CHAPTER 9 MINERALS

A. Kench, J. Grunert, J. Heyward & J. Anderson

As part of a comprehensive nutrition review, both macro- and micronutrients (vitamins and minerals) are assessed in CF. This chapter will cover the key minerals that are considered to be at risk of deficiency for people with CF.

9.1 Iron

Iron status is often compromised in adults and children with CF [96,412-415]. Iron is a component of haemoglobin, which circulates in the blood via erythrocytes (red blood cells) and is responsible for the transport of oxygen around the body [43]. It is also found in readily metabolised body stores as ferritin, in the muscle as myoglobin, and in a variety of enzymes used for metabolic processes including oxygen and electron transport [43]. Iron is found in animal and plant-based food sources. Meat, fish and poultry provide good amounts of dietary iron. Less biologically available plant-based sources include wholegrain cereals and leafy green vegetables.

Disease Aetiology

Anaemia is defined as a deficiency in haemoglobin or the number of circulating red blood cells. Iron deficiency is the most common form of anaemia [416]. Iron deficiency is usually classified as absolute or functional iron deficiency [417].

ABSOLUTE IRON DEFICIENCY

- Iron stores are depleted and thus unavailable for erythropoiesis [417]

FUNCTIONAL IRON DEFICIENCY (ANAEMIA OF CHRONIC DISEASE OR INFLAMMATION)

- Iron stores are adequate or even higher than normal but there is insufficient iron available at the site of erythroblast production [417].

It is thought that both absolute and functional iron deficiency play a role in the pathophysiology of iron deficiency in the paediatric CF population [415]. Functional iron deficiency is the primary cause of iron deficiency in the adult CF population [96,412-414].

Iron deficiency usually occurs after a period where losses or requirements exceed intake and/or absorption of iron [418]. Iron deficiency is therefore more common in the following populations, with or without CF [418]:

- The paediatric population, especially during periods of rapid growth
- Pregnant, breastfeeding and menstruating women
- Endurance athletes
- Blood donors

The following factors also contribute to iron deficiency, especially in the CF population [415,419,420]:

- Chronic inflammation
- Inadequate dietary intake - particularly for people following a vegetarian or vegan diet
- Gastrointestinal co-morbidities – malabsorption, small intestinal bacterial overgrowth or gastro-oesophageal reflux (GOR)
- Haemoptysis
- Chronic bacterial colonisation of the airways

Although a direct causal relationship has not been established, it has also been suggested that chronic colonisation by Pseudomonas aeruginosa (PA) may cause iron deficiency in CF due to:

- PA using extracellular iron for growth [421]
- PA stimulating the production of cytokines, diverting iron from haemoglobin synthesis and in turn promoting local iron storage in the airways of people with CF [420]

The prevalence of iron deficiency in children with CF has been reported to be 17-33% [415,419,422], increasing to >60% in the adult CF population [414,419,422].

Assessment

When assessing iron status for a person with CF, it is important to consider the following:

- Adequacy of dietary iron intake
- Clinical indicators of potential iron deficiency
- The underlying cause of iron deficiency
- Biochemical markers for iron status

DIET

Normal iron absorption is known to vary from 10% or less in iron-fortified infant cereals, to 50% in breast milk [43]. On average, less than 20% of the iron available in the western diet is absorbed [418]. The following factors are thought to contribute to the proportion of iron absorbed from food [43]:

- An individual's iron status
- The overall iron content of foods consumed
- Type of iron consumed (haem vs. non-haem iron)
    - Haem iron is found primarily in meat, seafood and poultry and is more bioavailable than non-haem iron. In the western population, haem iron contributes to 10-15% of total iron intake [423].
    - Non-haem iron is less bioavailable than haem iron and is present in both animal (meat, seafood and poultry) and plant-based food sources (wholegrain cereals and green leafy vegetables) as well as iron-fortified foods.
- The impact of other nutrients on the absorption of iron
    - Vitamin C and organic acids such as citric, lactic or malic acid as well as the consumption of meat, fish and poultry can enhance the absorption of non-haem iron.
    - Calcium, phytates (found in legumes, rice and other grains) and tannins (found in tea) can inhibit the absorption of haem and non-haem iron.

Wholegrain cereals, meats, fish and poultry are the major contributors to iron intake in Australia and New Zealand [43], see Table 9b. Iron requirements for the general Australian and New Zealand population are outlined in Table 9a.

Table 9a. Recommended Dietary Intake (RDI) of iron for people in Australia and NZ, mg/day [43].
Available at: http://www.nrv.gov.au/

Recommended Dietary Intake (RDI) for Iron		
	Males (mg/day)	**Females** (mg/day)
Infants		
0-6 months	0.2	0.2
7-12 months	11	11
Young children		
1-3 years	9	9
4-8 years	10	10
Children & adolescents		
9-13 years	8	8
14-18 years	11	15
Adults		
19-30 years	8	18
31-50 years	8	18
51-70 years	8	8
<70 years	8	8

Table 9b. Iron containing foods (mg per serve) [424]

