

# Zinc deficiency, excess and supplementation

## The role of zinc in the body

Zinc is an essential trace element and has a number of roles and functions in the human body.

- It is an essential component/cofactor for more than 300 enzymes involved in the synthesis and metabolism of carbohydrates, lipids, proteins, nucleic acids and other micro-nutrients.
- It stabilises cellular components and membranes and so is important for cell and organ structure and integrity.
- It is essential for cell division and is needed for normal growth and development during pregnancy, childhood and adolescence.
- It is involved in DNA synthesis and the process of genetic expression.
- It is important for immune function (both cellular and humoral immunity).
- It is involved in wound healing and tissue repair.
- It is needed for the senses of taste and smell.

## How much zinc per day?

- **The recommended daily zinc intake (reference nutrient intake) for an adult man in the UK is 9.5 mg.**
- **The recommended daily zinc intake for an adult woman in the UK is 7 mg.**
- An average-sized adult male has a body level of 1.4 to 2.3 g of zinc.<sup>[1]</sup>

- Approximately 60% of the total body zinc content is found in skeletal muscle and 30% in bone mass.
- The choroid of the eye and prostatic fluid have high concentrations of zinc.
- Zinc is absorbed predominantly in the duodenum and proximal jejunum, and excreted mainly in the faeces.
- There are no body stores of zinc and so daily intake of zinc is needed to maintain adequate body levels.
- Mean consumption of zinc for an adult is about 10–15 mg daily.<sup>[1]</sup>
- The Department of Health in the UK advises that intake of zinc should not exceed 25 mg per day.

## Dietary sources of zinc

Zinc-rich foods:

- Red meat and poultry (these are the main sources of zinc for many).
- Oysters, crab, lobster and other shellfish (oysters contain more zinc per serving than any other food).
- Pulses, nuts and legumes.
- Wholegrain cereals.
- Fortified breakfast cereals.
- Dairy products such as cheese.

Note that phytates in wholegrain bread, cereals, legumes and some other foods inhibit zinc absorption and so affect the bioavailability of zinc from plant foods.

## Zinc deficiency

### Risk factors

- Inadequate diet.
- Gastrointestinal diseases including [ulcerative colitis](#), [Crohn's disease](#), short bowel syndrome and [chronic diarrhoea](#).

- Chronic liver disease.
- Chronic kidney disease.
- Alcohol dependency (decreases zinc absorption and increases urinary zinc excretion).
- Sickle cell disease.
- Diabetes.
- Pregnancy and breastfeeding.
- Vegetarian diet.
- People taking large amounts of iron supplementation (iron can interfere with zinc absorption).

### **Symptoms of zinc deficiency**

This depends on the severity of zinc deficiency.

- Anorexia, lethargy, diarrhoea.
- Growth restriction (delayed bone maturation).
- Impaired immune function and susceptibility to infection.

Severe cases can lead to:

- Delayed sexual maturation, impotence, hypogonadism and hypospermia.
- Alopecia, dermatitis, paronychia.
- Intellectual disability, impaired nerve conduction and nerve damage.
- Weight loss.
- Macular degeneration.
- Impaired taste and smell.
- Impaired wound healing.
- Impaired iron absorption.<sup>[2]</sup>

### **Investigations**

- Diagnosis may be difficult to confirm because plasma and serum zinc levels do not necessarily reflect cellular zinc status.
- Clinical signs and effects of zinc deficiency may be present with normal laboratory values.
- Clinicians need to have a high index of suspicion, particularly if risk factors are present.

## **Treatment**

- This is based on both treatment of any underlying cause and zinc supplementation.
- Dietary advice should also be given.

## **Acrodermatitis enteropathica**

- Acrodermatitis enteropathica can either be inherited or acquired.<sup>[3]</sup>
- The acquired form can arise in people with a zinc-deficient diet.

- The inherited form is a rare autosomal recessive disorder leading to failure to generate a transport protein that enables zinc to be absorbed in the intestine:
  - Symptoms usually begin after an infant is weaned from breast milk.<sup>[4]</sup>
  - It presents with a characteristic pustular rash over the mucocutaneous junctions, particularly around the mouth and around the anus and genital areas.<sup>[4]</sup>
  - Hair loss, nail dystrophy, failure to thrive and severe diarrhoea are also features.
  - Atrophy of the brain cortex can lead to irritability and emotional disturbances.
  - Secondary bacterial and fungal infections may also occur.
  - Treatment is with zinc supplements.
  - If treated early, most of the symptoms are reversible and usually leave no sequelae.
  - Therapy is lifelong and total compliance is essential.

## Zinc excess and zinc toxicity

### Risk factors

- Zinc may accumulate in [acute kidney injury](#).
- Those with [haemochromatosis](#) may absorb larger amounts of zinc.
- Various pesticides contain zinc salts.
- Compounds used to make paints, rubber and dyes may also contain zinc.

