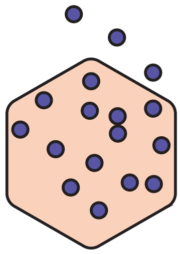
Impaired active absorption

- Atrophic gastritis
- Pernicious anemia
- GI surgery

1-2 % = 10 mcg

Sufficient to correct deficiency

Well above the RDA of 2.4 mcg



Passive diffusion of a high oral dose (1000 mcg), it is absorbed independently of active transport.

Why is a high dose needed in dietary deficiencies?

Even if Vitamin B12 deficiency is due to dietary factors (inadequate intake, as in vegans, WFPB practitioners, vegetarians, etc.), it is still appropriate to use 1000 mcg/day of oral B12 during the correction phase.

- Even in people without malabsorption, B12 absorption can be inefficient at higher doses due to the saturable nature of the active transport mechanism.
- A high dose ensures enough B12 is absorbed through both active and passive pathways, helping to restore tissue stores more rapidly.
- Safety: B12 has low toxicity; excess is excreted, making high doses safe for repletion.

Why is a high dose needed in IM/ IV?

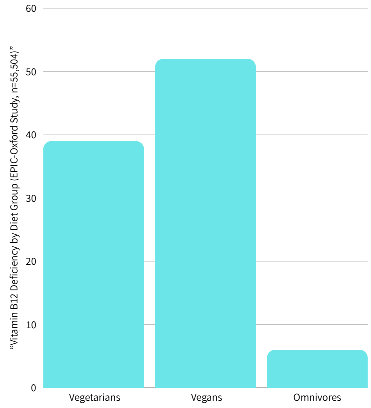
Although intramuscular and intravenous Vitamin B12 close to 100% bioavailability, 1000 mcg doses are commonly used to rapidly replenish depleted tissue stores (2–5 mg), compensate for ongoing malabsorption (e.g., pernicious anemia), and enable less frequent dosing. Given its excellent safety profile, high-dose B12 is both effective for correction and practical for long-term maintenance.

CLINICAL GUIDANCE PREVENTING B12 DEFICIENCY

PREVENTION OF B12 DEFICIENCY - PLANT BASED DIETARY PATTERNS

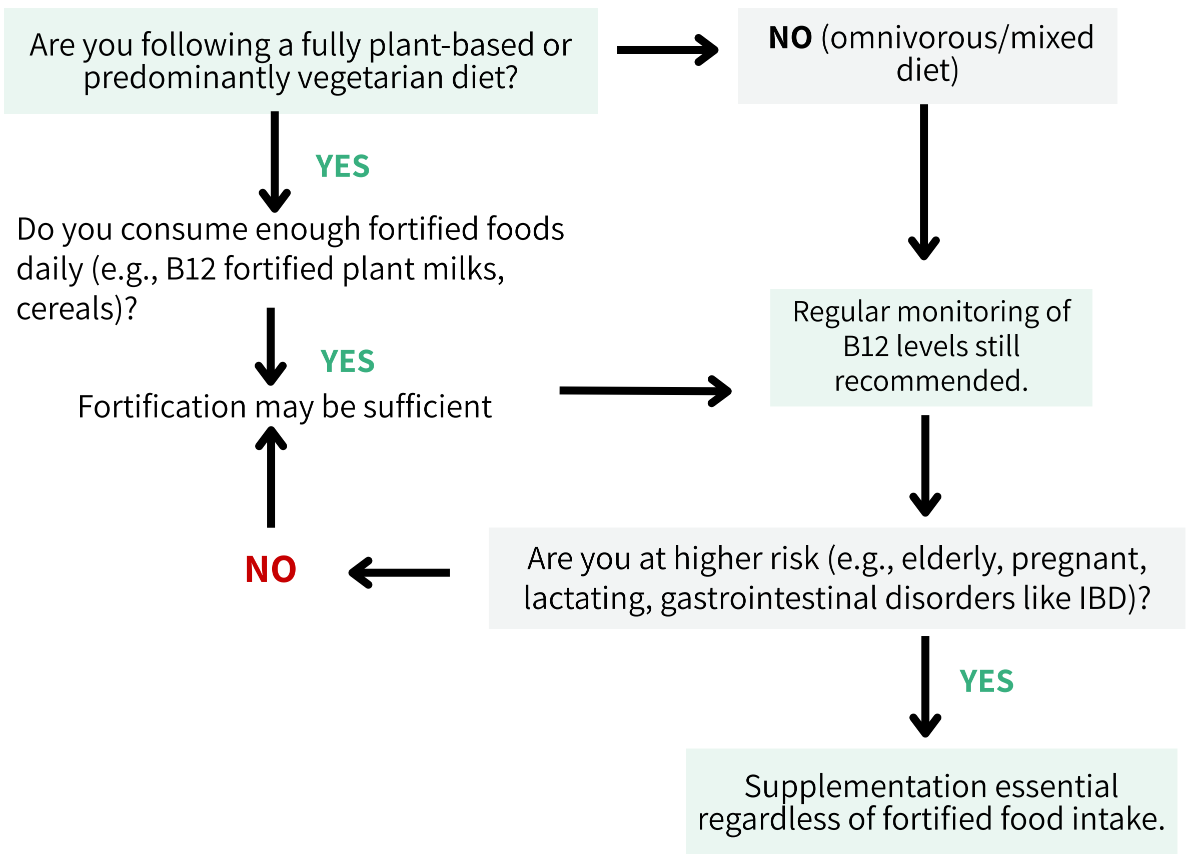
Despite the growing popularity of vegan and plant-based diets, major health bodies lack specific guidelines for people who follow plant based diet due to limited data and smaller population size.

