
Micronutrients in critical illness

K. Sriram MD FRCS(C) FACS
Chairman, Division of Surgical Critical Care,
Chief, Section of Surgical Nutrition; Stroger
Hospital (formerly Cook County Hospital)
Associate Professor of Surgery, Rush
University, Chicago, IL, USA

Outline of presentation

- Full text and references can be sent if requested (ksriram41@hotmail.com)
 - Actual dosages and numbers will not be used; only general guidelines are presented
 - General discussion of absorption, interactions and toxicity
 - Specific micronutrients will be addressed focusing on clinical situations
 - Detailed discussion on anti-oxidants is beyond the scope of this presentation
 - Information of practical use
-

Definitions

- The term “micronutrient” includes vitamins and trace elements
 - Vitamins are substances not generally synthesized by the body and are cofactors for various enzymes
 - Trace elements are metals present in very minute quantities and act as cofactors or as part of the structure of specific enzymes
-

General functions

- Micronutrients affect fundamental biological processes
 - Deficiencies affect various biochemical processes and enzymatic functions.....
resulting in organ dysfunction, poor wound healing and altered immune status
with deleterious sequelae
-

An important component of nutritional support

- Comparison to a music symphony
 - Comparison to a digital music system
 - Contribution of micronutrients to the overall efficacy of nutritional support is substantial
-

CLASSIFICATION

- Vitamins: Fat or water soluble
- Trace elements: More complex



CLASSIFICATION:

Trace elements can be classified into three groups:

1. **Cationic elements:** Zn, Fe, Mn and Cu which are absorbed from the gut with variable efficiency

and whose homeostatic control is mediated by the liver and gastrointestinal tract

2. **Anionic elements**: Cr, Se, Mo and I which are absorbed efficiently by the gut and excreted mainly in the kidneys

3. Those that exist as **organic compounds**, eg selenoamino acids, Cr in “glucose tolerance factor”, heme Fe and Co in cobalamin

Requirement guidelines

- The American Medical Association has established guidelines for the 13 essential vitamins and for trace elements (Cr, Cr, Co, Fe, Fl, I, Mo, Mn, Se, Zn)
- Typically applicable to the general healthy population. Requirements in critically ill patients are unknown

1. Nutrition Advisory Group, *JPEN J Parenter Enteral Nutr*, 3, 1979
 2. American Medical Association, Dept of Foods and Nutrition, *JAMA*, 241, 2051, 1979
-

Requirement guidelines, pitfalls

- Decreased serum levels do not indicate actual deficiencies and represent redistribution; may actually be a beneficial and adaptive response, as some vitamins at high doses function as pro-oxidants.
 - Benefits of supplementation, which may not result in increased serum levels, are also unclear
-

Requirements in diseased states

The Food and Drug Administration (FDA)(USA) has recognized that IV vitamin requirements (specifically vitamins B₁, B₆, C and K) are increased in disease states

Manufacturers are instructed to modify their products but a similar recommendation for trace elements has not been initiated

Food and Drug Administration (FDA) Parenteral multivitamin products; Drugs for human use; Drug efficacy study implementation; Amendment, Federal Register, 65(77), 21200-21201, 2000

Time before deficiency

Earliest Time on TPN Before Deficiency Reported



Zinc :	2 weeks
Copper :	5 weeks
Selenium :	4 weeks
Chromium :	5 months

Guidelines

- Vitamins and trace elements should be components of all parenteral nutrition solutions and enteral formulas (Level A recommendation)

ASPEN – Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN 26: 31SA, 2002

Absorption of vitamins

- Water soluble vitamins - proximal gastrointestinal (GI) tract
 - Fat soluble vitamins - the mid and distal ileum due to the necessity for fat digestion facilitated by bile and pancreatic lipase
 - Absorption of fat soluble vitamins is affected by all conditions with fat malabsorption (pancreatic insufficiency, bile loss.)
 - Vitamin B₁₂ is absorbed in the terminal ileum
-

Absorption of trace elements

- Paucity of information about the exact location in the GI tract where a specific trace element is absorbed.
 - Zn and Se is absorbed mainly in the duodenum and also in the jejunum
 - Fe is also absorbed in the duodenum and proximal jejunum
 - Cr and Cu are absorbed in the ileum
-

