# Selenium –

# rol in organism

**M.Păpurică**
**UMF "Victor Babes" Timisoara**

# Selenium in intensive care ?

## Probably not a magic bullet but an important adjuvant therapy

Critical Care Medicine:
January 2007 - Volume 35 - Issue 1 - pp 306-307
doi: 10.1097/01.CCM.0000251943.86292.87

**Berger, Mette M. MD, PhD; Shenkin, Alan MD, PhD**


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Ru Rh Pd Ag Cd
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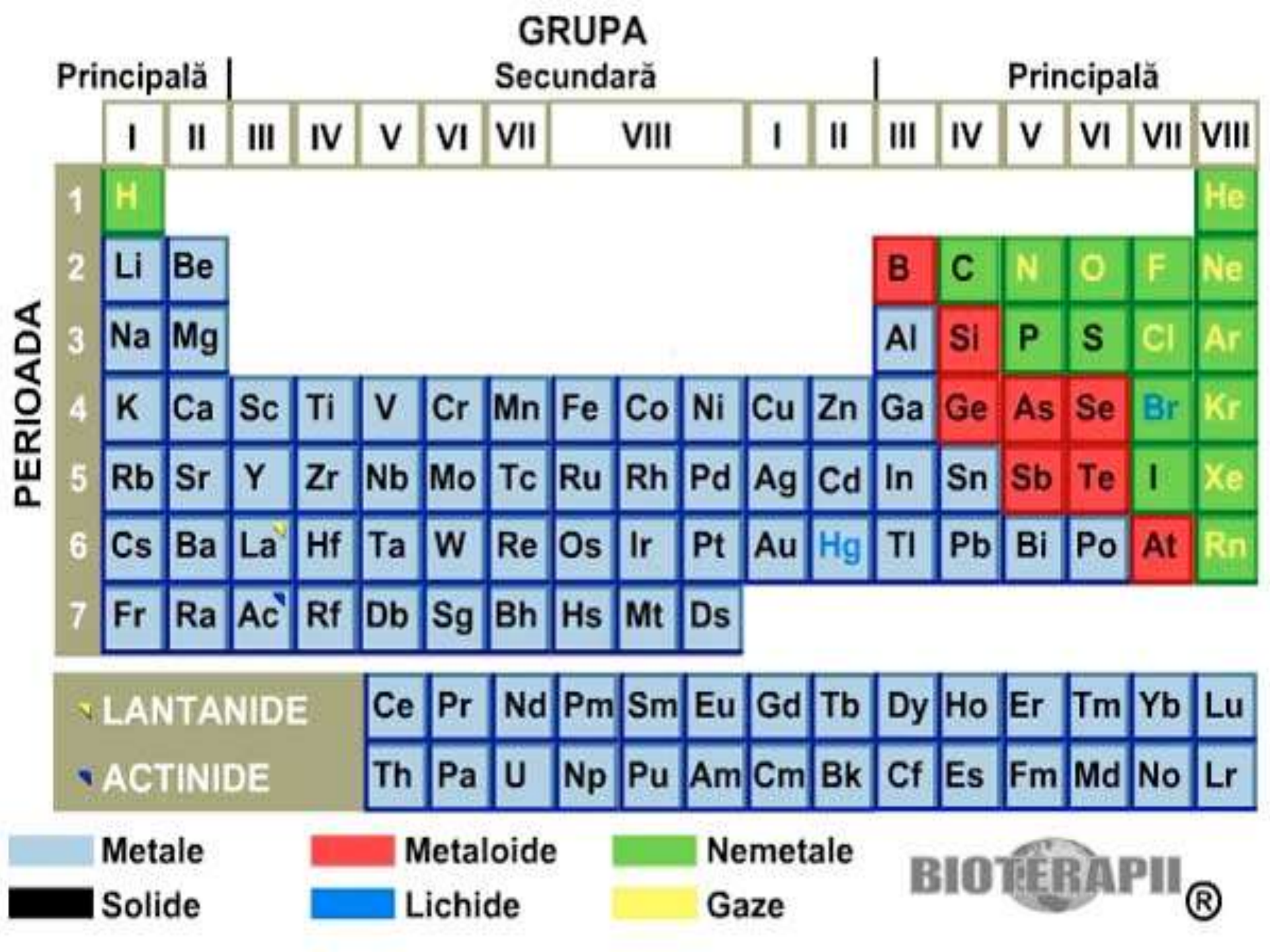
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Metale
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Lichide
Gaze
BIOTERAPII ®

# Industry

# Human

**Incorporated in selenocompounds - small molecular weight that influence human health.**

**selenoproteins**

# Micronutrients

Called *micronutrients* because they are needed only in **minuscule amounts,** these substances are the **"magic wands"** that enable the body to produce enzymes, hormones and other substances essential for proper growth and development

- **Microminerals (trace elements)**
- **Vitamins**

# Essential micronutrients

| Trace elements | Vitamins |
|---|---|
| Cu | A Retinol |
| Se | D Cholecalciferol |
| Zn | E Alpha-tocopherol K |
| Fe | Phyloquinone B1 Thiamin |
| Mn | B2 Riboflavin |
| Mo | B3 Niacin(PP) |
| Cr | B5 Pantothenic acid B6 |
| F | Pyridoxine |
| I | B8 Biotine(H) |
| Co | B9 Folic acid |
| | B12 Cobalamin |
| | C Ascorbic acid |

Fores Nillsen, New esential trace elements for the life sience, Bilogical Trace Element Research, 1989, 599-611

