INTERNATIONAL
IV NUTRITIONAL THERAPY
GLOBAL PHYSICIAN EDUCATION

Parenteral Vitamins and Minerals

Advanced IV Therapy: Chronic Disease and Infections
by
Virginia Osborne, ND, Brenden Cochran, ND and Shawna Kiker, ND

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IV Solution Physiology / Kinetics:

- When you infuse an IV you directly access the vascular (plasma) compartment.
- You very quickly effect the ECF and then the ICF of most all cells.
- Remembering the osmotic balances between these compartments is critical to proper IV therapy safety and beneficial outcomes.

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Classes of Vitamins

- Parenteral vitamins come in two general classifications, water-soluble and fat-soluble.
- Water-soluble vitamins consist of all of the B vitamins and vitamin C. The B vitamins and vitamin C are relatively non-toxic as they do not accumulate in the body. However, the patient may experience nausea when B vitamins are infused too quickly or given in higher doses.

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Fat Soluble Vitamins

- The fat-soluble vitamins, including A, D, E, K and biotin are available in “water soluble” forms as stable emulsions.
- The fat soluble vitamins can accumulate if given in too high dose over time and may result in toxicity.

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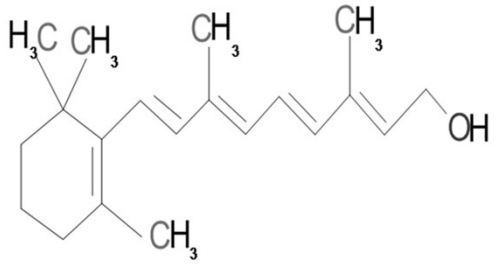
Vitamin A



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Vitamin A

- Aquasol A, water-miscible vitamin A Palmitate
- Standard concentration is 50,000 IU/mL
- Labeled for I.M. use only.
- **<u>DO NOT</u>** give to patients with liver disease or liver cancer.
- <u>Absolute contraindication if pregnant</u>
- Concentrated vitamin A given i.v. may induce anaphylactoid or anaphylactic reactions and death

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Vitamin A Functions

- essential for immune function,
  - Anti-viral
- Aids in the differentiation of stem cells to develop into red blood cells.
- Supports mucus membrane IgA
- Deficiencies can allow for more sensitivities to aflatoxin
  - PMID: 323066 (Interrelationships of mycotoxins with nutrition)

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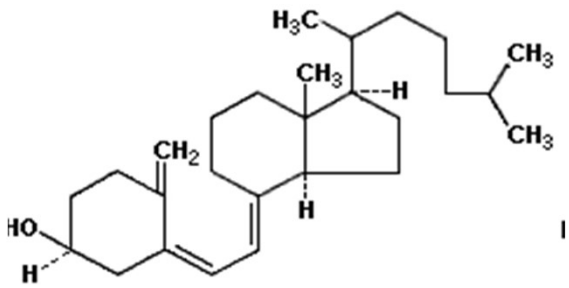
Vitamin D



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Vitamin D3, Cholecalciferol

- Calcitriol Injection (U.S. and Canada), 1-25 Vitamin D3 (Active form)
- Ergocalciferol Injection (U.S. and Canada), Vitamin D2
- Paricalcitol Injection (U.S.)
- Parenteral dosage
  - Adults and teenagers-Start at 1 mcg a day
  - Increment to no more than 12 mcg a week

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Vitamin D

- Administration - IM:
  - Supplied in 1 mL ampules containing 500,000 IU/mL
    - Mayo clinic online (400,000 iu in elderly IM q 6-12 mos)
  - Calciferol In Oil Injection may be given undiluted deep IM
  - Compounded product is generally 10,000 to 50,000 IU / mL
- Adverse Reactions:
  - Generally seen only with excessive vitamin D administration
  - Early and late signs of overdose are hypercalcemia, which leads to weakness, muscle and bone pain, hypertension, cardiac arrhythmia and headache

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Vitamin D

- Contraindications
  - Primary hyperparathyroidism
- Drug Interactions
  - Vitamin D levels are increased by: Estrogen, Isoniazid, Thiazide diuretics, Calcium channel blockers (magnesium)
  - Vitamin D levels can be decreased by: Cholestyramine, Phenobarbital, phenytoin, mineral oil, Orlistat
- Deficiencies can allow for more sensitivities to aflatoxin
  - PMID: 323066 (Interrelationships of mycotoxins with nutrition)

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VITAMIN – D and Calcium Metabolism

7-OH Cholesterol --(Skin)→ Cholecalciferol (D3) [UV Light]

(Liver)

25 hydroxylase

Parathyroid Gland ++ due to Falling Serum Ca PTH

25-Hydroxycholecalciferol 25(OH)D3

PTH (-) 24 Hydroxylase

24,25-Hydroxycholecalciferol
24,25 Dihydroxy D3

NET EFFECTS:
- **Ca INTO Bone**
- **Ca Absorption in Gut**
- ***LOWERS SERUM Ca***

(Kidney)

1-α-hydroxylase
(-) Phos(+) (PTH)

1,25-Hydroxycholecalciferol
dihydro D3

NET EFFECTS:
- **Ca OUT of Bone**
- **Ca Absorption in Gut**
- **Ca Renal Reabsorption**
- ***RAISES SERUM Ca**

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Inflamm. Res. (2014) 63:803–819
DOI 10.1007/s00011-014-0755-z