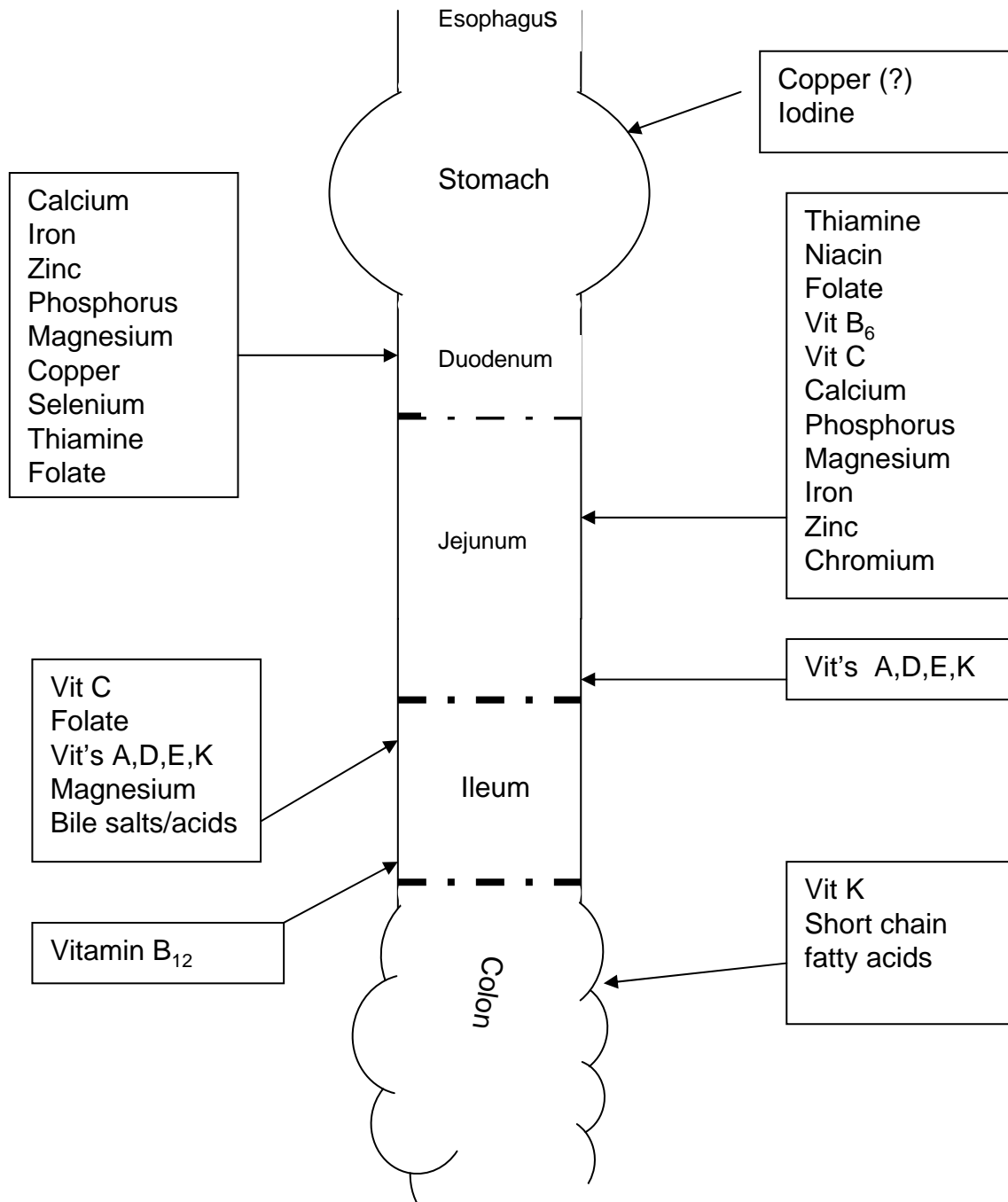
Interactions between trace elements

- Numerous interactions exist between trace elements affecting absorption via the GI tract
 - Factors affecting bioavailability of trace elements are various: dietary factors include chemical form of nutrient (e.g., organic form of Cr is better absorbed than ionic form)
 - Fiber decreases Zn and Fe absorption
-

Interactions between trace elements

- Competitive interactions (e.g., Fe depresses the absorption of Cu and Zn; Zn depresses Cu absorption and vice versa)
- Administration of ferrous sulfate with enteral nutrition can result in zinc deficiency.

Kenny F, Sriram, K, and Hammond, J, Clinical zinc deficiency during adequate enteral nutrition, *J Am Coll Nutr*, 8(1), 83, 1989



Storage

- Like vitamins, the storage site of most trace elements is the liver

TOXICITY OF MICRONUTRIENTS: Vitamins

- Toxicity from water soluble vitamins is unlikely and up to 100 times the RDA can be safely administered.
 - Fat soluble vitamin toxicity do not occur until over 10 times the RDA.
-

TOXICITY OF MICRONUTRIENTS: Trace elements

- In the doses recommended, toxicity of Zn and Se has not been reported
 - Up to 100 mg of Zn can be administered parenterally over 24 hours and is well tolerated.
 - Se is “safe” up to 400 µg/day (parenteral)
 - Cu and Mn can be toxic in liver dysfunction
-

