INTERNATIONAL
IV NUTRITIONAL THERAPY
GLOBAL PHYSICIAN EDUCATION

Parenteral Vitamins and Minerals

Advanced IV Therapy

by

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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.

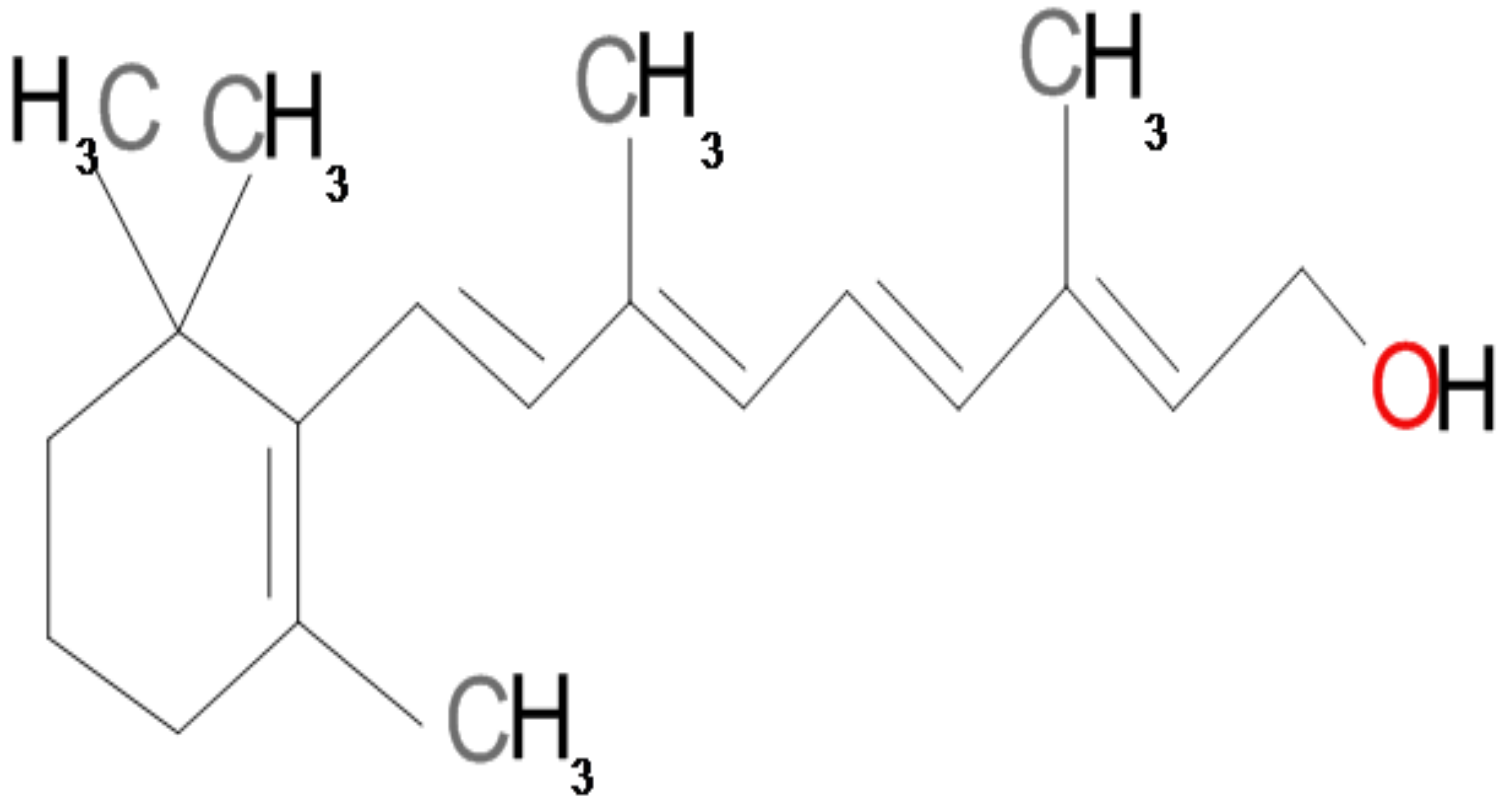
Classes of Vitamins

- 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.

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.

Vitamin A



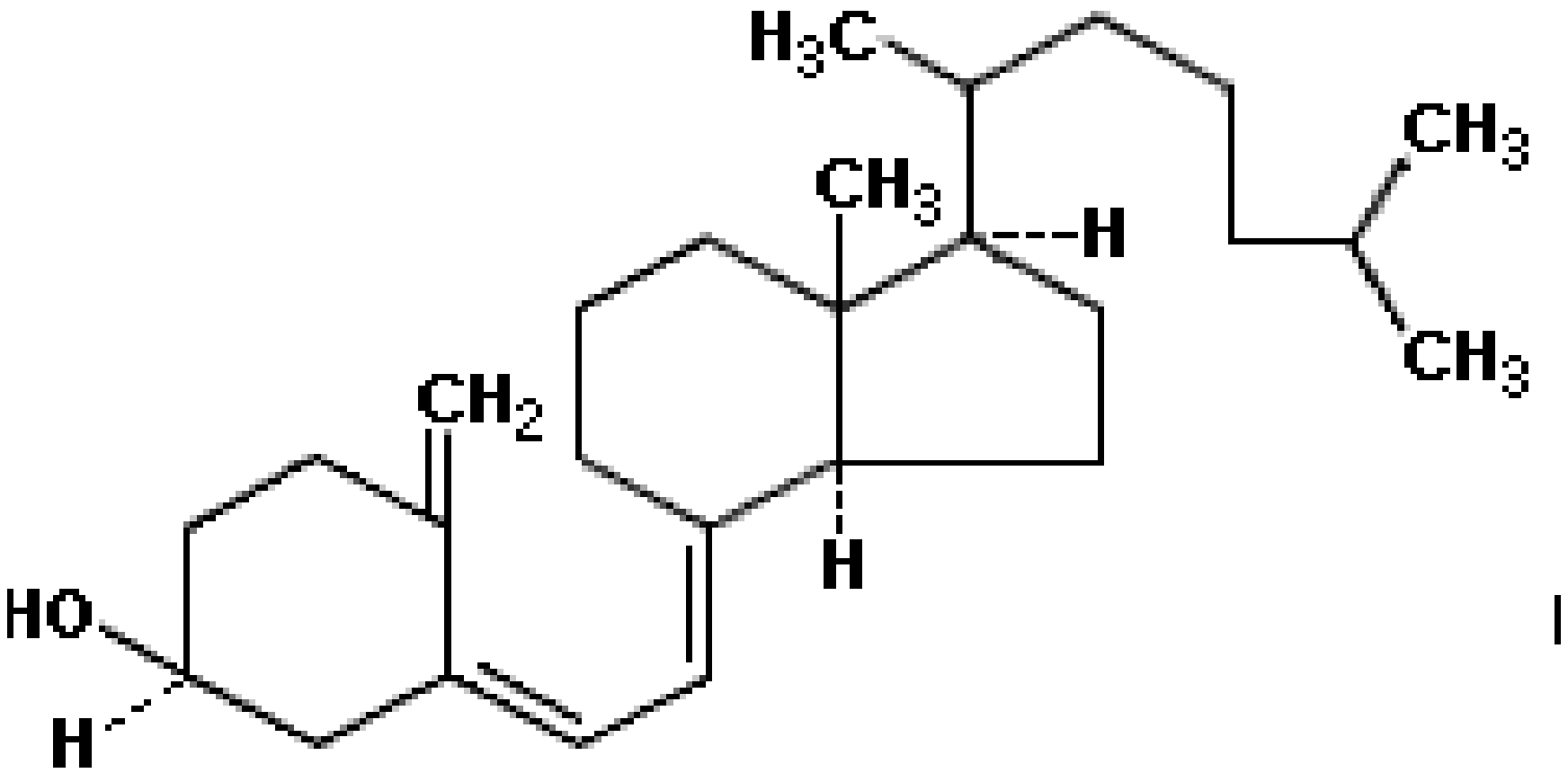
Vitamin A

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

Vitamin A Functions

- Vitamin A effects:
- gene expression
- is needed for:
- normal vision,
- essential for immune function,
- effects fetal growth and development
- Aids in the differentiation of stem cells to develop into red blood cells.

Vitamin D



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

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 50,000IU / 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

IV Vitamin D

- Available as Calcitriol for injection, 1mcg (500 IU) single dose vials.
  - All other parenteral Vitamin D (in the US) is for IM use only.
- Dose recommended is 1 to 4 mcg (500 to 2000 IU) on the first dose, and 4 mcg or higher on successive doses.
  - Often dosed weekly. Check serum Ca, Vit. D and PTH if using long term.
  - Following the first dose, dose recommendations are 4 to 10 mcg weekly if needed.
    - On the high end: Muindi et. al. used 57 mcg weekly in a pharmacokinetic study with decadron in cancer patients.

IV Vitamin D

- Mix without ionic additives in D5W (normally 250 mL D5W run over 45 – 60 minutes to check patient tolerance.)
- Other IV formulae may be run either before or after.

Muindi JR, et. al. A phase I and pharmacokinetics study of intravenous calcitriol in combination with oral dexamethasone and gefitinib in patients with advanced solid tumors. Cancer Chemother Pharmacol. 2009 Dec;65(1):33-40. Epub 2009 Apr 26.

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

Vitamin D

- Other effects
  - Vitamin D may enhance effects of cancer drug doxorubicin.
- Calcium levels should be followed closely if vitamin D is taken with digoxin
  - Vitamin D improves absorption of calcium, and in turn, can increase the likelihood of a toxic reaction from digoxin

Vitamin D

- Hormone effect:
- Formed in the dermal layers (skin) by action of ultraviolet rays upon the precursors, 7-dehydrocholesterol and ergosterol (plants only, not in animals), and acts on vitamin D receptors to regulate calcium in opposition to parathyroid hormone.
    - A vitamin that includes both CHOLECALCIFEROLS and ERGOCALCIFEROLS (plant derived D2), have the common effect of preventing or curing rickets in animals.

VITAMIN – D and Calcium Metabolism

UV Light

7-OH Cholesterol --(Skin)→ Cholecaliferol (D3)

(Liver)

25 hyrdrolase

Parathyroid Gland ++ due to Falling Serum Ca

PTH

25-Hydroxycholecalciferol 25(OH)D3

PTH (-)

24 Hydroxlase

(Kidney)

1-α-hydroxlase

(-) Phos(+) (PTH)

24,25-Hydroxycholecalciferol

24,25 DihydroD3

NET EFFECTS:

- **Ca INTO Bone**
- **Ca Absorption in Gut**

- ***LOWERS SERUM Ca***

1,25-Hydroxycholecalciferol

dihydro D3

NET EFFECTS:

- **Ca OUT of Bone**
- **Ca Absorption in Gut**
- **Ca Renal Reabsorption**

***RAISES SERUM Ca**

Measuring Vitamin D Levels

- The preferred test for determining vitamin D
  - 25-hydroxyvitamin D (25(OH)D3)
  - Optimal levels upper 25 percentile of reference range
  - Dr. Michael Hollick, top vitamin D researcher, and Dr. John Cannell (Vit D newletter / research) have advocated for higher reference ranges

- Levels below 20 ng/mL* indicate serious deficiency and will increase the risk of breast and prostate cancer, autoimmune diseases, and upper respiratory illness during winter months
  - *ng/mL x 2.496 = nmol/L

Dawson-Hughes B, et al; Estimates of optimal vitamin D status. Osteoporos Int. 2005 Jul;16(7):713-6. Epub 2005 Mar 18.

- Vitamin D has captured attention as an important determinant of bone health, but there is no common definition of optimal vitamin D status.

- The opinions of the authors on the minimum level of serum 25(OH)D that is optimal for fracture prevention varied between 50 and 80 nmol/l. However, for five of the six authors, the minimum desirable 25(OH)D concentration clusters between 70 and 80 nmol/l.

- The authors recognize that the average older man and woman will need intakes of at least 20 to 25 mcg (800 to 1,000 IU) per day of vitamin D(3) to reach a serum 25(OH)D level of 75 nmol/l.

- Based on the available evidence, we believe that if older men and women maintain serum levels of 25(OH)D that are higher than the consensus median threshold of 75 nmol/l, they will be at lower risk of fracture.

Review of Vit D Benefits

- Benefits of Vit D3
- Intestinal: activates detoxification
- Bone: aids in metabolism and calcium asbsorption
- Apoptotic
- Angiogenesis inhibitor
- An up regulator of tumor suppressor genes p27 and p21
- Calcium, folate and soy genistein block the nutrializing of Vit D in the presence of cancer cells. G. DiSilva MD A4M International Conference April 11, 2013

Rheumatol Int. 2012 Aug;32(8):2279-83. doi: 10.1007/s00296-011-1943-6. Epub 2011 May 10.

The effect of oral and parenteral vitamin D supplementation in the elderly: a prospective, double-blinded, randomized, placebo-controlled study.

Sakalli H, Arslan D, Yucel AE.

Source

Internal Medicine, Adana Numune Training and Research Hospital, 01960 Adana, Turkey. hakansakalli1@yahoo.com

Abstract

Hypovitaminosis D in the elderly causes falls and fractures as a result of impaired neuromuscular functions and also may be a reason for nonspecific musculosceletal pain. The aim of this study is to investigate the benefits of a single dose per os or parenterally administrated vitamin D on increasing the quality of life and functional mobility and decreasing the pain in the elderly. The community-dwelling elderly subjects over 65 years age were included in the study. The subjects were given 300.000 IU Vitamin D via per os and parenteral route and assessed after 4 weeks. The serum creatinine, calcium, phosphorous, ALT, ALP, 24-h urine calcium excretion, PTH, and vitamin D levels, as well as VAS (visual analog scale) for pain assessment, functional mobility with TUG (timed up and go test) and quality of life with SF-36 before and after the treatment were evaluated. The serum vitamin D levels were measured by the RIA method. The subjects were divided into four groups each consisting of 30 subjects. The 1st group took i.m. vitamin D, the 2nd group took i.m. placebo, the 3rd group took p.o. vitamin D, and the 4th group took p.o. placebo. The mean age of all the participants was 70.1 ± 4.3 years. There was no difference in the age and gender between the groups ($P > 0.05$). After treatment, the PTH level of first group was decreased ($P = 0.0001$) and the vitamin D level increased ($P = 0.0001$) significantly. In the third group, the PTH level of first group was decreased ($P = 0.0001$) and the vitamin D level increased ($P = 0.004$) and the 24-h calcium excretion in urine ($P = 0.015$) increased significantly. When the pain, the functional mobility, and the quality of life were evaluated, in the first group, the TUG ($P = 0.0001$) and the VAS ($P = 0.0001$) decreased significantly, whereas the SF-36 subtitles: physical functioning ($P = 0.0001$), role physical (0.006), bodily pain ($P = 0.0001$), general health ($P = 0.007$), social functioning ($P = 0.05$), and mental health ($P = 0.048$) increased significantly. In group two, the VAS ($P = 0.001$) decreased, the role physical ($P = 0.009$), and role emotional ($P = 0.034$) increased significantly; In group three, the TUG ($P = 0.0001$) and the VAS ($P = 0.002$) decreased, whereas the physical function ($P = 0.0001$) and role physical (0.001) increased significantly; In group four, the VAS ($P = 0.007$) decreased significantly**. The megadose vitamin D administration increases quality of life, decreases pain, and improves functional mobility via po or im route in the elderly.**

PMID:
21556746
[PubMed - indexed for MEDLINE]

Vitamin E

- Vitamin E acetate, (check pharmacy availability)
- MVI – Multivitamin for injection, 1 mg/mL
- Administration and dose
  - ½-1 mL acetate (aqueous) in 500 mL solution
  - MVI 10 mL in 500 mL solution
  - IM admin leads to pain, swelling, tenderness at site
- CI side effects: No reports of harmful effect when physiologic doses are given

Vitamin K

- Essential cofactor for carboxylase, important clotting, will drive calcium into cells
- **WARNING** — INTRAVENOUS AND INTRAMUSCULAR USE Severe reactions, including fatalities, have occurred during and immediately after INTRAVENOUS injection of phytonadione, even when precautions have been taken to dilute the phytonadione and to avoid rapid infusion. Severe reactions, including fatalities, have also been reported following INTRAMUSCULAR administration. Typically these severe reactions have resembled hypersensitivity or anaphylaxis, including shock and cardiac and/or respiratory arrest. Some patients have exhibited these severe reactions on receiving phytonadione for the first time. Therefore the INTRAVENOUS and INTRAMUSCULAR routes should be restricted to those situations where the subcutaneous route is not feasible and the serious risk involved is considered justified.

