
Comments on Inorganic Arsenic Key Science Issue 8: Nutrition and Dose and Effect

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Gradient

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Science Issue 8: Nutrition and Dose and Effect

Folate deficiency

- Reduces availability and activity of s-adenosyl methionine for sequential methylation of iAs \rightarrow MMA \rightarrow DMA
- Bangladesh studies, up to 700 μ g iAs /L water (Howe *et al.*, 2014, Gamble *et al.*, 2005 & 2007)
 - Reduced folate associated with \uparrow MMA and \downarrow DMA in blood and in urine
 - Folate deficiency - preferential use of SAM in first methylation step
 - Folate deficiency - increased internal dose of trivalent metabolites

Science Issue 8: Nutrition and Dose and Effect (cont.)

Folate deficiency (cont.)

- High homocysteine/low folate associated with increased OR for skin lesions (Pilsner *et al.*, 2009)
 - Plasma folate mean 9 nmol/L in study population
 - 5th percentile in US of 12.4 nmol/L (NHANES, 2012)
- Betel nut use in Bangladesh
 - Impact on folate status (Gamble *et al.*, 2005)
 - Independent risk factor for skin lesions (Pilsner *et al.*, 2009) and atherosclerosis (McClintock *et al.*, 2014)
- High homocysteine/low folate – independent risk factors for CVD

Science Issue 8: Nutrition and Dose and Effect (cont.)

BMI

- Lower BMI associated with \uparrow MMA and \downarrow DMA (Heck et al, 2007)
- 38 % in study BMI < 18.5 versus 10 % < 18.5 in US men

Selenium

- Prospective case-cohort in Bangladesh (Chen *et al.*, 2007)
 - Inverse association between selenium blood level and skin lesions
 - High selenium (169.9 – 262.6 $\mu\text{g/L}$) – almost 50 % reduction in skin lesions
- US – only 3 % < required amount selenium

Science Issue 8: Nutrition and Dose and Effect (cont.)

Comments

- Nutrition needs to be considered as a modifier of both dose and effect
 - Nutritional differences between populations with high arsenic concentration (nutritional deficiencies) and US (nutritionally sufficient) population need to be considered in differences across countries
 - Exposure → dose
 - Dose → response