FACTORS AFFECTING MICRONUTRIENT REQUIREMENTS: Pre-existing

- Micronutrient status is altered in alcohol abuse (esp. deficiency of thiamine, folate, zinc)
elderly patients (esp. those in long-term care facilities)

Chandra, *Lancet*, 340, 1124, 1992

Johnson et al. , *Clinics in Geriatric Medicine* 18(4), 773, 2002

Diseases affecting micronutrient requirements

- Gastrointestinal losses (such as fistulas, diarrhea) result in loss of all vitamins and multiple trace elements, especially Zn and Se
 - Pancreatic enzymes are needed for optimal vitamin B₁₂ absorption and deficiency can occur with pancreatitis
-

Re-instillation of gastric aspirate

- Deficiencies can occur with gastrointestinal (GI) losses (high output fistulas; excessive diarrhea).
- Re-instillation of upper GI secretions into the jejunum will facilitate absorption of fat soluble vitamins (that require bile and pancreatic secretions) and will avoid the loss of trace elements

Sriram, K. & Sridhar, R., Gastroduodenal decompression & nasoenteral nutrition: "Extracorporeal gastrojejunostomy", *Nutrition*, 12(6), 440, 1996.

Diseases affecting micronutrient requirements: Renal failure

- Pyridoxine, folic acid and vitamin C
- Hemodialysis -, Vitamins C and E, folic acid and pyridoxine, (Se, Zn)
- Peritoneal dialysis - Zn and Se deficient, but this is not because of loss in the dialysate

Kopple, J.D, In Shils, M.E., et al , Eds., *Modern Nutrition in Health and Disease*, 9th ed., Williams & Wilkins, Baltimore, 1999, 1439.

Story, DA, et al *Crit Care Med*, 27(1), 220, 1999.

Fortin M.-C. et al *Intens Care Med*, 25, 594, 1999.

Sriram K, Abraham G, *Nutrition*, 16 (11/12), 1047, 2000.

FACTORS AFFECTING MICRONURIENT REQUIREMENTS : Treatment modalities

Gastrectomy or terminal ileum resection - and vitamin B₁₂ deficiency
Nitrous oxide administration during anesthesia is known to cause acute folic acid and vitamin B₁₂ deficiencies

Schilling, R.F. *JAMA* 255(12), 1605, 1986

Drug-nutrient interactions

- Folate deficiency due to trimethoprim/sulfamethoxazole
 - Vitamin K deficiency due to administration of antimicrobials which alter intestinal flora
-

Vitamin K

Role: Coagulation, newly recognised role in bone health, immunity

Possible deficiency states:

No storage forms of vitamin K.

Sources of vitamin K: diet, and bacterial synthesis

Alterations in microbiologic flora (antibiotics)
diminish bacterial synthesis

Manifestations of deficiency: Estimation of prothrombin time (PT) may not detect sub-clinical vitamin K deficiency states, which may become pronounced after surgery or resuscitation

Vitamin K, dosage

Recommendations:

- Standard RDA (150 μg) in enteral feeding
 - Parenteral multivitamin preparations have been recently reformulated to provide 150 μg per day
-

Vitamin K, precautions

- Fat emulsions contain a “hidden” source of vitamin K. However, the amount is variable, from 0 to 290 mcg/L in 20% lipid emulsions ¹
- When TPN is discontinued, the prothrombin time needs to be carefully monitored; the dose warfarin often needs to be decreased

1. Lennon, C. *JPEN J Parenter Enteral Nutr* 17:142-144, 1993

Vitamin K : toxicity & adverse effects

- Rapid intravenous administration can result in hypotension
 - Excessive administration of vitamin K results in inability to adequately anticoagulate patients with warfarin
-

Vitamin A

- *Role:* Maintenance of mucosal integrity (bacterial translocation)
- *Possible deficiency states:* GI losses, patients on steroids
- *Manifestations of deficiency:* Poor wound healing, mucosal and skin changes, diarrhea

Stephensen, C.B. *Annu Rev Nutr*, 21, 167, 2001
Ehrlich, J.P., Hunt, T.K., *Surg*, 167, 324, 1968

Vitamin A and steroids

- Steroid and retinoids have antagonistic effects on growth factors and collagen deposition in wound healing

Wicke, Arch Surg 2000; 135:1205

Vitamin A: toxicity

- Vitamin A levels are increased in renal failure patients
- In the absence of a modified multivitamin preparation tailored for renal failure, only standard doses are recommended