# Forms

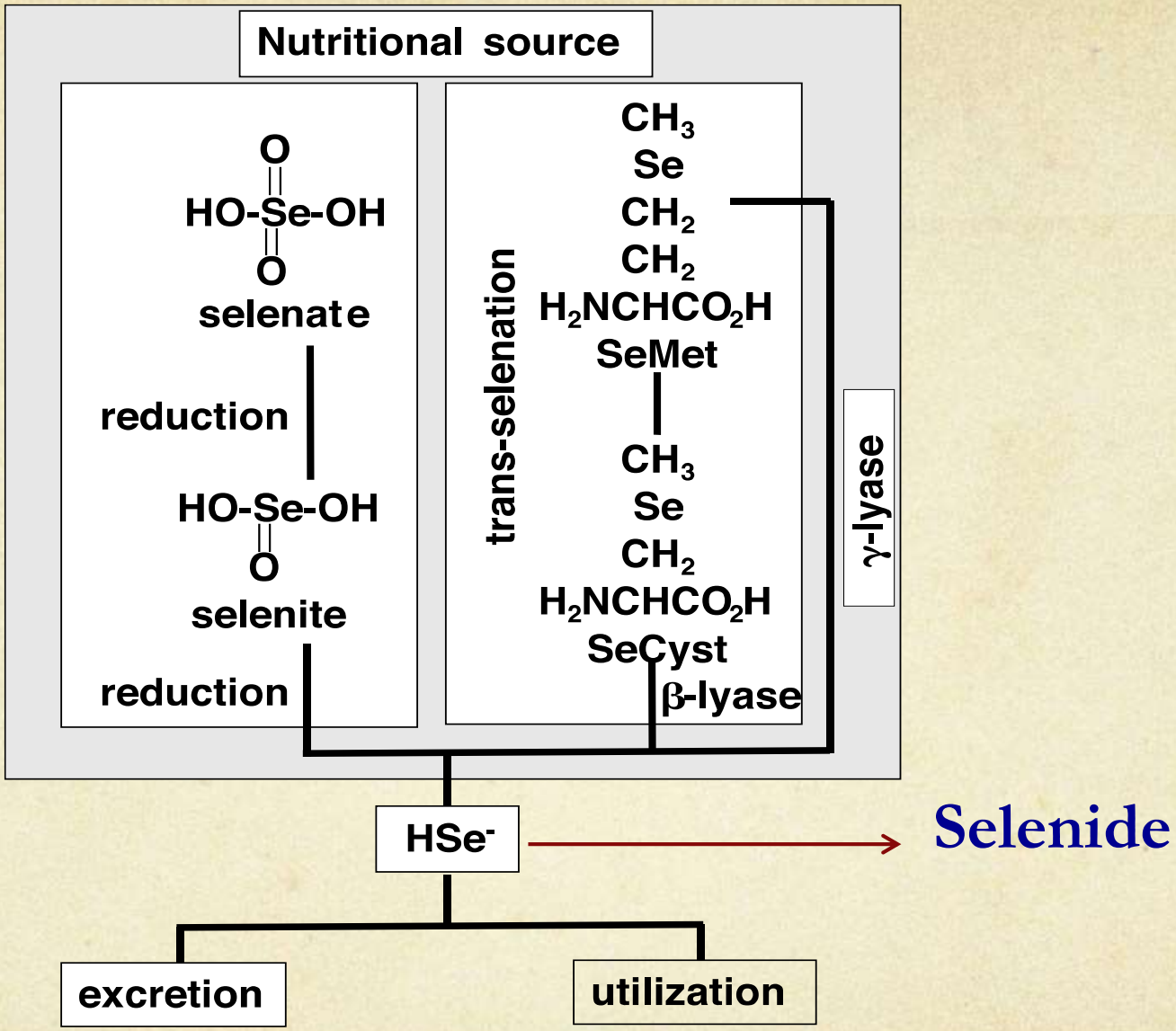
## Inorganic forms

- metallic forms
- oxyanions - selenite $SeO(OH)_2$
  - selenate $SeO_2(OH)_2$

## Organic forms

- selenocisteina SeCys
- seleomethionine SeMet

Suzuki, K. T. and Ogra, Y. (2002) Metabolic pathway for selenium in the body: Speciation by HPLC-ICP MS with use of enriched Se. *Food Addit.Contam.*, **19**, 974–983




**Kazuo T. Suzuki Metabolomics of Selenium: Se Metabolites Based on Speciation Studies**
*Journal of Health Science,* **51**(2) 107–114 (2005)

# Sourses of Selenium

- **SeCys** is present in plants and animals (vegetables and meats in foods)
- **SeMet** in general proteins in foods (vegetables and meats)
- **selenite and selenate** in drinking water and foods

Ogra, Y., Ishiwata, K., Encinar, J. R., Lobinski, R. and Suzuki, K. T. (2004) Speciation of selenium in selenium-enriched shiitake mushroom, *Lentinula edodes*. *Anal. Bioanal. Chem.*, **379**, 861–866.

# Sourses of Selenium

## Selenium accumulators

- **selenite-accumulators (broccoli and cucumber),**
- **SeMet-accumulators (grains such as wheat, and mushroom)**
- **MeSeCys-accumulators (garlic and onion)**

Ogra, Y., Ishiwata, K., Encinar, J. R., Lobinski, R. and Suzuki, K. T. (2004) Speciation of selenium in selenium-enriched shiitake mushroom, *Lentinula edodes*. *Anal. Bioanal. Chem.*, **379**, 861–866.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OUR PICKLES CAN MAKE A SOURPUSS SMILE


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Benefits of


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# Human active forms

- **Glutation peroxidaza (GPx)**
- **Thioredoxin reductaza**
- **Thyroid hormone deiodinase**
- **Selenoproteins**

## Antioxidant/Redox Reactions Involving Selenoproteins

1. *Detoxification of peroxides:*

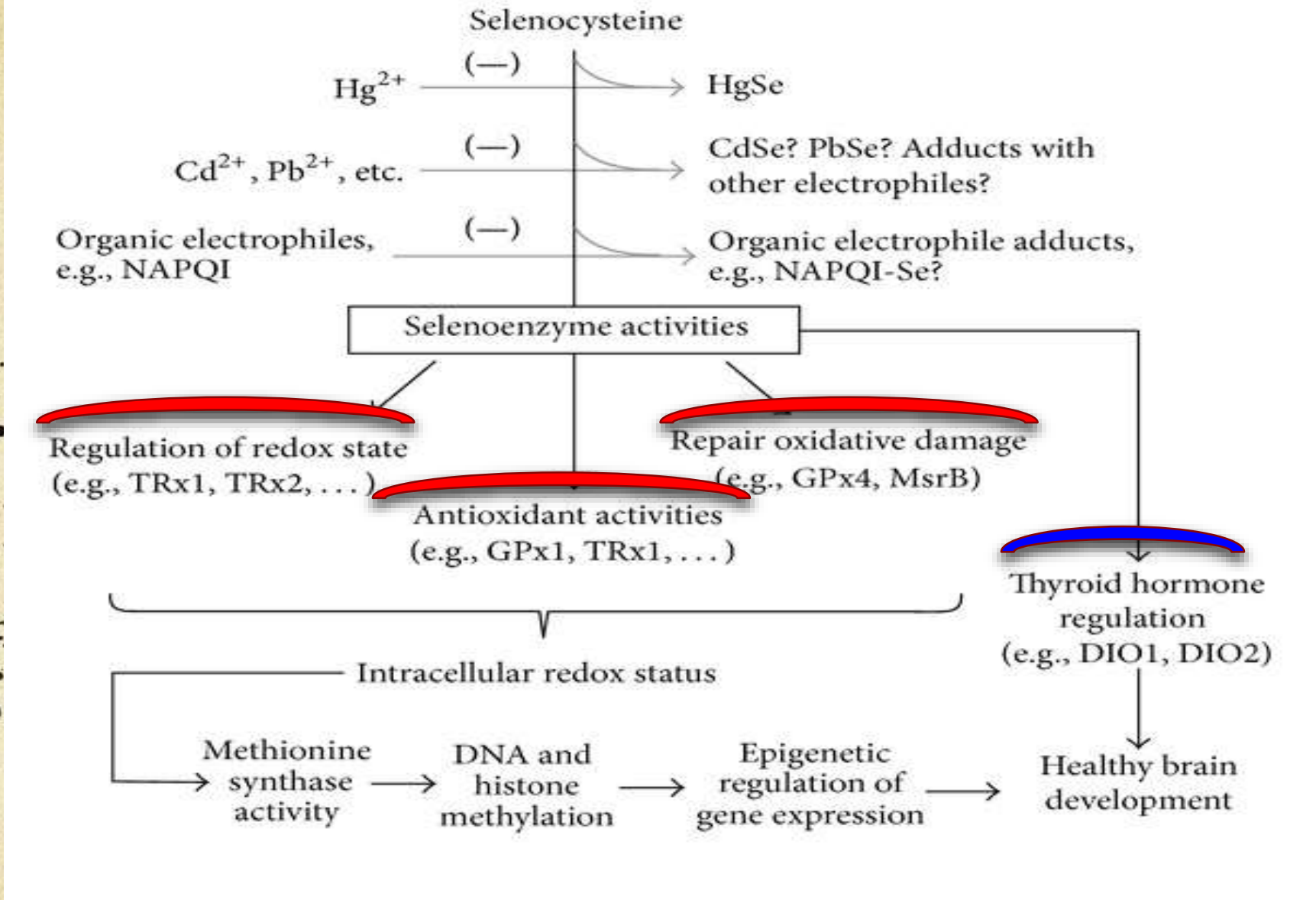
$$R\text{-}O\text{-}O\text{-}H + 2GSH \xrightarrow{GPx} R\text{-}O\text{-}H + GSSG + H_2O$$

