MedNut Mail

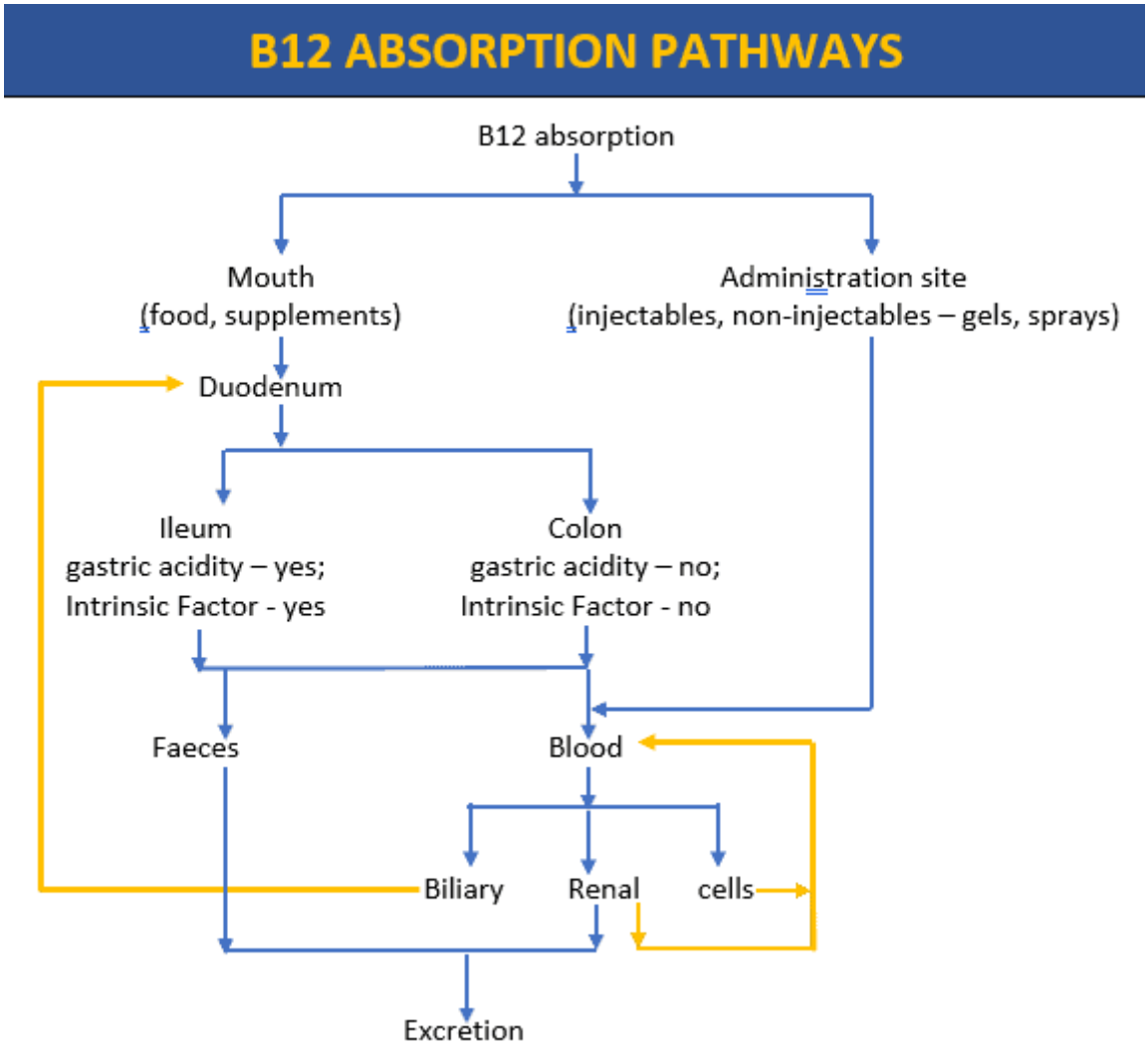
The How, What, Which, Where, When and Why of pharmaconutrition

B12 absorption

Y Coleman

24thMarch 2026

https://medicationsandnutrition.com/mednut-mail/



B12 absorption is a surprisingly complex process as it encompasses both feast and famine scenarios.