Vitamin K

- Vitamin K1: Give **subcutaneous** whenever possible
- Protect from light at all times
- Can be diluted with Normal Saline, D5W or D5NS
- Should get preservative free form. Benzyl alcohol associated with toxicity in newborns.

The Anticancer Effects of Vitamin K (Lamson D and Plaza S. *Altern Med Rev* 2003;8(3):303-318)

Abstract

Vitamin K, an essential nutrient often associated with the clotting cascade, has been the focus of considerable research demonstrating an anticancer potential. Much of this research has focused on vitamin K3, although vitamins K2 and K1 have also been shown to have anticancer effects. Early studies of vitamin K3 employed an oxidative model to explain the anticancer effects seen in both *in vitro* and *in vivo* studies; however, this model does not adequately address the action of vitamins K1 and K2. Recent research has demonstrated the anticancer action of vitamin K may act at the level of tyrosine kinases and phosphatases, modulating various transcription factors such as Myc and Fos. Tyrosine kinases associated with cyclins have also been shown to be affected by vitamin K, which can lead to cell cycle arrest and cell death.

Vitamin K

- Preferred tx. Vitamin K3
- 1 gram K3 per 100 grams IVC (1 L SWI)
- Nausea is possible, many report severe but transient abdominal pain. You MUST warn patient of muscle spasms, abdominal cramping, masseter spasms.

Vitamin K

- If adding K3
- 250 mg with 25 G IVC
- 500 mg with 50 G IVC
- 750 mg with 75 G IVC
- 1000 mg with 100 G IVC

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.

Vitamin B1, Thiamine

- Supplied as Thiamine hydrochloride
- 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
- An intradermal skin test may be used if a sensitivity to thiamine is suspected
- The risk of allergic reactions is very low when thiamin is given with other B-vitamins
- Doses up to 200 times the daily maintenance dose (1.5 mg/day) has not been associated with toxic effects

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

Vitamin B1: Thiamine HCl

- Deficiency leads to slow function of the HMP Shunt and the TCA cycle (1)
  - Consider in:
    - Chronic fatigue
    - Depleted patients
    - Therapies attempting to boost glutathione function

- Deficiency can be caused by: (1)
  - Loop diuretics
  - Digitalis

Vitamin B2: Riboflavin

- Low toxicity due to renal dumping of excess

- FMN (flavinoidmononucleotide)
- FAD (flavinadeninedinucleotide)

- Depressed B2 status leads to slow beta-oxidation of fats (1)

- Part of Glutathione Reductase & Synthase enzyme systems
  - Increase use with oxidative therapies
    - H2O2
    - Vit C

- Average IV dose 1 to 10 mg.

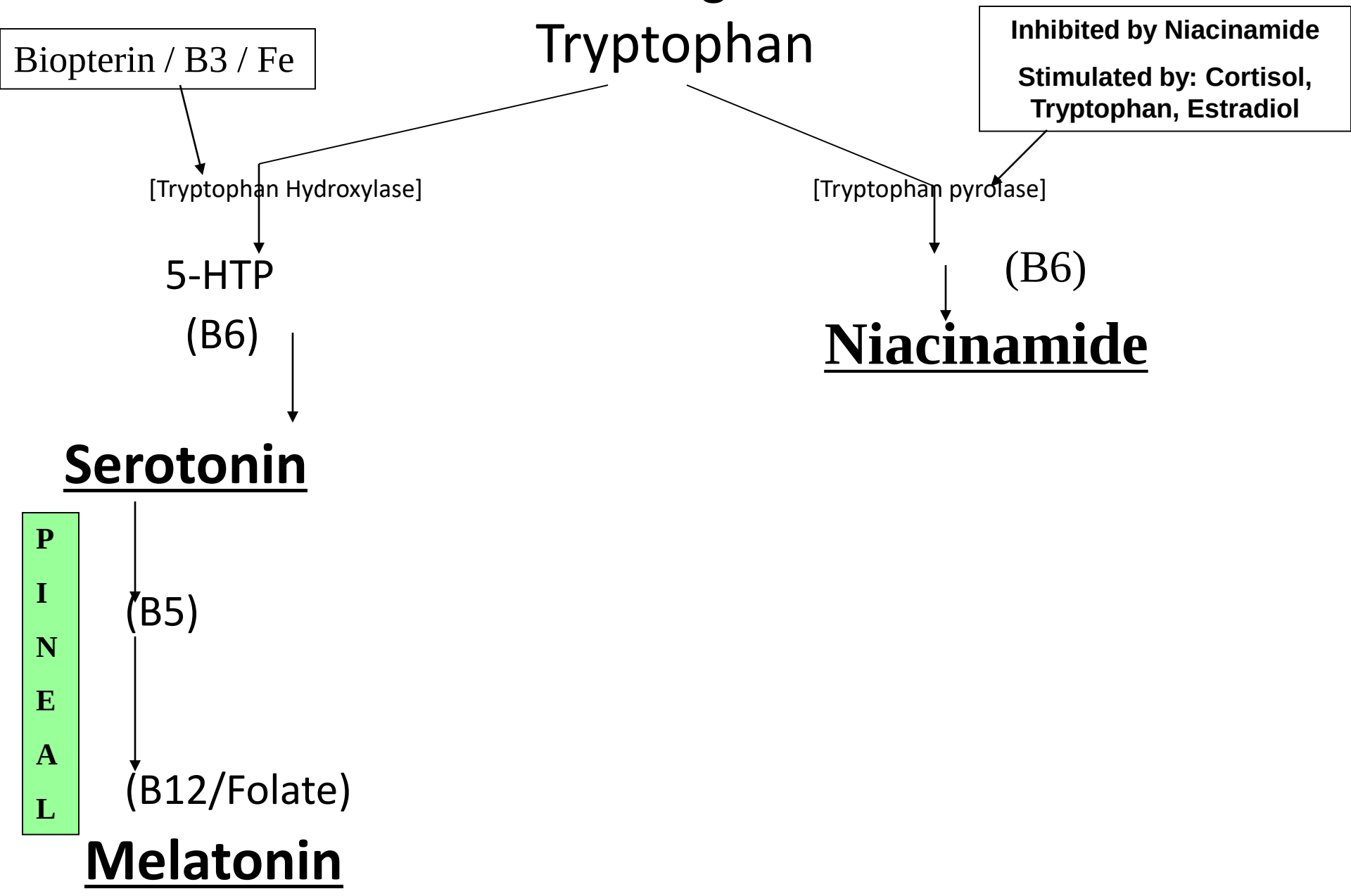
Vitamin B3: Niacinamide

- 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.

Serotonin Augmentation



Vitamin B5, Dexpanthenol

- Supplied as the alcohol form of pantothenic acid, 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 500 mg in a drip
- Physiologic doses are very safe
- Pharmacologic doses of 2500-3000 mg may prolong the effects of succinylcholine

Vitamin B5, Dexpanthenol

- Drug reactions:
  - Rare allergic reactions during use of parenteral dexpanthenol and some antibiotics, barbiturates and opiates when used concomitantly
- 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

Vitamin B6, Pyridoxine

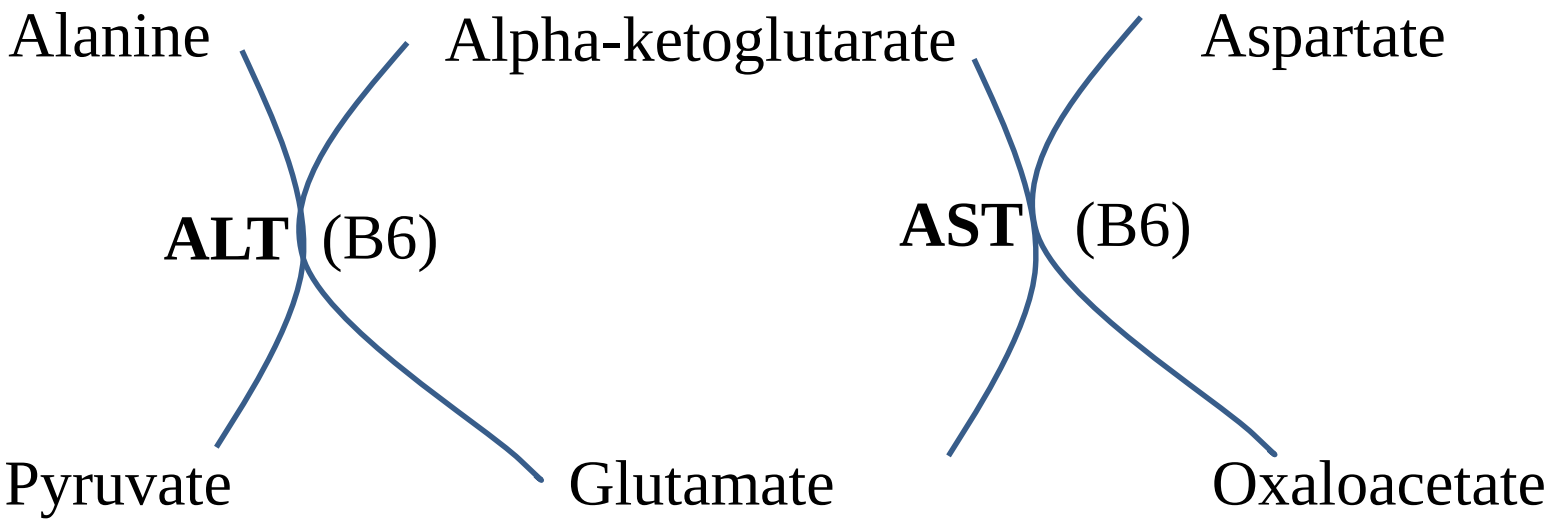
- Supplied as Pyridoxine hydrochloride
- Standard concentration is 100 mg/mL
- Dose and administration
  - Prophylactic dose for i.m. or i.v. administration is 2-4 mg daily
  - Therapeutic dose is 10-15 mg one to three times daily
  - Nutritional protocols generally include 100 mg diluted in at least 30 mL carrier solution

Vitamin B6, Pyridoxine

- Adverse Reactions:
  - When given as undiluted i.v. injection may cause dizziness, faintness and irritation of tissue
- Drug Reactions:
  - Doses higher than 5 mg daily can reverse the therapeutic effect of levodopa by increasing its metabolism in peripheral tissues. With a combination of carbidopa and levodopa(sinemet) this antagonistic effect is less noticeable

Vitamin B6, Pyridoxine

- Pyridoxine acts as a coenzyme in metabolic reactions for carbohydrate, lipid and amino acid metabolism
- B6 deficiency can be induced by malabsorption, malignancies, many diseases, long-term drug therapy as well as total parenteral nutrition (TPN).
- Ethanol increases the breakdown of pyridoxine



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

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 candidasis).
  - Long term TPN depletes biotin
- Pregnant women tend to have high risk of biotin deficiency

Biotin

- Biotin is an important vitamin for cellular function and growth and, therefore, essential for fetal development. The fetus is exclusively dependent on maternal biotin supply. Since biotin is not produced within the body, maternal biotin levels depend on dietary intake. In order to investigate the biotin status of the human fetus, we measured the plasma biotin levels in 15 pregnant women and their fetuses who underwent amniocentesis and fetal blood sampling at 18 to 24 weeks of gestation for prenatal diagnosis of thalassemia. Maternal biotin was found to be 131 + or - (SD) 102 ng/L and fetal biotin 784 + or - 327 ng/L (p less than 0.0001). Our findings are indicative of an active transport mechanism of biotin through the placenta in favor of the fetus.[Mantagos S et al; Biol Neonate 74(1): 72-4 (1998)] PubMed Abstract

Biotin Research

- …Or how we relate to Rats and Pigs biochemically

The presence of biotin in select regions of rat CNS, as revealed with a monoclonal antibody directed against biotin and with avidin- and streptavidin-conjugated labels /is described/. Detectable levels of biotin were primarily found caudal to the diencephalon, with greatest expression in the cerebellar motor system and several brainstem auditory nuclei. Biotin was found as a somatic label in cerebellar Purkinje cells, in cell bodies and proximal dendrites of cerebellar deep nuclear neurons, and in red nuclear neurons. Biotin was detected in cells of the spiral ganglion, somata and proximal dendrites of cells in the cochlear nuclei, superior olivary nuclei, medial nucleus of the trapezoid body, and nucleus of the lateral lemniscus. Biotin was further found in pontine nuclei and fiber tracts, the substantia nigra pars reticulata, lateral mammillary nucleus, and a small number of hippocampal interneurons. Biotin was detected in glial cells of major tract systems throughout the brain but was most prominent in tracts of the hindbrain.

