

## 28. Selenium

### Physiology

The total body content of selenium (3-30 mg) varies according to the geochemical environment and dietary intakes. Selenium is an integral part of the enzyme glutathione peroxidase (GSHpx), one of the mechanisms whereby intracellular structures are protected against oxidative damage <sup>1</sup>. Less than 2 % of selenium in plasma exists as glutathione peroxidase. Most is associated with  $\alpha$ - and  $\beta$ -globulins, and with glycoproteins amongst which one, selenoprotein P, may be involved specifically with selenium transport <sup>2</sup>.

Selenium deficiency (in animal models) has been associated with defective microsomal oxidation of xenobiotics and rat hepatic microsomal type 1 iodothyronine 5'-deiodinase is a seleno-enzyme <sup>3,4</sup>. Other selenoproteins have been isolated from mammalian tissues. One may be essential for normal morphology of mammalian sperm <sup>5</sup> but the roles of the others have not yet been identified. Additionally cellular immune functions are disturbed by selenium deficiency <sup>6</sup>.

Selenium is present in foods mainly as selenomethionine and selenocysteine. Selenoamino acids are probably absorbed by energy-dependent and sodium co-transport mechanisms similar to their sulphur analogues. Although the bioavailability of inorganic selenium is less than that of organic forms, this is probably of little practical significance because all usual dietary forms are absorbed quite efficiently <sup>1,7</sup>.

The pool of selenomethionine in protein is subject to factors influencing methionine metabolism, and its constituent selenium is not necessarily available for selenium-dependent processes. For example, when methionine intake is limiting, selenomethionine is incorporated into methionine sites even if there is a concomitant selenium deficiency. However if the methionine supply is adequate, selenium released from degraded selenomethionine is available to the active selenium pool. The biologically active pool of selenium depends on selenocysteine, which can be synthesised endogenously.

Homoeostasis of organic selenium is achieved by adaptations in urinary excretion, and to a lesser extent intestinal absorption. Systemically selenoamino acids can be

degraded to yield amino acid residues and selenite. Excess selenium is successively reduced to methylated and other derivatives, which are excreted in the urine.

## Deficiency and excess

In man the most striking selenium-responsive syndrome is that of Keshan disease, a selenium-responsive cardiomyopathy which affects predominantly children, adolescents and young women in China. Other factors probably contribute to the pathogenesis of Keshan disease, but related cardiomyopathies have been observed in patients on total parenteral nutrition. Less severe deficiencies, involving skeletal myopathy with increased plasma creatine kinase activities, macrocytosis and lightening of skin and hair pigmentation, have been documented. An increased degree of haemolytic sensitivity of red cells *in vitro* to peroxide, as evidence of significantly reduced GSHpx activity, may be the only detectable feature.

At excessive intakes of selenium a volatile dimethylated compound  $[(\text{CH}_3)_2\text{Se}]$  is formed, which when lost via expired air gives a characteristic garlic odour. Dietary intakes of 3.2-6.7 mg/d cause severe selenosis, encompassing an erythematous, bullous dermatitis, dystrophic nails, alopecia and neurological abnormalities involving parasthesia, paralysis and hemiplegia <sup>9</sup>.

## Requirements

### Adults

Customary adult daily intakes of selenium vary between 20 and 300  $\mu\text{g}/\text{d}$ . In China dietary intakes range from 11-5000  $\mu\text{g}/\text{d}$ , at which extremes deficiency and toxicity syndromes occur.

In New Zealand and Finland habitual intakes of 15-40  $\mu\text{g}/\text{d}$  have not been associated with selenium-responsive disease although whole blood GSHpx activity was below its possible peak activity, which occurs with whole blood selenium concentrations about 100  $\mu\text{g}/\text{L}$  <sup>7,8</sup>. In China populations with intakes of selenium of less than 12  $\mu\text{g}/\text{d}$  experience Keshan disease, and those with intakes of 19  $\mu\text{g}$  or more do not <sup>9,10</sup>. If allowance is made for the smaller size of individuals in China, 20  $\mu\text{g}/\text{d}$  can be proposed as the European LTI <sup>11</sup>. Studies based on the saturation of GSHpx activity suggest that an Average Requirement would be about 40  $\mu\text{g}/\text{d}$  <sup>10</sup>, which would give a PRI of 55  $\mu\text{g}/\text{d}$ .

Disturbed metabolism of selenium occurs at intakes above 750 µg/d and early features of nail dystrophy have been described at intakes of 900 µg/d <sup>12</sup>. Since the intake beyond which there is no discernible benefit is much lower than this, it is suggested that the maximum safe intake from all sources should be 450 µg/d.

### *Children*

No extensive investigations have been made on selenium requirements in children. Blood concentrations at 1 year of age are about 80% of those of adults, increase to adult values by 3 years, and then remain fairly constant <sup>13</sup>. The PRIs have been calculated from adult values, on the basis of body weight, and should cover the relatively much smaller requirements for growth (0.2 ng/g weight gain).

### *Pregnancy and lactation*

Adaptive changes in the metabolism of selenium occur during pregnancy <sup>14</sup>, so no recommendation is made for any extra increment.

To maintain the selenium concentration in infants' serum at about 70 ng/ml, a daily intake from breast milk of about 8-10 ng/ml is necessary <sup>15</sup>. In the absence of more specific information, the extra requirement during lactation has been calculated on the basis of 60% absorption from the diet, and milk with a selenium content of 12 ng/ml, to give an increment of 15 µg.

## Summary

<i>Adults</i>	$\mu\text{g/d}$
<b>Average Requirement</b>	40
<b>Population Reference Intake</b>	55
<b>Lowest Threshold Intake</b>	20
<b>Maximum safe intake</b>	450

### *Population Reference Intakes of other groups*

Age Group	PRI ( $\mu\text{g/d}$ )
6 - 11 m	8
1 - 3 y	10
4 - 6 y	15
7 - 10 y	25
11-14 y	35
15-17 y	45
Pregnancy	55
Lactation	70

## References

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