The **EPIC-Oxford study** (n=55,504) found that 39% of vegetarians had B12 deficiency despite consuming dairy and eggs, compared to 52% of vegans and 6% of omnivores (38).



The Academy of Nutrition and Dietetics specifically notes that without reliable supplemental or fortified sources, vegans are at high risk for subclinical and clinical B12 deficiency, which can manifest as megaloblastic anemia and irreversible neurologic damage (71).

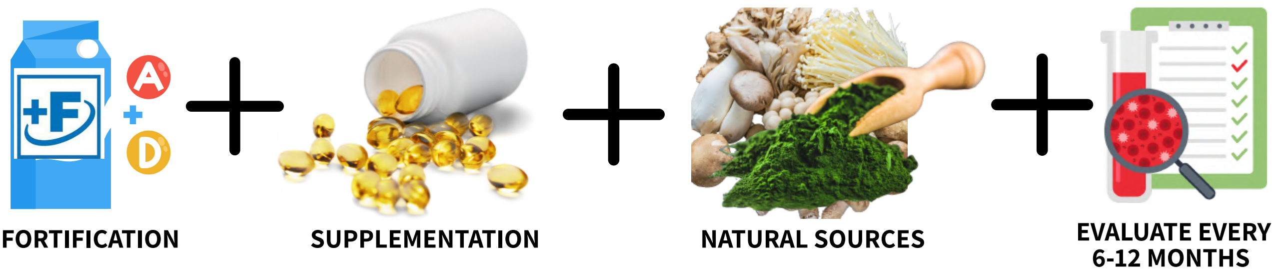
Although recent studies offer promising data on certain natural plant-based sources of Vitamin B12, current evidence is insufficient to support general recommendations. More robust research is needed to confirm the consistency, reliability, and bioavailability of these sources. In contrast, omnivorous diets typically provide 4-7 µg of B12 per day well above the 2.4 µg RDA through meat, dairy, eggs, and fish, although absorption can decline with age or due to gastrointestinal conditions. As a result, most evidence-based guidelines recommend mandatory B12 supplementation for individuals following vegan diets, either through daily supplements (e.g., 50–100 µg cyanocobalamin) or consistent intake of fortified foods (15, 30).



PREVENTION OF B12 DEFICIENCY - PLANT BASED DIETARY PATTERNS

A MULTIPRONGED APPROACH TO PREVENT VITAMIN B12 DEFICIENCY IN PLANT-BASED DIETS

Ensuring Vitamin B12 adequacy in individuals following a plant-based diet requires an integrated strategy combining dietary sources, supplementation, and regular monitoring:



Dietary approach: Fortified foods and natural plant-associated sources:
Incorporate Vitamin B12 fortified foods (such as fortified plant milks, cereals, nutritional yeast, or meat alternatives) 2–3 times daily, aiming for at least 4–6 mcg per serving. Additionally, explore natural plant-associated sources like B12 enriched mushrooms (e.g., shiitake) and certain algae (e.g., nori, chlorella), though their B12 content can be inconsistent and may include inactive analogues. While promising, these should be viewed as complementary rather than primary sources until further validated.