	Serving Size	Iron (mg)	mg/100g
Animal-based iron sources			
Chicken liver	100 g	11	11
Beef	100 g	3.5	3.5
Kangaroo	100 g	3.2	3.2
Lamb	100 g	2.5	2.5
Salmon	100 g	1.3	1.3
Tinned tuna	100 g	1.1	1.1
Pork	100 g	0.8	0.8
Chicken	100 g	0.4	0.4
Snapper	100 g	0.3	0.3
Plant-based iron sources			
Weet-Bix™	30 g	4.2	14
All Bran™	30 g	3.2	10.7
Kidney beans	1 cup	3.1	2.1
Green lentils	1 cup	3	6.8
Tofu	100 g	3	3
Chickpeas	1 cup	2.7	1.8
Cooked wholemeal pasta	1 cup	2.3	1.8
Cashew nuts	20 nuts	1.5	5
Raw spinach	1 cup	1.2	3.2
Rolled oats	30 g	1.1	3.7
Almonds	30 g	1.1	3.7
Dried apricots	5 apricots	0.9	3.1
Broccoli	1 cup	0.9	0.8
Cooked brown rice	1 cup	0.7	0.5

DIETARY CONSIDERATIONS FOR INFANTS

- The bioavailability of iron in breast milk is high although not enough to meet the iron requirements for infants greater than 6 months in age. Iron-rich foods, including iron-fortified cereals and pureed meats should also be included at the time of introduction of solids [425].
- Cow's milk is low in iron and as a result, should not be recommended as the main drink for infants less than 12 months of age [425]. The excess consumption of cow's milk, replacing iron-rich food sources, should also be considered as a potential cause of iron deficiency in toddlers.

CLINICAL

Symptoms of iron deficiency may include [43,418]:

- Reduced physical work capacity and fatigue
- Delayed psychomotor development in infants
- Impaired cognitive function
- Impaired immunity
- Adverse pregnancy outcomes
- Faltering growth during infancy

In addition to the factors contributing to potential iron deficiency in CF *(as outlined in disease aetiology)*, the following should also be considered as potential underlying causes [418]:

- Gastrointestinal conditions – cow's milk protein allergy, coeliac disease, gastrointestinal blood losses
- Parasitic infections

BIOCHEMICAL AND LABORATORY DATA

Anaemia is defined as serum haemoglobin (Hb) levels below the reference range for age and gender [418]. However, anaemia is not always a result of iron deficiency. A corresponding low mean corpuscular volume (MCV) or mean corpuscular haemoglobin (MCH) usually indicates anaemia resulting from iron deficiency [418].

If iron deficiency is suspected, further testing of iron studies, including serum iron, transferrin, transferrin saturation, ferritin +/- soluble transferrin receptor (sTfR) should be requested [418]. Overall serum ferritin, which reflects the size of the iron store, is most commonly used to assess iron status in the general population [426]. However, serum ferritin is also an acute phase protein and is elevated during periods of inflammation. Care should be taken when interpreting biochemical markers of iron status in conditions that are complicated by chronic inflammation, as is often the case in CF, as serum ferritin levels may be within normal limits or falsely elevated when iron stores are low [96]. A summary of the biochemical markers used to assess iron status and their interpretation is outlined in Table 9c.

Table 9c. Interpretation of biochemical markers used to assess iron status in the general population*

Diagnosis	Haemoglobin (Hb)	Mean cell volume (MCV)	Serum ferritin (µg/L)	Transferrin or total iron binding capacity	Transferrin saturation	Soluble transferrin receptor (sTfR)	Serum iron
Iron deficiency	Normal	Normal (or low)	Low	Normal to High	Low to Normal	Normal to High	Low
Iron deficiency anaemia (absolute)	Low	Low	Low	High	Low	High	Low
Anaemia of chronic disease or inflammation	Low	Normal	Normal to High	Normal	Low	Normal	Low
Iron deficiency anaemia with chronic disease (functional)	Low	Low	Low to Normal	Normal to High	Low	High	Low

*Adapted with permission from Parischa et al. [418]

How should iron status be assessed in people with CF? PICO 9.1.1

[Grade C] The level of evidence to guide practice for assessing iron status in CF is insufficient. Further research or expert consensus is required. Until further evidence is available, it is suggested that iron status in CF be assessed as per guidelines for the general population. [96,97]

Intervention

How should iron deficiency be treated in people with CF? PICO 9.1.2

[Ungraded] There is insufficient evidence available regarding the treatment of iron deficiency in CF.

Key points to consider in the treatment of iron deficiency:

- Increasing dietary iron intake alone is often inadequate in the treatment of iron deficiency [418]. However, dietary iron intake should still be optimised and the impact of iron enhancers and inhibitors on absorption should be considered.
- Treatment of iron deficiency should depend on the underlying cause.

Absolute iron deficiency: A prescribed iron supplement is usually required. Available preparations in Australia and NZ can be found in Table 9d [412,415,420].

- If a prescription supplement is required, suggested oral treatment doses [418]:
  - Children: 3-6mg/kg/d elemental iron for 2-3 months after serum Hb normalises
  - Adolescents & adults: 100-200mg elemental iron daily for 3-6 months after serum Hb normalises
- Intravenous (IV) supplementation may be required for some patients who do not respond to oral treatment[418].

Functional iron deficiency: Aim to treat the underlying source of inflammation. A prescribed iron supplement is not always required [412,415,420].

Table 9d. Readily available iron supplements in Australia

	Preparation	Dose	Elemental iron (mg)
Ferro-Gradumet ®	Tablet	1	105
Ferrograd C®	Tablet	1	105
Ferro-Liquid ®	Liquid	5ml	30

Refer to http://www.pharmac.govt.nz/Schedule for a list of current iron supplements available in New Zealand.