B12 Absorption mechanisms and processes

Sources

Two primary sources of B12 include -

- exogenous – produced outside the body, and includes foods of animal origin, supplements, injectables, and non-injectables;

- endogenous – produced within the intestinal microbiota.

Absorption

B12's absorption processes include 2 separate capacity-limited pathways, each with their own site of absorption and mechanism of action.

I. **Intrinsic Factor to ileum pathway.**

Requires 4 factors, being -

i. **gastric acidity within pH 1-2.** Gastric acidity is required to activate pepsin, the protease that releases B12 from foodstuffs;

ii. **receptor capacity.** The IF-B12 receptor has a limited number of sites which means B12 absorption is determined by receptor capacity;

iii. **calcium availability**. The binding of IF-B12 complex to IF-B12 receptor requires calcium in order to gain entry into the enterocytes.

iv. **absorption refractory period**. IF-B12 complex uptake is restricted for ~ 6 hours whilst the IF-B12 receptor density regenerates. For example, consumption of a B12-containing foodstuff at 08:00 means the IF-B12 complex receptors won't be available again until ~ 14:00.

II. **Mouth to colon pathway.**

Excessive B12 intake, microbiota-generated B12, and other unabsorbed B12 can be partially absorbed in the colon. This pathway is commonly referred to as "passive diffusion".

Some early evidence indicates the colonic B12 contribution to B12 status is much more important than currently believed.

"Passive diffusion" seems to be code for unknown transporter(s). The limited "passive" absorption in the colon implies limited capacity of an absorbing mechanism. The body's tight regulation and many fail-safe options indicate uncontrolled transfer of substances from gut to blood is highly unlikely.

Reabsorption

Renal

Renal resorption of B12 can be quite variable.

High B12 levels, eg post injection, may exceed TCII binding capacity which means renal excretion of the excess.

Biliary

Some B12 is syphoned from the hepatocytes into the biliary system which releases into the duodenum. This pathway means B12 can re-enter the intestinal tract for reabsorption or excretion.

The process by which B12 enters the biliary system is yet to be established.

B12 absorption from food	
From food to blood	
Mouth	Small amounts of free, non-protein-bound B12 bind to haptocorrin (HC) also known as Transcobalamin I (TCN1, TCI, TC1).
Stomach	Gastric acidity (released from parietal cells) is essential for pepsin activation. Activated pepsin releases B12 from foodstuffs, and then B12 then binds to TCI for transfer to duodenum.
Duodenum	B12 is released from TCI by proteases trypsin and chymotrypsin and then binds to Intrinsic Factor (IF). (Intrinsic Factor is a capacity-dependent transporter released by gastric parietal cells). IF+B12 complex moves to the ileum.
Distal Ileum	IF+B12 complex binds to the IF+B12 complex receptor– a calcium-dependent process that enables entry into enterocytes. The ileal IF+B12 complex receptors are capacity-dependent.
Enterocytes	B12 is released from the IF+12 complex in the lysosomes by cathepsins B & L. ABCD4 (ATP Binding Cassette Subfamily D Member 4 protein) and LMBD1 (lysosomal cobalamin transport-escort protein) co-operatively transfer free B12 from the lysosome to the cytosol. B12 required for within-cell requirements is processed within the cytosol. Free B12 is exported from the cytosol to the interstitial fluid by MRP1 (multidrug resistance protein 1). The location where B12 binds to TCII (transcobalamin 2) to form the TCII+B12 complex is indeterminate. Some authors infer TCII binds to B12 within the interstitial fluid, whilst others state it occurs in the blood. TCII+B12 complex is B12s primary distribution mechanism.
colon	B12 absorption amount and mechanism are yet to be identified.
From blood to cells	
Cells	TCII+B12 binds to cell receptor CD320, which is a calcium-dependent process.
	B12 that will be utilised by the cell is delivered to – - **cytoplasm**. Both cytoplasmic methionine synthase (MS) and MS reductase (CblE) utilize MeCbl (methylcobalamin), or - **mitochondria**. Both mitochondrial methylmalonyl-CoA mutase (MMCM) and adenosyltrasferase (CblB) utilize AdoCbl (5'-deoxyadenosylcobalamin). B12 not utilised by the cell is delivered back into the bloodstream for distribution.