2. *Regeneration of reduced thioredoxin:*

$$Trx\text{-}S_2 + NADPH + H^+ \xrightarrow{Trxrd} Trx\text{-}(SH)_2 + NADP^+$$

3. *Reduction of oxidized methionine residues:*

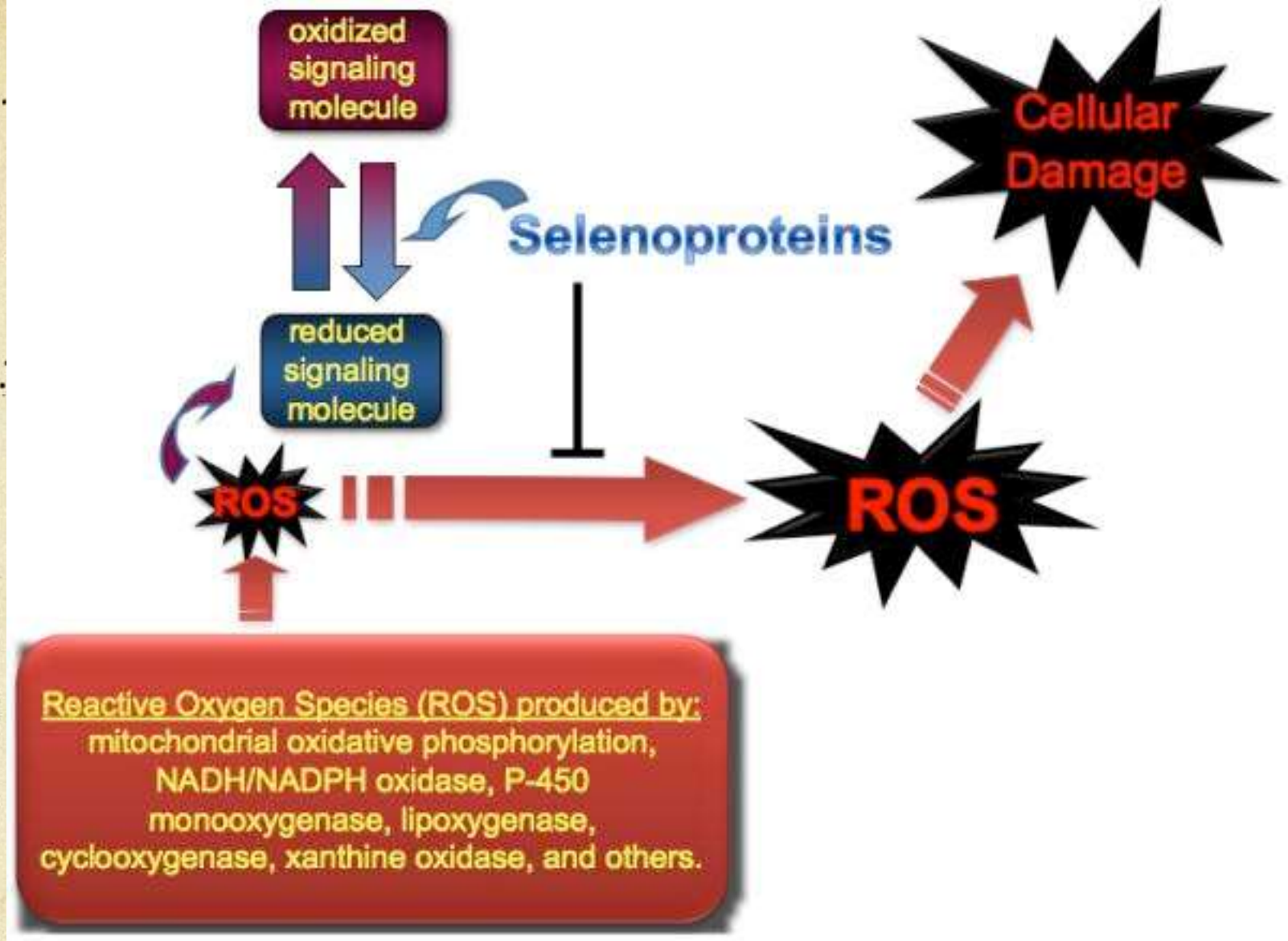
$$peptide\text{-}Met\text{-}R\text{-}O + Trx\text{-}(SH)_2 \xrightarrow{Sel\ R} peptide\text{-}Met + Trx\text{-}S_2 + H_2O$$




Autism Res Treat. 2014;2014:164938. doi: 10.1155/2014/164938. Epub 2014 Mar 5.

Potential Role of Selenoenzymes and Antioxidant Metabolism in relation to Autism Etiology and Pathology.

Raymond LJ, Deth RC, Ralston NV




Autism Res Treat. 2014;2014:164938. doi: 10.1155/2014/164938. Epub 2014 Mar 5.

Potential Role of Selenoenzymes and Antioxidant Metabolism in relation to Autism Etiology and Pathology.

Raymond LJ, Deth RC, Ralston NV

# Role ……. in the body

- Sepsis, septic shock[1]
- Antioxidant
- Decreased the risk of lung, colorectal, and prostate cancers[2,3]
- Antitoxic (Pb. Hg, Ar )
- Imunomodulator


1. Matthias W. A. Angstwurm, Selenium in ICU SIRS – sepsis patients, Crit Care Med 2007 Vol. 35, No. 1

2.Taylor PR, Albanes D. Selenium, vitamin E, and prostate cancer--ready for prime time? J. Natl. Cancer Inst 1998;90:1184–1185.

3. Clark LC, Combs GF Jr. Turnbull BW, Slate EH, Chalker DK, Chow J, Davis LS, Glover RA, Graham GF, Gross EG, Krongrad A, Lesher JL Jr. Park HK, Sanders BB Jr. Smith CL, Taylor JR. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial, Nutritional Prevention of Cancer Study Group. JAMA 1996;276:1957–1963.

# Role ……. in the body

- Alfa 1 antitripsina deficiency [1]
- Autism[2]
- Masculin infertility
- Regulate thyroid hormone synthesis
- Cardioprotection in cardiomyopathyc disease


1. Catherine M. Greene et all., s There a Therapeutic Role for Selenium in Alpha-1 Antitrypsin Deficiency? Nutrients 2013, 5, 758-770
2. **Laura J. Raymond et all., Potential Role of Selenoenzymes and Antioxidant Metabolism in relation to Autism Etiology and Pathology** Autism Research and Treatment, volume 2014, Article ID 164938, 15 pages

# Main actors


- Glutathione Peroxidases (GPx1 -6)
- Thioredoxin Reductases
- Deiodinases
- Selenoprotein (H - W)
- Selenophosphate-synthetase 2

# Glutathione Peroxidases (GPx1)

- the most abundant and ubiquitously expressed selenoproteins
- highly sensitive to changes in Se status
- oxidative stress has been shown to reduce levels of GPx1
- GPx1 recovers most rapidly
- role for GPx1 in cancer prevention
- plays an important role in protecting against neurodegenerative diseases

# Glutathione Peroxidases (GPx1)

- slightly higher risk of type-2 diabetes in Se supplemented humans as described above as well as the strong correlation found between **increased erythrocyte GPx1 activity and insulin resistance** in gestational diabetic women

Chen X, Scholl TO, Leskiw MJ, Donaldson MR, Stein TP. Association of glutathione peroxidase activity with insulin resistance and dietary fat intake during normal pregnancy. J. Clin. Endocrinol. Metab 2003;88:5963–5968.

# Glutathione Peroxidases (GPx2)

- expressed in the gastrointestinal tract, in liver
- protect intestinal epithelium from oxidative stress
- GPx2 is upregulated in cancers of gastrointestinal tract (1)
- A recent study show that lower expression of GPx2 increased migration and invasion of cancer cell clones, but decreased their growth (2)

1.Serewko MM, Popa C, Dahler AL, Smith L, Strutton GM, Coman W, Dicker AJ, Saunders NA. Alterations in gene expression and activity during squamous cell carcinoma development. Cancer Res 2002;62:3759–3765.
2. Banning A, Kipp A, Schmitmeier S, Lowinger M, Florian S, Krehl S, Thalmann S, Thierbach R, Steinberg P, Brigelius-Flohe R. Glutathione Peroxidase 2 Inhibits Cyclooxygenase-2-Mediated Migration and Invasion of HT-29 Adenocarcinoma Cells but Supports Their Growth as Tumors in Nude Mice. Cancer Res 2008;68:9746–9753

# Glutathione Peroxidases (GPx3)

- source of GPx3 in plasma is the kidney
- decreased GPx3 activity led to platelet hyper- reactivity and an increased risk of thrombosis [2]
- GPx3 and Sel P role for this selenoprotein in modulating NO concentration or other aspects of the vascular environment.
- affects susceptibility to stroke or other cardiovascular disorders [3]

1Yoshimura S, Watanabe K, Suemizu H, Onozawa T, Mizoguchi J, Tsuda K, Hatta H, Moriuchi T. Tissue specific expression of the plasma glutathione peroxidase gene in rat kidney. J. Biochem 1991;109:918–923.
2. Freedman JE, Loscalzo J, Benoit SE, Valeri CR, Barnard MR, Michelson AD. Decreased platelet inhibition by nitric oxide in two brothers with a history of arterial thrombosis. J. Clin. Invest 1996;97:979–987.
3. Kenet G, Freedman J, Shenkman B, Regina E, Brok-Simoni F, Holzman F, Vavva F, Brand N, Michelson A, Trolliet M, Loscalzo J, Inbal A. Plasma glutathione peroxidase deficiency and platelet insensitivity to nitric oxide in children with familial stroke. Arterioscler. Thromb. Vasc. Biol 1999;19:2017–2023.