Is iron supplementation contraindicated in people with CF who are chronically colonised with Pseudomonas aeruginosa? PICO 9.1.3

[Grade D] There is insufficient evidence from clinical trials to suggest that iron supplementation is contraindicated in adults and children with CF who are chronically colonised with Pseudomonas aeruginosa. When indicated, an iron supplement should be prescribed for adults and children with CF who are chronically colonised with pseudomonas aeruginosa. [98]

Monitoring and Evaluation

It is recommended that iron status be assessed annually in the CF population [78]. If iron deficiency is suspected, then the frequency of monitoring should increase [78]. If oral iron supplementation is required, the recommended duration of treatment will depend on the severity of iron deficiency at diagnosis. After commencing oral supplementation at the prescribed therapeutic dose, it is expected that reticulocytosis will occur within the first few days [418,427]. Haemoglobin (Hb) levels are then expected to rise by approximately 20g/L every few weeks [418]. Iron stores should be restored within 2-3 months of Hb stabilisation in the paediatric population and 3-6 months in the adult population [418,427].

The following should be considered when reviewing patients with iron deficiency:

- Tolerability of supplementation - nausea, epigastric pain and constipation are common side effects of prescribed iron supplements [427].
- Adherence to supplementation - poor adherence to iron supplementation is common, especially due to the above gastrointestinal side effects [418,427].

Iron studies should be repeated at the end of treatment to ensure that iron deficiency has resolved.

Practice Points PICO 9.1.1, 9.1.2 and 9.1.3

Increased risk of iron deficiency in CF due to chronic inflammation, inadequate dietary intake, gastrointestinal comorbidities and haemoptysis. Iron studies are difficult to interpret in CF due to chronic inflammation. Aim to assess iron status during clinical stability.

Interpretation of biochemical markers in CF - Serum ferritin is an acute phase protein (rises during periods of inflammation) and may be unreliable. Inflammatory markers, including C-reactive protein (CRP) should be taken into consideration.

- Serum transferrin receptor (sTfr) is not readily available but should be considered as it is not affected by inflammation. A raised sTfR may be a useful indicator of functional iron deficiency in CF.

Absolute iron deficiency - Iron stores are depleted, as indicated by serum ferritin (low), serum iron (low), transferrin (high), transferrin saturation (low), sTfR (high), CRP (normal)

- Oral iron supplementation is recommended

Functional iron deficiency - Iron stores are normal-high but not available at the site of erythroblast production. Serum ferritin (low – normal), serum iron (low), transferrin (normal-high), transferrin saturation (low), sTfR (high), CRP (high)

- Oral iron supplementation may be required

Dietary considerations
Increasing dietary iron intake is often inadequate in the treatment of iron deficiency in CF. Iron is available in food as haem iron (more bioavailable) and non-haem iron (less bioavailable).

- Meat, seafood and poultry are good sources of haem iron.
- Plant-based foods (wholegrain cereal and green leafy vegetables) and iron-fortified foods (infant rice-cereal) are good sources non-haem iron.
- Foods high in vitamin C improve the absorption of iron.
- Foods high in calcium, phytates (legumes, rice and other grains) and tannins (tea) can inhibit the absorption of iron.

Oral iron supplement considerations
Prescribe an iron supplement, in addition to dietary change, for 2-3 months to treat diagnosed iron deficiency. Suggested treatment doses:

- Children: 3-6mg/kg/d elemental iron for 2-3 months after serum Hb normalises
- Adolescents & adults: 100-200mg elemental iron daily for 3-6 months after Hb normalises
- Gastrointestinal complaints (including constipation and epigastric pain) are common side effects of oral iron supplements.

Multivitamins are not recommended in the treatment of iron deficiency. Concerns regarding potential drug-nutrient interactions should be discussed with the CF pharmacist.

Iron supplementation is not contraindicated for people with CF with chronic Pseudomonas aeruginosa infection.

Intravenous iron supplementation

Iron (ferric carboxymaltose) 500mg/10ml injection is associated with fewer adverse events than other IV iron supplements. It is also available on the pharmaceutical benefits scheme (PBS) in Australia and via PHARMAC in New Zealand (District Health Board hospitals only).

9.2 Magnesium

Magnesium is an abundant mineral found in the body and acts as a cofactor in more than 300 enzymatic reactions, including those involved in regulation of muscle and nerve function, heart rhythm, platelet-activated thrombosis and bone formation [43,428]. Plant and animal-based foods such as green vegetables, unrefined cereals, legumes, nuts, and shellfish provide good sources of magnesium [428]. Highly processed foods such as highly refined flours, oils and fats are low in magnesium [43,428]. Hypomagnesaemia, defined as low serum magnesium, is not common but has been observed in the CF population [429-431].

Disease Aetiology

Magnesium homeostasis is primarily controlled by the kidneys [429,432]. Causes of hypomagnesaemia in the general population include [432]:

- Redistribution of magnesium – often seen in refeeding syndrome
- Reduced dietary intake of magnesium
- Gastrointestinal malabsorption
- Renal disease
- Endocrine – diabetes mellitus and hyperaldosteronism
- Drug-nutrient interactions

People with CF may be at risk of hypomagnesaemia but the mechanism for why it occurs in CF is largely unknown [429-431]. The following reasons are thought to potentially contribute to hypomagnesaemia in CF [429]:

- Frequent use of aminoglycosides that may result in long-term renal damage and tubular leak of magnesium
- CF-related diabetes with increased sodium and magnesium losses via diuresis [433]
- Malabsorption whereby magnesium binds to fat in faecal fat excretion [434]

Hypomagnesaemia has been reported in a retrospective analysis of biochemical parameters for patients referred for lung transplant, whereby 57% of patients had serum magnesium levels below the reference range for age and sex [429]. However, the true prevalence of magnesium deficiency and/or hypomagnesaemia in CF is unknown [429,430].