Gleghorn, EE et al., *Am J Clin Nutr*, 44, 107, 1986

Vitamin D: Deficiency

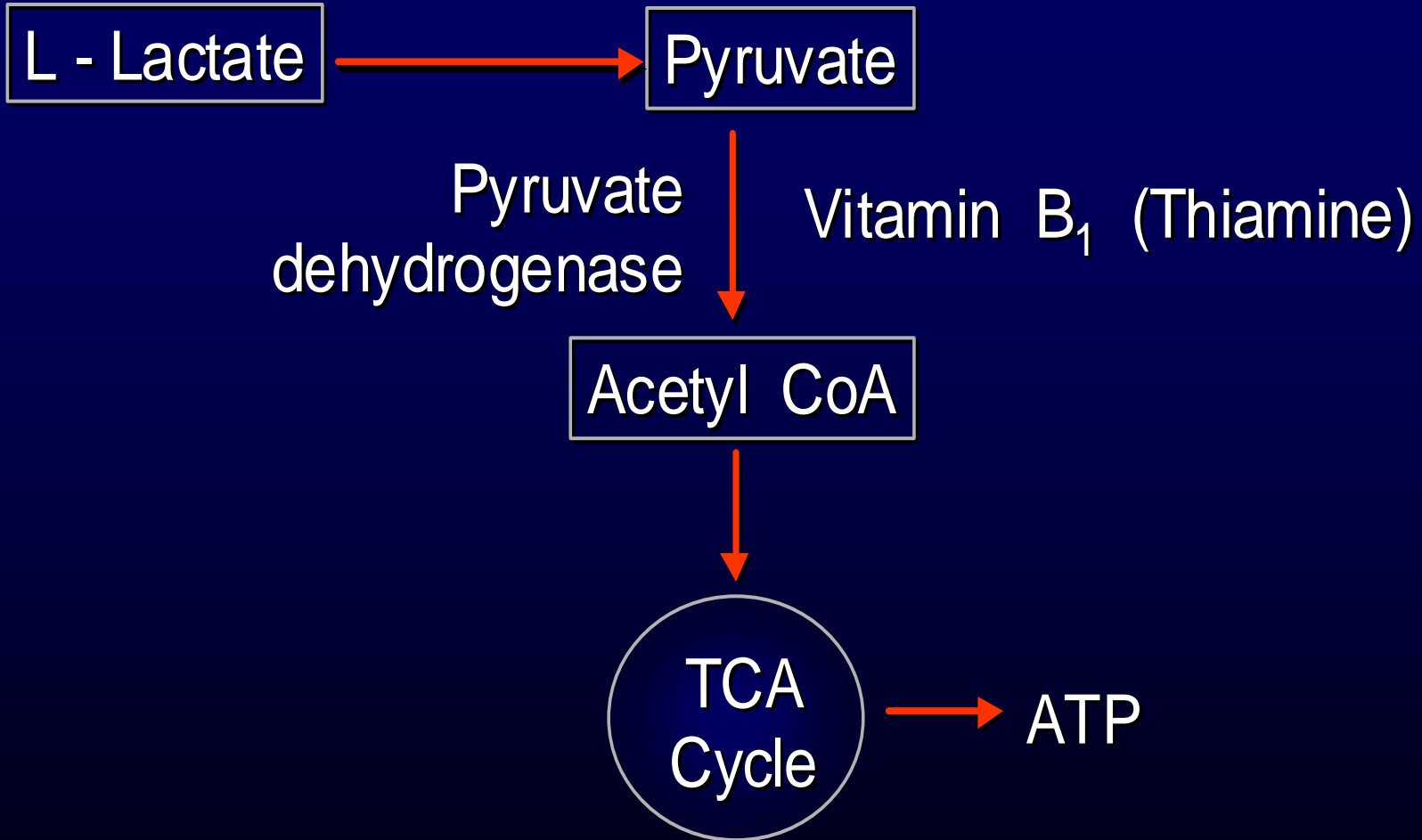
- **Possible deficiency states:** Lack of sunlight (common in elderly and in long-term care institutions), hepatic and renal insufficiency (as vitamin D needs to be converted into its active hydroxylated form), prolonged critical illness¹
- **Manifestations of deficiency:**
Osteomalacia and osteoporosis are not relevant for critically ill patients
Immune dysfunction²

1. Van den Bergh. J Clin Endo Metab 2003, 88:4623
 2. Hollick MF: Mayo Clin Proc 2003, 78(12): 1457-1459
-

Vitamin B₁: Role

- Thiamine is a cofactor for oxidation of pyruvate, alpha ketoacids and branched chain amino acids

Lactic dehydrogenase



Role of Thiamine

Thiamine : Deficiency

- *Possible deficiency states:* Alcoholics, high carbohydrate intake, as a component of “re-feeding syndrome”, iatrogenic insufficient thiamine)
- *Manifestations of deficiency:* Refractory metabolic (lactic) acidosis.