Biotin is thus expressed in select regions of rat CNS with a distribution that correlates to the known clinical sequelae associated with biotin deficiencies.[McKay BE et al; J Comp Neurol 473(1):86-96 (2004)] PubMed Abstract

The authors/ sought to determine whether the urinary excretion rates of biotin and biotin metabolites in rats are similar to those reported in humans. D-(Carbonyl-(14)C-biotin was injected intraperitoneally at physiologic doses in 6- to 10-wk-old rats; HPLC and radiometric flow detection were used to specifically identify and quantify biotin and metabolites in urine. Substantial amounts of bisnorbiotin and biotin sulfoxide, the two principal human metabolites, were detected. The excretion rates of biotin and metabolites were strikingly dependent on the dose of biotin. When the dose of (14)C-biotin was 30% of the daily dietary intake (a physiologic dose), 50% of the administered (14)C was excreted within 24 hr; more than half of the excretion was the unchanged vitamin. After day 1, (14)C-bisnorbiotin was the major form excreted. For the cumulative 5-day excretion, (14)C-biotin accounted for 46 + or - 9%, (14)C-bisnorbiotin accounted for 47 + or - 11 %, and (14)C-biotin sulfoxide accounted for 8 + or - 4% of the total of biotin, bisnorbiotin, and biotin sulfoxide recovered radioactivity (mean + or - 1 SD, n = 6). These proportions are similar to those reported in humans: biotin = 52 + or - 12%, bisnorbiotin = 35 + or - 9%, and biotin sulfoxide = 13 + or - 4% of total biotin plus metabolites (mean + or - 1 SD, n = 10). Thus, these studies confirm the earlier identification of bisnorbiotin and biotin sulfoxide as the two principal biotin metabolites and provide evidence that the rat is an appropriate model for human biotin metabolism.[Wang K S et al; J Nutr 126(7): 1852-7 (1996)] PubMed Abstract

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-Cambrough 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]

- Ren Fail. 1996 Jan;18(1):131-7.
- **Oral glucose tolerance test after high-dose i.v. biotin administration in normoglucemic hemodialysis patients.**
- Koutsikos D, Fourtounas C, Kapetanaki A, Agroyannis B, Tzanatos H, Rammos G, Kopelias I, Bosiolis B, Bovoleti O, Darema M, Sallum G.
- **Source**
- Department of Nephrology, Aretaieon University Hospital, Athens, Greece.
- **Abstract**
- Abnormal glucose metabolism in uremia may result from a complex interplay between decreased insulin secretion and insulin resistance. Recent studies report beneficial effect of biotin administration in glucose metabolism in diabetic animals and in a small number of patients with diabetes mellitus. The aim of the present study was to evaluate the response of oral glucose tolerance test (OGTT) to the i.v. administration of large doses of biotin in hemodialysis patients. Eleven hemodialysis patients aged 56.90 +/- 11.20 (32-76) years on regular hemodialysis thrice a week for 2.72 +/- 1.79 (1-7) years were studied. Fasting venous plasma glucose, glucosylated hemoglobin (%GH), and plasma glucose concentration 2 h after the administration of a 75-g glucose load were measured before, and 2 weeks and 2 months after administration of 50 mg of biotin i.v. postdialysis, and after a 2-month washout period. During the study, dialysis schedule and patients' medication, diet, and dry weight were kept unchanged. OGTT was abnormal in 4 patients before biotin administration and became normal in 3 patients (75%). Our results offer support to the findings of other studies about the **beneficial effect of biotin in experimental or clinical diabetes mellitus, and argue for the involvement of biotin in glucose metabolism.**
- PMID: 8820510 [PubMed - indexed for MEDLINE]

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

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

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,

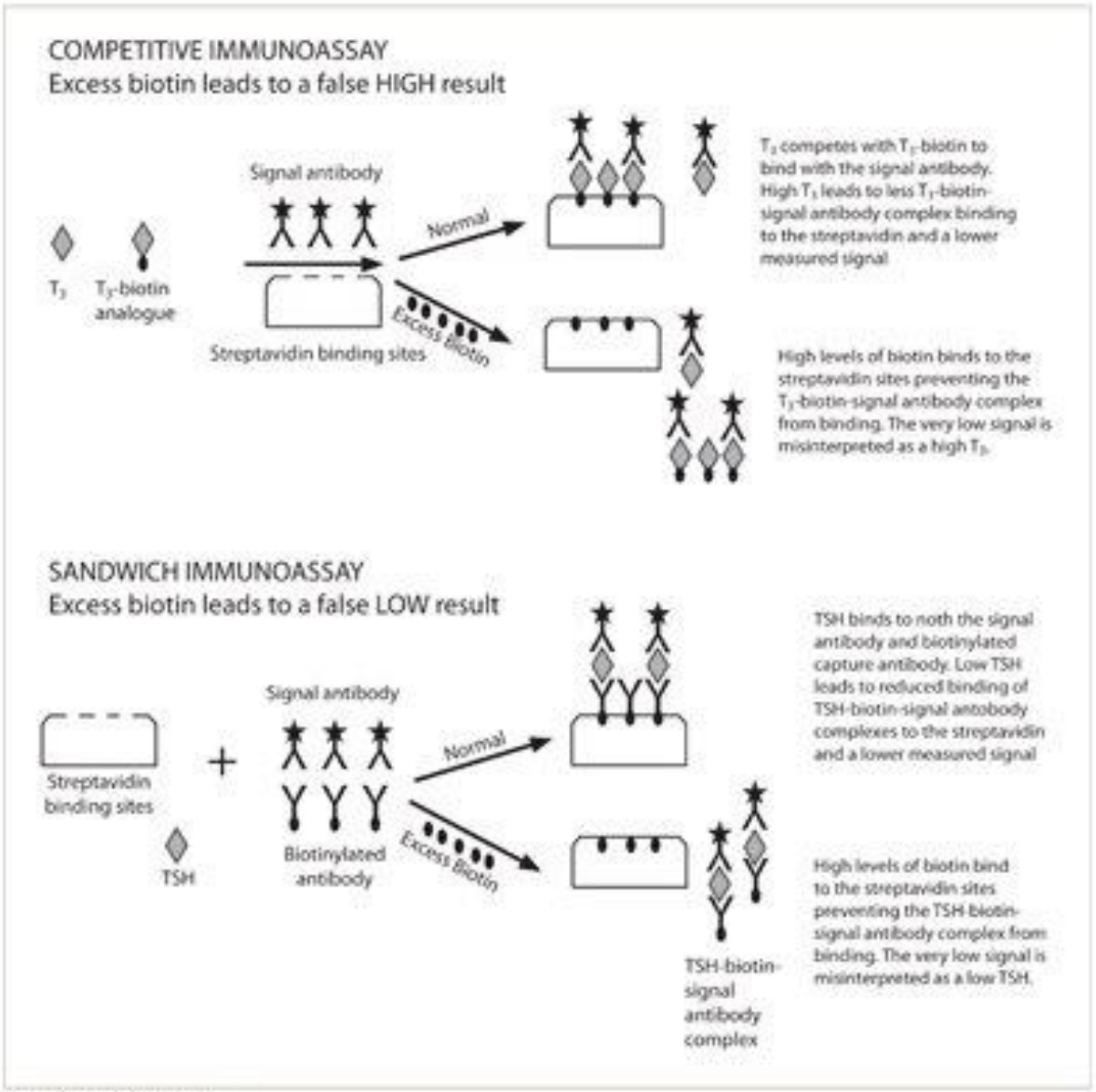
DC: ILSI Press; 1996:220-235

Biotin

- No known drug interactions

- Krause KH, Bonjour JP, Berlit P, Kochen W. Biotin
  status of epileptics. Ann N Y Acad Sci 1985;447:297-313.
- 52. Krause KH, Bonjour JP, Berlit P, et al. Effect of long-term treatment with antiepileptic drugs on the vitamin status. Drug Nutr Interact 1988;5:317-343.
- 53. Mock DM, Dyken ME. Biotin catabolism is accelerated in adults receiving long-term therapy with anticonvulsants. Neurology 1997;49:1444-1447.
- 54. Mock DM, Mock NI, Nelson RP, Lombard KA. Disturbances in biotin metabolism in children undergoing long-term anticonvulsant therapy. J

High-Dose biotin can interfere with labs



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

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	Falsely Lowered	

Dosage

- Therapeutic dosages range widely;
- IV: 10-20mg
- 2.5 mg daily has been used successfully for brittle nails,
- 15 mg daily for improving lipid levels (particularly triglycerides), and 9-16 mg daily to decrease glucose levels
- in diabetes. Both oral (uremic neurological syndrome)
- and intramuscular (diabetic neuropathy) doses of 10 mg daily have been used successfully to treat peripheral neuropathy. An optimal daily biotin intake for healthy adults has not been established at this time
- Mock DM. Biotin. In: Ziegler EE, Filer LJ, eds. Present Knowledge in Nutrition, 7th ed. Washington, DC: ILSI Press; 1996:220-235

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

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
  - Hydoxocobalamin 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

Vitamin B12, Cobalamin

- Methyl-B12 is required to convert homocysteine to methionine and to synthesize and maintain myelin sheaths on nerves
- Methionine is required for the metabolism of choline and betaine
- These facts help explain some of the neurological damage caused by B12 deficiency

Vitamin B12, Cobalamin

- Adverse reactions
  - Vitamin B12 has been shown to be nontoxic at doses that exceed daily requirements by 10,000 times
  - Preservative can result in hypersensitivity reactions but allergies to PF B12 are rare
- Drug reactions
  - Colchicine causes malabsorption of oral cobalamin

Folic Acid

- Folic Acid
- 5mg/ml
- Dosage and Administration:
  - IM: up to 10 mg intermittent
  - Folate deficiency with megaloblastic anemia is treated with 0.5-1 mg/day i.m.
  - IV: 5-10 mg diluted in i.v. solution, intermittent
- Adverse Reactions and Toxicity
  - The toxicity of folic acid is very low
  - Adults showed no adverse effects after receiving 400 mg/day for five months or 10 mg/day for five years.

Folinic Acid, Leucovorin Calcium

- Leucovorin Calcium Powder
  - 50 mg
    - Reconstitute with 5 mL Bacteriostatic Water for Injection, USP and use within 7 days, or with Sterile Water for Injection, USP and use immediately
    - Each mL of solution contains 10 mg Leucovorin.
  - Leucovorin Calcium Powder, 100 mg
  - Leucovorin Calcium Powder, 350 mg

Folinic Acid, Leucovorin Calcium

- Dosage and administration
  - 1-2 mL (10-20 mg) in at least 50 mL solution at conclusion of HDIVC (specific protocol for CA)
  - Other Protocol: 10 mg (adult)

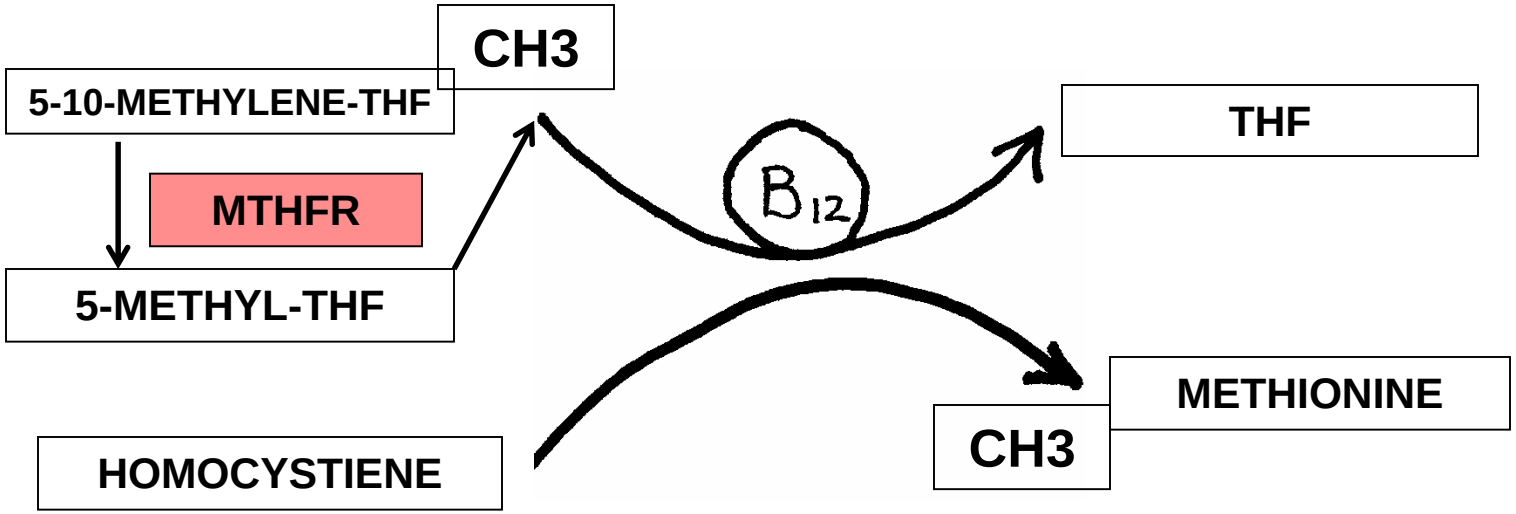
Methyl Transfer - B12 & FOLATE

THF (TetraHydroFolate) is active in methyl group transfer.

The CH3 transfer helps DNA in new cell production.

MTHFR enzyme reduces the 5-10 Methylene form to the 5 Methyl form, making B12 activity possible

B12 frees FOLATE from its bound form (5-Methyl-THF) to its coenzyme form (THF). It does this via a CH3 release in the following reaction:



Folic acid & MTHFR gene mutations

- Gene name is methylenetetrahydrofolate reductase (NAD(P)H), designated MTHFR
- Gene provides instructions for making the enzyme methylenetetrahydrofolate reductase
- Enzyme converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate.
- Reaction is required for the multistep process that converts homocysteine to methionine

Folic acid & MTHFR gene mutations

- Health conditions associated with MTHFR mutations: Homocysteinemia, homocysteinuria, anencephaly, spina bifida
- Polymorphisms in the MTHFR gene are associated with heart disease, stroke, high blood pressure (hypertension), preeclampsia, glaucoma, psychiatric disorders, and certain types of cancer

Ref: http://ghr.nlm.nih.gov/gene/MTHFR

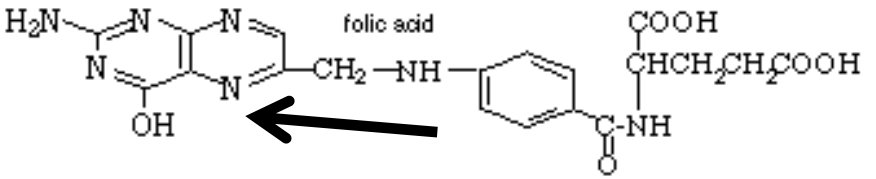
MTHFR gene mutations

- 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-Methyl tetrahydrofolate) supplements, typically 1 or 5 mg/capsule
  - Never, however, use these alone as you will aggravate other deficiencies.

Forms of Folate:

- Folic Acid

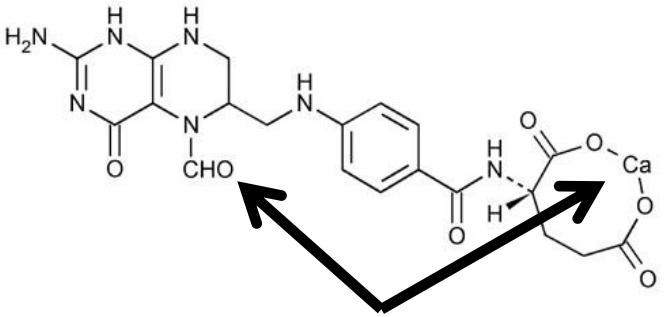
  requires DHFreductase



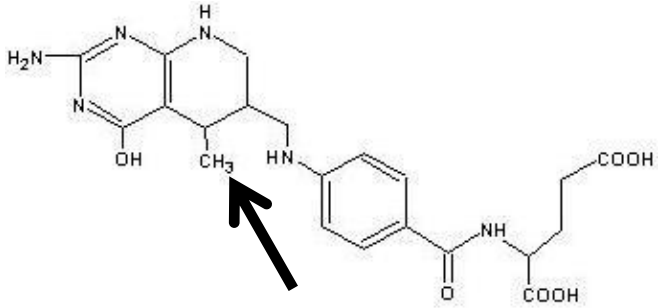
FOL→NADH/B3→THF→B3+DHF-reductase

- Folinic Acid / Leukovorin (formyl-THF)