### Symptoms of zinc toxicity

- Zinc toxicity may be acute or chronic.

- Acute toxicity (ingesting more than 200 mg/day of zinc) can cause:
  - Abdominal pain, nausea, vomiting and diarrhoea.
  - Other reported effects - these include gastric irritation, headache, irritability, lethargy, anaemia and dizziness.
- Prolonged intake of zinc ranging from 50-150 mg/day can lead to:
  - Disturbance of copper metabolism, causing low copper status, reduced iron function, red blood cell microcytosis, neutropenia and reduced immune function.
  - It can also lead to reduced levels of high-density lipoproteins and so it has been suggested that excessive zinc intake may be atherogenic.
  - Excess zinc can also affect cardiac function and can impair the pancreatic enzymes amylase and lipase.

## Investigations

- Blood zinc levels can be measured to assess toxicity.

## Treatment

- Treatment is symptomatic. <sup>[5]</sup>

## Metal fume fever

- Inhalation of fumes containing zinc oxide may cause metal fume fever.
- Metal fume fever can also follow inhalation of fumes of copper, magnesium, aluminium, antimony, iron, manganese and nickel during welding, galvanising or smelting. <sup>[5]</sup>
- Symptoms may occur within 3-10 hours of exposure and usually resolve within 1-2 days.
- Symptoms include cough, dyspnoea, sore throat, chest pain, headache, fever, rigors, myalgia, arthralgia and gastroenteritis.

- Management of metal fume fever includes removing the patient from exposure, oxygen as required, and symptomatic treatment for pain and fever.<sup>[5]</sup>

## Zinc supplements

- A number of different forms of zinc are available as supplements, including zinc sulfate, zinc gluconate and zinc acetate.
- Zinc supplements must be used with caution in view of the dangers of zinc excess and zinc toxicity.

### Indications for zinc supplementation

These include:

- Proven zinc deficiency and zinc-losing conditions.
- Zinc acetate is used to treat Wilson's disease.<sup>[6]</sup>
- Total parenteral nutrition regimens usually include trace amounts of zinc. If necessary, further zinc can be added to intravenous feeding regimens.

### Supplementation during acute diarrhoea in children

- The World Health Organization (WHO) recommends zinc supplementation for 10–14 days (20 mg daily; 10 mg daily for children aged under 6 months) in children with acute diarrhoea in countries where the prevalence of malnutrition is high because studies have shown that this shortens the course of the diarrhoea.<sup>[7]</sup>

### Supplementation as treatment for the common cold

- Lozenges containing at least 75 mg have been the most widely studied but their use needs to be balanced against side-effects of nausea and bad taste.<sup>[8]</sup>
- No sufficient evidence was found to support prophylactic zinc supplementation for the common cold.

### Supplementation for age-related macular degeneration (AMD)

- The Age-Related Eye Disease Study (AREDS) was a large, randomised, placebo-controlled trial looking at the effect of high-dose antioxidant (beta-carotene, vitamin C and vitamin E) and zinc supplements on the development of advanced AMD in people who already had different degrees of AMD. [9]
- When both antioxidants and zinc were taken, the risk of developing advanced AMD was significantly reduced and visual acuity loss was reduced as well.
- Supplementation with zinc alone reduced the risk of advanced AMD in high-risk individuals but not in the total study population.
- Zinc supplementation alone did not have a significant effect on visual acuity loss.
- A Cochrane review also supported the use of antioxidant and zinc supplementation in those with AMD but with caution and recommendation for further studies. [10]

## Cautions

- Zinc may accumulate in [acute kidney injury](#).
- Those with [haemochromatosis](#) may absorb larger amounts of zinc.
- Excess zinc supplementation can interfere with iron and copper absorption.
- It can also reduce magnesium and calcium absorption.

## Interactions

- Quinolone and tetracycline antibiotics may interact with zinc supplements, leading to reduced absorption of the supplement and the antibiotic.
- Zinc supplementation can reduce the absorption of penicillamine.
- Prolonged use of thiazide diuretics increases urinary excretion of zinc and so can reduce tissue levels.

## Side-effects

- Irritability, headache, lethargy.



- Unpleasant taste in the mouth.
- There have been reports of anosmia with intranasal zinc preparations.
- Gastrointestinal effects, including abdominal pain, dyspepsia, nausea, vomiting, diarrhoea, gastric irritation, and gastritis. This is more likely when supplements are taken with little or no food.
- Prolonged use of high doses of zinc can result in deficiency of copper.

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## Further reading

- [Saper RB, Rash R](#); Zinc: an essential micronutrient. Am Fam Physician. 2009 May 1;79(9):768–72.

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