Mental changes, confabulation, confusion and congestive heart failure “wet beri beri”

Cruickshank, AM, Intens Care Med, 14,384, 1988

Cho YP et al, Hepatogastroenterology 2004; 51(55):253-255

Gastrointestinal beri-beri

- Gastrointestinal syndrome of nausea, vomiting, abdominal pain, similar to ischemia of bowel
- Associated with lactic acidosis
- Responds to thiamine administration

Donnino M. *Ann Int Med* 141(11):898, 2004

Vitamin C: Role

- Non-enzymatic antioxidant
 - Collagen synthesis and wound healing
 - Synthesis of carnitine (important for the metabolism of long chain triglycerides)
-

Vitamin C : Deficiency

- *Possible deficiency states*: Previous high intake with abrupt cessation of intake (“rebound scurvy”), burns
- *Manifestations*: Peri-follicular petechiae, poor wound healing, gingivitis, glossitis

Olson, R.E. In Beers, M.H., Berkow, R., Eds, The Merck Manual, Whitehouse Station, NJ, USA, Merck and Co., 1998, 32-51

Vitamin C: toxicity

- Vitamin C can sometimes function as a pro-oxidant
- It can increase free Fe which promotes bacterial proliferation and decreases bacteriocidal activity.
- High intakes produces hyperoxaluria with renal calculi formation

Halliwell, B., *Free Radic Res*; 25, 57, 1996

Folic Acid (“B9”)

- *Role:*
 - Coenzyme in the metabolism of nucleic & amino acids
 - Prevents megaloblastic anemia,
 - Homocysteine metabolism, of interest in hypercoagulable conditions
 - *Possible deficiency states:* Alcoholism, nitrous oxide exposure, renal replacement therapy (dialysis), antiepileptic drugs
-

Zinc: Role

The Zn content of the human body is the highest for any trace element, except for Fe. (Total body content of zinc: 1.4 to 2.3 grams ; compared to Total body content of iron: 3 to 5 grams)

Zinc: Role

About 95% of body Zn is intracellular

The functions of Zn fall under 3 major categories:

- formation of metalloenzymes
- RNA conformation and membrane stabilization,
- Protein and carbohydrate metabolism
- Immune system

Over 70 metalloenzymes of Zn are known -carbonic anhydrase, alkaline phosphatase, alcohol dehydrogenase, superoxide dismutase, angiotensin-converting enzyme (ACE) and DNA polymerase

Key enzyme function of zinc

More than 90% of enzymatic zinc is present in erythrocytes as carbonic anhydrase, responsible for maintenance of acid base balance

Zinc: Metabolism

Zn is well absorbed in the gut (primarily from the duodenum and jejunum)

Zn is bound mainly to albumin (about 60%) and to alpha2-macroglobulin (about 30%)

Then taken up by the hepatocytes and excreted in the bile, and is thus involved in enterohepatic circulation

Zinc: Excretion

Zn is excreted primarily (about 90%) in feces via GI and pancreatic secretions

Normally urinary Zn loss is low

but in conditions such as burns, trauma, and sepsis, and when parenteral aminoacids are infused, the urinary excretion is high

Zinc, deficiency

- *Possible deficiency states:*
 - Excessive GI losses (protracted diarrhea, emesis, high-output fistulas), short bowel syndrome, pancreatic insufficiency
 - Trauma, burns
 - Alcoholism
 - Renal insufficiency
 - High dose steroids probably secondary to proteolysis
 - HIV infection, malignancies
-

Zinc: Deficiency

- Skin rash (scaly, hyperpigmented lesions involving elbows and knees, also called acrodermatitis enteropathica), characteristic rash around ala nasi
-

Zinc deficiency, other features

- Glucose intolerance
 - Poor wound healing
 - Abnormal hemostasis, immune dysfunction,
 - Loss of hair
 - Altered taste (dysgeusia) and smell perception, diarrhea
 - Decreases work capacity of muscles - detrimental effects on respiratory function
 - Worsens hepatic dysfunction
-

Zinc, toxicity

- *Recommendations:* Parenteral, 2.5-4 mg/day
Enteral RDA is 15 mg.

Additional doses are given when indicated.

- *Toxicity and adverse effects:* High doses of Zn results in immune dysfunction.

At doses recommended for clinical use, toxicity does not occur.