Supplementation: A daily supplement of 30–100 µg, or 1000 µg twice weekly, is recommended for healthy adults particularly vegans, the elderly, and others at elevated risk of deficiency. Oral, chewable, or sublingual formulations are preferred for improved absorption. These doses are safe for long-term use and have been shown to maintain adequate B12 status in clinical studies. However, given inter-individual variability in absorption and differences across international guidelines, specific dosage requirements may vary (95).

- **Daily dosage:** (Ages 11-65) 50 mcg a day, (Ages 65+) 1,000 mcg a day.
- **Weekly dosage:** 1000 to 2000 mcg, even up to 5000 mcg is considered safe (15).
- **Vegan pregnancy and lactation:** 1000 µg/day for 4 months + B12 fortified foods regularly in meals (if Serum B12 < 75 pmol/L) (10).

If Serum B12 levels are normal: 50 µg/day (single dose) or 1000 µg × 2 (weekly dose) (10).

Regular monitoring: Given individual variability in absorption and intake, biochemical monitoring every 6–12 months is advised. Recommended markers include serum B12, holotranscobalamin (active B12), methylmalonic acid (MMA), and homocysteine, which help detect early functional deficiency and guide timely intervention.

A ONE-DAY PLANT-BASED DIETARY PATTERN TO SUPPORT VITAMIN B12 ADEQUACY

A well-planned plant-based diet can meet daily B12 requirements through fortified foods and appropriate supplementation enhancing B12 intake without relying on animal products.

BREAKFAST

Fortified cornflakes (1/2 cup) ~0.8 mcg

+

Fortified soy milk (1/2 cup) ~0.6 mcg

+

Mixed fruits (1 cup) + 1 tbsp nutritional yeast = 4 mcg

LUNCH

Salad + dressing made with lemon juice, olive oil and 1 tsp chlorella -6.6 mcg

Scramble tofu + 1 tbsp nutritional yeast = 4 mcg

Brown rice + dal negligible

EVENING

Chana chaat with miso paste 1 tbsp ~0.04 mcg

DINNER

Stir fry vegetables + 2tbsp kimchi = 0.1 mcg

TOTAL = ~ 15.7 mcg (~2.2 mcg estimated B12 absorbed)

Fortified foods are a practical alternative

In a study by Del Bo' et al. (2019), researchers found that fortified nutritional yeast (a food-based source) and oral B12 supplements were equally effective in raising B12 levels among vegans. Interestingly, many participants preferred the fortified food option (nutritional yeast) over taking pills, likely due to convenience or a desire for more natural approaches (12).

RETHINKING B12: EMERGING STRATEGIES AND NATURAL PLANT-ASSOCIATED SOURCES

As global dietary patterns continue to shift toward plant-based eating, ensuring adequate Vitamin B12 intake has become a pressing nutritional challenge. Plant-only diets exclude conventional B12 sources, mostly animal-derived foods, hence supplementation or fortification becomes absolutely necessary. However, growing interest in natural, food-based solutions has sparked research into novel plant-associated B12 sources and alternative strategies to prevent deficiency.

In a world moving toward plants, B12 strategies must evolve too.

Natural B12-rich foods (supplementary sources):

Several plant-based foods, such as nori (Porphyra), chlorella, shiitake mushrooms, tempeh, and kimchi, have been studied for their B12 content. Among these, nori and chlorella show the most promise in delivering bioactive B12.

Prevention of Vitamin B12 deficiency: Inconclusive, but caution is advised

- Some studies report that regular intake of fortified foods or nutritional yeast can maintain adequate B12 levels (>300 pg/mL) without supplementation (79). Additionally, nori/chlorella-based supplements have shown potential to deliver bioactive B12, while spirulina products largely contain inactive pseudocobalamin (124).
- Clinical observations in long-term raw vegans have further suggested that daily intake of ≥3 μg of B12 from fortified nutritional yeast may suffice to prevent deficiency, maintaining serum levels above 300 pg/mL (79).
- A study by Watanabe et al. (1999) in the Journal of Agricultural and Food Chemistry found that Porphyra species (nori) **contain bioactive, bioavailable Vitamin B12 capable of raising serum levels in humans** (129).

The road ahead: Unlocking the potential of plant-associated B12 sources

While early findings are promising, there is a pressing need for rigorous, large-scale trials to confirm the long-term reliability of B12 bioavailability from plant-associated sources. Currently, these sources remain inconsistent in content, stability, and bioactivity affected by processing, microbial contamination, and growing conditions, making them unsuitable as standalone options. As research progresses, validated natural sources could enhance food-based strategies, support better adherence, and reduce reliance on synthetic supplements. Advancing this field will require continued investment in nutritional biochemistry, microbial synthesis, and bioavailability research.