# Glutathione Peroxidases (GPx4)

- subcellular localization between cytosol, nuclear, and mitochondria[1]
- protective role (reversing oxidation of lipid peroxides)
- involved in metabolism of lipids (arachidonic acid and linoleic acid) [2]
- contribute to the pathogenesis of Parkinson Disease or Alzheimer's Disease [3]
- protective role in cardiovascular disease (decreasing lipid peroxidation and inhibiting the sensitivity of vascular cells to oxidized lipids) [4]
- associated with infertility [5]

1Conrad M, Schneider M, Seiler A, Bornkamm GW. Physiological role of phospholipid hydroperoxide glutathione peroxidase in mammals. Biol. Chem 2007;388:1019–1025.
2. Chen CJ, Huang HS, Chang WC. Depletion of phospholipid hydroperoxide glutathione peroxidase up-regulates arachidonate metabolism by 12S-lipoxygenase and cyclooxygenase 1 in human epidermoid carcinoma A431 cells. FASEB J 2003;17:1694–1696
3. Chen L, Na R, Gu M, Richardson A, Ran Q. Lipid peroxidation up-regulates BACE1 expression in vivo: a possible early event of amyloidogenesis in Alzheimer's disease. J. Neurochem 2008;107:197–207.
4 Guo Z, Ran Q, Roberts LJ 2nd, Zhou L, Richardson A, Sharan C, Wu D, Yang H. Suppression of atherogenesis by overexpression of glutathione peroxidase-4 in apolipoprotein E-deficient mice. Free Radic. Biol. Med 2008;44:343–352.
5. Foresta C, Flohe L, Garolla A, Roveri A, Ursini F, Maiorino M. Male fertility is linked to the selenoprotein phospholipid hydroperoxide glutathione peroxidase. Biol. Reprod 2002;67:967–971.

# Thioredoxin Reductases (Trx)

- **catalyze the reduction of oxidized thioredoxin (1)**
- **exists in all living cells**
- **defense against oxidative damage due to oxygen metabolism, and redox signaling using molecules like hydrogen peroxide and nitric oxide (2)**
- **In cancer treatment: is essential for cell growth and survival, it is a good target for anti-tumor therapy (4)**
- **In cardiomyopathy: two mutations in the TrxR2 gene are found in patients diagnosed with DCM and not in a control population( control oxidative damage in cardiac myocytes) (3)**


1. Arner ES, Holmgren A. Physiological functions of thioredoxin and thioredoxin reductase. Eur. J. Biochem 2000;267:6102–6109
2. Meyer, Yves; Bob B. Buchanan, Florence Vignols, and Jean-Philippe Reichheld (2009). "Thioredoxins and glutaredoxins: unifying elements in redox biology". *Annual Reviews Genetics* **43**: 335–367
3. Hashemy SI, Ungerstedt JS, Zahedi Avval F, Holmgren A (April 2006). "Motexafin gadolinium, a tumor-selective drug targeting thioredoxin reductase and ribonucleotide reductase". *J. Biol. Chem.* **281** (16): 10691–10697
4. Nilsonne G, Sun X, Nyström C, Rundlöf AK, Potamitou Fernandes A, Björnstedt M, Dobra K (September 2006). "Selenite induces apoptosis in sarcomatoid malignant mesothelioma cells through oxidative stress". *Free Radic. Biol. Med.* **41** (6): 874–885.

# Iodothyronin Deiodinases

- **three enzymes: types 1, 2, and 3 (1)**
- **thyroid hormone metabolism** (3)
- **regulated (D2) stability in response to changes in iodine supply, to cold exposure, and changes in thyroid gland function (2)**

1.Bianco AC, Salvatore D, Gereben B, Berry MJ, Larsen PR. Biochemistry, cellular and molecular biology, and physiological roles of the iodothyronine selenodeiodinases. Endocr. Rev 2002;23:38– 89.
2. Gereben B, Goncalves C, Harney JW, Larsen PR, Bianco AC. Selective proteolysis of human type 2 deiodinase: a novel ubiquitin-proteasomal mediated mechanism for regulation of hormone activation. Mol. Endocrinol 2000
3.Dumitrescu AM, Liao XH, Abdullah MS, Lado-Abeal J, Majed FA, Moeller LC, Boran G, Schomburg L, Weiss RE, Refetoff S. Mutations in SECISBP2 result in abnormal thyroid hormone metabolism. Nat. Genet 2005;37:1247–1252.

# Selenoproteins

| | | | |
|---|---|---|---|
| H | - relatively high in early stages of embryonic development | P | - Se transporter<br>- glutathione peroxidase activity, heparin binding, and heavy metal ion complexation<br>- important defense against heavy metals<br>- lower circulating Sel P during inflammatory conditions like sepsis and Crohn's disease |
| I | - involved in a phospholipid biosynthesis pathway | R | - protection from neurodegeneration , lens cell viability, and oxidative damage during aging |
| K | - localized to the endoplasmic reticulum membrane, human heart<br>- function of Sel K remains unclear | S | - participate in the removal of misfolded proteins from the ER lumen for degradation and to protect cells from oxidative damage and ER stress-induced apoptosis<br>- associated with genetic variations in Sel S : cardiovascular disease and stroke, preeclampsia, rheumatoid arthritis, and gastric cancer |
| M | - role for this selenoprotein in limiting the development of cancer | T | - biological role for Sel T in calcium mobilization ? |
| N | - a transmembrane protein localized to the ER membrane<br>- high expression of Sel N in fetal tissue and proliferating cells are suggestive role in early muscle formation | V | - potential roles of Sel V in male reproductive biology |
| O | - no information regarding its tissue distribution, subcellular location, or physiological role | W | - functions in muscle growth and differentiation by protecting the developing myoblasts from oxidative stress |



M. A. Reeves, P. R. Hoffmann; The human selenoproteome: recent insights into functions and regulation
*Cell Mol Life Sci.* 2009 August ; 66(15): 2457–2478