Selenium: Role

- Antioxidant functions, closely linked with that of vitamin E.
 - Se present in two forms:
 - Selenomethionine
 - Selenocysteine (regulated)
-

Selenium: Functions

- An essential component of glutathione peroxidase, a "scavenger" enzyme that removes Reactive Oxygen Species
- Important for thyroid hormone production
- Se also inhibits nuclear transcription factor κ B (NF kappa B) expression which is a key step in the development of inflammation

Berger, M.M., *Intens Care Med*, 27, 91, 2001

Flohe´ Ligelius-Flohe´, *Free Radic Biol Med*, 22, 1115, 1997

Selenium : Metabolism

- Seleno aminoacids (diet) form the main source of Se and over 50% is absorbed. Inorganic Se absorption does occur but is less efficient
 - Absorption is the duodenum and proximal jejunum
 - After absorption, Se is transported in blood bound to proteins
 - 50 - 60% of Se is excreted in the urine and the rest via the GI tract
-

Selenium, risks of deficiency

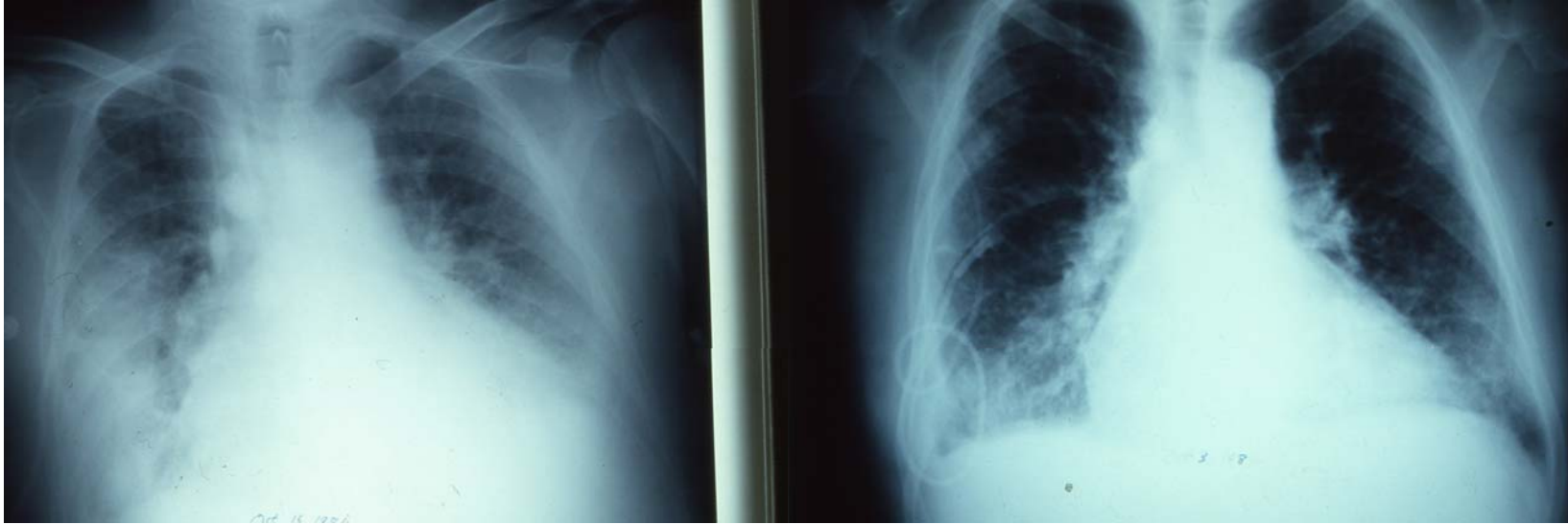
- Administration of Se-free TPN or EN
 - Alcoholism
 - Surgical resection of duodenum and proximal jejunum especially when EN formulas deficient in Se are used
 - Trauma patients are often Se deficient
-

Selenium : Clinical deficiency

- *Clinical signs of deficiency*: Specific to critically ill patients, Se deficiency manifests as congestive heart failure and arrhythmias.
- Involvement of peripheral muscles is manifested as myositis, with weakness and muscle cramps

Johnson, R.A., et al., *N Eng J Med*, 304, 1210, 1981.

Selenium and congestive heart failure



- Sriram, K., Petersen, J.K., et al: Clinical improvement of congestive heart failure after selenium supplementation in total parenteral nutrition. Proceedings of Nordic Symposium on Metabolism of Trace Elements Related to Human Disease, Nordfjord, Norway, June, 1985.

Selenoprotein dysfunction with statins

- HMG-CoA reductase inhibition (statin group of drugs) may lead to myopathy by interfering with formation of selenocysteine tRNA and by causing abnormalities in selenoproteins

Moosmann B. Lancet 2004; 363:892

Selenium increases diabetes risk

- 50% increased risk with long term Se supplementation (200 mcg/day), compared to placebo
- Study on 1202 patients, no diabetes at baseline, lived in low soil Se area in USA

Stranges S. Ann Intern Med 2007; 147:217

Selenium in critical care, 2007

A prospective randomized, placebo-controlled, multiple-center study in patients with severe systemic inflammatory response syndrome, sepsis, and septic shock

- 249 patients with severe systemic inflammatory response syndrome, sepsis, and septic shock and an Acute Physiology and Chronic Health Evaluation (APACHE) III score >70.