Assessment

DIET

Magnesium deficiency due to inadequate dietary intake is not common [432]. However, adequacy of intake should still be considered as part of a thorough nutrition assessment, especially for people with CF who have poorly controlled fat absorption or show signs/symptoms of a potential deficiency.

Foods high in magnesium are outlined in Table 9e below. These include green leafy vegetables (i.e. spinach), nuts and seeds, fish, legumes and unrefined cereals [43]. The recommended RDI of magnesium based on age and sex is outlined in Table 9f [43].

Table 9e. Magnesium containing foods (mg per serve) [435]

Foods containing Magnesium	Serving Size	Magnesium content (mg)
Animal-based sources		
Chicken	100g	28
Beef (mince)	100g	29
Salmon	100g	29

...table continued overleaf

Foods containing Magnesium	Serving Size	Magnesium content (mg)
Plant-based sources		
Almonds	30g	78
Cashews	30g	75
Peanuts	30g	48
Soy milk	1 cup	55
Peanut butter	1 Tbspn	45
Wholemeal bread	2 slices	50
Rice (brown) cooked	½ cup	44
Yoghurt	1 cup	39
Oats (raw)	¼ cup	31
Banana	1 banana	30
Potato (baked)	1 potato	26
Cow's milk	1 cup	26
Kidney beans	½ cup	28

Table 9f. Recommended Dietary Intakes of magnesium for people in Australia and NZ, mg/day [43]. *Available at: http://www.nrv.gov.au/*

Recommended Dietary Intake (RDI) for Magnesium		
Age	**Male** (mg/day)	**Female** (mg/day)
Infants		
0-6 months	30*	30*
7-12 months	75	75
Young children		
1-3 years	80	80
4-8 years	130	130
Children & adolescents		
9-13 years	240	240
14-18 years	410	360
Adults		
19-30 years	400	310
31-50 years	420	320
51-70 years	420	320
>70 years	420	320

* Adequate Intake (AI)

CLINICAL

Early clinical symptoms of magnesium deficiency may include [428]:

- Loss of appetite
- Nausea and vomiting
- Fatigue and weakness

As magnesium deficiency worsens, symptoms may include [428]:

- Numbness and tingling
- Muscle contractions and cramps
- Seizures
- Sudden changes in behavior and personality changes
- Abnormal heart rhythm and coronary spasms

Symptoms of magnesium deficiency are often not experienced until serum magnesium levels drop below 0.5mmol/L [432]. It is not uncommon for patients to present with no signs or symptoms of magnesium deficiency, even with severe hypomagnesaemia, if serum concentration declined gradually [428]. Hypomagnesaemia commonly co-exists with other micronutrient deficiencies, particularly hypokalemia and hypocalcaemia [432].

BIOCHEMICAL AND LABORATORY DATA

Serum magnesium concentration does not reflect total body magnesium levels as only 1% of total body magnesium is present in the extracellular fluids [428]. Magnesium is primarily concentrated in the bones and muscles [436,437]. Total body magnesium deficiency may therefore exist in people with normal serum magnesium levels [428].

Serum magnesium measures short-term intake variation and is most helpful in detecting rapid extracellular changes [99,428]. While not always practical, a 24-hour urinary magnesium is a better marker of body stores [428].

- High urinary excretion indicates renal wasting of magnesium
- Low urinary excretion suggests an inadequate intake or absorption of magnesium

INTERVENTION

It has been hypothesised that oral magnesium supplementation may improve respiratory musculature in the CF population. However, only one small study has investigated this hypothesis to date. While improvements in respiratory muscle strength were shown amongst the paediatric patients studied, there is currently insufficient evidence to recommend routine supplementation of magnesium above reference intake values [99].

Does supplementing magnesium above the RDI improve nutrition and/or respiratory outcomes in people with CF? PICO 9.2.1

[Grade D] There is insufficient evidence to support that routine magnesium supplementation above the RDI improves health outcomes in people with CF. Explore the use of oral magnesium supplementation only when dietary intake is unable to meet the RDI. [99]

Monitoring and Evaluation

There is no evidence to guide practice for the ongoing monitoring and evaluation of magnesium status in CF. Clinical judgment should be applied when determining if or when to review magnesium status for a person with CF.

Practice Points PICO 9.2.1

Encourage people with CF to achieve adequate consumption of magnesium as part of a varied diet.

- Foods high in magnesium include green leafy vegetables, unrefined cereals, legumes, nuts & shellfish
- Magnesium deficiency is likely to co-exist with other micronutrient deficiencies. A nutrition review should therefore consider overall micronutrient adequacy.

Oral magnesium supplementation is considered safe and cost-effective. High dose magnesium supplementation may result in gastrointestinal side effects, especially diarrhoea. This is most commonly seen in patients on higher dose magnesium supplements after lung transplantation.

9.3 Calcium

This section provides a general outline of the nutrition considerations for calcium and CF. Due to a lack of supporting literature no PICOs have been answered for this chapter. Refer to Chapter 13 for more detailed information about the relationship between calcium and bone health.

Calcium plays a crucial role in the development and maintenance of the skeleton with 99% of the body's calcium found in the form of *'hydroxyapatite'* (bone mineral) [438]. Calcium is also involved in cardiac function and neuromuscular facilitation [43]. Calcium status may be compromised in the CF population due to vitamin D deficiency or inadequate intake of dietary calcium [78].