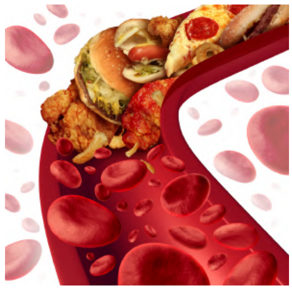
VITAMIN B12 FROM ANIMAL FOODS: A NUTRITIONAL ADVANTAGE WITH HEALTH TRADE-OFFS

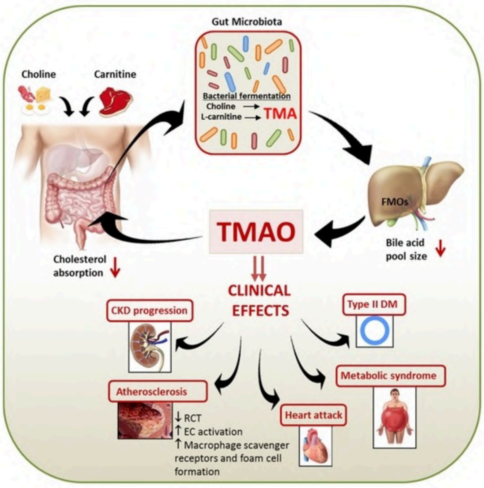
ANIMAL-BASED DIETS PROVIDE VITAMIN B12 BUT MAY COMPROMISE LONG-TERM HEALTH

While animal-sourced foods are rich in Vitamin B12, **diets high in red and processed meats, full-fat dairy,** and certain fish may increase the risk of cardiovascular disease, certain cancers, and exposure to environmental toxins. Balancing B12 intake by prioritising plant-based, nutrient-rich foods supports both nutritional adequacy and long-term health.

Saturated Fats and LDL Cholesterol: CVD Risk Factors

Animal-based foods rich in saturated fats, such as meat, dairy, and eggs, elevate LDL cholesterol, a key contributor to atherosclerosis. Clinical trials have shown that reducing saturated fat intake and replacing it with unsaturated fats or complex carbohydrates can lower the risk of cardiovascular events by approximately 20% (3, 47, 52).





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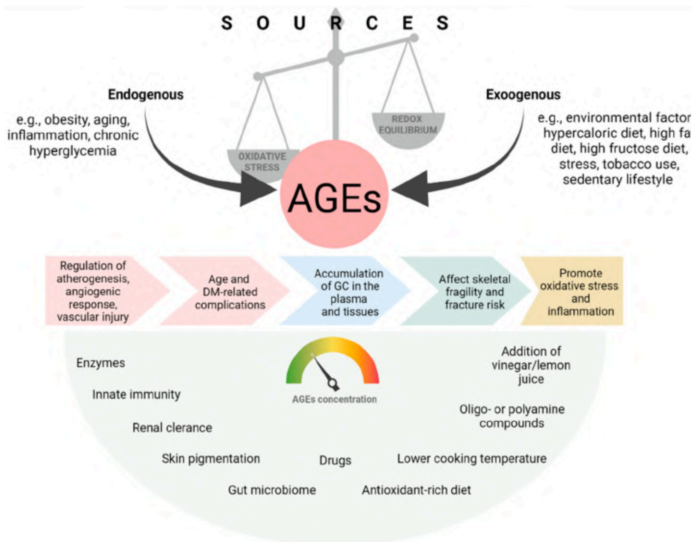
Trimethylamine N-oxide (TMAO) levels

Red meat contains carnitine and choline, found abundantly in red meat, eggs, and certain fish are metabolised by gut bacteria into trimethylamine (TMA), and then oxidised by the liver into TMAO. Elevated TMAO levels are linked to inflammation and arterial plaque buildup, raising CVD risk. Studies show red meat eaters have higher TMAO levels than vegetarians (117).

Advanced Glycation End Products & Health Risks

Animal-based foods, when cooked at high temperatures (e.g., grilling, frying), produce advanced glycation end products (AGEs). These compounds promote oxidative stress and inflammation which may accelerate aging, contributing to chronic disease risk (51).