Matthias W. A. Crit Care Med 2007; 35:118

Selenium in critical care, 2007, contd

- *Interventions:* Patients received 1000 micrograms of sodium-selenite as a 30-min bolus injection, followed by 14 daily continuous infusions of 1000 micrograms intravenously, or placebo.
- *Conclusion :* The adjuvant treatment of patients with high dose sodium-selenite reduces mortality rate in patients with severe sepsis or septic shock.

Matthias W. A. Crit Care Med 2007; 35:118

Update on Se

- Some benefit in burns, trauma
- No benefit in pancreatitis

Geoghegan M, Curr Opinions in Critical Care, 2006; 12:36.

Selenium and HIV

- Daily oral selenium supplementation can suppress the progression of HIV-1 viral burden and provide indirect improvement of CD4 count
- This study on 450 patients supports the use of Se as a simple, inexpensive and safe adjunct therapy in HIV

Hurwitz BE et al. *Arch Int Med* 167:148, 2007

Iron

Fe is an oxygen carrier and during critical illness free Fe is released into the circulation

This interferes with reticulo endothelial system activity, decreases macrophage activity and promotes growth of microorganisms, especially gram negative bacilli

Demling, R.H. & De Biase, M.A., Micronutrients in critical illness, *Crit Care Clin*, 11, 651, 1995.

Iron, continued

Supplemental Fe is not recommended during acute illness but may be used during the recovery phase, with or without erythropoietin.

When Fe needs to be added to PN, the dextran formulation appears to be safe and is devoid of lipid peroxide formation, and is the preferred form of addition rather than using free Fe

Lavoie JC, Chessex P. J Pediatr Gastroenterol Nutri 1997; 25:307-311

New evidence: Safety of IV Fe

- Intravenous iron following cardiac surgery does NOT increase the infection rate
- Data on 863 patients, 39 developed infections (4.52%).
- Fe treated group (n=12, 3.97%)
- Control group (n=27, 4.81%)
- “Safe to use Fe in postoperative setting”

Torres S. *Surgical Infections* 7(4):361, 2006

Copper, Manganese

- Cu is important for wound healing and antioxidant defense, immune function, collagen synthesis (component of lysyl oxidase)
- Deficiency causes pancytopenia
(anemia, thrombocytopenia, neutropenia)

(Sriram, K, : JPEN, 10(5):530-532, 1986)

Cu deficiency and neutropenia

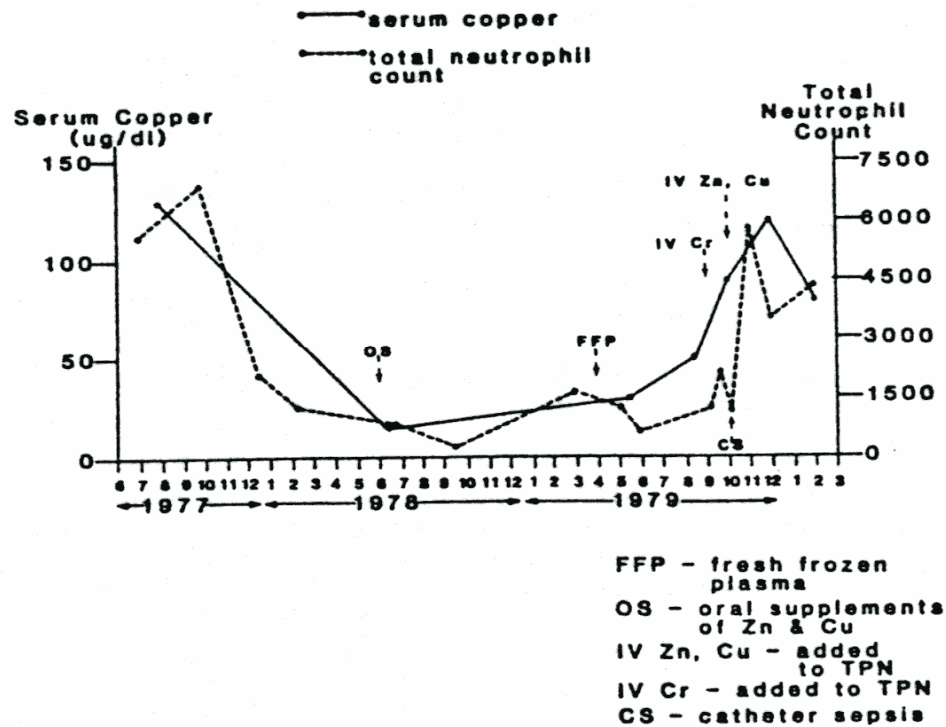


FIG. 1. Effect of Cu on total neutrophil count.

Sriram, K. et al : Neutropenia due to copper deficiency in total parenteral nutrition. *Journal of Parenteral and Enteral Nutrition*, 10(5):530-532, 1986.