Disease Aetiology

Parathyroid hormone (PTH) and 1,25-dihydroxycholecalciferol ($1,25(OH)_2D$) controls calcium homeostasis [438].

- PTH – increases distal tubular renal calcium resorption and bone resorption [438]
- $1,25(OH)_2D$ – increases intestinal calcium absorption [438]

Negative calcium balance enhances resorption of bone to maintain extracellular calcium homeostasis [439]. For the general population and people with CF, a negative calcium balance is known to increase the risk of low bone mineral density and fractures [149]. The pathogenesis of negative calcium balance and low bone mineral density in CF remains uncertain. It is thought to be multifactorial with potential causes including:

- Dietary - inadequate calcium intake, poor nutritional status and high protein and sodium intakes which may increase urinary calcium excretion [440]
- Infection and inflammation [149,441]
- Glucocorticoid use [149,442]
- Hormonal status [443]
- The incorporation of calcium into insoluble micelles with dietary fat [444]
- Vitamin D - increased prevalence of vitamin D deficiency in people with CF may exacerbate dietary calcium deficiency through reduced gastrointestinal absorption [445]
- Malabsorption – even with optimal pancreatic enzyme replacement (PERT) dosing, some calcium may be lost via dietary malabsorption and increased endogenous faecal losses [391,446]

The prevalence of negative calcium balance in the CF population is unknown [149]. However, it is well established that people with CF have a high prevalence of low bone mineralisation [441].

Assessment

When assessing calcium intake, bone health (Chapter 13) and vitamin D (Chapter 8) should also be considered.

DIET

Review dietary intake of calcium containing foods, see Table 9g. Foods high in calcium include dairy foods (i.e. cow's milk, cheese & yoghurt), fortified plant-based milks (i.e. soy milk), firm tofu & bony fish. Legumes, nuts and some green vegetables also contain small amounts of calcium.

Calcium intake should be assessed annually and compared to national recommendations for age and sex in the general population [391]. As seen in Table 9h, the recommended dietary intake (RDI) for calcium varies throughout different life stages [43]. Overall calcium requirements are higher during periods of rapid growth i.e. infancy and throughout the pubertal growth spurt [438].

CLINICAL

In addition to dietary calcium intake, the following should be considered when assessing calcium status in the context of CF:

- Vitamin D status – vitamin D deficiency may exacerbate dietary calcium deficiency through reduced gastrointestinal absorption [445]
- The impact of poor nutrition status and high protein and sodium intake on urinary calcium excretion [440]
- The impact of infection and inflammation on bone remodelling [149,441]

- Drug-nutrient interactions [438]
  - Proton pump inhibitors may indirectly reduce calcium salt solubility due to a reduction in gastric acid
  - Glucocorticoid use may result in poor gastrointestinal calcium absorption and increased renal calcium excretion
  - Calcium can interfere with the absorption of other medicines (particularly bisphosphonates, iron and some antibiotics e.g. ciprofloxacin)
- Pancreatic enzyme replacement therapy (PERT)
  - Poor adherence or under-dosing of PERT may result in malabsorption and increased endogenous faecal calcium losses [446]
  - Adequate PERT is required for lipolysis to prevent the excretion of calcium in soaps [78]

Potential side effects of excessive calcium supplementation, above the RDI (Table 9h) include [439]:

- Hypercalcaemia and hypercalcuria
- Nephrolithiasis
- Constipation
- Vascular and soft tissue calcification
- Interactions with zinc and iron absorption

Table 9g. Calcium containing foods (mg per serve) [435]

Calcium containing foods	Serving Size	Calcium content (mg)	mg/100 g
Dairy sources			
Milk	1 cup	304	124
Natural yogurt	200g	386	193
Cheddar cheese	1 slice	160	739
Vanilla ice cream	1 scoop	48	93
Vanilla custard	100g	130	130
Non-dairy sources			
Tofu (firm)	1 cup	832	320
Pink salmon (canned in water)	1 small can	279	310
Snapper	1 fillet	163	160
Tahini	1 Tbspn	66	330
Almonds	10 almonds	30	220
Dried figs	6 figs	160	200
Dried apricots	6 apricots	32	67
Brazil nuts	10 nuts	53	150
Bok choy	1 cup	65	83
Silverbeet	½ cup	87	72
Lebanese cucumber	1 cup	68	63
Broccoli	2 florets	15	32
Baked beans in tomato sauce	1 cup	43	39
Chickpeas (canned)	1 cup	90	45
Soy beans (canned)	1 cup	106	59
Boiled egg	1 egg	21	39
Licorice	1 stick	34	280

Table 9h. Recommended Dietary Intake of calcium for people in Australia and NZ, mg/day [43].
Available at: http://www.nrv.gov.au/

Recommended Dietary Intake (RDI) for Calcium		
	Males (mg/d)	**Females** (mg/d)
Infants		
0-6 months	210*	210*
7-12 months	270*	270*
Young children		
1-3 years	500	500
4-8 years	700	700
Children & adolescents		
9-11 years	1000	1000
12-13 years	1300	1300
14-18 years	1300	1300
Adults		
19-30 years	1000	1000
31-50 years	1000	1000
51-70 years	1000	1300
>70 years	1300	1300

* Adequate Intake (AI)

BIOCHEMICAL AND LABORATORY DATA

There are no simple biochemical measures available to assess calcium status [149,391]. It is recommended that dietary calcium intake, as assessed by a dietitian, be considered in conjunction with vitamin D status (Chapter 8) and additional bone health considerations (Chapter 13) [439,447].