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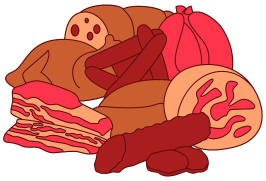
Chronic Inflammation: Saturated fats, dietary cholesterol, TMAO and AGEs all contribute to systemic inflammation. Animal products displace fiber and antioxidants from the diet while increasing pro-inflammatory factors- "displacement" effect (8).

Animal vs. Plant-Based Sources of B12: Nutritional and Health Implications



VS

VS

Red meat- ground beef (3 oz):

- ~2.5 µg B12 (100% DV)
- ~5 g saturated fat
- ~75 mg cholesterol

Nori (4 g)

- ~1.5-2.4 µg B12 (60-100% DV)
- ~0 g saturated fat
- ~0 mg cholesterol

Fortified nutritional yeast (1 tbsp):

- ~4 µg B12 (>100% DV)
- 0 g fat
- 0 mg cholesterol.

Cardiometabolic Impact

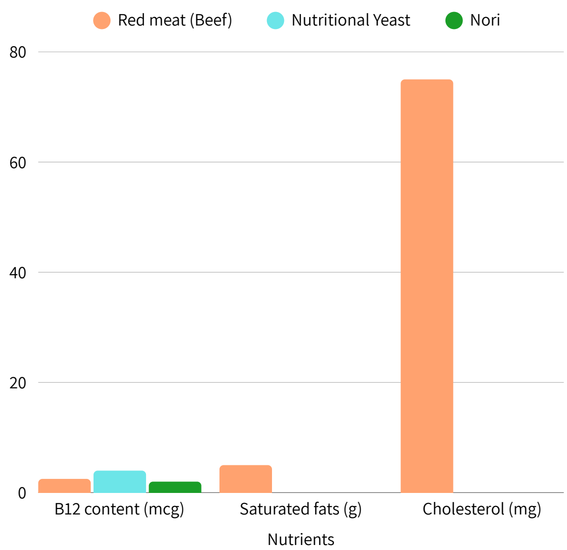
- Red Meat: Contains saturated fats and cholesterol; high in carnitine and TMAO, heme iron, AGEs, protein, and zinc components linked to increased risk of cardiovascular disease and colorectal cancer.
- Nori: Free of atherogenic lipids, contains bioactive compounds with anti-inflammatory benefits. Beneficial in moderation, some forms of nori may contain high sodium.
- Fortified Nutritional Yeast: Low in fat and free of cholesterol, it provides protein and B-Vitamins (like B6 and folate), and is low in sodium.

Carcinogenic Potential

- Red Meat: Classified as a Group 2A carcinogen (probably carcinogenic to humans) by the WHO, with processed red meat classified as Group 1 (carcinogenic to humans)
- Nori & Fortified Nutritional Yeast: No known association with carcinogenicity when consumed in moderation. Nori has antioxidant and immune-supportive properties.

Environmental Footprint

- Red Meat: High environmental impact, including significant greenhouse gas emissions, land, and water use. (62)
- Nori & Fortified Nutritional Yeast: Produced with minimal environmental impact.



Source: https://tools.myfooddata.com/nutrition-facts/100067124/wt1

Choosing plant-based B12 sources like nori, chlorella, and mushrooms with proper supplementation over red meat lowers chronic disease risk and supports environmental sustainability. This shift supports both long-term public health goals and national sustainability efforts.

POLICY, PUBLIC HEALTH & EDUCATION

HOW CAN INDIA ELIMINATE B12 CRISIS?

Vitamin B12 deficiency remains an underrecognized public health issue in India, especially among vegetarians, low-income groups, and rural populations.

Scale up supplementation programs

Integrate B12 supplementation into public health schemes (e.g., anemia programs, antenatal care, school meal plans). Target high-risk groups: pregnant/lactating women, children, the elderly, and vegans.

Mandatory & widespread fortification

Mandate B12 fortification of staples (e.g., wheat flour, rice, plant milks). Ensure quality control and monitoring to avoid variable dosing. Subsidize fortified foods and supplements & strengthen rural distribution channels.

Public & clinical awareness campaigns

Educate healthcare professionals and the public on the importance of B12, risks of deficiency, and reliable sources. Dispel myths about fermented or traditional foods as sufficient sources.

Monitoring & surveillance

Integrate B12 testing in national surveys and promote regular biochemical screening in clinical practice. Use combined testing (serum B12 + MMA/homocysteine). Develop guidelines for early diagnosis and management.