Inflammation Research

REVIEW

Inflammation and vitamin D: the infection connection

Meg Mangin · Rebecca Sinha · Kelly Fincher

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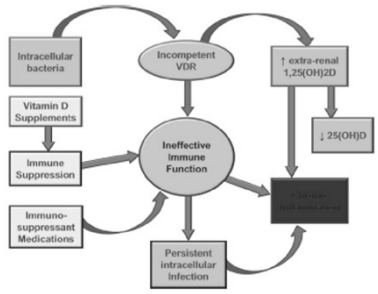

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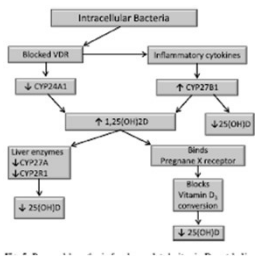
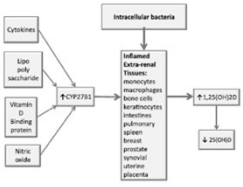
Why do I have a low 25-OH?





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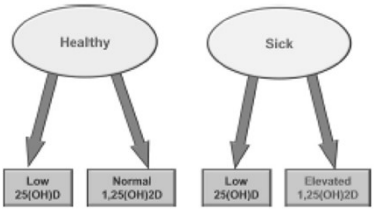

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Water Soluble Vitamins

- Water soluble vitamins, and vitamin like nutrients, generally are transported in plasma bound or attracted to plasma proteins.
- Their kinetics are complicated with respect to distribution and elimination, but are highly dependent upon hepatic uptake, plasma protein binding, renal transport effect, blood brain barrier physiology and many other factors which all come into play upon infusion.

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Vitamin B1, Thiamine

- Standard concentration is 100 mg/mL
- Can be administered i.m. or i.v. and should be diluted when given i.v., 30 mL minimum dilution
- Anaphylaxis has been rarely seen with thiamine HCl administered as a single agent
- Common dosing IV 100 – 200 mg

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Vitamin B1, Thiamine

- Thiamine is a coenzyme in oxidative decarboxylation reactions
- Important for reactions in energy metabolism
- Requirement is related to energy intake in the form of carbohydrates
- Essential in aldehyde metabolism

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Vitamin B1: Thiamine HCl

- Deficiency leads to slow function of the HMP Shunt and the TCA cycle
  - Consider in:
    - Chronic fatigue
    - Depleted patients
    - Therapies attempting to boost glutathione function
- Deficiency can be caused by:
  - Loop diuretics
  - Digitalis
  - Ethanol intake
  - Chronic aldehyde exposure

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Acetaldehyde and Nutrient Deficiencies:Thiamine

In addition to its toxic effects, acetaldehyde induces deficiencies of nutrients used for its detoxification.
Ex: vitamin B1 (thiamine) is depleted through alcohol and acetaldehyde detoxification. (Thiamine) B1 is essential in carbohydrate metabolism for energy production, of which the brain uses 20 percent.

Acetaldehyde-induced B1 depletions exacerbate the already low B1 levels common in the population due to diuretics and other drugs, over-consumption of simple carbohydrates (dysglycemia) and adrenal stress. In addition to its many functions, thiamine, the "nerve vitamin," is critical to nerves and neurotransmitters.
Even mild, chronic B1 deficiency can produce brain-related symptoms such as emotional instability, confusion, depression, fatigue, irritability, headaches, sensitivity to noise, insomnia, decreased short-term memory, brain-fog and a feeling of impending doom. (Lonsdale, Williams)

- Takabe M, Itokawa Y. Thiamine depletion after ethanol and acetaldehyde administration to rabbits. J Nutr Sci Vitaminol (Tokyo). Oct. 1983;29(5):509-14.
- Lonsdale D, Shamberger. Red cell transketolase as an indicator of nutritional deficiency. Am J Clin Nutr 1980;33:205-11.
- Williams RR, et al. Induced Thiamin (vitamin B1) Deficiency in Man. Arch Int Med. 1942;69:721-38.

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Acetaldehyde and Nutrient Deficiencies: Thiamine

Vitamin B1 deficiency-related lactic acidosis can make people more vulnerable to bug bites, since many insects, particularly mosquitoes, are attracted to mild acids.

(Fradin) Furthermore, people with chemical sensitivities to aldehydes may also be sensitive to seemingly unrelated substances like sulfites (preservatives) from wines and foods, and the smell of chlorine from pools and bleach.

Wernicke-Korsakoff syndrome results from thiamine deficiency.

The treatment is replacement of this essential vitamin. Previously, the usual dose was 100 mg/day via oral, intravenous, or intramuscular administration. However, the US and International standard of care appears to be shifting towards high-dose thiamine (500 mg tid) for a brief period (2-3 days), then reassessing the patient for improvement. In cases in which the patient is alert and is demonstrating improvement, parental (intravenous/intramuscular) thiamine should continue as long as the patient continues to improve, usually at 250 mg daily. (emedicine)

- Fradin MS. Mosquitoes and Mosquito Repellents: A Clinician's Guide. Ann Intern Med. June 1998;128(11):931-940.
- http://emedicine.medscape.com/article/288379-medication

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Acetaldehyde and Nutrient Deficiencies: Molybdenum

The under appreciated essential trace mineral molybdenum is also involved with acetaldehyde metabolism.
A **molybdenum deficiency** not only affects this process but also other enzymes in the body that require molybdenum as a cofactor—for example, sulfite oxidase, responsible for converting irritating sulfites into harmless sulfates for use in liver detoxification and cartilage.
Sulfur-containing amino acids, as important free radical scavengers, also use this molybdenum-dependent pathway. Molybdenum has been shown to reduce sulfite sensitivity by increasing sulfite oxidase activity. (AltMedRev)