Intervention

Calcium should be optimised via dietary sources where possible [149,438]. In particular, dairy products are recommended as good sources of dietary calcium [78]. If unable to meet nation specific recommendations for daily calcium intake, an oral calcium supplement is recommended, see Table 9i [78,149,438].

Points to consider with oral calcium supplementation:

- The timing of oral calcium supplements should be considered in the context of the patient's overall management goals.
- Where possible, calcium supplements should not be taken at the same time as medications with a known drug-nutrient interaction e.g. bisphosphonates, iron supplementation and some antibiotics e.g. ciprofloxacin.
- Glucocorticoids and proton pump inhibitors may inhibit the gastrointestinal absorption of calcium.

Table 9i. Readily available calcium supplements in Australia (mg per serve)

	Calcium (mg) per tablet	Vitamin D (IU) per tablet
Caltrate®	600	-
Caltrate with Vitamin D®	600	400
Ostelin Kids Vitamin D and Calcium®	350	300
Ostelin Vitamin D and Calcium®	600	500

Refer to http://www.pharmac.govt.nz/Schedule for a list of current calcium supplements available in New Zealand.

Monitoring and Evaluation

It is recommended that calcium intake be assessed annually, in conjunction with a thorough nutrition assessment whereby adequacy of energy and protein intake is also assessed [78,149,438]. More frequent review of dietary intake is recommended for people with poor height growth velocity or weight loss [78,149]. Where possible, it is also recommended that intake is assessed by a dietitian with specialist CF knowledge [149,438].

For CF patients with renal impairment, serum calcium levels should be monitored closely [438].

9.4 Sodium

All people with CF are at increased risk of sodium deficiency as a result of increased sweat losses [1,279]. Sodium plays a role in fluid balance and blood volume maintenance [43,448]. Sodium chloride, most commonly referred to as 'salt', is found naturally in some foods in small amounts. The vast majority of dietary sodium is added to food as a flavour enhancer or preservative.

Disease aetiology

The primary defect in CF, a mutation in the CF transmembrane conductance regulator (CFTR) gene, affects the function of cell chloride channels and prevents the usual flow of sodium and chloride ions and water in and out of cells. As a result, people with CF have abnormally high sodium and chloride losses via sweat glands and are at an increased risk of dehydration, hyponatraemia (low serum sodium) and hypochloridaemia (low serum chloride) [449,450]. The sodium concentration of sweat in the CF population is usually 3-5 times that of the general population [451].

Factors identified that increase the risk of sodium deficiency (hyponatraemia and dehydration) in CF include:

INFANCY

- Increased requirements due to periods of rapid growth and a large body surface area [279]. Overall infants have increased salt losses via their skin, especially in hot and humid temperatures [202].
- Lower sodium content of breastmilk (approximately 7mmol/L) compared with infant formula (up to 15mmol/L) [452,453]
- Low sodium content of many first complementary foods [78]

ILLNESS

- Reduced sodium intake associated with poor appetite [1]
- Increased losses when febrile [1]
- Increased losses via ileostomy (common in infancy post bowel surgery for meconium ileus) [1]

COMPOSITION OF ORAL AND ENTERAL NUTRITION SUPPORT SUPPLEMENTS

- Relatively low sodium composition of supplementary oral and enteral feeds [1]

SWEAT COMPOSITION AND RATE

- People with CF have been found to have higher sweat rates, particularly during exercise [454-456].
- The excretion of sweat is nearly isotonic to plasma and can diminish the thirst drive [451,455,457] .

EXERCISE

- In the healthy population, an individual's sodium sweat losses with exercise vary depending on dietary intake, sweat rate, hydration and heat acclimatisation [458]. Prolonged and strenuous physical activity, especially in the heat can result in significant sodium losses [458].
- When exercising in hot and humid conditions, CF sweat sodium losses can be 10 times that found in the non-CF population [279].
- Children with CF have been found to drink less during exercise, likely as a result of a reduced hyperosmotic trigger diminishing thirst drive [100,450].

How do environmental factors and exercise impact on sodium requirements for people with CF compared to those without CF? PICO 9.4.1

[Grade C] Climate (heat and humidity) is thought to have an impact on salt requirements in CF. There is also some evidence to support an altered thirst drive for people with CF. However, at this time, there is insufficient evidence available to conclude how environmental factors and exercise impact on sodium requirements for the wider CF population. [100-102]

The prevalence of sodium deficiency in the CF population is unknown. The literature is primarily limited to case studies, especially in infants [202].

Assessment

DIET

As part of a thorough nutrition assessment, a CF individual's sodium intake should be considered as well as their potential risk of sodium deficiency and hyponatraemia [285]. Check for the following:

- Periods of illness, due to reduced intake associated with poor appetite and increased losses if febrile
- Periods when regular dietary intake is decreased and is replaced by oral fluid supplements or enteral nutrition support, which have low sodium content
- Periods of increased exercise and/or exposure to hot/humid environments
- Intake during infancy
- Canned, processed and convenience/fast foods are generally high sodium containing foods

CLINICAL

Signs and symptoms of sodium deficiency to consider as part of a thorough nutrition assessment include: nausea and/or vomiting, muscle cramps, deposition of salt crystals on the skin, fatigue, poor growth (especially in infants), headaches, difficulty expectorating sputum, constipation, DIOS and hyponatraemia [1,411,459]. Some antidepressant medications, particularly selective serotonin reuptake inhibitors (SSRIs), may cause increased sweating and hyponatraemia, especially on commencement.