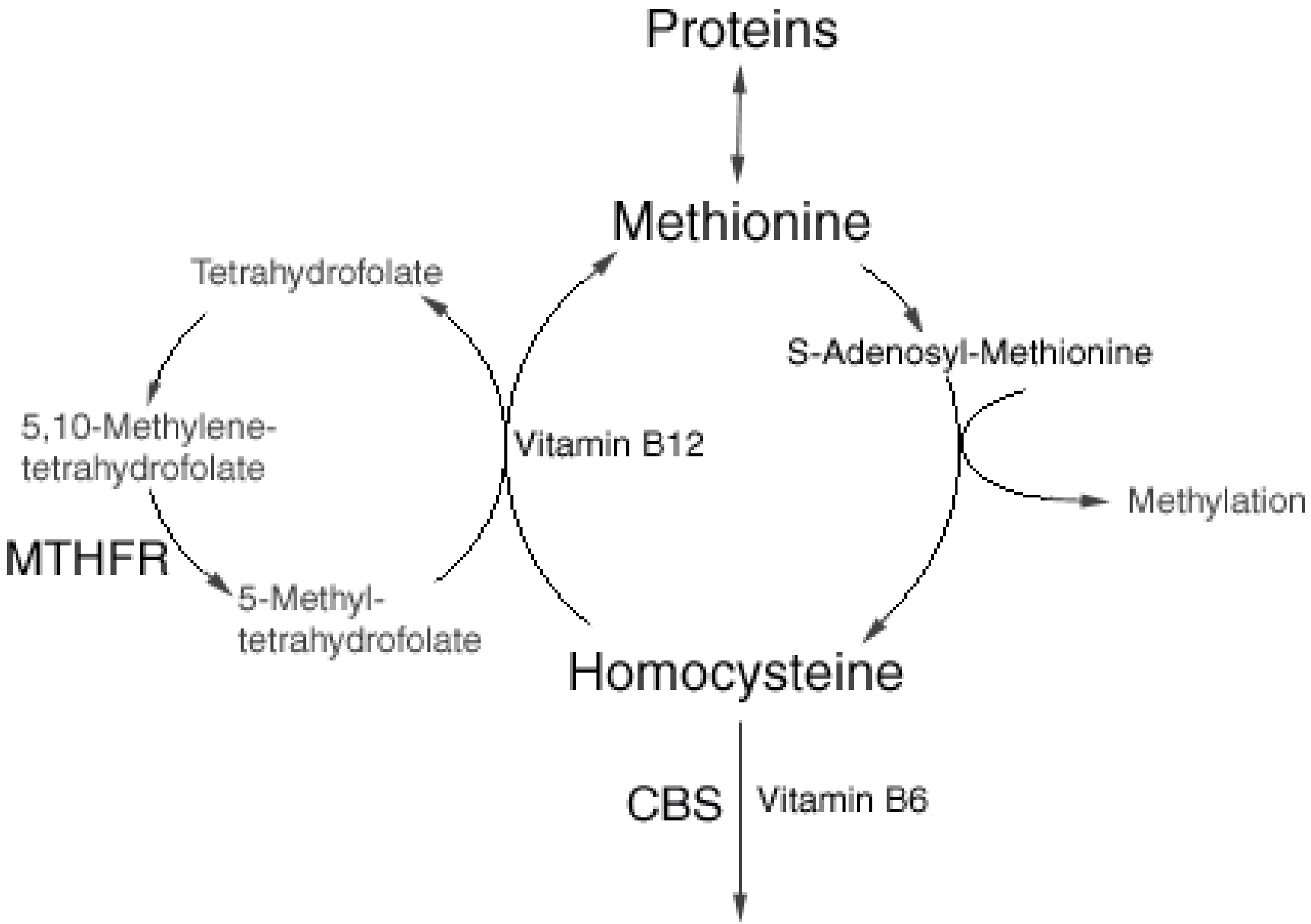
  No DHFreductase required



- 5-Methyltetrahydrofolate



(Graphics) http://web2.iadfw.net/uthman/nutritional_anemia/nutritional_anemia.html



- Succinyl CoA (TCA cycle)
- PAPS (Supports Dopamine production)
- Glutathione
- Taurine
- GABA
- Uric Acid

OPTIONS FOR AND DOSING OF ORAL SUPPORT AGENTS

- Methyl Donor Support
  - Methyl B-12: 1-5 mg SL / QD

- Collateral Pathway Support
  - Pyridoxal-5-phosphate: 50 – 100 mg BID
  - Betaine HCl: 3 – 9 grams divided doses with meals
  - NAC: 500 mg QD to BID
  - Niacin or Niacinamide: 100 to 500 mg BID to TID

- Direct 5-MTHF Support
  - 5-MTHF: ramp up 1 to 15 mg QD
  - B-2 & B-3 as obtained in a high potency b-complex.

IV – IM DOSE AND ADMINISTRATION

(NOTE: Oral supportive agents are recommended to augment these parenteral agents if tolerated by the patient. And – all IM doses can be higher if tolerated in an IV formula.)

- **Methyl Donor Support**
  - Methyl B-12 2.5 - 5 mg IM once to twice weekly [Methyl B-12 can be compounded from 2.5 to 10 mg/mL]
- **Collateral Pathway (CBS) Support**
  - Pyridoxine HCl 25 – 50 mg IM once to twice weekly [Pyridoxine is generally 100 mg/mL]
- **Direct 5-MTHF Pathway Support**
  - 5-MTHF ramp up 1 - 10 mg IM once to twice weekly [5-MTHF can be compounded as 2.5 to 10 mg/mL]
  - B-2 & B-3 as obtained in parenteral B-100 complex - [1 mL B-100 contains: 100 mg Thiamine HCl; 2 mg Dexpanthenol; 2 mg Riboflavin 5 phosphate-Na; 100 mg Niacinamide; 2 mg Pyridoxine HCl]

[From: Methyl Cycle Support: Parenteral Therapy Overview; © Paul S. Anderson 2012]

Most Important:

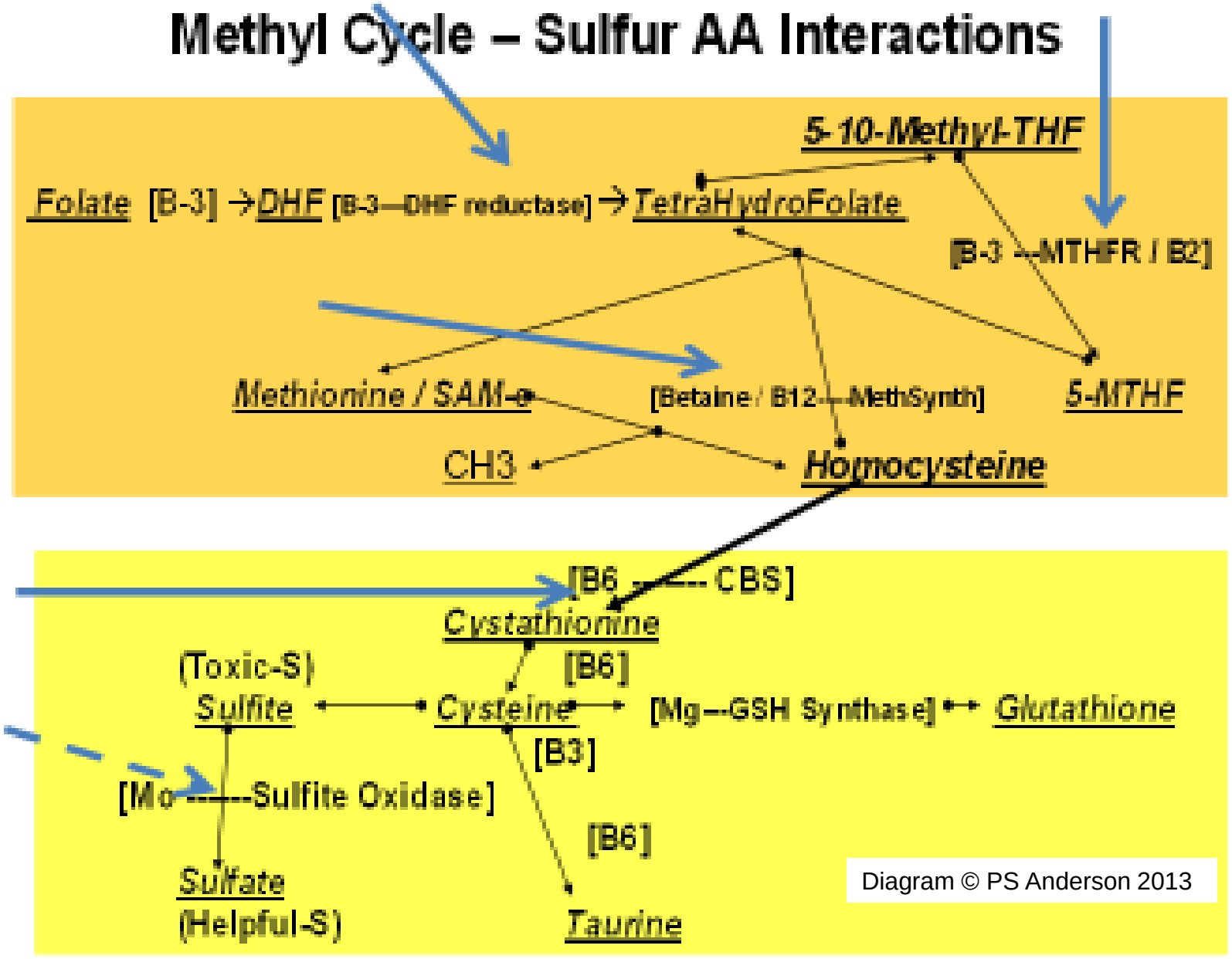
- Since you do not know how toxic or how many SNP's they have – Be as balanced in supplementation as possible and work up.

- Most homo MTHFR eventually require 10-15 mg 5MTHF daily until replete, but without collateral support they will crash (even with it sometimes).

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.

Methyl Cycle – Sulfur AA Interactions



Methylation References:

[1] Guenther, B.D. , C.A. Sheppard, P. Tran, R. Rozen, R.G. Matthews, and M.L. Ludwig. The structure and properties of methylenetetrahydrofolate reductase from Escherichia coli suggest how folate ameliorates human hyperhomcyseinmia. Nature Structural Biology 6, 359-365 (1999).

[2] Rosenblatt, D. S. Inherited disorders of folate transport and metabolism. In The Metabolic Basis of Inherited Disease (eds Scriver, C.R., Beaudet, A.L., Sly, W. S., & Valle, D.) 2049-2063 (McGraw-Hill, New York, 1989).

[3] Ogier de Baulny H, Gérard M, Saudubray JM, Zittoun J. Remethylation defects: guidelines for clinical diagnosis and treatment. Eur J Pediatr. 1998 Apr;157 Suppl 2:S77-83.

[4] Buccianti G, et.al. 5-methyltetrahydrofolate restores endothelial function in uraemic patients on convective haemodyalisis. Nephrol Dial Transplant (2002) 17: 857-864

[5] Anderson, PS (2012, August). Active comparator trial of addition of MTHFR specific support versus standard integrative naturopathic therapy for treating patients with diagnosed Fibromyalgia (FMS) and Chronic Fatigue Syndrome (CFS). Poster Presentation, presented at the American Association of Naturopathic Physicians annual convention, Bellevue, WA.

Vitamin B Complex

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

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

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

Vitamin B Complex

Life Sci. 2012 Dec 10;91(23-24):1187-95. doi: 10.1016/j.lfs.2012.08.025. Epub 2012 Aug 24.

- **B vitamins relieve neuropathic pain behaviors induced by infraorbital nerve constriction in rats.** Kopruszinski CM[1], Reis RC, Chichorro
  - suggest that B vitamins might constitute a relevant adjuvant to control some aspects of the pain afflicting patients suffering from trigeminal neuropathic pain

B Vitamins alleviate indices of neuropathic pain in diabetic rats.

- Jolivalt CG, Mizisin LM, Nelson A, Cunha JM, Ramos KM, Bonke D, Calcutt NA.
- Eur J Pharmacol. 2009 Jun 10;612(1-3):41-7. doi: 10.1016/j.ejphar.2009.04.028. Epub 2009 Apr 23.
- PMID: 19393643

MVI – Multi Vitamin Infusion

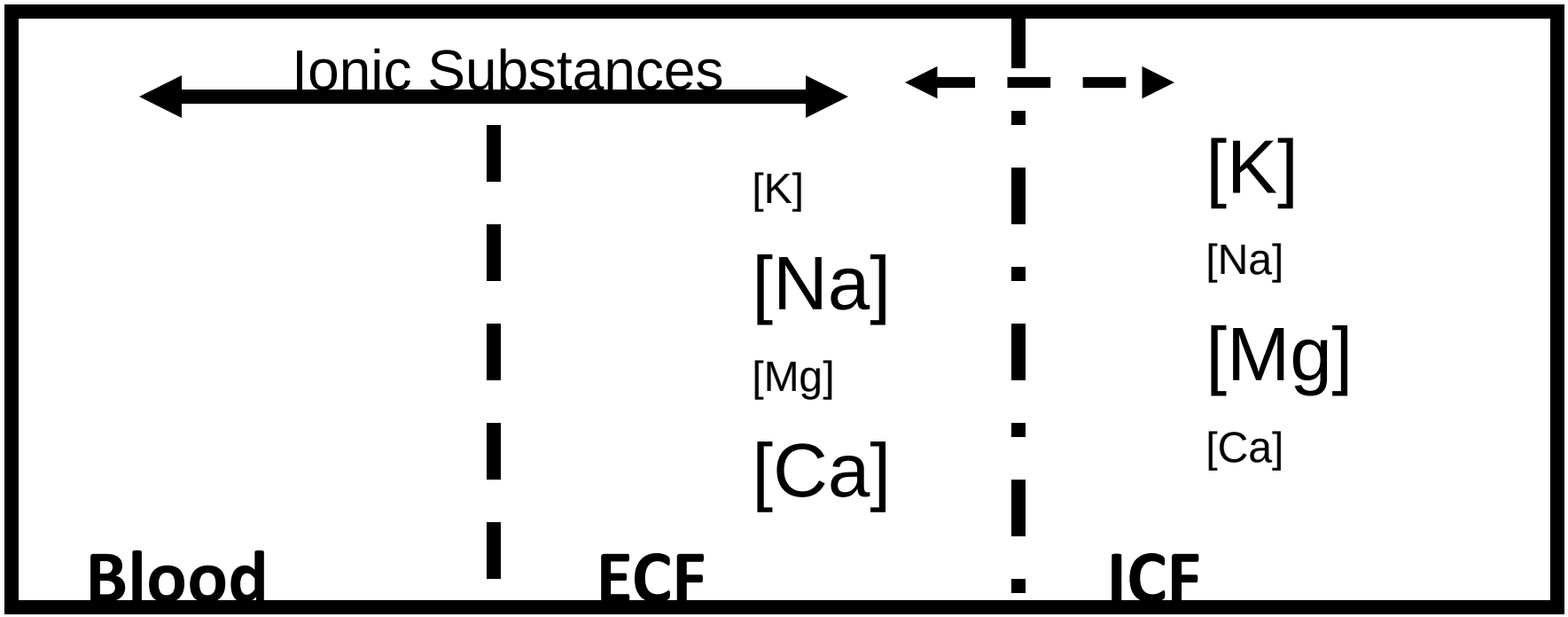
- Mixture of Vitamins:
  - Commercial Solution
    - **Ascorbic Acid** **200 mg**
    - **Vitamin A** **1 mg**
    - **Vitamin D** **5 mcg**
    - **B1: Thiamine HCl** **6 mg**
    - **B2: Riboflavin-5-phos-Na** **3.6 mg**
    - **B6: Pyridoxine HCl** **6 mg**
    - **B5: Dexpanthenol** **15 mg**
    - **B3: Niacinamide** **40 mg**
    - **Vitamin K** **150 mcg**
    - **Vitamin E** **10 mg**
    - **Biotin** **60 mcg**
    - **Folic Acid** **600 mcg**
    - **Cyanocobalamin** **5 mcg**
- Used in depleted patients as an additive nutrient mix
- Average IV dose: One vial

Points to remember:

- Ionic substances (Na, Ca, K…) act the same way they do in normal physiology!
  - So, what if you infuse a high volume of an ion normally found in the ICF?

- Water soluble small molecules are going to go through the capillaries and be available to cells through normal uptake mechanisms.
  - Vitamin C will still favor the ECF and the Cytosolic portion of the ICF
  - Lipid will still access the CM (vascular and cellular, and the lymphatics.)

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.