Sulfites also destroy vitamin B1's biological activity, contributing to a deficiency. Nutrient depletion leads to sensitivity to other chemicals that use these same pathways. This has been demonstrated in patients with Candidiasis as the excess stress put on the enzyme systems to detoxify acetaldehyde often leave them with sensitivities to multiple chemicals especially fragrances. Supplementing with the appropriate cofactors may improve an individual's ability to handle Candida-generated acetaldehyde. (Schmitt)

- Molybdenum. Monograph. Altern Med Rev. 2006;11(2):156-161.
- Schmitt WH, et al. Molybdenum for Candida albicans Patients and other Problems. The Digest of Chiropractic Economics. Jan-Feb. 1991;31(4):56-63.

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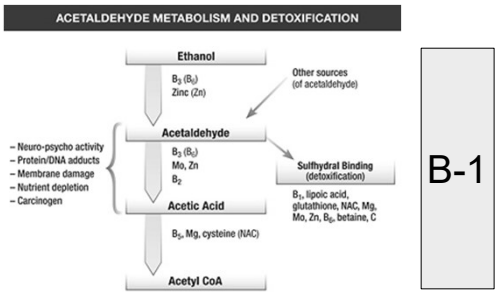

B-1

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Vitamin B2: Riboflavin

- Low toxicity due to renal dumping of excess
- Depressed B2 status leads to slow beta-oxidation of fats
- Deficiencies can allow for more sensitivities to aflatoxin
  - PMID: 323066 (Interrelationships of mycotoxins with nutrition)
- Helps prevent against mycotoxin hepatotoxicity
- Part of Glutathione Reductase & Synthase enzyme systems
  - Increase use with oxidative therapies
    - H2O2
    - Vit C
- Average IV dose 1 to 10 mg.

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Vitamin B3: Niacinamide

- Supports SEROTONIN synthetic pathways
- Part of the glucose tolerance factor
- Heavy use in enzyme systems
  - Used in *Dehydrogenase reactions*.
  - H+ Transfers
  - NAD
- Average IV dose: 100 to 1000 mg.

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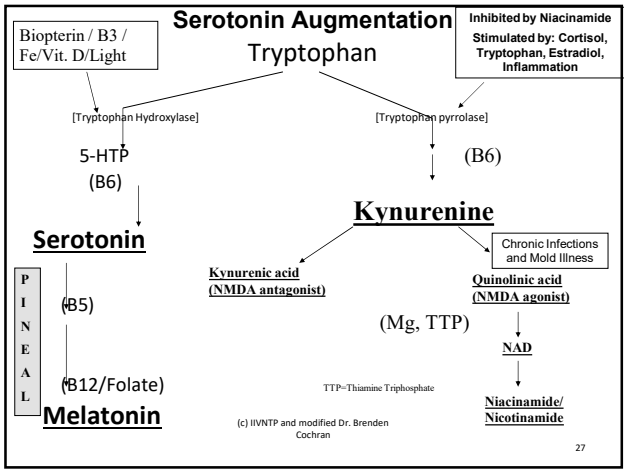

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NAD

- NAD 50 mg /mL
- Initial test dose: 1 ml /100 ml Normal Saline or in any Vitamin/Mineral protocol
- **NADH is the reduced** coenzyme form of vitamin B3
- **NAD is the oxidized** coenzyme form of vitamin B3.
- NAD and NADH are converted into each other in numerous different metabolic activities.

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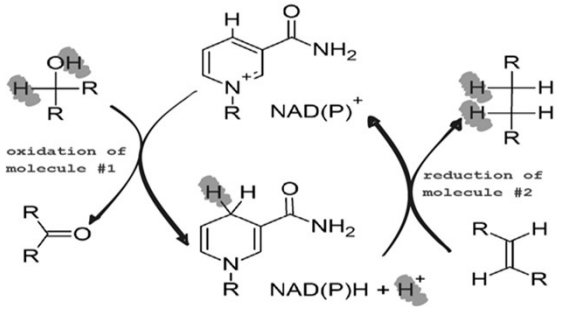
NAD(P) – NAD(P)H Cycle



https://commons.wikimedia.org/wiki/File:NAD_NADH_cycle.png

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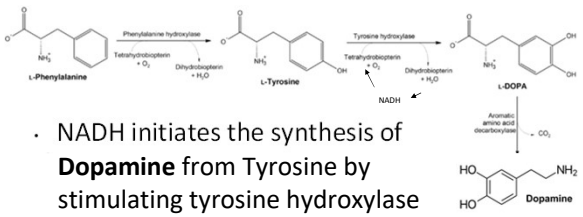
NAD

- It is used in the synthesis of Tyrosine



- NADH initiates the synthesis of **Dopamine** from Tyrosine by stimulating tyrosine hydroxylase in the biopterin pathway as a rate limiting factor.

https://upload.wikimedia.org/wikipedia/commons/thumb/d/dd/Conversion_of_phenylalanine_and_tyrosine_to_its_biologically_important_derivatives.png/800px-Conversion_of_phenylalanine_and_tyrosine_to_its_biologically_important_derivatives.png

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NAD

- **NAD** and **NADH** also serve to activate various enzymes.
- **NAD** is the first of 5 enzyme complexes of the electron transport chain, where ATP is synthesized and runs every biological process of the body.