**Selenium status varies by country and corresponds to dietary selenium intake and dietary supplements.**

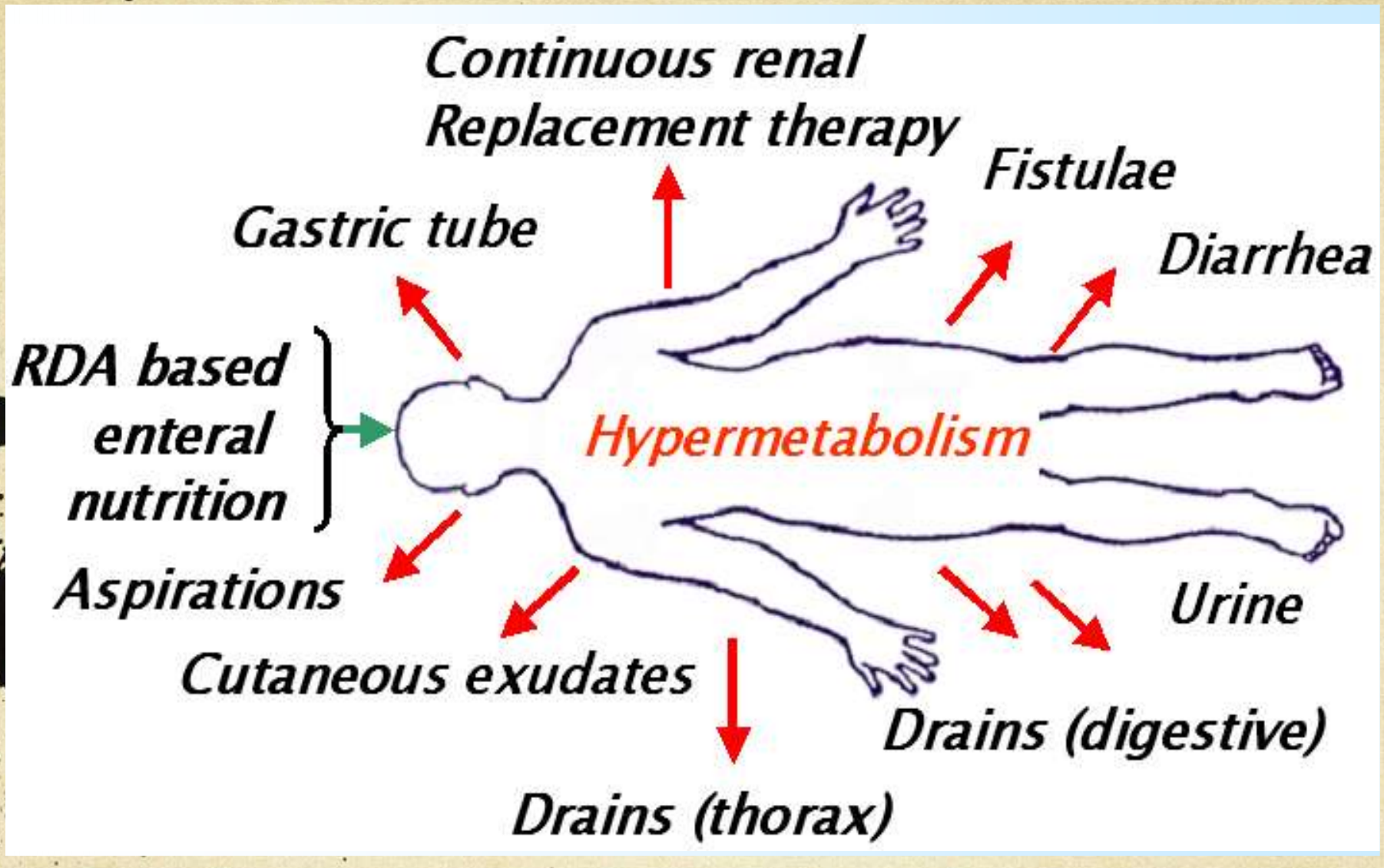
**- in the USA, 50% of the population takes dietary supplements**

Rayman MP: Selenium and human health. Lancet 2012, 379:1256–1268.