Activities of agents on the CNS

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

Calcium

- 10% Calcium gluconate
- 10% Calcium chloride,
- 10%Calcium glycerophosphate (Calphosan), contains 50 mg calcium glycerophosphate and 50 mg calcium lactate
- Dosage and administration
  - Gluconate 100-2000 mg (0.465-9.3 mEq) i.v.
    - Infusion rate never greater than 1 mEq/min.

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 – room temperature to avoid precipitation

Calcium

- Adverse reactions: hypotension, bradycardia, arrhythmia, tingling sensations, syncope, cardiac arrest

- Parenteral effects are mainly on nerve conduction and muscle contraction

Calcium

- May have increased requirement for Ca in IV's under some circumstances such as:
  - Chelation remineralization
  - Hypocalcemic patients
  - High dose IV – Vitamin C use

Calcium

- Role:
  - (8.5 – 10.5 mg. / dL Normal range)
  - **Neuromuscular regulation**
  - Skeletal / Bone maintenance
  - Influence enzyme activity
  - Prothrombin → Thrombin conversion
  - **Calcium and Phosphate have a reciprocal relationship**

- Hypercalcemia:
  - Causes:
    - Hyperparathyroid / overdose of Vit. D or Antacids / Multiple myeloma / Parathyroid adenoma
  - Effects:
    - **Arrhythmias / N-V / Constipation / Lethargy** / Anorexia / Dehydration **/ Coma**

Calcium

- Hypocalcemia: **(Life threatening complication: laryngospasm)**
  - Causes:
    - Hypoparathyroidism / Mg. & Vit. D. deficiency
    - Diarrhea / Infection / Trauma / Burns
  - Effects: **(All effects aggravated by High K and low Mg.)**
    - Cramping (See next 2 slides), Neurological sx's
    - **Prolonged Q-T interval**

Calcium deficit: Chovestek's sign

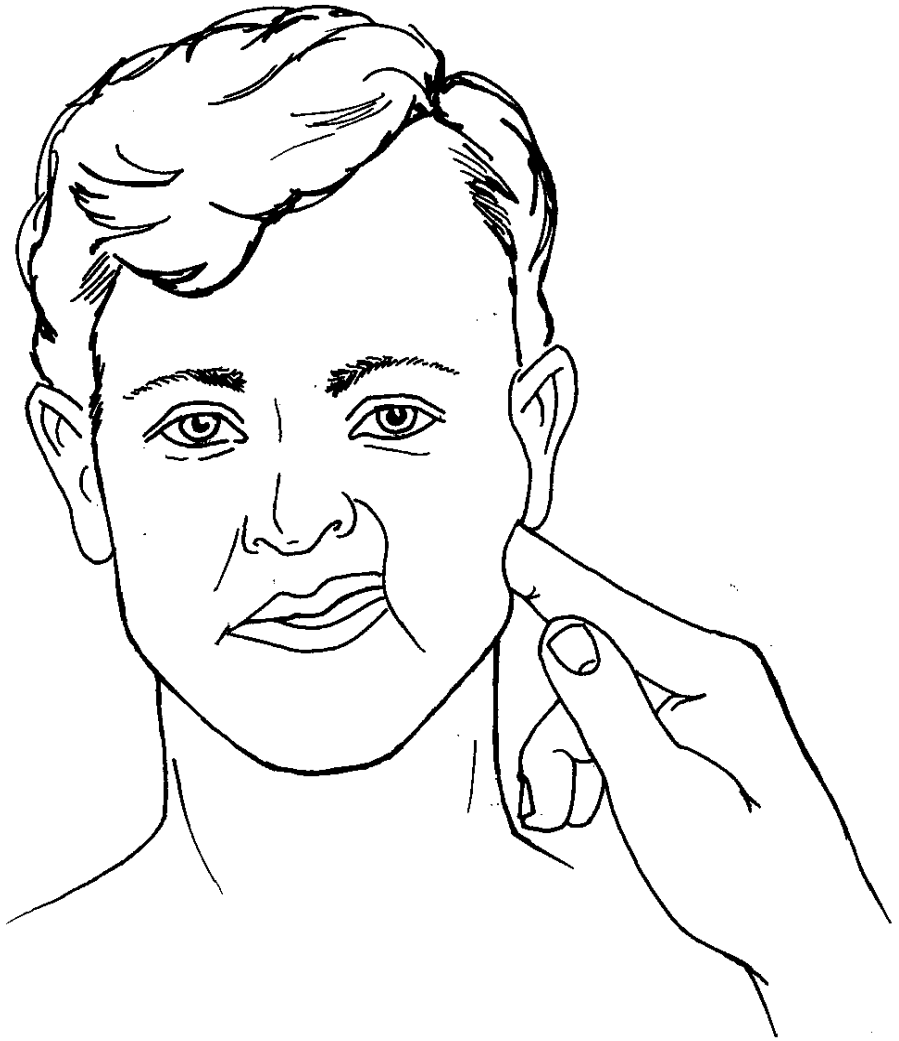


FIG. 4–5. Positive Chvostek's sign, which occurs after tapping the facial nerve approximately 2 cm anterior to the earlobe. Unilateral twitching of the facial muscle occurs in some patients with hypocalcemia or hypomagnesemia.

Calcium deficit: Trousseau's sign

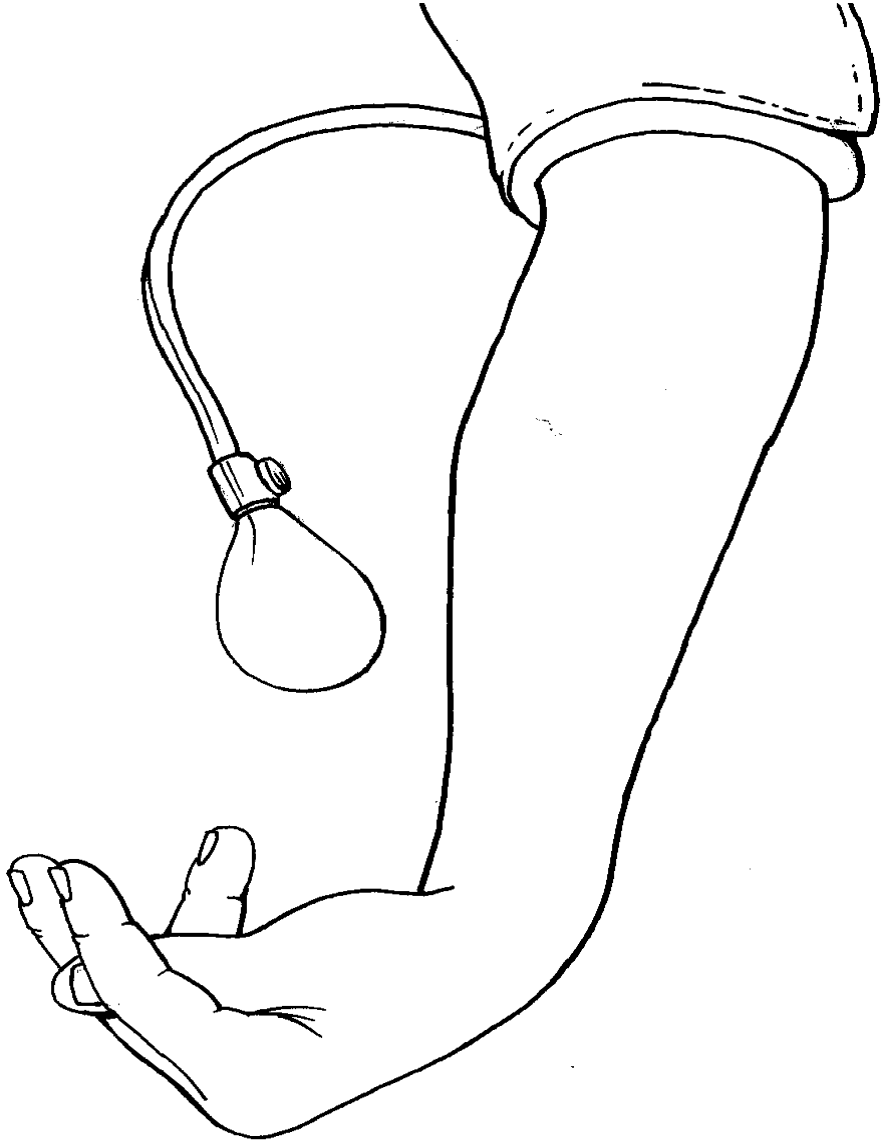


FIG. 4–4. Positive Trousseau's sign. Carpopedal attitude of the hand when blood pressure cuff is place on the arm and inflated above systolic pressure for 3 minutes. A positive reaction is the development of carpal spasm.

Magnesium

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

Magnesium

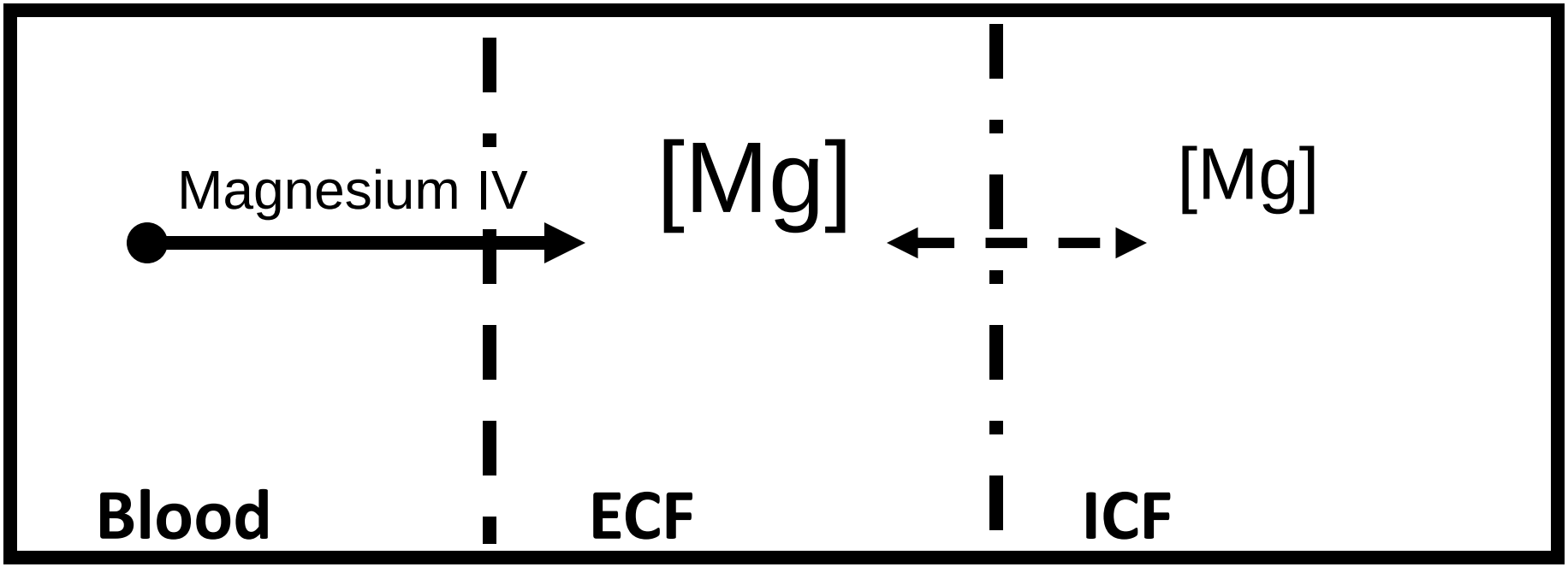
- Dosage & Administration
  - IM: Up to 3 mL 50% adults
    - 1-3 mL 20% pediatric
  - IV: given normal renal function, up to 50 mEq over 4-6 hours (12.5 mL 50% Mg Sulfate)
  - Clinical use
    - Up to 3 mL 50% over 20-30 min, watch for O.D. Sx
    - Up to 6 mL 50% over 2 hours in drip

Magnesium – Clinical

Using Mg Salt in appropriate protocols

- 50% Mg Sulfate: Asthma, muscle cramps, migraine
  - 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

Compartment Dynamics: Magnesium Administration



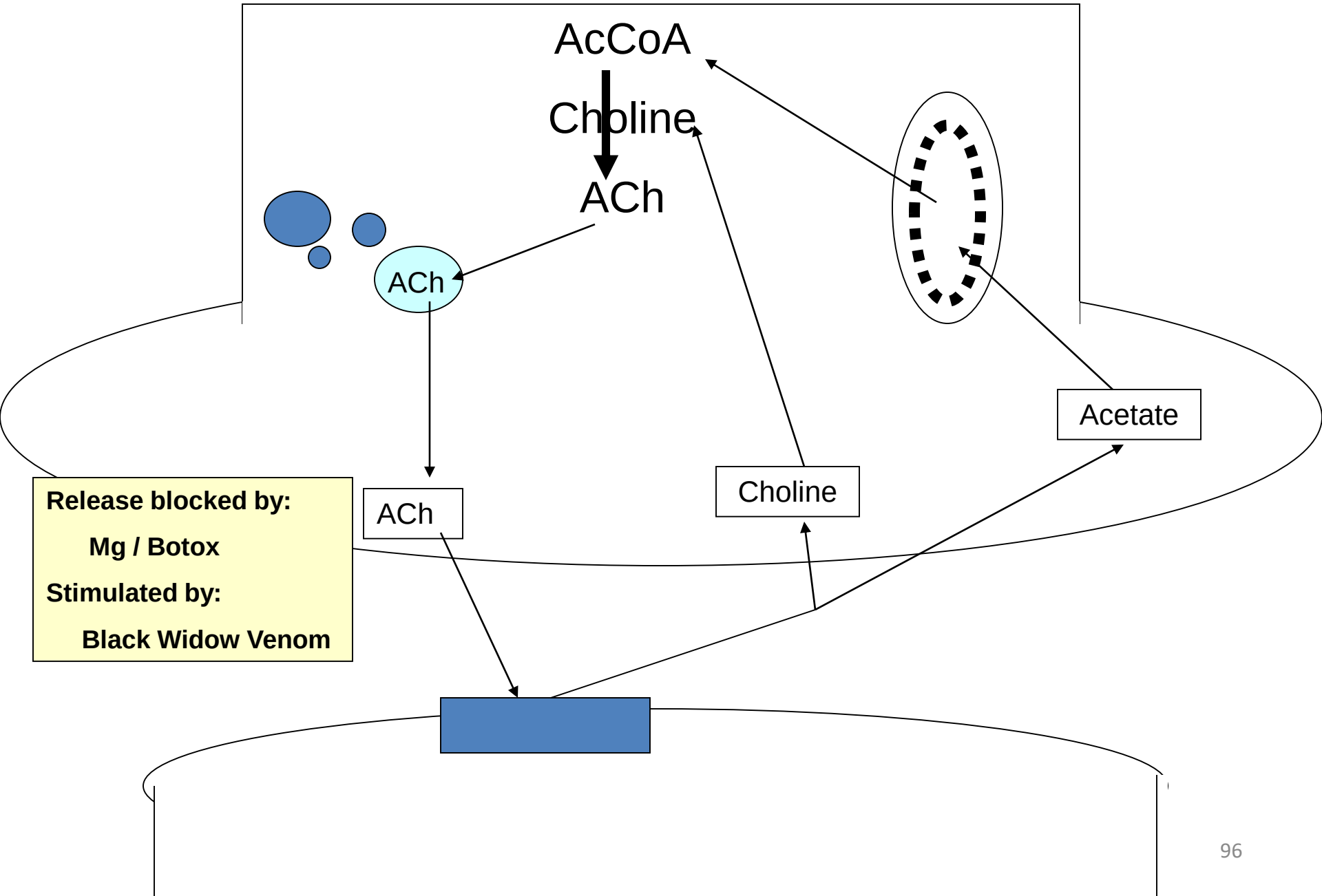
For a time (until the Mg and Ca+ channel gates can equilibrate) The abnormally high ECF Mg will cause a dampening of the normally high Ca ECF and High Mg ICF gradient. The membrane will thus lose some (or all) excitability!