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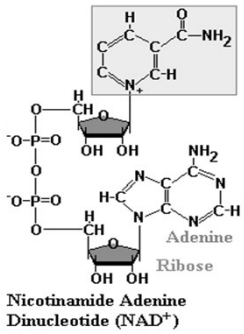
NAD versus B3



- NAD holds two "B-3" molecules

&

- Two Ribose Molecules

https://www.chem.uwec.edu/webpapers2001/claremm/pages/intro/nadintro.html

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Vitamin B5, Dexpanthenol

- Standard concentration is 250mg/mL
- Dose is 250-500 mg i.m., i.v. dose is up to 250 mg diluted in a push and 2000 mg in a drip
- Physiologic doses are very safe
- Pharmacologic doses of 2500-3000 mg may prolong the effects of succinylcholine
- MOST well tolerated by mold toxic patients in our experience

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Vitamin B5, Dexpanthenol

- Pantothenic acid functions as a component of coenzyme A and as part of the acyl carrier protein for fatty acid synthetase
- Has major influences on the synthesis and breakdown of carbohydrates and fatty acids as well as the synthesis of steroid hormones and hemoglobin
- Essential in histamine elimination (NAT2)

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Vitamin B6, Pyridoxine

- Standard concentration is 100 mg/mL
- Dose and administration
  - Prophylactic dose for i.m. or i.v. administration is 2-4 mg daily
  - Nutritional protocols generally include 100 mg diluted in at least 30 mL carrier solution

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Vitamin B6, Pyridoxine

- Adverse Reactions:
  - When given as undiluted i.v. injection may cause dizziness, faintness and irritation of tissue

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Vitamin B6, Pyridoxine

- Pyridoxine acts as a coenzyme in metabolic reactions for carbohydrate, lipid and amino acid metabolism
- Ethanol increases the breakdown of pyridoxine

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P-5-P Injection??

- Occasionally available
- Generally one can use 1/3 the dose of P5P IM or IV that is dosed in the Pyridoxine form.

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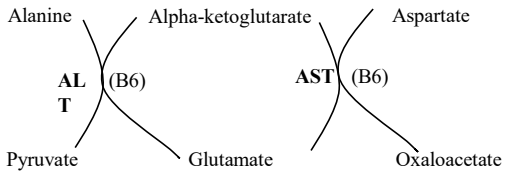

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BIOTIN

- Vitamin H or B7
- 5 mg/mL
- Cofactor in the metabolism of fatty acids and amino acids/ leucine, plays a role in the citric acid cycle and gluconeogenesis.
- Responsible for carbon dioxide transfer in several carboxylase enzymes

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Signs of Biotin Deficiency

- Appetite and growth decreased.
- Dermatologic symptoms:
  - Dermatitis, alopecia, achromotrichia (absence or loss of hair pigment) Perosis, Fatty liver and Kidney syndrome, hepatic steatosis, rash, seizures
- Neurologic symptoms: (adults)
  - Depression, lethargy, hallucination, and numbness and tingling of the extremities.
  - Hereditary disorders of biotin metabolism result in functional biotin deficiency and leads to impaired immune system function, with increased susceptibility to bacterial and fungal infections (one case of vaginal candidiasis).
- Pregnant women tend to have high risk of biotin deficiency

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J Nutr. 2001 Apr;131(4):1271-8.

The clearance and metabolism of biotin administered intravenously to pigs in tracer and physiologic amounts is much more rapid than previously appreciated.

Wang KS, Kearns GL, Mock DM.

Source
Department of Biochemistry & Molecular Biology,
University of Arkansas for Medical Sciences and Arkansas
Children's Hospital Research Institute, Little Rock, AR 72205, USA.

Abstract
Understanding of biotin pharmacokinetics and regulation of metabolism is essential for the determination of the biotin requirement for humans. Using Landrace-Cambroug h pigs as a model, we initially demonstrated that biotin binding to protein accounts for only a small percentage of the total biotin in plasma. A physiologic amount of [14C]biotin was administered intravenously to three pigs; nine blood samples were collected over 48 h. Plasma concentrations of 14C-labeled metabolites were negligible for the first 2 h after biotin infusion. Disappearance curves of total 14C and of [14C]biotin were similar; both fit a triexponential function consistent with a three-compartment, open model. To characterize the rapid early phase of disappearance more precisely, a physiologic amount of [14C]biotin was administered intravenously to five pigs; eight blood samples were collected over the first hour and 16 total samples over 48 h. Again a triexponential function provided an excellent fit. The mean half-life values (+/- 1 SD) for the three phases were 0.11 +/- 0.07, 1.43 +/- 0.42 and 22 +/- 4 h. The [14C]biotin accumulated primarily in the liver, kidney and muscle. When administered intravenously at tracer doses to three pigs, [3H]biotin exhibited similar early pharmacokinetics; however, substantial quantities of a 3H-labeled metabolite appeared after 1 h. These studies provide evidence that egress of biotin from plasma is more rapid than previously appreciated.
The slower second and third phases may represent transport into the cytosol, biotransformation into intermediates and covalent binding to intracellular proteins.
Similar pharmacokinetics are likely to be seen in humans.

PMID:
11285337
[PubMed - indexed for MEDLINE]

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- Biotin seen to reverse disease progression in significant proportion of patients with progressive multiple sclerosis.