# Impact on micronutrient status

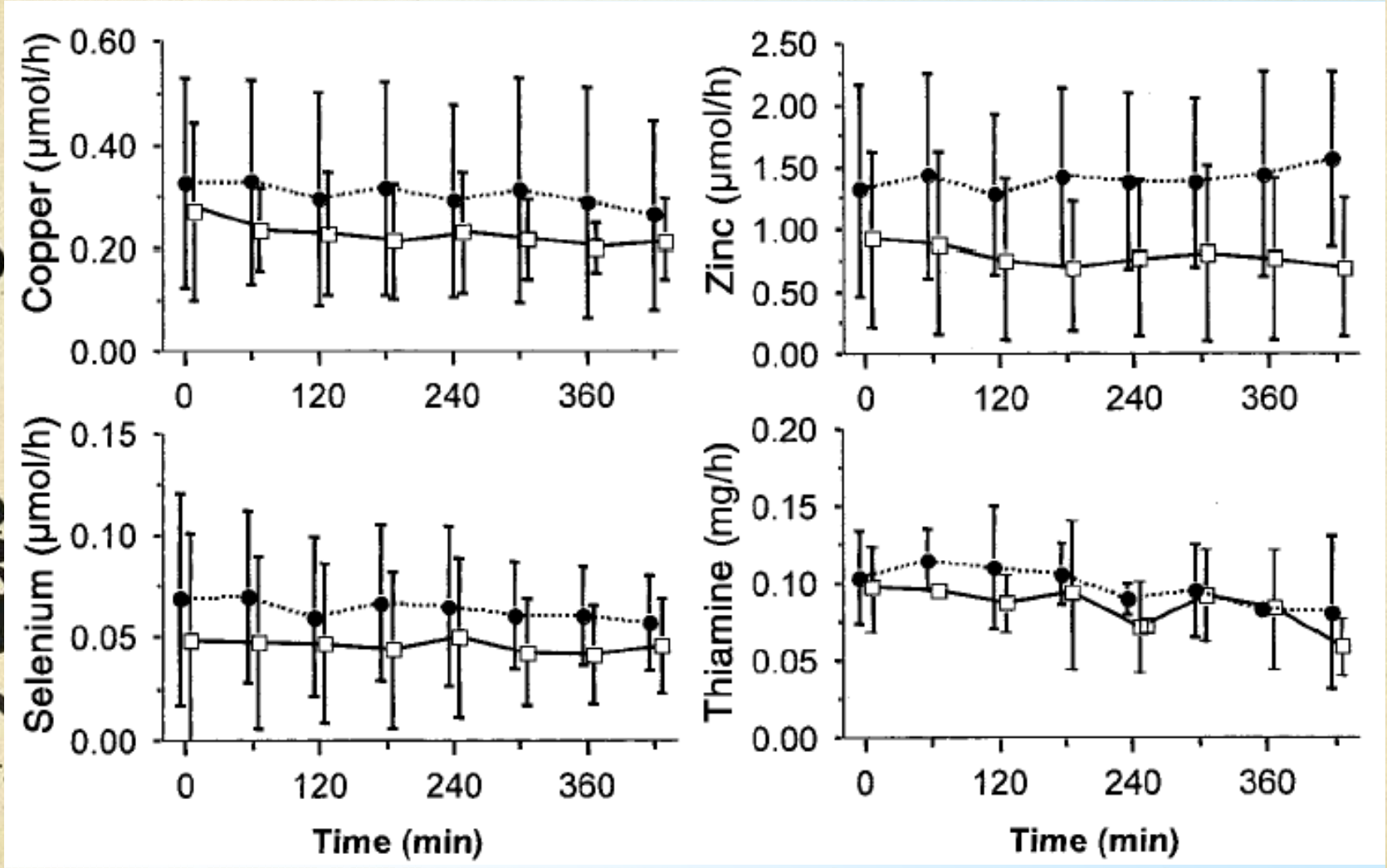
## Selenium in ICU

- Oxidative stress
- Inflammation
- Organ failure



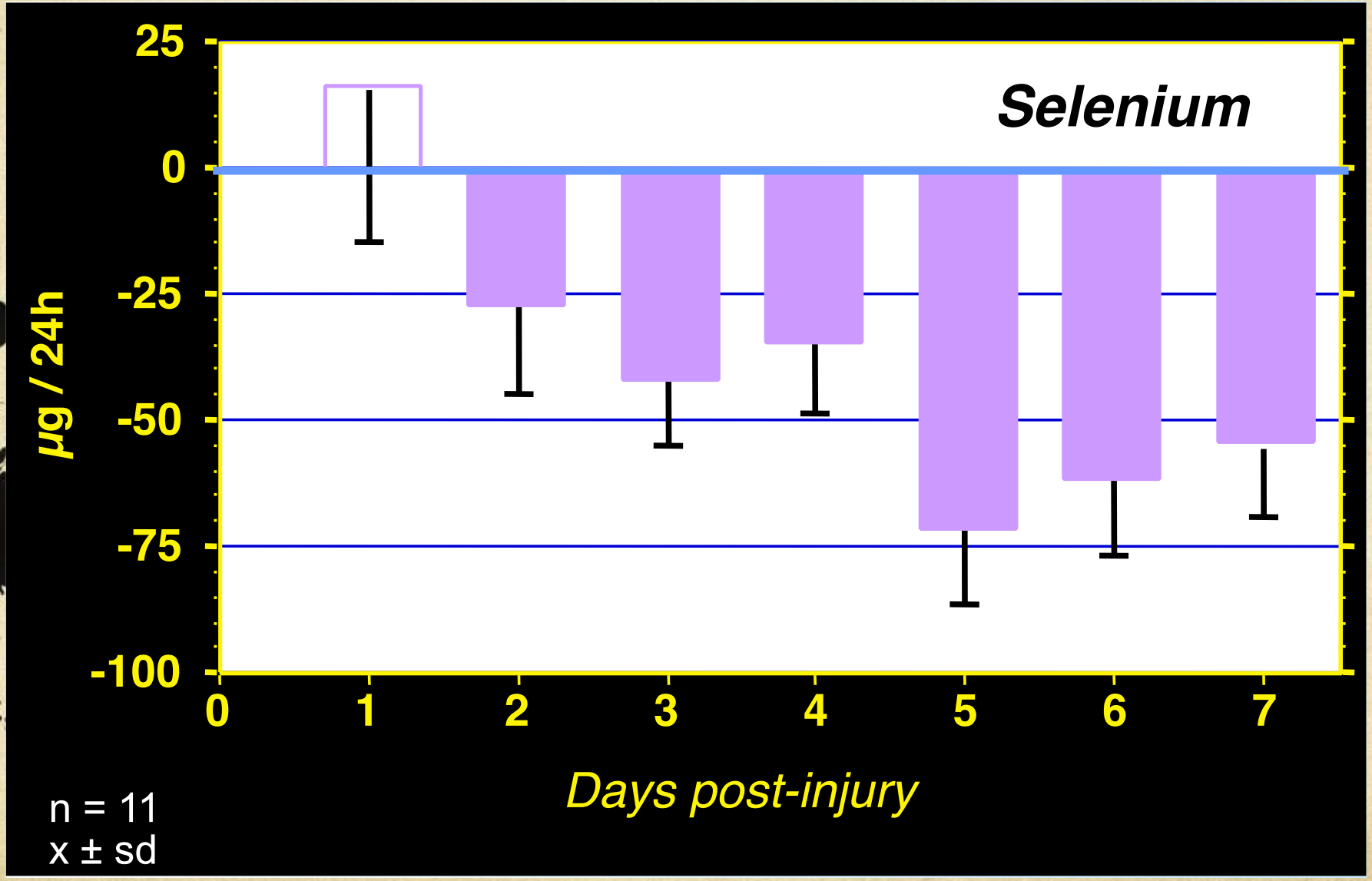

Berger, Negative balances – the causes in critically ill, NCP 21: 438, 2006

# Micronutrients losses during CVVH



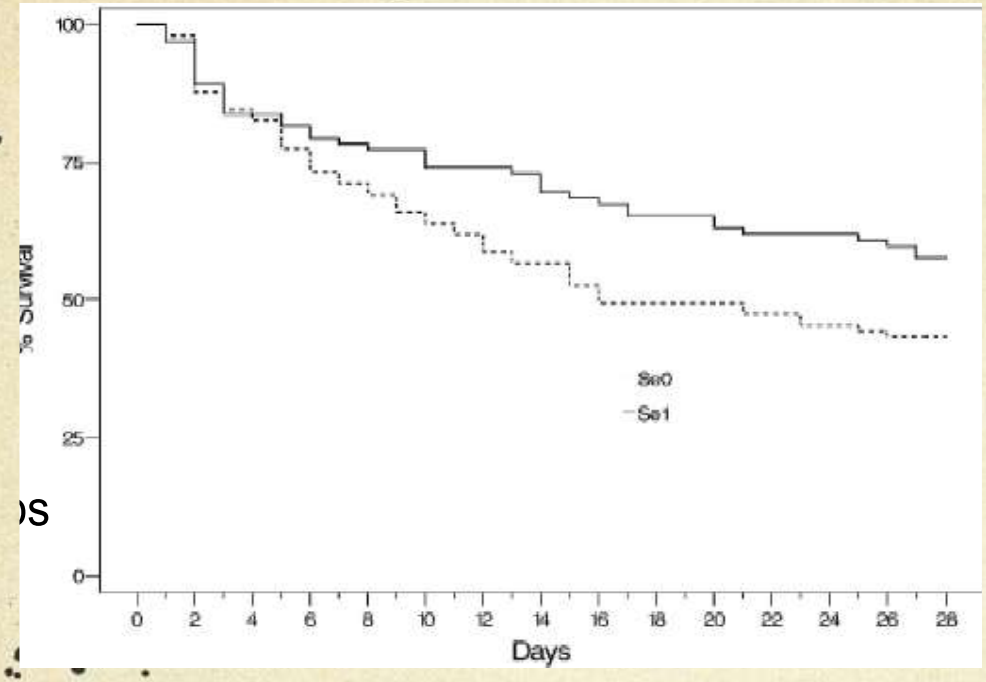

Berger MM et all., Amer.J Clin Nutr, 410, 2004

# Se balance after major trauma




Berger MM et all., J Trauma 40:103, 1996

# Matthias W. A. Angstwurm, Selenium in ICU SIRS – sepsis patients, Crit Care Med 2007 Vol. 35, No. 1




249 patients in severe sepsis or septic shock: 1000 mcg Se or placebo daily for 2 weeks after a loading dose

- the estimated mean survival time was 19.7 days in Se1 patients compared with 16.4 days in the Se0 group ($p < .0476$)

- - the absolute mortality reduction with adjuvant selenium treatment was 17.6% ($p < .024$; OR, 0.48; 95% CI, 0.25–0.91)

- - the 28-day mortality rate was with 14.3%, significantly lower, in Se1patients

Matthias W. A. Angstwurm, Selenium in ICU SIRS – sepsis patients, Crit Care Med 2007 Vol. 35, No. 1

## Secondary End Points

- APACHE II score decreased from day 1 to day 28 in the Se1 group (27.6%, $p < .0002$), comparable to the Se0 group (24.1%, $p < .0002$).
- the incidence of ARDS also was not significantly different in Se1 (5.4%) and Se0 (4.1%) patients.
- the maximum serum Selenium concentrations were found on day 14

# Disscution

- selenoprotein P is rapidly generated (1), preventing endothelial cells from oxidative damage followed by a diminished activation
- decreased tumor necrosis factor-α-induced intercellular adhesion molecule and selectin expression (2)
- GPx and thioredoxin reductase diminish the production of inflammatory prostaglandins and leukotrienes