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

Magnesium Effect on Muscle Tissue:

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

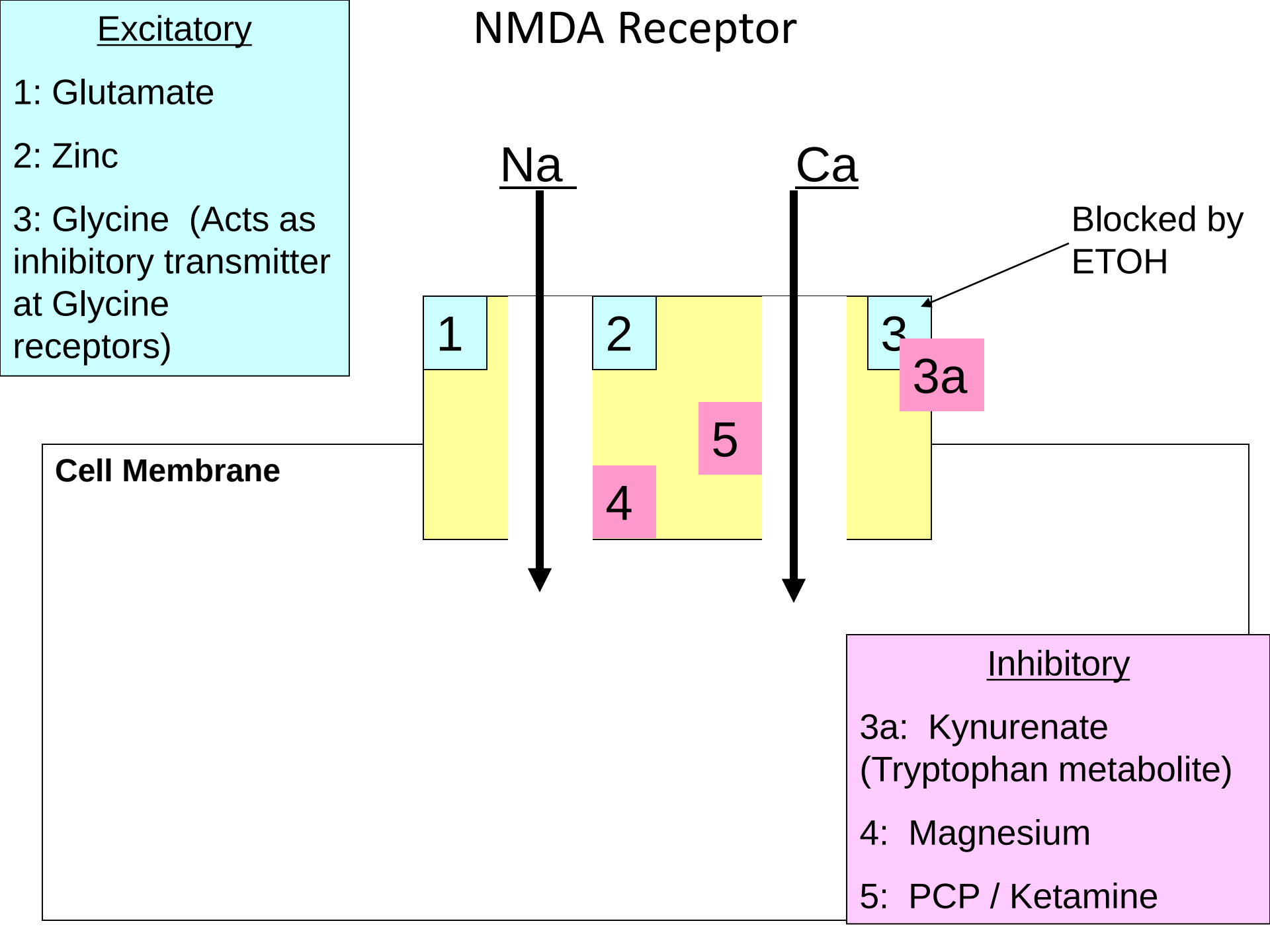
Acetylcholine Synapse



NMDA Receptor

- Primary excitatory receptor complex
- Often categorized with other excitatory "Glutamate" class receptors
  - N-methyl-D-aspartate (Na/Ca/K)
  - Kainate (Na/K ?)
  - AMPA (Na/K)
  - AP4 (Presynaptic inhibition)
  - ACPD (IP3 / DAG)

NMDA Receptor



Can J Anaesth. 2003 Aug-Sep;50(7):732-46.

The therapeutic use of magnesium in anesthesiology, intensive care and emergency medicine: a review: [L'usage therapeutique du magnesium en anesthesiologie, reanimation et medecine d'urgence].

Dube L, Granry JC.
Department of Anesthesiology, University Hospital, Angers, France.

==========

PURPOSE: To review current knowledge concerning the use of magnesium in anesthesiology, intensive care and emergency medicine.

METHODS: References were obtained from Medline(R) (1995 to 2002). All categories of articles (clinical trials, reviews, or meta-analyses) on this topic were selected. The key words used were magnesium, anesthesia, analgesia, emergency medicine, intensive care, surgery, physiology, pharmacology, eclampsia, pheochromocytoma, asthma, and acute myocardial infarction.

Can J Anaesth. 2003 Aug-Sep;50(7):732-46. (Continued)

Principal findings:

- Hypomagnesemia is **frequent postoperatively and in the intensive care** and needs to be detected and corrected to prevent increased morbidity and mortality.
- Magnesium **reduces catecholamine release** and thus allows better control of adrenergic response during intubation or pheochromocytoma surgery.
- It also **decreases the frequency of postoperative rhythm disorders in cardiac surgery as well as convulsive seizures in preeclampsia and their recurrence in eclampsia**.
- The use of **adjuvant magnesium during perioperative analgesia may be beneficial for its antagonist effects on N-methyl-D-aspartate receptors**.
- The precise role of magnesium in the treatment of asthmatic attacks and myocardial infarction in emergency conditions needs to be determined.

CONCLUSIONS: Magnesium has many known indications in anesthesiology and intensive care, and others have been suggested by recent publications. Because of its interactions with drugs used in anesthesia, anesthesiologists and intensive care specialists need to have a clear understanding of the role of this important cation.

PMID: 12944451 [PubMed - in process]

Magnesium Modulation of Calcium Accumulation in Cardiac Mitochondria

- **Respiration-supported Ca ++ uptake in isolated heart mitochondria is decreased by the presence of Mg ++. ……. Differential responses of mitochondrial respiration, as indicated by cytochrome b redox states indicate that the presence of Mg ++ "protects" the ability of heart mitochondria to phosphorylate ADP after Ca ++ uptake. Modulation of Ca ++ uptake by Mg ++ may, therefore, play an important role in protecting intact mitochondrion structural-functional relationships during ischemic episodes. These data thus indicate a role of Mg ++ as a modulator of both uptake of Ca ++ and the form it takes in cardiac mitochondria in response to ischemia and during normal metabolism, through its stimulation. ……**

Burton B. Silver, PhD

Development of Cellular Magnesium Nano-Analysis in Treatment of Clinical Magnesium Deficiency Journal of the American College of Nutrition, Vol. 23, No. 6, 732S-737S (2004)

Mg $^{++}$ has biologic effects that parallel the pharmacologic effects of Ca $^{++}$ blocker drugs. To determine whether increased i.c. levels of Mg $^{++}$ [Mg $^{++}$] $_i$ enhance brachial artery (BA) vasoreactivity, prospectively flow-mediated endothelium-dependent (FMED) and endothelium-independent sublingual nitroglycerin (NTG) BA vaso-reactivity (BRT) were determined in 49 stable CAD patients (40 men, 9 women, mean age 68 ± 9 years)

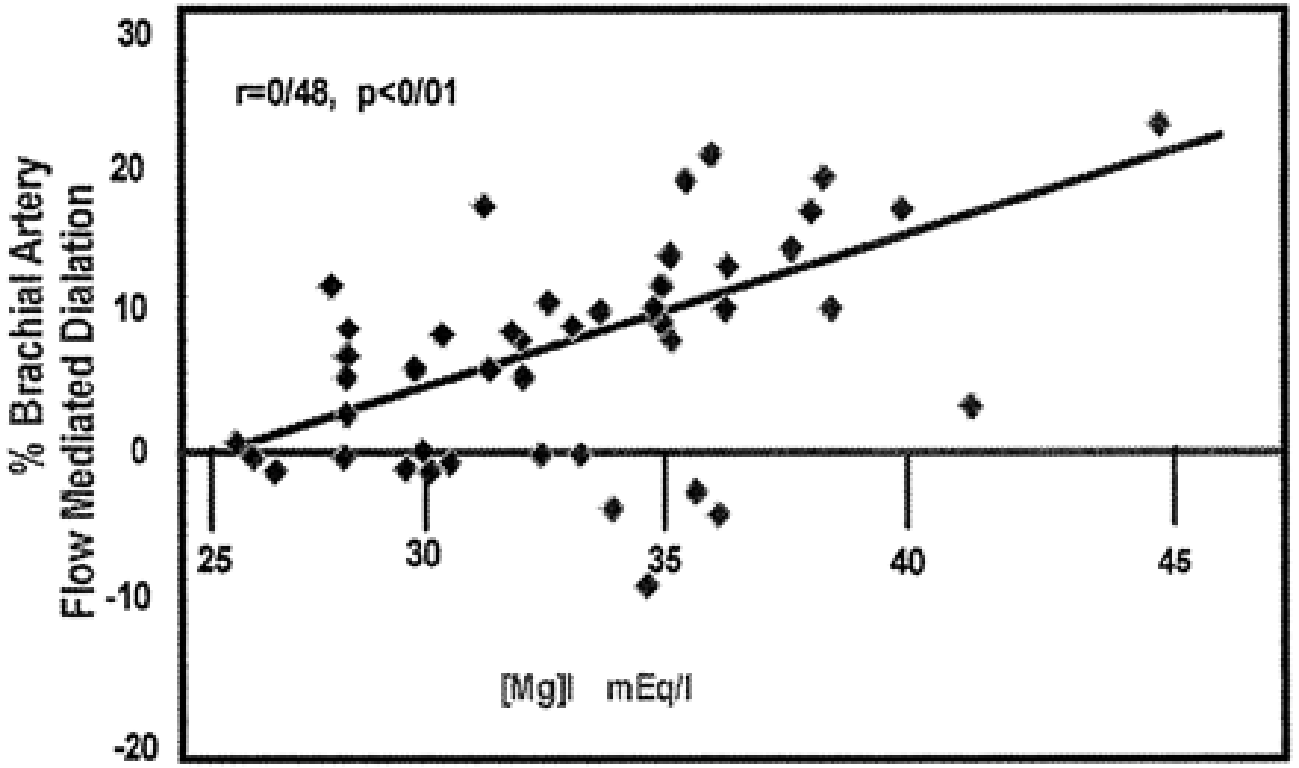


Fig. 7. Correlation of percent change in baseline brachial artery flow-mediated vasodilation (%FMD) and baseline intracellular lever, ([Mg]i), in 50 subjects showing a linear correlation.

Burton B. Silver, PhD

Development of Cellular Magnesium Nano-Analysis in Treatment of Clinical Magnesium Deficiency Journal of the American College of Nutrition, Vol. 23, No. 6, 732S-737S (2004)

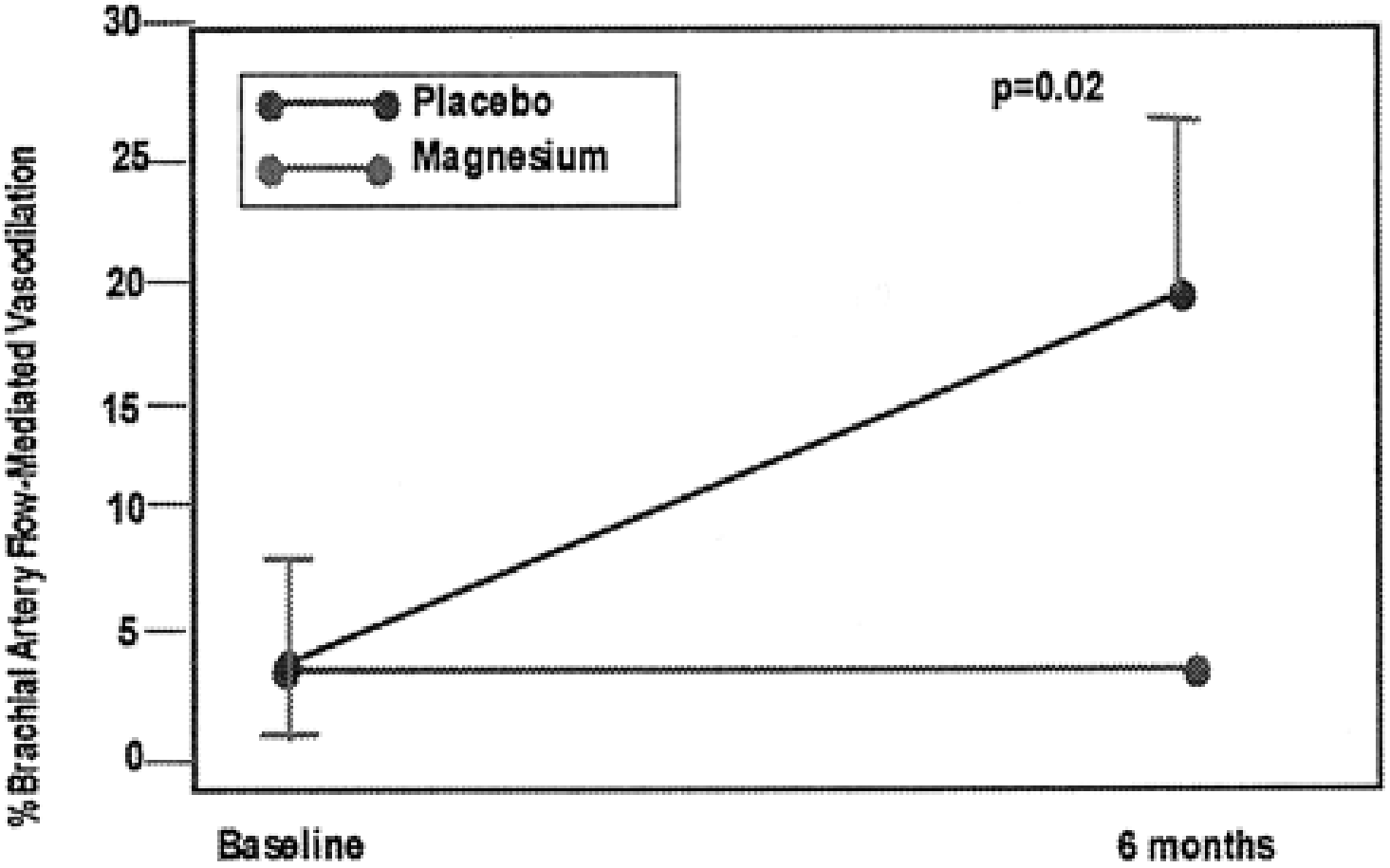


Fig. 8. Percent change in endothelium-dependent brachial artery flow-mediated vasodilation (%FMD) in placebo (horizontal line) (n = 25) and magnesium (diagonal line) (n = 25) at baseline and after 6 months.