Elevated B12

B12 levels are rarely monitored once prophylactic maintenance interventions commence.

Some interesting research found that when B12 levels are –

- either low or within range, then uptake is accelerated,

- elevated, then uptake is diminished.

Diagnosing deficiency

B12 availability can be impaired by multiple factors, including prescribed medications such as the acid inhibitors and metformin.

Plasma homocysteine reflects adequacy of B12 status for metabolic function and its concentrations increase once serum B12 < 300 pmol/L.

Professor A. David Smith (VITACOG) defines B12 status as suboptimal < 300 pmol/L.

Clinical concerns

B12 has very well-developed safety mechanisms surrounding its absorption during feast and famine periods. Although the liver is the primary storage site, significant levels of B12 are also stored in the biliary system. In fact, a proportion of B12 is syphoned to the biliary system at every intake.

Regardless of the intestinal pathways utilized, the absorption mechanisms have maximum loads, above which B12 is no longer absorbed. In the ileum, the key receptors also shut down for 4-6 hours once maximum load is exceeded.

The famine protection mechanisms are similarly curious. Reabsorption strategies are a key retention strategy and include both renal and biliary processes.

Some questions that arise include –

What benefit/protection is conferred by absolutely limiting B12 uptake during a “feast” period?

What is the upper B12 limit for absorption cessation via the ileum pathway?

Why don’t we know and fully understand the B12 absorption process in the colon, including its mechanisms and range limits?

What benefit/protection is being conferred by utilizing a system that recycles B12 every food intake episode (via the biliary system)?

What necessitates the storage of a specific water-soluble vitamin in the biliary system?

If prescribed medications alter biliary function, do they also alter the availability of B12? And what are their mechanisms of action?

Do any prescribed medications alter B12 binding to TCII?

Clinical questions

What actions will you initiate when you see someone prescribed a B12 intervention -

- would you recommend monitoring levels and if elevated then reducing either intervention frequency or dose?
- and has ongoing low B12 levels – would you question whether any prescribed medications are inhibiting release of B12 from the ileum or colon?

Conclusions

B12 absorption processes include both feast and famine management strategies.

Researched and written by the author.

Cite: Coleman, Y. 2026. B12 and acid inhibitors. MedNut Mail https://medicationsandnutrition.com/b12-absorption/Accessed (date)

Bibliography

Bibliography
Al-Awami, HM., Raja, A. & Soos, MP. 2023. Physiology, Gastric Intrinsic Factor. [Updated 2023 Jul 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546655/. Accessed 2026-03-08
Allen, LH., Miller, JW., de Groot, L., Rosenberg, IH., Smith, AD., Refsum, H. & Raiten, DJ. 2018. Biomarkers of Nutrition for Development (BOND): Vitamin B-12 Review. **Journal of Nutrition 148:**1995S–2027S. ttps://doi.org/10.1093/jn/nxy201.
Boachie, J., Adaikalakoteswari, A., Goljan, I., Samavat, J., Cagampang, FR. & Saravanan, P. 2021. Intracellular and Tissue Levels of Vitamin B12 in Hepatocytes Are Modulated by CD320 Receptor and TCN2 Transporter. **International Journal of Molecular Science 22(6):**3089. https://creativecommons.org/licenses/by/4.0/
CLOUD-CLONE CORP.(CCC) https://www.cloud-clone.com/products/RPG794Hu01.html. Accessed 2026-03-08
Fedosov, SN., Nexo, E. & Heegaard, CW. 2024. Kinetics of Cellular Cobalamin Uptake and Conversion: Comparison of Aquo/Hydroxocobalamin to Cyanocobalamin. **Nutrients 16(3):**378. https://doi.org/10.3390/nu16030378.
Heda, R., Toro, F. & Tombazzi, CR. Physiology, Pepsin. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Accessed 2026-02-25; https://www.ncbi.nlm.nih.gov/books/NBK537005/
Kashyap, S., Gowda, P., Pasanna, RM., Sivadas, A., Sachdev, HS., Kurpad, AV. & Devi, S. 2024 The Oral Bioavailability of Vitamin B_{12} at Different Doses in Healthy Indian Adults. **Nutrients 16:**4157. https://doi.org/10.3390/nu16234157
Kuldyushev, NA., Simonenko, SY., Goreninskii, SI., Pallaeva, TN., Zamyatnin, AA Jr. & Parodi, A. 2025. From Nutrient to Nanocarrier: The Multifaceted Role of Vitamin B12 in Drug Delivery. **International Journal of Molecular Science 26(11):**5119. https://doi.org/10.3390/ijms26115119
Miller, JW. 2018. Proton Pump Inhibitors, H2-Receptor Antagonists, Metformin, and Vitamin B-12 Deficiency: Clinical Implications. **Advances in Nutrition 9(4):**511S-518S. https://doi.org/10.1093/advances/nmy023