Neurology Reviews. 2016 August;24(8):13,17

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Biotin

- Side Effects and Toxicity
- No biotin toxicity has been reported in:
- 200 mg orally
- 20 mg intravenously per day.

- Mock DM. Biotin. In: Ziegler EE, Filer LJ, eds. Present Knowledge in Nutrition, 7th ed. Washington, DC: ILSI Press; 1996:220-235

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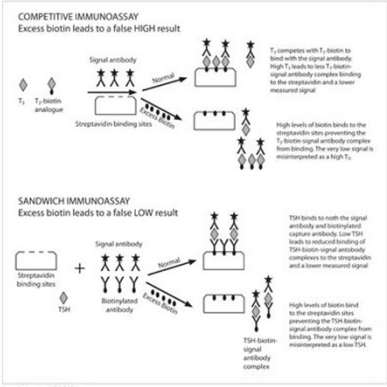
High-Dose biotin can interfere with labs



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High-Dose biotin can interfere with labs

- Single ingestion of biotin 30 mg interfered with the following labs for 8 hours
  - Estradiol
  - DHEA
  - Testosterone
- TSH was low and Free T4, Free T3 high for up to 24 hours.

Brennan, James and Lee, Stephanie. High-Dose biotin supplement can interfere with common laboratory tests. Endocrinology Today. https://www.healio.com/endocrinology/thyroid/news/print/endocrine-today/%7B0ff7371d-93a3-4865-b502-60fde9c98122%7D/high-dose-biotin-supplement-can-interfere-with-common-laboratory-tests

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Test Name	Test Code	Effect on Result	Comment
Cortisol	CORTI	Falsely Elevated	The results of this assay can be **falsely elevated** due to the consumption of Biotin. Please instruct patients to discontinue the use of vitamins or supplements that contain Biotin 12 hours before blood draw.
Cortisol Stimulation Baseline	CORB	Falsely Elevated	
Cortisol Stimulation 30 Minutes	COR30	Falsely Elevated	
Cortisol Stimulation 60 Minutes	COR60	Falsely Elevated	
Folate(FOL)	FOL	Falsely Elevated	
Hepatitis A Total Antibody with Reflex	HAAB2	Falsely Elevated (Falsely Positive)	
Homocysteine	HCY	Falsely Elevated	
Testosterone	TESTO2	Falsely Elevated	
Estradiol	ESTRA	Falsely Lowered	The results of this assay can be **falsely lowered** due to the consumption of Biotin. Please instruct patients to discontinue the use of vitamins or supplements that contain Biotin 12 hours before blood draw.
HCG for Accutane Monitoring	HCGAC2	Falsely Lowered	
HCG for Pregnancy	HCGS	Falsely Lowered	
HCG Quantitative	HCGTUM	Falsely Lowered	
Hepatitis A Antibody, IgM	HAIGM2	Falsely Lowered (False Negative)	
Hepatitis B Surface Antibody	HBABQ2	Falsely Lowered (False Negative)	
Hepatitis B Surface Antigen	HBSAG	Falsely Lowered (False Negative)	
Hepatitis B Core Antibody	HBCOR	Falsely Lowered (False Negative)	
Hepatitis C antibody	HCSCR2	Falsely Lowered (False Negative)	
HIV 1 & 2 Antibody	HIVSCN	Falsely Lowered (False Negative)	
HIV, Rapid 1 & 2 Antibody	HIVSS2	Falsely Lowered (False Negative)	
NT-proBNP	NTBNP	Falsely Lowered	
Parathyroid Hormone, Intact	PTHIN	Falsely Lowered	
Parathyroid Hormone, Intact, Intraoperative	PTHOP	Falsely Lowered	
Sex Hormone Binding Globulin	SHBG2	Falsely Lowered	
Troponin I	TROPI	Falsely Lowered	
Thyroid Stimulation Hormone	TSH3	Falsely Lowered	
Vitamin B12	B12	False	

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Vitamin B12, Cobalamin

- Three types of parenteral B12 available
  - Cyanocobalamin, 100 mcg/mL, 1000 mcg/mL
  - Hydroxocobalamin, concentration as prescribed, compounded
  - Methylcobalamin, concentration as prescribed, compounded
- Dose and administration
  - 1000 mcg is common dose, although 2000 mcg is also very safe

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Vitamin B12, Cobalamin

- Cyanocobalamin is best used i.m. as much of the dose is lost as blood circulates through the kidneys
- Hydroxocobalamin, also known as long acting B12, binds to serum proteins better than Cyano. Suitable for i.m. or i.v. use
  - Hydroxocobalamin is used as a treatment for cyanide poisoning, 5-10 g i.v.
- Methylcobalamin is a metabolically active form of B12, especially suited for neurological complaints

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~~Folic Acid~~

- Folic Acid
- 5mg/ml
- Dosage and Administration:
  - IM: up to 10 mg intermittent
  - IV: 5-10 mg diluted in i.v. solution, intermittent

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Folinic Acid, Leucovorin Calcium

- Leucovorin Calcium Powder
  - 50 mg
  - Leucovorin Calcium Powder, 100 mg
  - Leucovorin Calcium Powder, 350 mg

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Folinic Acid, Leucovorin Calcium

- Dosage and administration
  - 1-5 mL (10-50 mg) in at least 50 mL solution

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MTHFR gene mutations

- MTHFR testing indicated when:
  - Elevated homocysteine, venous thromboembolism, coronary artery disease, and/or stroke.
  - History of pregnancy complications including neural tube defects, stillbirths, and/or recurrent pregnancy loss
  - Or really – on all patients as screening
- Treat with 5-methyltetrahydrofolate
  - Rx Deplin(7.5 mg or 15 mg)
  - 5-MTHF (5-Methyltetrahydrofolate) supplements, typically 1 or 5 mg/capsule
  - Never, however, use these alone as you will aggravate other deficiencies.