BIOCHEMICAL AND LABORATORY DATA

Serum sodium alone is not a sensitive marker for salt depletion in CF [1]. The interpretation of biochemical markers for assessing salt depletion in people with CF should therefore be done in conjunction with a thorough clinical assessment[1]. If total body salt depletion is suspected, spot urine sodium analysis should be conducted [460]. Sodium deficiency is confirmed with urinary sodium concentrations <10 mmol/L [285].

Intervention

What is the recommended daily sodium requirement for people with CF compared to those without CF? PICO 9.4.2

[Grade D] There is a lack of research available to guide sodium requirements for people with CF. As a result, recommendations vary in international consensus and review documents. Recommendations for daily sodium requirements in CF are:

- Infants - 500-1000mg
- Children - 1000-4000mg
- Adolescents and adults - 6000mg

(unchanged from the '*2006 Australasian Clinical Practice Guidelines for Nutrition in CF*[1])

Table 9j. Recommended daily sodium requirements (mg/d) for people with CF in Australia and NZ[1] compared to the general population [43].

	Recommended Dietary Intake for Sodium mg/d (mmol/d)	
Age	**CF population**	**General population**
Infants	500-1000 (22-44)	120-170 (5-7)
Children	1000-4000 (44-174)	200-800 (9-35)
Adolescents and adults	6000 (261)	460-920 (20-40)

As shown with the broad range of sodium requirements provided for each age group in Table 9j, it is important to remember that sodium targets should be individualised. There is likely to be variability in sodium requirements within and between individuals. The recommended sodium dose to correct a confirmed deficiency is 1 to 2 mmol/kg/day with ongoing monitoring of serum sodium, electrolytes and urinary sodium until corrected [285,411].

Monitoring and Evaluation

The sodium requirement for a person with CF may change over time. It is important that adequacy of sodium intake, including supplementation, is reviewed on a regular basis. Particular times or periods in which this may be the case include:

- Seasonal variation - sodium requirements are likely to be higher during the warmer months of the year
- Changes in levels of physical activity and exercise patterns
- Change in work environments (particularly if required to work outdoors)
- Major changes to nutrient sources that may impact on dietary sodium intake e.g. reliance on enteral nutrition or oral supplements

A spot urine sodium analysis should be considered if sodium depletion is suspected or supplementation significantly changes. While not commonly used in clinical practice in Australia and New Zealand, other ways to monitor sodium status include:

- Fractional excretion of sodium (FENa) – aiming for a level 0.5-1.5% [78]
- Urinary sodium : creatinine ratio – aiming for 17-52mmol/mmol [78]

CF patients and the families of young children should also be taught to identify times when sodium requirements may be elevated, signs and symptoms of potential salt depletion and be provided with a guide to increase sodium supplementation as required. It is important to remember that level of thirst should not be relied on to estimate fluid requirements because a low serum osmolality may diminish thirst drive [100].

Practice Points PICO 9.4.1

Take into account the following when evaluating sodium requirements:

- Infants & people with CF exposed to hot / humid environments or illness are at high risk of sodium depletion & hyponatraemia.
- Signs & symptoms of sodium depletion include nausea, vomiting, muscle cramps, deposition of salt crystals on the skin, fatigue, poor growth (especially in infants) and/or hyponatraemia
- Sweat sodium losses vary amongst individuals (with and without CF)
- Dietary intake, sweat rate, hydration and heat acclimation can impact on sodium losses.

Sweat rates/sodium losses are elevated and thirst drive potentially diminished for people with CF in hot / humid conditions and during exercise. Dehydration/hyponatraemia is a risk under these conditions.

Practice Points PICO 9.4.2

- Clinicians should continue to use nation-specific guideline/consensus documents (including the '*2006 Australasian Clinical Practice Guidelines for Nutrition in Cystic Fibrosis*' in addition to a thorough nutrition assessment and clinical judgment as a guide when recommending sodium supplementation to people with CF [1].
- Serum sodium is not a sensitive marker for salt depletion in CF.
- Undertake a spot urine sodium analysis if sodium depletion is suspected or supplementation significantly changes.
- Clinicians should be guided by local climate-based recommendations and clinical judgment when individually tailoring sodium supplementation to people with CF.

Translating into Practice

Tips to increase sodium intake during infancy:

- Formula fed infants – divide recommended salt dose across a minimum of 3-4 formula bottles.
- Breastfed infants – a small amount of salt can be placed on a clean finger and the infant can suck the salt from the finger prior to a feed. Parents usually measure the recommended dose out at the beginning of the day and work through this with each feed.
- Pancreatic insufficient infants – salt can be added to the apple (or fruit) puree used to administer the pancreatic enzyme replacement therapy (PERT).
- Salt solution – recommended salt can be mixed with a small amount of water and administered to infants via a syringe in small doses throughout the day. This is best given prior to a feed as may cause vomiting in some infants.