Invest in research on plant-associated B12 sources

Support bioavailability research, microbial fortification, and innovative plant-based solutions such as B12 enriched fungi or algae that, if validated, could enhance dietary adherence and offer affordable, scalable, and culturally acceptable options.

Should we recommend universal supplementation or fortification?

Given the high prevalence of deficiency, especially among vegetarians, adolescents, and pregnant women, public health strategies like supplementation and fortification may play a key role, particularly for high-risk groups. While supplementation is effective, it depends on individual adherence. A combined approach of fortification plus targeted supplementation may offer greater impact.

Food fortification has proven successful in improving micronutrient status globally. There is growing interest in mandatory Vitamin B_{12} fortification to address widespread deficiencies. However, more randomized trials, product stability studies, and careful monitoring are needed. These strategies should be part of a broader, well-monitored response to the B12 deficiency challenge.

CONCLUSION SUMMARY

CONCLUSION: GUIDING EVIDENCE-BASED B12 SUFFICIENCY IN A SHIFTING DIETARY LANDSCAPE

Concluding perspectives: Ensuring Vitamin B12 sufficiency in plant-based diets

Vitamin B12 deficiency presents a significant public health concern, particularly in the context of a global shift toward more sustainable, plant-based dietary patterns. Given its essential role in DNA synthesis, red blood cell formation, and neurological function, B12 is a non-negotiable nutrient. Left unaddressed, deficiency can lead to irreversible consequences, making prevention and early detection a clinical imperative.

As dietary habits evolve to align with climate and public health goals, clinicians must move beyond outdated paradigms and lead this transformation. Physicians are uniquely positioned to guide patients toward dietary choices that are both nutritionally adequate and environmentally responsible without compromising scientific integrity.

High-risk groups including older adults, pregnant and lactating women, individuals with malabsorption disorders, and those following long-term vegetarian or vegan diets require particular attention. In countries like India, where vegetarianism is deeply rooted, deficiency rates exceed 70%. Given the often silent progression of B12 deficiency, routine biochemical screening (serum B12, methylmalonic acid, and homocysteine) should become standard preventive care for at-risk individuals, even in the absence of symptoms.

While animal-derived foods remain concentrated sources of Vitamin B12, excessive consumption especially of red, processed meats etc has been consistently linked to elevated risks of chronic diseases, including cardiovascular disease and certain cancers. In light of this evidence, physicians have a critical role in guiding patients toward predominantly plant-based dietary patterns that not only support long-term health and chronic disease prevention, but also significantly reduce environmental impact.

However, it is important to recognise the limitations of relying solely on plant-based sources for Vitamin B12. While certain algae, mushrooms, and fermented plant products may contain active forms in meaningful amounts, current evidence remains insufficient to confirm their consistency, potency, and bioavailability. Therefore, these sources alone should not be considered reliable for preventing or correcting deficiency. For individuals following plant-based diets, a combined approach, including naturally occurring sources (where applicable), fortified foods (such as plant milks, cereals, and nutritional yeast), and appropriately dosed supplements, remains the most effective strategy for maintaining B12 sufficiency.

Vitamin B12 deficiency has reached near-pandemic levels in some regions, with prevalence rates exceeding 70% in certain populations. This underscores the urgent need for greater awareness, routine screening, and expanded access to fortified foods. Strengthening food fortification policies, especially in affordable, commonly consumed staples, alongside education on supplementation, is essential to address this growing public health concern. Physicians should counsel patients on these options and encourage regular monitoring to ensure adequacy.

We are living in a time where the climate crisis is inseparable from the health crisis. Plant-based diets not only improve individual health outcomes, but also contribute to lower greenhouse gas emissions, reduced deforestation, water conservation, and biodiversity protection. This makes them a vital lever for advancing both personal and planetary well-being.

> *Vitamin B12 deficiency is entirely preventable within a plant-based dietary framework when guided by evidence-based strategies that include fortified foods, appropriately dosed supplementation, and naturally occurring sources where applicable.*

Healthcare providers have a unique responsibility to lead this shift. By placing nutrition, lifestyle, and prevention at the core of care, we can help forge a resilient, health-promoting, and environmentally conscious food system. Healing today begins not only in clinics, but also in kitchens and communities. When clinicians integrate evidence-based nutrition with global sustainability awareness, they don't just treat disease they help shape a healthier, more sustainable future.

And when thoughtful minds collaborate with purpose, they don't just heal patients they help build a healthier, more sustainable world.

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