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Most Important:

- Since you do not know how toxic or how many SNP's they have – Be as balanced in supplementation as possible and work up.
- Most homo MTHFR eventually require 10-15 mg 5MTHF daily until replete, but without collateral support they will crash (even with it sometimes).

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How do you know if it is a 'detox' reaction from the methyl pathway support or a GI Dysbiotic problem?

- Do a trail of parenteral pathway and methyl support.
- A GI problem (i.e. dysbiotic or infected) will be fine with IV or IM nutrients.

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Vitamin B Complex

- B-complex contains the following ingredients/mL:
  - Thiamine HCl 100 mg
  - Riboflavin-5-phosphate 2 mg
  - Niacinamide 100 mg
  - Dexpanthenol 2 mg
  - Pyridoxine 2 mg.

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Vitamin B Complex

- Dosage and Administration:
- IM: 1 mL
- IV: 0.5-2.0 mL diluted in i.v. solution
  - One mL given as part of a 30 mL i.v. push (Myers Cocktail) has been administered countless times without adverse reaction
  - For doses higher than 1 mL it is recommended that B-complex be diluted in at least 100 mL i.v. solution

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Vitamin B Complex

- Adverse reactions & toxicity
  - GI upset (nausea) is the most common complaint with oral preparations and can occur with too rapid i.v. infusions

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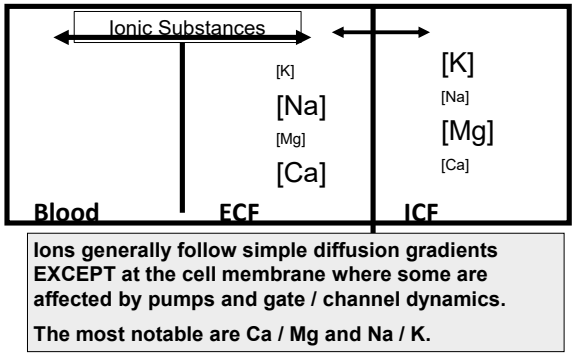
Compartment Dynamics



Ions generally follow simple diffusion gradients EXCEPT at the cell membrane where some are affected by pumps and gate / channel dynamics.

The most notable are Ca / Mg and Na / K.

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Activities of agents on the CNS

AGENT	EXCITE CNS	SEDATE CNS
Calcium		****
Magnesium		****
H+		****
Bicarbonate	****	
Phosphate	****	

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Calcium

- 10% Calcium gluconate
- 10% Calcium chloride,
- Dosage and administration
  - Gluconate 100-2000 mg (0.465-9.3 mEq) i.v.
    - Infusion rate never greater than 1 mEq/min.

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Calcium

- Calcium salts administered i.m. can cause local necrosis and abscess
- Calcium added to lipid emulsions has resulted in non-visible precipitates, patient deaths
- Storage – Calcium gluconate room temperature to avoid precipitation

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Magnesium

- Magnesium sulfate 500 mg/mL (50%)
- Magnesium chloride, 200 mg/mL (20%)

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Magnesium

- Dosage & Administration
  - IM: Up to 3 mL 50% adults
    - 1-3 mL 20% pediatric
  - IV: given normal renal function, up to 50 mEq over 4-6 hours (12.5 mL 50% Mg Sulfate)
  - Clinical use
    - Up to 3 mL 50% over 20-30 min, watch for O.D. Sx
    - Up to 6 mL 50% over 2 hours in drip

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Magnesium – Clinical

Using Mg Salt in appropriate protocols

- 50% Mg Sulfate: Asthma, muscle cramps, migraine, pain
  - 3 mL in push to 6 mL drip
- 20% Mg Chloride: Arrhythmia
  - 10 mL in drip with other mineral chloride salts
- Many (most likely most) patients are Mg deficient and benefit from an appropriate degree of Mg replacement during IVMT

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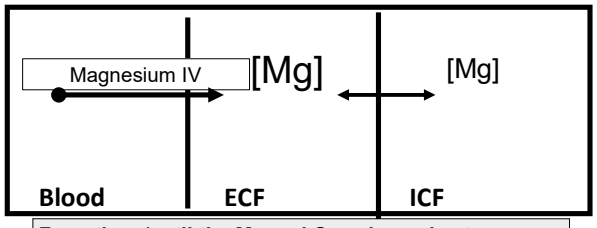
Compartment Dynamics: Magnesium Administration



For a time (until the Mg and Ca+ channel gates can equilibrate) The abnormally high ECF Mg will cause a dampening of the normally high Ca ECF and High Mg ICF gradient. The membrane will thus lose some (or all) excitability!