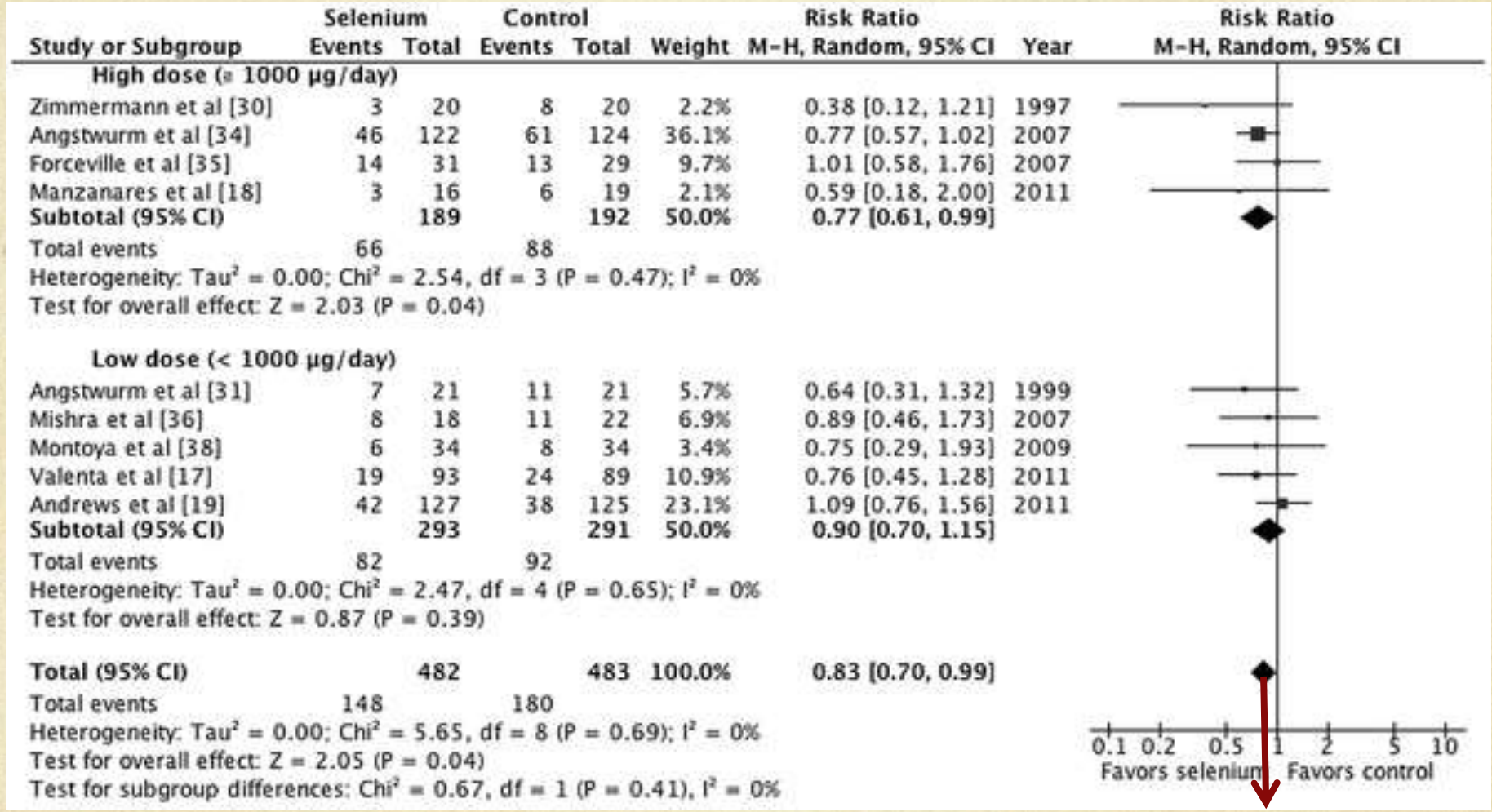
1.Schomburg L, Schweizer U, Kohrle J: Sele- nium and selenoproteins in mammals: Ex- traordinary, essential, enigmatic. *Cell Mol Life Sci* 2004; 61:1988 –1995

2. Miller S, Walker SW, Arthur JR, et al: Selen- ite protects human endothelial cells from oxidative damage and induces thioredoxin reductase. *Clin Sci* 2001; 100:543–550

# Is there any evidence that selenium supplementation in ICU patients is beneficial?

| Author and year | Critical illness | No. of patients | Daily Se/ebselen | Mortality Se+ | Mortality Se- | Included in meta-analysis* |
|---|---|---|---|---|---|---|
| Kuklinski 1991[31] | Pancreatitis | 17 | Se 500 g 8 days | 0/8 | 8/9 | Avenell Heyland (+/-) |
| Zimmerman 1997[21] | SIRS | 40 | Se 1000 g bolus + 1000 g 28 days | 3/20 | 8/20 | Avenell Heyland |
| Berger 1998[24] | Burns | 20 | Se 159 g 8 days | 1/10 | 0/10 | Heyland |
| Angstwurm 1999[12] | Sepsis/SIRS | 42 | Se 535 g for 3 days then reducing | 7/21 | 11/21 | Avenell Heyland |
| Porter 1999[27] | Trauma | 18 | Se 200 g ? days | 0/9 | 0/9 | Heyland |
| Berger 2001[28, 29**] | Trauma | 32 | Se 500 g 5 days | 2/20 | 1/12 | Heyland |
| Berger 2001[28**] | Trauma | 21 | Se 500 g 5 days | 2/9 | 1/11 | Avenell |
| Berger 2004[***26] | Burns | 21 | Se 380 g 14-21 days | 1/11 | 1/10 | Heyland |
| Lindner 2004[33] | Pancreatitis | 70 | Se 2000 g bolus + 1000 g 7 days | 5/35 | 3/35 | Avenell |
| Mishra 2007[13] | Sepsis/SIRS | 40 | Se 474 g for 3 days then reducing | 11/18 | 15/22 | Avenell |
| Forceville 2007[22] | Septic shock | 60 | Se 4000 g on first day, then 1000 g/day 9 days | 14/31 | 13/29 | No |
| Angstwurm 2007[14] | Sepsis/SIRS | 249 | Se 1000 g bolus then 1000 g/day 14 days | 46/116 | 61/122 | Avenell Heyland |

## Forest plot comparing mortality among selenium-treated patients to controls by treatment dosages.



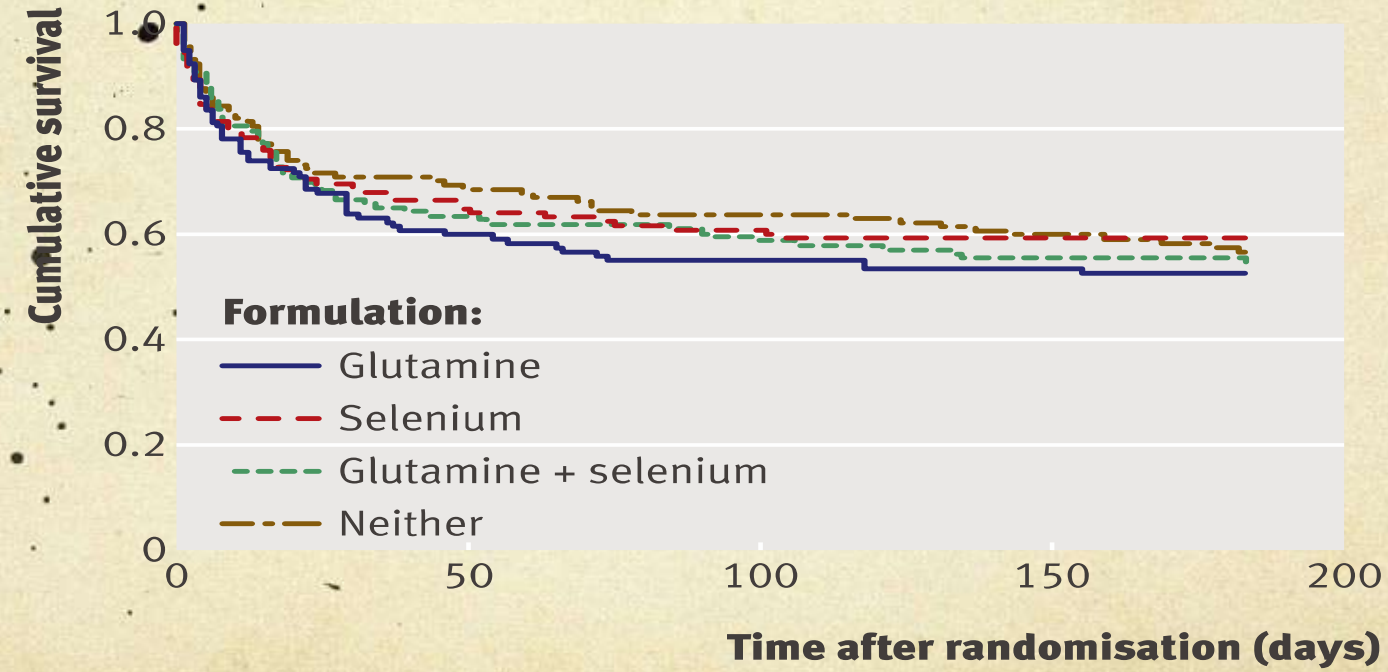

**Huang** T-S, Shyu Y-C, Chen H-Y, Lin L-M, et al. (2013) Effect of Parenteral Selenium Supplementation in Critically Ill Patients: A Systematic Review and Meta-Analysis. PLoS ONE 8(1): e54431. doi:10.1371/journal.pone.0054431
http://www.plosone.org/article/info:doi/10.1371/journal.pone.0054431

