Selenium

Selenium is an essential mineral and micronutrient. It is fundamental to human health and found in many foods. It is found in meat, grain cereals, egg yolk, milk, brazil nuts, mushrooms, garlic and seafood (hence, selenium levels are high in populations with high intake of seafood, like the Inuit population).\(^\text{[1, 2]}\)

Selenoproteins are important constituents of a number of enzymes with a range of functions including antioxidant function, thyroid hormone metabolism, male fertility and immune mechanisms. A decline in blood selenium levels in the UK and other European countries has raised concern about possible public health implications, particularly in relation to cancer and cardiovascular disease. Whilst there is some understanding of the role of these proteins in health and disease (and some interesting theories and research), there are many unanswered questions and much debate about supplementation. More research is repeatedly called for.\(^\text{[2]}\) Deficiency is linked with a wide variety of medical problems but excessive intake can have toxic effects and may even be carcinogenic.\(^\text{[3]}\)

How much selenium is recommended?

Dietary recommendations for selenium differ between countries. This is because there is uncertainty over what constitutes ‘optimal selenium status’.\(^\text{[4]}\) The average daily intake of selenium in in the UK has been falling over a 30-year period. In the UK, the recommended daily allowance (RDA) is 75 micrograms/day for men and 60 micrograms/day for women.\(^\text{[5]}\) In the USA, the RDA is 55 micrograms/day for adults. The World Health Organization (WHO) RDA for selenium is 70 micrograms/day to 350 micrograms/day. Some are recommending supranutritional supplements of 200 micrograms/day to 800 micrograms/day. Toxic effects probably occur at around 40x the RDA.

How are selenium levels measured?

Erythrocyte, serum and tissue levels of glutathione peroxidase (GP) can be measured to assess selenium status.\(^\text{[6]}\) Selenium in hair and nails can also be measured. Discuss with your laboratory before deciding which method to use.

Why is selenium essential?

Dietary recommendations were made over 20 years ago on the basis of blood levels of GP. This intracellular enzyme converts hydroxyl radicals or hydrogen peroxide into water and this requires selenium as a co-factor. Levels of this enzyme have thus been taken to correlate with selenium levels. Since then, over 30 new selenoproteins have been identified and about half of these have an identified biological function.\(^\text{[7, 8]}\) These selenoproteins include:

- Four GP enzymes, a major class of functionally important selenoproteins and the first to be characterised:
  - Classical GP x 1.
  - Gastrointestinal GP x 2.
  - Plasma GP x 2.
  - Phospholipid hydroperoxide GP x 4.

- Thioredoxin reductase (TR), a selenocysteine-containing enzyme important in regulating metabolic activity.
- Selenoprotein P (60% of plasma selenium is held in this form) may have a role in the transport of selenium but also may have other functions.
- Several iodothyronine deiodinase enzymes. These are responsible for conversion of the prohormone thyroxine to the active thyroid hormones (triiodothyronine, or T3).
- Sperm capsule selenoprotein which may be responsible for maintaining integrity of the sperm flagella (and hence motility of sperm).
- Selenoprotein W. This is involved in muscle metabolism.

What harm does deficiency of selenium cause?

Deficiency of selenium may cause a variety of problems but the health implications of a decline in selenium levels in the UK over 25 years have not been systematically investigated. In general, selenium is thought to be important in a number of varied aspects of health: for a healthy immune system, for a protective effect against some forms of cancer, to maintain and enhance male fertility, for a reduction in cardiovascular mortality and to regulate inflammatory markers in asthma. Research is in progress and there is a lot of interest in the results of this research. Although there are still many unanswered questions, so far selenium has been linked with:

- Counteracting the development of virulence and inhibiting HIV progression to AIDS.\(^9\)\(22\) Trials are small and results mixed but more research is called for.\(^{10}\)
- Enhancing sperm motility.\(^{11}\)
- A possible role in preventing pre-eclampsia.\(^{12}\)
- A possible relationship between mood disturbance and selenium deficiency.\(^{13}\)
- A possible association between elevated selenium intake and reduced cancer risk. The association between selenium status and cancer risk remains enigmatic and epidemiological studies have failed to consistently link low selenium levels with increased cancer risk in men and women.\(^{14}\) It is possible that there may be gender differences in susceptibility to cancer risk with men being more susceptible to the risk of low selenium. In the Nutritional Prevention of Cancer Trial, daily supplementation of selenium significantly reduced prostate cancer in men.\(^{15}\) It is thought that the greatest benefit from selenium supplementation will be in low selenium status populations, although the biggest primary and secondary prevention trials - SELECT (= Sel enium and Vitamin E Cancer Prevention Trials) - were carried out in the USA where selenium status is good.\(^{16}\) Some were predicting that the SELECT results in 2013 would show benefit.\(^{17}\) However, the trial was discontinued because there was no evidence of a benefit from either vitamin E or selenium on prevention of prostate cancer.\(^{18}\) Concern was also raised about a link between selenium supplementation and an increased risk of developing type 2 diabetes.\(^{19}\)
- In asthma, some epidemiological studies suggest that deficiencies of selenium, zinc and other nutrients (vitamins A, C, D and E) may be associated with the development of allergic disorders and asthma.\(^{20}\) Although a number of trials suggest supplementation with selenium may help symptoms of chronic asthma, only one small trial, according to the Cochrane review, showed evidence of this.\(^{21}\)
- Cardiovascular disease.\(^{22}\) The hypotheses that low selenium concentrations are associated with increased cardiovascular disease and that selenium supplements prevent coronary heart disease are unproven. Selenium supplementation cannot currently be recommended for cardiovascular disease prevention.\(^{23}\) Deficiency is associated with cardiomyopathy in general, but particularly in Keshan disease, a congestive cardiomyopathy associated with Coxsackievirus and selenium deficiency.\(^{24, 25}\)
- Deficiency in trauma and burns patients. One study reports improved recovery with selenium supplementation in trauma and burns patients.\(^{26}\)
- The thyroid gland contains more selenium than any other tissue. Selenium deficiency may help to precipitate hypothyroidism and autoimmune thyroid disease and supplementation may contribute to prevention of these diseases.\(^{27}\)

Who is at risk of selenium deficiency?

Risk factors include:

- Poor dietary intake. Because selenium is found in meat and seafood, vegetarians in areas with low environmental selenium may become deficient.
- Smoking.\(^{28}\)
- Socio-economic status. Lower levels have been found in people receiving state benefits or with lower educational attainment.
- The elderly living in residential or nursing homes had lower levels of selenium when compared with ‘free-living’ elderly patients.
- The elderly, particularly in areas where low intake is common.
- Where you live:
  - Areas with a low selenium soil environment are associated with deficiency. The elderly in such areas are particularly at risk and one study from New Zealand demonstrated suboptimal levels of selenium in a significant proportion of 103 elderly New Zealand women.\(^{29}\)
  - The levels of selenium are higher in the south of England than in the north.\(^{28}\) The selenium status may vary within countries according to factors such as the selenium in the local soil but is also affected by the levels of selenium in imported crops.
- Patients on total parenteral nutrition (TPN).\(^{30, 31}\)
- Trauma and burns patients.\(^{26}\)

Indications for supplementation
Those at high risk of deficiency should have their selenium status measured. If deficient in selenium, such patients should certainly be given supplements. As with many nutritional components, distinction must be drawn between the basic nutritional requirement to prevent deficiency and supplementation to prevent, for example, chronic disease and cancer.\[32, 33\] According to a report from the USA, 99% of over 17,000 subjects were 'selenium replete' according to plasma selenium levels and not in need of routine supplementation.\[33\]

There is widespread questioning of the use of RDAs and some questioning of methods of assessing deficiency in this as in other areas of nutrition.\[36, 37\] Evidence of benefit at supranutritional levels of dietary intake is needed to support what has been called the 'nutraceutical' approach to supplementation. Further studies are needed and are being undertaken to support such beneficial effects.\[34\] If such evidence is forthcoming then health professionals will need to use dietary and clinical assessment methods to ensure that those at risk of cancer or inflammatory or infectious disease be appropriately advised about selenium intake.\[34\]

Further reading & references