Burton B. Silver, PhD

Development of Cellular Magnesium Nano-Analysis in Treatment of Clinical Magnesium Deficiency Journal of the American College of Nutrition, Vol. 23, No. 6, 732S-737S (2004)

Effect of IV Mg ++ in Patients with ST elevation and Acute Myocardial Infarction

Using the EXA tm sublingual cell evaluation, magnesium intravenous intervention studies were done on 22 myocardial infarct patients who were compared to healthy controls and noncardiac patients. Mean Mg ++ in infarct patients was 30.7 ± 0.4 compared to 15 control subjects whose cellular Mg ++ levels were 35.0 ± 0.5, p < .0001. Infarct patients received a mean dose of 36 ± 6 mmol/24 hrs of intravenous Mg 2SO 4. No Mg ++ was given after the second 24 hours of the study. Intracellular [Mg 2+] i rose significantly in the infarct patients over the first 24 hours and the magnitude of the increase was greater in those who received higher doses of intravenous magnesium sulfate. Despite the fact that Mg 2SO 4 was not given after the first 24 hours, mean sublingual magnesium **continued to rise for 48 hours after the first dose of magnesium sulfate** (from 30.7 ± 0.4 to 35.2 ± 0.6 mEq/L) suggesting that magnesium may be moving from the vascular space to the tissues over 48 hours

- **Burton B. Silver, PhD**
- **Development of Cellular Magnesium Nano-Analysis in Treatment of Clinical Magnesium Deficiency** Journal of the American College of Nutrition, Vol. 23, No. 6, 732S-737S (2004)

I.V. Mg Research-Migraines

Bigal, M. E., C. A. Bordini, et al. (2002). "Intravenous magnesium sulfate in the acute treatment of migraine without aura and migraine with aura. A randomized, double-blind, placebo-controlled study." Cephalalgia 22(5): 345-53.

- Sixty patients in each group were assigned at random to receive magnesium sulfate, 1000 mg intravenously, or 0.9% physiological saline, 10 ml. We used seven parameters of analgesic evaluation and an analogue scale to assess nausea, photophobia and phonophobia. Mg sulfate can be used for the treatment of all sxs in migraine with aura, or as an adjuvant therapy for associated symptoms in patients with migraine without aura.

I.V. Mg Research-Bronchial Hyper-reactivity

Schenk, P., K. Vonbank, et al. (2001). "Intravenous magnesium sulfate for bronchial hyper-reactivity: a randomized, controlled, double-blind study." Clin Pharmacol Ther 69(5): 365-71.

- In the magnesium group, 30% of the subjects reached a normal PC(20) or decrease of FEV in 1 second by 20% compared with 10% in the placebo group. We conclude that intravenous magnesium sulfate significantly improved bronchial hyper-reactivity and may serve as an adjunct to standard treatment.

Calcium and Magnesium IV Products

- Between ‘salt’ forms calculating mg / mL based on product concentration may not yield an equivalent dose of the electrolyte in the IV solution.
- Example:
  - Calcium in the chloride and gluconate forms are both 10% solutions (100 mg/mL).
  - 10 mL Calcium gluconate (1000 mg) yields 4.65 mEq Ca++
  - 10 mL Calcium chloride (1000 mg) yields 13.6 mEq Ca++

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

Calcium and Magnesium IV Products

- Therefore on an equivalent ionic basis:
  - 1 mL Calcium chloride is equal to 2.92 mL Calcium gluconate
  - 1 mL Calcium gluconate is equal to 0.34 mL Calcium chloride
  - 1 mL Magnesium sulfate is equal to 2.06 mL magnesium chloride
  - 1 mL Magnesium chloride is equal to 0.49 mL Magnesium sulfate

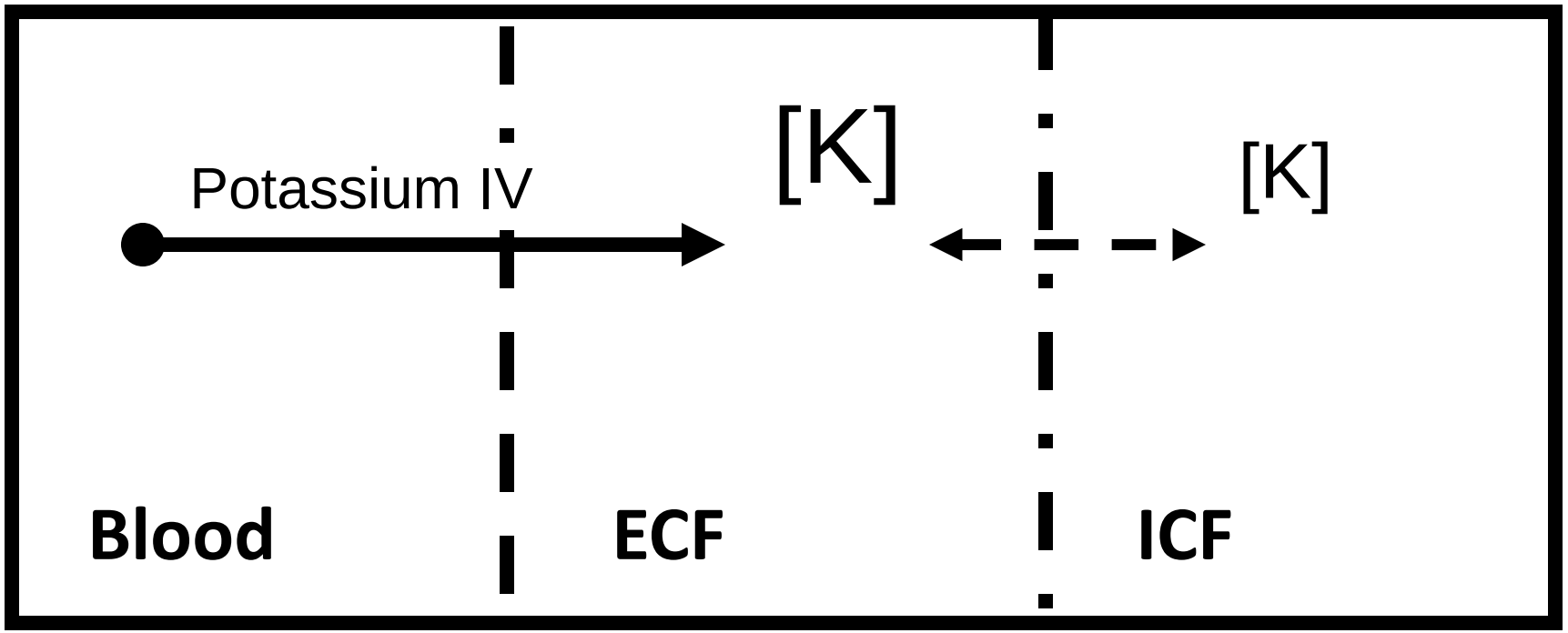
Potassium

- Potassium chloride, 2mEq/mL is principle 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

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

Compartment Dynamics: Potassium Administration

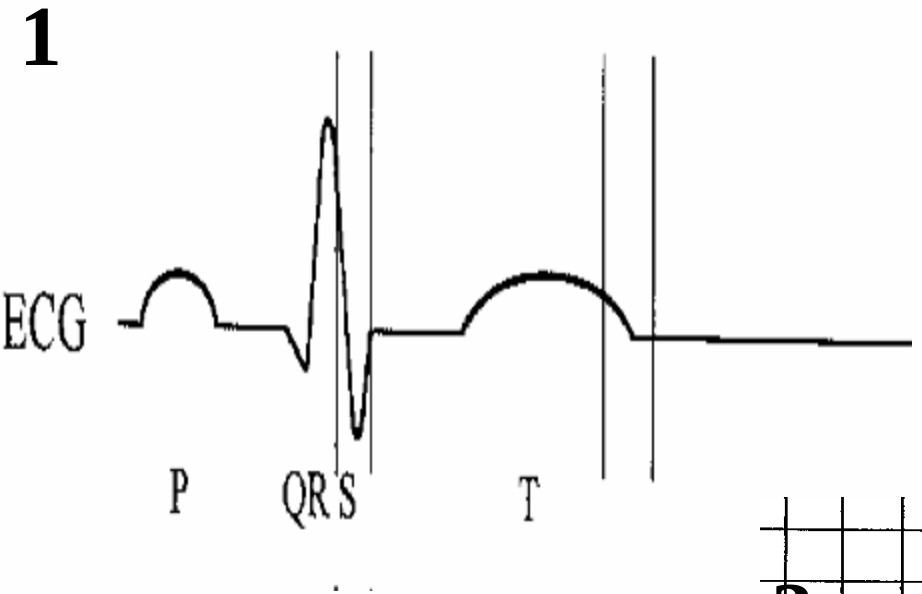


For a time (until the Na/K pump and channel gates can equilibrate) The abnormally high ECF K+ will cause a dampening of the high Na ECF and High K ICF gradient. The membrane will thus lose some (or all) excitability!

ECG Changes and Potassium

1: Normal ECG 2: Hypokalemia 3: Hyperkalemia

1



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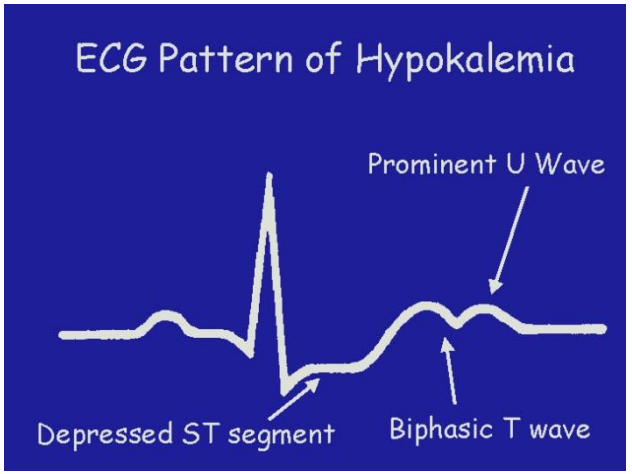

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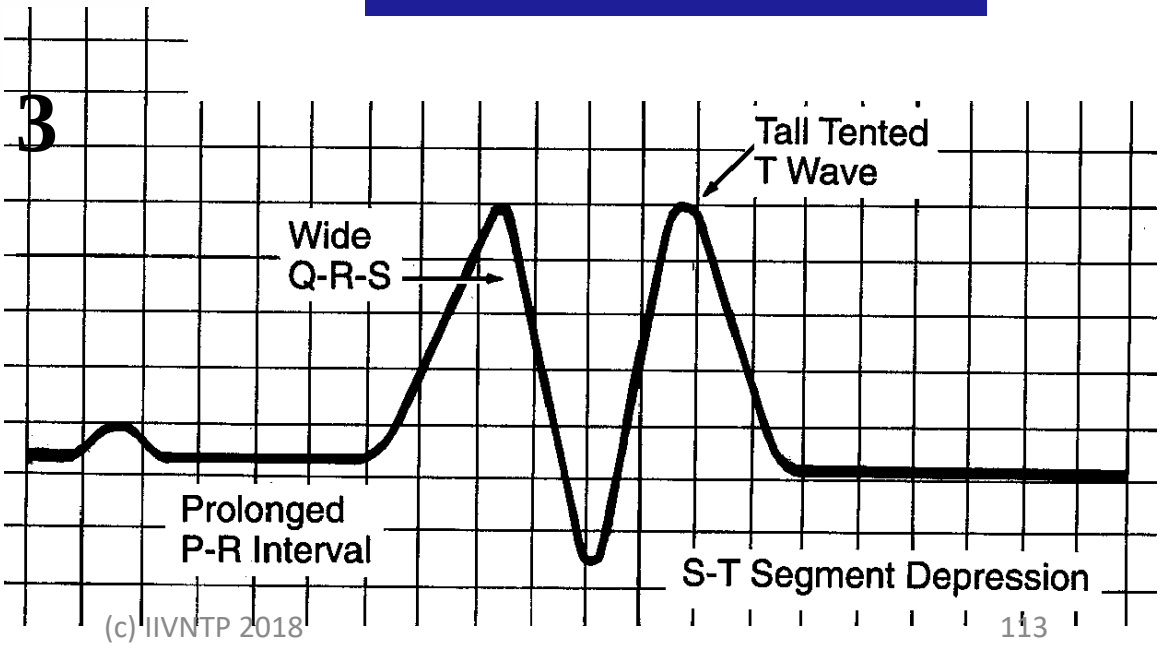


NEVER GIVE POTASSIUM IM OR SQ !!!!!

CRITICAL GUIDELINES FOR ADMINISTRATION OF POTASSIUM

Never give a potassium I.V. push.

Potassium chloride (KCl) should be added to a nondextrose solution such as isotonic saline to treat severe hypokalemia because administration of KCl in a dextrose solution may cause a small reduction in the serum potassium level.

Never administer concentrated potassium solutions without first diluting them as directed.

KCl preparations greater than 60 mEq/L **should not** be given in a peripheral vein. Concentrations greater than 8 mEq/100 mL can cause pain and irritation of peripheral veins and lead to postinfusion phlebitis (Rapp, 1987).

When adding KCl to infusion solutions, especially plastic systems, make sure the KCl mixes with the solution thoroughly. Invert and agitate the container to ensure mixing. ***Do not add KCl to a hanging container!***

For patients with any degree of renal insufficiency or heart block, Zull (1989) recommends reducing the infusion by 50 percent. For example, 5 to 10 mEq/h rather than 10 to 20 mEq/h.

Administer potassium at a rate not to exceed 10 mEq/h through peripheral veins (Kokko & Tannen, 1990; Gahart, 1994).

For patients with extreme hypokalemia, rates should be no more than 40 mEq/h while ECG is constantly monitored (Kokko & Tannen, 1990).

If KCl is administered into the subcutaneous tissue (infiltration), it is extremely irritating and can cause serious tissue loss. Use extravasation protocol in this situation.

CRITICAL GUIDELINES FOR REMOVAL OF POTASSIUM

Treatment Guidelines

- **Sodium polystyrene sulfonate** is a cation exchange resin that removes potassium from the body by exchanging sodium for potassium in the intestinal tract. This method should not be the sole treatment for severe hyperkalemia because of its slow onset.

Oral sodium polystyrene sulfonate (15 to 30 g); may repeat every 4 to 6 hours as needed; it removes potassium 1 to 2 hours.

Rectal sodium polystyrene sulfonate (50 g) as retention enema; when administered, use an inflated rectal catheter to ensure retention of the dissolved resin for 30 to 60 minutes; it removes potassium in 30 to 60 minutes; each enema can lower the plasma potassium concentration by 0.5 to 1.0 mEq/L (Rose, 1989)

- **Dialysis** is used when more aggressive methods are needed. Peritoneal dialysis is not as effective as hemodialysis. Whereas peritoneal dialysis can remove approximately 10 to 15 mEq/h, hemodialysis can remove 25 to 35 mEq/h (Kokko & Tannen, 1990).
- **Glucose and insulin**

Insulin facilitates potassium movement into the cells, reducing the plasma potassium level. Glucose administration in nondiabetic patients may cause a marked increase in insulin release from the pancreas, producing desired plasma potassium-lowering effects (Rose, 1989).

500 mL of 10 percent dextrose with 15 to 10 U of regular insulin over 1 hour: The potassium-lowering effects are delayed about 30 minutes but are effective for 4 to 6 hours (Zull, 1989).

- **Emergency measures**

Calcium gluconate: 10 mL of 10 percent calcium gluconate administered slowly over 2 to 3 minutes. Administer only to patients who need immediate myocardial protection against toxic effects of severe hyperkalemia. Protective effect begins within 1 to 2 minutes and lasts only 30 to 60 minutes (Spital, 1989).