Bibliography

Moravcová, M., Siatka, T., Krčmová, LK., Matoušová, K. & Mladěnka, P. 2024. Biological properties of vitamin B12. **Nutrition Research Reviews 38(1):**338-370. https://doi.org/10.1017/S0954422424000210

Mucha, P., Kus, F., Cysewski, D., Smolenski, RT. & Tomczyk, M. 2024. Vitamin B_{12} Metabolism: A Network of Multi-Protein Mediated Processes. **International Journal of Molecular Science 25(15):**8021 https://doi.org/10.3390/ijms25158021

O'Leary, F. & Samman, S. 2010. Vitamin B12 in health and disease. **Nutrients 2(3):**299-316. https://doi.org/10.3390/nu2030299

Quadros, EV., Regec, AL., Khan, KMF., Quadros, E. & Rothenberg, SP. 1999. Transcobalamin II synthesized in the intestinal villi facilitates transfer of cobalamin to the portal blood. **American Journal of Physiology-Gastrointestinal and Liver Physiology 277:**1, G161-G166. https://doi.org/10.1152/ajpgi.1999.277.1.G161

Smith, AD. 2016. Hippocampus as a mediator of the role of vitamin B-12 in memory. **American Journal of Clinical Nutrition 103:**959–60.

Smith, AD., Warren, MJ. & Refsum, H. 2018. Chapter six – vitamin B12. **Advances in Food and Nutrition Research 83:**215-279. https://doi.org/10.1016/bs.afnr.2017.11.005

Sobczyńska-Malefora, A., Delvin, E., McCaddon, A., Ahmadi, K. R., & Harrington, D. J. 2021. Vitamin B_{12} status in health and disease: a critical review. Diagnosis of deficiency and insufficiency – clinical and laboratory pitfalls. **Critical Reviews in Clinical Laboratory Sciences 58(6):**399–429. https://doi.org/10.1080/10408363.2021.1885339

The Mechanism of Absorption of Vitamin B12 (cobalamin) in the GI Tract

https://www.ebmconsult.com/articles/vitamin-b12-absorption-mechanism-intestine-intrinsic-factor. Accessed 2026-02-11

Editor-in-Chief: Anthony J. Busti, MD, PharmD, FNLA, FAHA

Reviewer: Jon D. Herrington, PharmD, BCPS, BCOP

Vitamin B12. 2025. National Institutes of Health. Accessed 2026-02-03

Please read this as it is important …

The information in this article is provided to support Health Professionals. It is not an exhaustive protocol and Health Professionals are advised that adequate professional supervision is accessed to ensure that Duty of Care obligations with respect to safe administration of medicines is met for each consumer.

Medications have profoundly and positively changed health outcomes however they do generally come with some nutritional harms. By identifying and addressing the nutritional harms, optimal health outcomes are closer to being achieved.

You may be interested in some of our other products …

MedNut Mail is our free weeklyish email that identifies and comments upon various aspects of pharmaconutrition.

For more information click here.

For innovative clinicians wanting to include drug-nutrition interactions into their daily clinical practice in order to optimise outcomes for those in their care.

For more information click here.

Connect with us on