Cu & Mn in hepatic failure

- Cu and Mn are excreted in the bile.
- In hepatic insufficiency or cholestasis, delete or decrease from parenteral nutrition admixtures

Berger MM, Cutaneous zinc & copper losses in burns. *Burns* 1992; 18:373-380

A.S.P.E.N.: *JPEN J Parenter Enteral Nutr*, 26(1), Supplement, 1SA, 2002.

Chromium

- Cr should be deleted or decreased in renal insufficiency

Conclusion: Who needs supplementation?

- All critically ill patients need micronutrient supplementation as soon as nutritional support is initiated, by either the enteral or parenteral route
-

Timing

Largest increases in Reactive Oxygen Species (ROS) production occurs early in the course of acute illness

Decreased serum levels of micronutrients is seen in this period

Supplementation should begin early –

During the first 5 to 7 days, the emphasis is on antioxidant supplementation

After this period, routine micronutrient supplementation is provided

Route of administration

In critically ill patients, the intravenous route is the only reliable method by which micronutrients can be administered

Enteral route for micronutrient supplementation in critically ill patients has studied only in trauma & burns. Absorption is unpredictable, due to hemodynamic instability, bowel edema and alterations in blood supply

Porter et al. ,Ann Surg , 65, 478, 1999

Pochon, Kloti, Burns, 5, 123, 1979

Berger, MM, Crit Care Med , 28, 2217, 2000

Route of administration: Summary

Micronutrients are initially administered intravenously, either as a component of total parenteral nutrition or separately.

As and when enteral feeding is initiated and tolerated, micronutrient supplementation can be added to the enteral formula

Dose, vitamins

Standard RDA of vitamins and trace elements

Regarding routine higher doses, firm recommendations are not available

Additional modest doses of vitamins A (10000 IU/day), E (50-60 mg/day) and C (500 mg/day) will benefit critically ill patients

Specific vitamins are additionally supplemented in specific conditions (burns, trauma)

Grant, J.P. Nutritional support in critically ill patients, Ann Surg, 220(5), 610, 1994.

Dose, trace elements

Higher amounts of trace elements are administered whenever there are excess GI losses

Monitoring of trace elements with organ dysfunction

- In critically ill patients on parenteral nutrition with hepatic and/or renal insufficiency, inclusion of a specific trace element will require monitoring of serum levels

Dickerson RN. Manganese toxicity and TPN.
Nutrition 17(7-8): 689-693, 2001

Guidelines

- Vitamins and trace elements should be components of all parenteral nutrition solutions and enteral formulas (Level A recommendation)
- Vitamin and trace element levels should be monitored periodically during long term PN administration (Level C)

ASPEN – Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN 26: 31SA, 2002

Malaysian Dietician's Assn guidelines, 2005

Daily Trace Element Supplementation to Adult PN Formulation^a

Trace Element	Standard Intake (Fleming CR, 1989)
Chromium	10 – 15 mcg ^{b,c}
Copper	0.3 – 0.5 mg
Iron	Not routinely added
Manganese	60 – 100 mcg ^c
Selenium	20 – 60 mcg ^c
Zinc	2.5 – 5 mg

^a Standard intake ranges based on generally healthy people with normal losses.

^b The contamination level in various components of PN formulation can significantly contribute to total intake. Serum concentrations should be monitored with long-term use.

^c May not be required during short-term use of PN.

AusPEN guidelines, 2004, (Draft)

Nutrient	Amount	Source
Vitamins:		
Potassium	1-2 mmols/kg	E.S.P.E.N Guidelines
Calcium	5 – 7.5 mmol/day	E.S.P.E.N Guidelines
Magnesium	4 – 10 mmol/day	E.S.P.E.N Guidelines
Phosphorus	20 - 40 mmol/day	E.S.P.E.N Guidelines
Trace Elements		
Chromium	0.2 – 0.4 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines
Copper	5-20 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines
Fluoride	50 µg/day	B.A.P.E.N. guidelines
Iodine	1 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines
Iron	20 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines
Manganese	5 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines
Molybenum	0.4 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines
Selenium	0.5 – 1.5 µg/day	AuSPEN guidelines
Zinc	50 – 100 µg/day	AuSPEN guidelines B.A.P.E.N. guidelines

Conclusion

General and safe guidelines for the use of micronutrients and vitamins in critically ill patients have been presented

The information available is at best incomplete, but will facilitate the clinician to make individual choices

Conclusion

Routine inclusion or supplementation of standard doses of vitamins and trace elements with enteral and parenteral nutritional support is accepted

The data on antioxidant supplementation in critically ill patients is evolving but is considered safe and may be associated with a reduction in mortality in critically ill patients

Heyland DK. (Meta-analysis of 11 papers) *Intensive Care Medicine* 2005, 31(3):327