**** This is why Mg is a functional Ca-Channel blocker.**

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Magnesium Effect on Muscle Tissue:

Effect:	Skeletal Muscle	Smooth and Cardiac Muscle
Calcium Channel blockade	+++	+++
NMDA Receptor antagonist: * Via central regulation	+++	+++
Acetylcholine release blockade:	+++	

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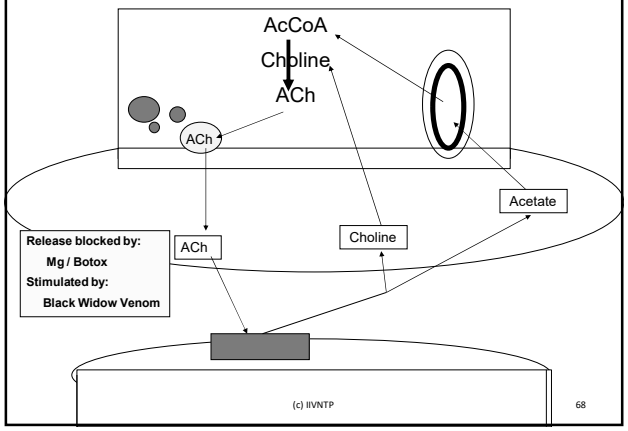
Acetylcholine Synapse



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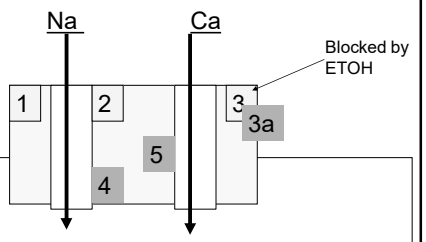
NMDA Receptor

Excitatory
1: Glutamate
2: Zinc
3: Glycine (Acts as inhibitory transmitter at Glycine receptors)



Inhibitory
3a: Kynurenate (Tryptophan metabolite)
4: Magnesium
5: PCP / Ketamine

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Calcium and Magnesium IV Products

Product	Percent	mg/mL	mEq / mL
Calcium Gluconate	10%	100	0.465
Calcium Chloride	10%	100	1.36
Magnesium Sulfate	50%	500	4.06
Magnesium Chloride	20%	200	1.97

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Potassium

- Potassium chloride, 2 mEq/mL is principal form used in IVMT
  - Potassium phosphate and acetate are available
- Dose and administration
  - Not for i.m. use
  - Never add potassium to an i.v. push
  - Always dilute appropriately prior to infusion

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Potassium - Clinical

- Typical IVMT dose is 2-5 mL in drip of 200-500 mL given over 1-3 hours
- It is useful to include potassium
  - When giving high dose vitamin C
  - When infusing solutions using D5W as carrier
  - Both of these treatments induce insulin and when insulin moves either glucose or vitamin C into cells potassium is required

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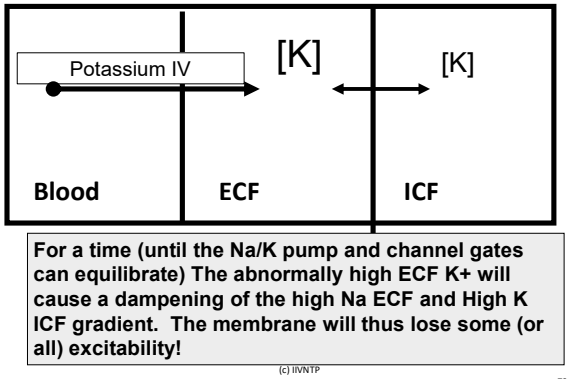
Compartment Dynamics: Potassium Administration



For a time (until the Na/K pump and channel gates can equilibrate) The abnormally high ECF K+ will cause a dampening of the high Na ECF and High K ICF gradient. The membrane will thus lose some (or all) excitability!

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Copper

- Copper sulfate, 0.4 mg/mL
- Copper chloride, 0.4 mg/mL
- Dosage and administration
  - IV: 1-2 mL as part of a drip infusion
- Caution: cholestasis, cirrhosis, Wilson's disease (copper storage disease)
- Indicated for depigmentation of hair, microcytic hypochromic anemia, neutropenia, skin pallor, skeletal demineralization

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Manganese

- Manganese chloride, 0.1 mg/mL
- Manganese sulfate, 0.1 mg/mL
- Dose and Administration
  - IM: Contraindicated
  - IV: Sulfate form is preferred
  - Adults 0.15-0.8 mg
  - Children 2-10 mcg/kg
- Adverse reactions: manganese excretion is primarily though bile, toxicity may result in patient experiencing cholestasis

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Molybdenum

Beneficial in copper toxicity

- more than 0.5 mcg/mL blood levels leads copper excretion to

Cautions:

- aggravates copper deficiency
- avoid in pregnancy
  - fetus can't excrete trace mineral sufficiently

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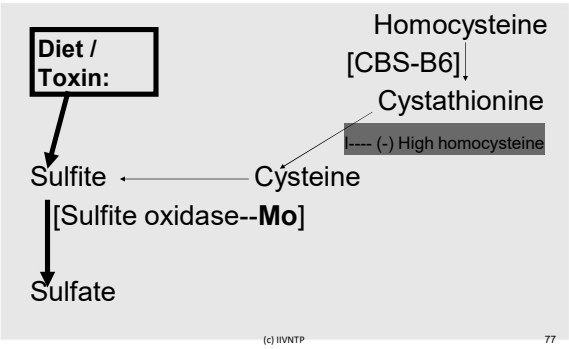
Catalytic role of Molybdenum in Sulfite clearance



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Molybdenum

Observational and experimental studies have shown an association between molybdenum and bipolar disorder (1). There is also strong evidence for the neuroprotective role of molybdenum (2,3,4).