Sodium bicarbonate: 45 mEq (1 ampule of 7.5% sodium bicarbonate) infused slowly over 5 minutes. This temporarily shifts potassium into the cells and is helpful in patients with metabolic acidosis.

Copper

- Copper sulfate, 0.4 mg/mL
- Copper chloride, 0.4 mg/mL

- Dosage and administraton
  - 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

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

Manganese

- Manganese can cause neuropsychiatric symptoms; irritability, excitement, compulsive behavior, Parkinson Disease like symptoms (Google Groote Syndrome)
- Essential nutrient, serves as enzyme activator as in H202 ; Mn-SOD, pyruvate carboxylase, cholinesterase
  - H_2O_2 + Mn H_2O + MnO

Molybdenum

- Ammonium molybdate, 25 mcg/mL

- Dose and administration
  - IV: 5 mL as part of mineral replacement protocols
  - 5-10 mL for patients deficient in liver phase II sulfation detoxification pathway

Molybdenum

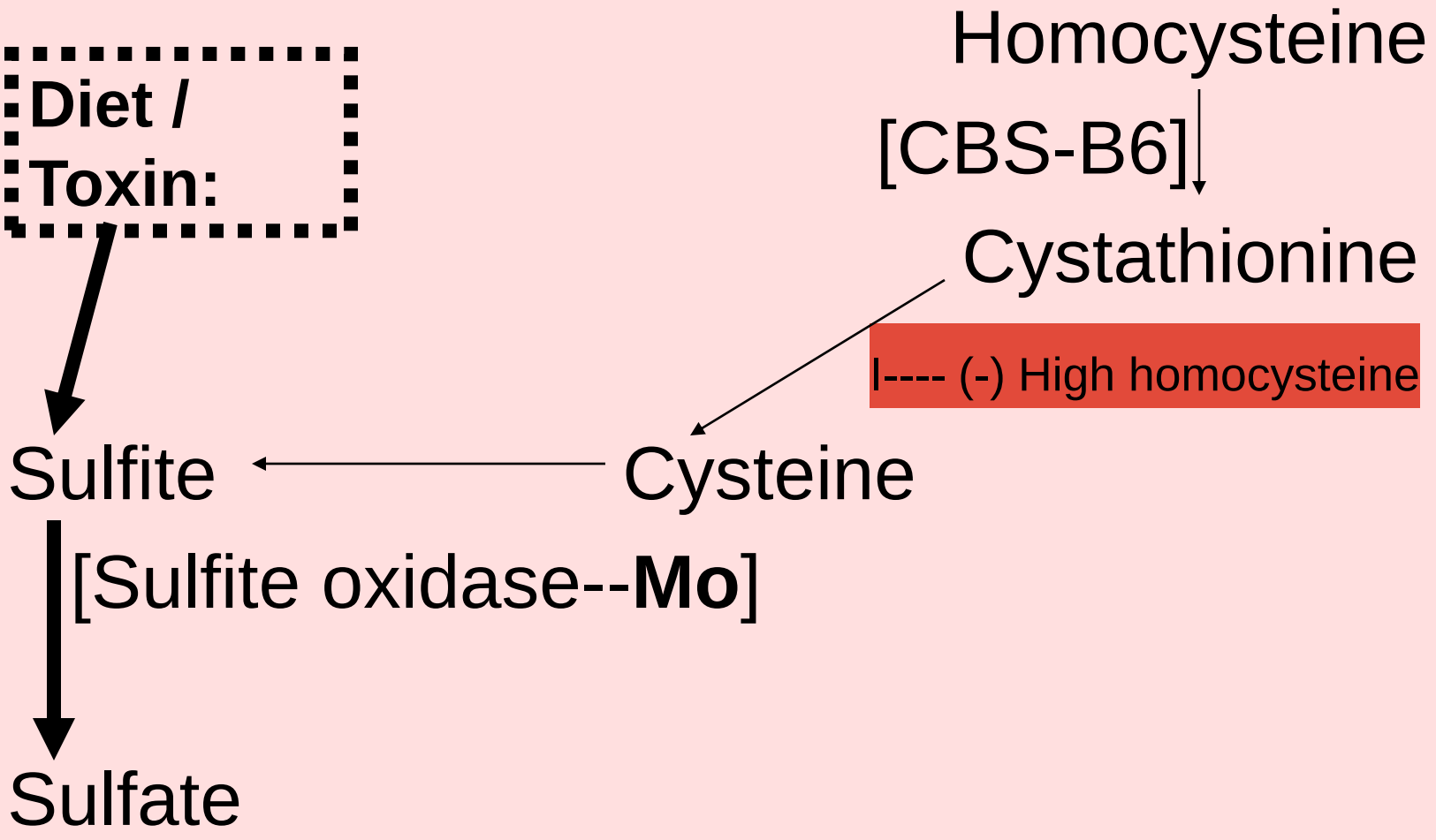
Beneficial in copper toxicity

– 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

Catalytic role of Molybdenum in Sulfite clearance



Molybdenum

Observational and experimental studies have shown an association between molybdenum and bipolar disorder (1). There is also strong evidence for the neuro-protective 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 sulferase gene that is responsible for xanthinuria type II. Metabolism. 2003 Nov; 52(11): 1501-4.

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
- Avoid exposing solution to sun, due to photo degradation

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

Stock Element Formulas:

Additive:	MTE-4	MTE-4 Conc.	MTE-5	MTE-5 Conc.
Zinc	1 mg	5 mg	1 mg	5 mg
Copper	0.4 mg	1 mg	0.4 mg	1 mg
Manganese	0.1 mg	0.5 mg	0.1 mg	0.5 mg
Chromium	4 mcg	10 mcg	4 mcg	10 mcg
Selenium	None	None	20 mcg	60 mcg

Zinc

- Zinc chloride, 1 mg/mL
- Zinc sulfate, 1 mg/mL and 5 mg/mL (concentrate)
  - Can be compounded in higher concentrations
- Dose and administration
  - IV: sulfate is best due to better solubility and stability characteristics
  - Concentration of zinc in infusates should not be greater than 10 mg/L
    - IF- given in continuous infusions over long periods.
      - If the patient's parenteral requirement is greater than 30 mg and administered in periodic IVMNT infusions - this 10 mg/L limit may be increased
  - Doses of 50-100 mg/day can be tolerated in zinc deficiency

Zinc

- Adverse and allergic reactions do not occur
- Toxic reactions to parenteral overdose range from mild to lethal
  - An error resulting in 23 mg in infusate lead to assymptomatic hyperamylasemia
  - 9.8 mg over one hour caused flushing, blurred vision, sweating
  - 1.6 gram error lead to death
- 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

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

Parenteral Iron

Globular protein structure human hemoglobin

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.

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

- Contraindications to parenteral iron: Hypersensitivity to any of the three parenteral iron products, anemias not associated with iron deficiency, suspected iron overload
- Iron sucrose at a dose of 100 mg can be administered safely and effectively by i.v. push (5 min) or infusion (15–30 min) without a test dose [*Van Wyck DB, Cavallo G, Spinowitz BS et al. Safety and efficacy of iron sucrose in patients sensitive to iron dextran: North American Clinical Trial. Am J Kidney Dis2000; 36: 88–97*].

- Hoigne [*Hoigne R, Breymann C, Kunzi UP, Brunner F. Parenteral iron therapy: problems and possible solutions. Schweiz Med Wochenschr1998; 128: 528–535*] analysed 160,000 doses of 100 mg iron sucrose administered to patients undergoing regular hemodialysis, calculated as 8100 patient-years. No cases of life-threatening adverse reactions occurred. There were five to seven instances of rapidly reversible hypotension, 10 cases of flushing, one case of urticaria and one case of vomiting with diarrhea

Iron

- Large intravenous doses, such as used with total dose infusions (TDI), have been associated with an increased incidence of adverse effects.
- The adverse effects frequently are delayed (1-2 days) reactions typified by one or more of the following symptoms: arthralgia, backache, chills, dizziness, moderate to high fever, headache, malaise, myalgia, nausea, and vomiting. The onset is usually 24-48 hours after administration and symptoms generally subside within 3-4 days.
- These symptoms have also been reported following intramuscular injection and generally subside within 3-7 days.

Other reactions – Iron dextran

Non-dose related: Hypersensitivity reactions characterized by anaphylactic shock, CV collapse, cardiac arrest, bronchospasm, oral or pharyngeal edema, or dyspnea

Sensitive patients, e.g. asthma, allergies, may benefit from pretreatment with 50 mg diphenhydramine

Contraindications to parenteral iron: Hypersensitivity to any of the three parenteral iron products, anemias not associated with iron deficiency, suspected iron overload

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.

Iron

How supplied

- Dexferrum, InFeD -- Iron Dextran
- Feraheme – Ferumoxytol
- Ferrlecit – Sodium Ferric Gluconate
- Venofer – Iron Sucrose
- Injectafer – Ferric carboxymaltose

Dose – based on iron dextran

- Calculate total dose using equations based on LBW then give 2ml i.m. (100mg) daily until calculated dose is given
- – OR, give IV infusion of total dose at once
- Dose(ml) = 0.0442(desired Hgb – observed x LBW + (0.26 x LBW)

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

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

Iron Dextran

Iron

- Iron Administration – Dextran

  IV: Dilute total dose in 250 to 1000ml of normal saline, use a few ml as a test dose, wait 15 minutes then infuse remainder over 4 to 6 hours
- Note: Due to the HIGH reaction rate (1 in 100 infusions) and the long administration time required IVNTP does NOT recommend using Iron Dextran as an IV additive.
- Additionally the other forms work better in the IV format.
- As an IM (Z-Track) it is better tolerated.

Iron

- Iron Administration for IM
  - Lay patient supine for iron administration i.m.
  - IM: Test dose of 0.5ml must be given over 30 seconds, wait 1 hour, then give remainder at 1ml (50mg) per minute
  - IM administration MUST be give deep i.m. using Z-track technique. Aspirate with syringe prior to injection

Iron - Sucrose

Iron sucrose

- Iron sucrose at a dose of 100 mg can be administered safely and effectively by i.v. push (5 min) or infusion (15–30 min) without a test dose
- [*Van Wyck DB, Cavallo G, Spinowitz BS et al. Safety and efficacy of iron sucrose in patients sensitive to iron dextran: North American Clinical Trial. Am J Kidney Dis2000; 36: 88–97*].

- Anaylsis of160,000 doses of 100 mg iron sucrose administered to patients undergoing regular hemodialysis, calculated as 8100 patient-years. No cases of life-threatening adverse reactions occurred. There were five to seven instances of rapidly reversible hypotension, 10 cases of flushing, one case of urticaria and one case of vomiting with diarrhea.

Hoigne [*Hoigne R, Breymann C, Kunzi UP, Brunner F. Parenteral iron therapy: problems and possible solutions. Schweiz Med Wochenschr1998; 128: 528–535*

Venofer® : Iron sucrose
Venofer (iron sucrose injection, USP) is a brown, sterile, aqueous, complex of polynuclear iron (III)- hydroxide in sucrose for intravenous use

• Each mL contains 20 mg elemental iron as iron sucrose in water for injection. Venofer is available in 5 mL single dose vials (100 mg elemental iron per 5 mL) and 10 mL single dose vials (200 mg elemental iron per 10 mL)
• The drug product contains approximately 30% sucrose w/v (300 mg/mL) and has a pH of 10.5- 11.1. The product contains no preservatives. The osmolarity of the injection is 1,250 mOsmol/L
• Venofer is available in both 100 mg/5 mL and 200 mg/10 mL single dose vials
• **Administration:** Venofer must only be administered intravenously either by slow injection or by infusion. Not for i.m. use!
• Venofer does not require a test dose prior to therapy. Staff vigilance when administering any intravenous iron product is recommended
• **Non-Dialysis Dependent-Chronic Kidney Disease Patients and iron deficient patients :** Venofer® is administered as a total cumulative dose of 1,000 mg over a 14 day period as a 200 mg slow IV injection undiluted over 2 to 5 minutes on 5 different occasions within the 14 day period.
• There is limited experience with administration of an infusion of 500 mg of Venofer®, diluted in a maximum of 250 mL of 0.9% NaCl, over a period of 3.5-4 hours on day 1 and day 14; hypotension occurred in 2 of 30 patients treated.

Venofer Hypersensitivity Reactions

In clinical studies, several patients experienced hypersensitivity reactions presenting with wheezing, dyspnea, hypotension, rashes, or pruritus. Serious episodes of hypotension occurred in 2 patients treated with Venofer at a dose of 500 mg.

The post-marketing spontaneous reporting system includes reports of patients who experienced serious or life-threatening reactions (anaphylactic shock, loss of consciousness or collapse, bronchospasm with dyspnea, or convulsion) associated with Venofer administration.

One hundred thirty (11%) of the 1,151 patients evaluated in the 4 U.S. trials in HDD-CKD patients (studies A, B and the two post marketing studies) had prior other intravenous iron therapy and were reported to be intolerant (defined as precluding further use of that iron product). When these patients were treated with Venofer there were no occurrences of adverse events that precluded further use of Venofer

A complete listing of treatment-emergent adverse events is available at http://www.rxlist.com/venofer-drug.htm#

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Iron - Gluconate

Ferrous Gluconate

Ferrous Gluconate for IV injection

- How Supplied
  - 5 mL per ampule: 10 ampules per package
- - contains 62.5 mg (12.5 mg/mL) of elemental iron:
- sodium salt of a ferric ion
- carbohydrate complex in an alkaline aqueous solution with approximately 20% sucrose (195 mg/mL) in water for injection,
- *sodium ferric gluconate complex in sucrose*

Ferrous Gluconate

- pH 7.7 – 9.7
- Preservative: Each mL contains 9 mg of benzyl alcohol as an inactive ingredient. (Avoid in all neonates).
- Therapeutic class: Hematinic

- Store at 20 – 25° C (68 – 77° F)
- Short term: stable to 15 – 30° C (59 – 86° F). Do not freeze.

Ferrous Gluconate

- Ferrous gluconate(as any of the iron products) may be expected to reduce the absorption of concomitantly administered oral iron preparations.
- Do not mix ferrous gluconate with other medications, or add to parenteral nutrition solutions for intravenous infusion.
  - The compatibility of ferrous gluconate with intravenous infusion vehicles other than 0.9% sodium chloride has not been evaluated.

- use immediately after dilution.

Ferrous Gluconate

- Typical dosing
- 62.5 mg in 100cc NS
- 125 mg in 100cc NS
- Initial infusion start with lower amount
  - after establishing no reaction to product, if a pt has had prior rx to any of the dextran products, a reaction maybe likely.
- Minimum infusion time for both = 1-1 ½ hour, longer often required due to better tolerance.

Ferrous Gluconate

- IM
- compounded
- Ferrus Gluconate 60mg, procaine 10mg, B12 5mg/ml. *
  - 2 ml vial
  - Short shelf life

*contributed by Dr. Werner Vosloo

Iron - carboxymaltose

Ferric carboxymaltose

- Typical dosing
- 750 mg in 100cc -250 NS
- 750 mg in 100cc – 250 NS
- Done with 2 infusions to reach max 1500 mg.
- Minimum infusion time= 15 min, we highly advise 1 hour or more.
- SPENDY!! Around $1050 per vial wholesale cost

Conclusion on Infusion of Fe

- General advice;
- Use either Ferlicit or Venofer (not Dexferrum) for IV
- Plan on a series of 10 IV's at 1X a week (1 Amp of Fe in 100-250 mL NS or D5W)
- Ideally follow each Fe IV with a small Vit-Min IV (just not in same bag)
- After the 10 IV Fe wait 3-4 weeks and re-run the CBC, Ferritin, TIBC etc
- Although less than Dexferrum recall that you need to be ready for allergic reactions with IV Fe

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