BMJ

RESEARCH

# Randomised trial of glutamine, selenium, or both, to supplement parenteral nutrition for critically ill patients

Peter J D Andrews, professor of critical care, consultant,[1,2] Alison Avenell, clinical senior lecturer,[3] David W Noble, consultant,[4] Marion K Campbell, director,[3] Bernard L Croal, consultant,[5] William G Simpson, consultant,[5] Luke D Vale, professor of health technology assessment,[3,6] Claire G Battison, trial manager,[1] David J Jenkinson, research fellow in medical statistics,[3] Jonathan A Cook, methodologist[3] and the SIGNET (Scottish Intensive care Glutamine or seleNium Evaluative Trial) Trials Group




parenteral nutrition supplemented with selenium for ≥5 days - reduction in new infections

Costa *et al. Critical Care* 2014, **18**:R92
http://ccforum.com/content/18/3/R92

CRITICAL CARE

RESEARCH Open Access

# Erythrocyte selenium concentration predicts intensive care unit and hospital mortality in patients with septic shock: a prospective observational study

Nara Aline Costa[1*], Ana Lúcia Gut[1], José Alexandre Coelho Pimentel[2], Silvia Maria Franciscato Cozzolino[2], Paula Schmidt Azevedo[1], Ana Angélica Henrique Fernandes[3], Bertha Furlan Polegato[1], Suzana Erico Tanni[1], Rafael Dezen Gaiolla[1], Leonardo Antonio Mamede Zornoff[1], Sergio Alberto Rupp de Paiva[1] and Marcos Ferreira Minicucci[1]

## Key messages

Erythrocyte selenium concentration is a predictor of

- ICU and hospital mortality in patients with septic

- not due to influence on GPx1 activity

# Products

## sodium selenite pentahidrat

**Decan** (Baxter, Aquettant) 153µg/40ml

**Microsol Selenium** (Boiron) 40µg/vial

**Nonan** (Baxter, Aquettant) 40µg/40ml

**Tracitrans** (Fresenius) 105,2µg/40ml

**Tracutil** (B.Braun) 78,9µg/10ml

**Addamel** (Fresenius) 32µg/10ml


# DOSES

- Recommended Daily Allowance (RDA) of selenium is 60 μg for women and 75 μg for men/ day
- The World Health Organisation suggests 40 μg/day of selenium is necessary to prevent disease
- in the UK, current intake is estimated at 34 μg/day

1.Expert group on vitamins and minerals. Safe upper levels of vitamins and minerals. Food Standards Agency London 2003: 232. http://cot.food.gov.uk/pdfs/vitamin2003

# What is the optimal dose of selenium for supplementation on the ICU?

**There may be a benefit from supplementing parenteral nutrition administered during critical illness with 500 µg of selenium daily for at least five days**

**- the safe upper limit for short term supplementation is 1,000 µg/day**

**- for long-term supplementation is 400-550 µg/day**


1. Peter J D Andrews et all., Randomised trial of glutamine, selenium, or both, to supplement parenteral nutrition for critically ill patients, BMJ 2011;342:d1542
2. Selenase® biosyn product literature http://www.pharmapal.com/ pharmapal/pdf/selenase.pdf Accessed December 2008.

# Products

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**Addamel** (Fresenius) 32µg/10ml


**Selenium Trace Element, 40 mcg/mL, 10mL Vial**

**Table 2: Selenium supplementation studies in critically ill patients**

| Author | Supplementation | Patients | No. of patients | Results |
|---|---|---|---|---|
| Zimmerman *et al.*[117] 1997 | 1000 μg/day Na-selenite IV vs no selenium. | SIRS+organ failure | 40 | Se supplementation reduced mortality. |
| Forceville *et al.*[61] 1998 | 40 μg/day Na-selenite+11.2IU Vit E + 500 mg Vit C IV | Adult ICU patients | 134 | 3-fold increase in morbidity and mortality in patients with low selenium concentrations. Efficacy of Se supplementation needs further investigation. |
| Berger *et al.*[116]1998 | 159 μg selenium +40.4 μmol copper +406 μmol zinc vs 32 μg selenium +20 μmol copper +100 μmol zinc | Major burn | 20 | Significant decrease in bronchopneumonia infection and shorter hospital stay with trace element supplementation. |
| Satio *et al.*[128] 1998 | 150 mg ebselen twice daily orally | Subarachnoid hemorrhage | 286 | Ebselen reduced brain damage and may be a promising neuroprotective agent. |
| Angstwurm *et al.*[118] 1999 | 535 μg/day Na-selenite (3 days), then 285 μg (3 days), then 155 μg (3 days) vs 35 μg/day IV | SIRS+APACHE>15 | 42 | Se replacement seems to improve clinical outcome and reduce incidence of acute renal failure requiring hemodialysis. |
| Porter *et al.*[114] 1999 | 50 μg q6h selenium IV+400IU Vit E, 100 mg VitC, 8 gm N-acetylcysteine q6h orally | Surgical ICU trauma patients | 18 | Antioxidant supplementation was associated with fewer infectious complications and fewer organ dysfunctions. |
| Berger *et al.*[113] 2001 | 500 μg Na-selenite only IV | | | |
| | 500 μg Na-selenite +150 mg α-tocopherol +13 mg zinc | Critically ill trauma patients | 31 | Earlier normalization of T4 and reverse T3 plasma levels with Se supplementation. |
| | Placebo | | | |
| Berger *et al.*[128] 2002 | 380 μg selenium + 59 μmol copper+574 μmol zinc vs placebo | Burn | 17 | Not estimable |
| Andrews *et al.*[128] 2004 | Glutamine containing and non-glutamine containing parenteral nutrition with or without Na-selenite 500 μg/day IV | ICU patients requiring parenteral nutrition | 500 | Not available-personal communication |
| Angstwurm *et al.*[129] 2004 | 500 μg/day Na-selenite (3 days), 250 μg(3 days) 125 μg (3 days) IV | ICU patients with nonthyroidal illness | 41 | Se supplementation in patients with nonthyroidal illness improved morbidity. |
| Mishra *et al.*[127] 2006 | 474 μg/day Na-selenite (3 days), 316 μg (3 days), 158 μg (3 days), then 31.6 μg/day IV vs 31.6 μg/day from the beginning | Severe sepsis | 40 | Se supplementation did not reduce oxidative damage or requirement for renal replacement therapy |
| Angstwurm *et al.* 2007[126] | 1000 μg/day Na-selenite IV vs placebo | Severe SIRS, sepsis and septic shock | 249 | Se supplementation reduced mortality in patients with severe sepsis and septic shock. |





Alaa Salama, Yasser Sakr, Konrad Reinhart, The role of selenium in critical illness: Basic science and clinical implications , Indian J Crit Care Med July-September 2007 Vol 11 Issue 3

# Normal value

0-3 mo: 18-64 µg/L

4-11 mo: 32-101 µg/L

1-5 y : 58-116 µg/L

6-16 y : 69-121 µg/L

**> 16 y: 74-139 µg/L**

Mayo Clinic, Mayo Medical Laboratories. Test Catalog. Selenium, Serum. www.mayomedicallaboratories.com. Ref Type: Internet Communication

**For optimal selenoprotein activity = 100 µg/L**

**EU average is 79 µg/L** (1)

**< 40 µg/L - Selenium defficit**

- loss of gluthation peroxidases activity

**1.Rayman MP**. Dietary selenium: time to act. *BMJ* 1997; 314: 387-88.

# Selenium monitoring – plasma When ?

Sepsis, septic shock

Burns

Trauma

pancreatitis

TPN

CVVH

# Warning !!!!!!!

**> 2.400µg/day TOXIC for human (1)**

**dose above 500–800 µg/day selenium should not be administered in routine practice in ICU patients (2)**

1.Laboratory Corporation of America. Directory of Services and Interpretive Guide. Selenium, Blood. www.labcorp.com 2010. Ref Type: Internet Communication

2.. Xavier Forceville et all. **Effects of high doses of selenium, as sodium selenite, in septicshock,** Critical Care 2007: Vol 11 No 4

# Conclusions - Se

- essential for its antioxidant function in critically ill patients
- dose of 500 μg/day seems to be safe and effectiv
- supplementation is inexpensive
- for ICU patients, in whom the literature suggests it should be supplemented parenterally
- reduce mortality rate in ICU


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