- 1. Naylor GJ, Smith AH, Bryce-Smith D, Ward NI. Trace elements in manic depressive psychosis. J Affect Disord. 1985 Mar-Apr; 8(2): 131-6.
- 2. Woo WH, Yang H, Wong KP, Halliwell B. Sulphite oxidase gene expression in human brain and in other human and rat tissues. Biochem Biophys Res Commun. 2003 Jun 6; 305(3): 619-23.
- 3. Johnson JL, Rajagopalan KV. The oxidation of sulphite in animals systems. Ciba Found Symp. 1979; (72): 119-33.
- 4. Yamamoto T, Moriwaki Y, Takahashi S, Tsutsumi Z, Tuneyoshi K, Matsui K, Cheng J, Hada T. Identification of a new point mutation in the human molybdenum cofactor sulfurase gene that is responsible for xanthinuria type II. Metabolism. 2003 Nov; 52(11): 1501-4.

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Selenium

- Selenium trace element, 40 mcg/mL
- Selenium trace element (compounded), most commonly 100 and 200 mcg/mL
- Dose and administration
  - IV: 200-800 mcg in drip protocol
- Contraindications: pregnancy, infants
- Caution renal disease, decreased excretion

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Selenium - Se

- Selenium is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes
  - Other selenoproteins help regulate thyroid function and play a role in the immune system
- Selenium is often depleted in mercury toxic patients
- Selenium can often be made from fermenting yeast (may not be tolerated by mycotoxin patients

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Zinc

- Zinc chloride, 1 mg/mL
- Zinc sulfate, 10 mg/mL

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Zinc

- Clinical: lowered immunity, impaired wound healing, impaired smell/taste, depression
- **Zinc Biochemistry, Physiology, and Homeostasis: Recent Insights and ...**
  *https://books.google.com/books?isbn=9401737282,https://www.springer.com/us/book/9781402002175*W. Maret - 2013 - Science

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REVIEW

Parenteral trace element provision: recent clinical research and practical conclusions

P Stehle[1], B Stoffel-Wagner[2] and KS Kuhn[1]

The aim of this systematic review (PubMed, www.ncbi.nlm.nih.gov/pubmed and Cochrane, www.cochrane.org; last entry 31 December 2014) was to present data from recent clinical studies investigating parenteral trace element provision in adult patients and to draw conclusions for clinical practice. Important physiological functions in human metabolism are known for nine trace elements: selenium, zinc, copper, manganese, chromium, iron, molybdenum, iodine and fluoride. Lack of, or an insufficient supply of, these trace elements in nutrition therapy over a prolonged period is associated with trace element deprivation, which may lead to a deterioration of existing clinical symptoms and/or the development of characteristic malnutrition syndromes. Therefore, all parenteral nutrition prescriptions should include a daily dose of trace elements. To avoid trace element deprivation or imbalances, physiological doses are recommended.

European Journal of Clinical Nutrition advance online publication, 6 April 2016; doi:10.1038/ejcn.2016.53

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Iron

- Indications
- Iron deficiency in patients where oral iron supplementation is ineffective.
- Iron replacement following significant blood loss.
- Iron deficiency anemia in patients with end-stage renal disease undergoing hemodialysis or receiving epoetin therapy.

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Iron

- Adverse reactions
  - Dose related: arthralgia, backache, chills, dizziness, moderate to high fever, headache, malaise, myalgia, N/V
  - Increased incidence of these effects with total dose infusions
  - Onset is 24-48 hours after administration
  - Effects subside within 3-4 days

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Iron – Lab Evaluation

- Monitoring iron levels
  - Serum iron may not be meaningful for 3 weeks
  - Serum ferritin peaks after about 7 to 9 days and slowly returns to baseline after 3 weeks
  - You can do a CBC the week following if checking the H&H (i.e. for pregnancy).
  - We wait 3 weeks following the end of IV Iron and run Ferritin, CBC, and a TIBC (UBC) panel.
  - Elevated Ferritin and low TIBC are normal and will return to stable values in 2-4 months. If Ferritin is not at a desired level (> 100) and TIBC is still high or high normal, consider more parenteral Iron therapy.

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Dexferrum, InFeD – Iron Dextran
- Supplied as 100 mg/2 ml SDV
- 100 mg or less given on daily basis
- Delivered over 1 hour, even longer
- Don't advise PUSH

Ferrlecit – Sodium Ferric Gluconate
- Supplied as 62.5 mg/5 ml SDV
- Max dose not to exceed 125 mg per dose, 1000 mg total cumulative
- Delivered over at least 1 hour

Venofer – Iron Sucrose
- Supplied as 50 mg/2.5 ml SDV, 100 mg/5 ml SDV, 200 mg/10 ml, 400 mg/ml SDV
- 100 – 400 mg can be given in single delivery, 1000 mg total cumulative
- Deliver in 15 minutes to 2.5 hours depending on dose

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Injectafer – Ferric carboxymaltose
- Supplied as 750 mg/15 ml SDV
- Not to exceed 750 mg per dose, 1500 mg total cumulative
- Delivered in at least 15 minutes

Feraheme – Ferumoxytol
- Supplied as 510 mg/17 ml SDV
- Not to exceed 510 mg per dose, 1020 mg total cumulative
- Delivered in at least 15 minutes
- NEVER PUSH

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References Iron

- http://www.rxlist.com/ferrlecit-drug.htm
- http://www.drugs.com/cdi/sodium-ferric-gluconate.html
- http://www.medscape.com/viewarticle/478589
- http://products.sanofi-aventis.us/ferrlecit/ferrlecit.html

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