Tips to increase sodium intake for children, adolescents and adults with CF:

- Add salt to food and cooking
- Encourage salty foods (see Table 9k below)
- Homemade salt capsules – fill empty gelatine capsules (available from retail pharmacy) with table salt.
- Commercial supplements (see Table 9l below)
- Homemade sports drinks – ¼ teaspoon salt (580 mg) added to 500 mL cordial solution

Useful sodium conversions

- 1 tsp salt (NaCl) = 2,300mg sodium
- 1mmol Na^+ = 23mg sodium
- 1g salt (NaCl) = 17.1mmol Na^+ = 393 mg sodium

Table 9k. Examples of foods high in salt [461]

Foods containing approximately 1/8 teaspoon salt (290mg sodium)	Foods containing approximately **¼ teaspoon salt (580mg sodium)**
50g packet salted potato or corn chips 1/3 cup salted peanuts or mixed nuts 1 cheese & crackers dip snack 2 slices of bread 1 wrap or piece of Lebanese bread 1 large croissant 1 ½ teaspoons Vegemite® 1 ½ tablespoons tomato or barbecue sauce 5 olives 3 small (2cm) cubes feta cheese 1 small can tuna (in brine, drained) 2 slices (60g) BBQ chicken, with skin 1 tablespoon capers	½ cup pretzels 2 slices processed meat (i.e. ham or salami) 1 rasher of bacon 2 slices processed cheese 1 slice haloumi cheese 1 meat pie 2/3 large sausage roll ¾ cup fried rice 6 chicken nuggets 1 ½ slices pizza ½ cup baked beans ½ serve 2 minute noodles (with flavouring) 2 teaspoons soy sauce 1 sausage (thick) 1 cheese and bacon roll

Table 9l. Commercial salt supplementation products available in Australia and New Zealand. Refer to http://www.pharmac.govt.nz/Schedule for a more detailed list of rehydration solutions available in New Zealand.

Product	Sodium (mg)	Sodium (mmol)
Commercial sports drinks		
Gatorade®per 100mL	51	2.2
Powerade®per 100mL	42	1.8
Gatorade Endurance®per 100mL	84	3.6
Staminade®per 100mL	29	1.3
Rehydration solutions		
Gastrolyte® (per 5g sachet)	278	12
Hydralyte® (per 5g sachet)	206	9
Glucolyte® (per 40g sachet)	248	10.7
Hydralyte Sports® (per 17.9g sachet)	690	30
Salt tablets		
Toppin® salt tablets (AUS)	240mg (per tablet)	10.4mmol (per tablet)
Slow Sodium 600mg tablets (NZ)	230mg (per tablet)	10mmol (per tablet)

9.5 Zinc

Zinc is essential for a number of diverse functions in the body. It plays a role in growth and development, reproduction, immune and sensory function, protein and DNA synthesis, wound healing, antioxidant protection and the stabilisation of membranes [362,462,463]. The main dietary source of zinc are animal foods as well as zinc fortified cereals [43,462].

Disease Aetiology

People most at risk of zinc deficiency:

- People with high physiological requirements – i.e. during periods of rapid growth in infancy, childhood and puberty [464]
- Pregnant and lactating women [464]
- Vegetarians due to a diet low in bioavailable zinc [463,465,466]
- Exclusively breastfed infants past 6 months of age [463,465,466]

Those with CF are also at increased risk of zinc deficiency due to pancreatic insufficiency, malabsorption and steatorrhoea. Chronic inflammation and increased oxidative stress further increases the risk of zinc deficiency in CF, as does the presence of liver disease, renal disease, diabetes, and protein energy malnutrition [463,465,466]. Treatment with pancreatic enzyme replacement therapy has been shown to improve zinc absorption [467,468].

The reported prevalence of zinc deficiency in children and adolescents with CF ranges from 0-40% [103,106,109,110,467,469]. Evidence for the prevalence of zinc deficiency in infants is limited. There have been several reports of infants presenting with signs and symptoms of severe zinc deficiency prior to the diagnosis of CF, though not all were found to be zinc deficient [467,470,471].

The clinical significance of marginal zinc deficiency is unclear. One study reports lower lung function and an increased prevalence of bone disease and impaired glycaemic status in people with CF who have sub-optimal zinc levels [108]. In contrast, no correlations between plasma zinc levels and growth, lung function and infection have been reported in other studies [103,107,109,110,472].

Zinc is generally considered to be relatively nontoxic [465]. There is no evidence of adverse effects from naturally occurring zinc in food [43,462].

Assessment

Zinc status is difficult to measure due to the absence of obvious signs and symptoms of deficiency and in the absence of a reliable biomarker or functional indicator. There is no universally accepted single measure suitable to accurately assess the zinc status of an individual [281,362]. Where zinc deficiency is suspected, diagnosis requires examination of the whole clinical picture to identify possible causes and consequences [464]. It is important to use a combination of dietary, biochemical and functional indicators such as growth (stunting or height for age) to assess those at increased risk of deficiency [466,473].

How should Zinc status be assessed for people with CF? PICO 9.5.1

[Grade D] The level of evidence to guide practice for assessing zinc status in CF is insufficient. Further research or expert consensus is required. [103]

DIET

As part of a thorough nutrition assessment consider dietary intake of foods high in bioavailable zinc such as meat, fish, poultry and fortified cereals. Phytates inhibit zinc absorption and a high intake of phytate containing foods e.g. unrefined cereals, legumes and nuts should also be considered with a dietary assessment. However, food processing, soaking and germination can reduce phytate content and increase absorption of zinc [251,466,473]. See Table 9m below for foods high in zinc. There is considerable individual variation in daily zinc intake which needs to be taken into account when assessing usual intake.

Zinc requirements for the general Australian and New Zealand population are outlined in Table 9n.

Table 9m. Zinc containing foods [474]

	Serving Size	Zinc content (mg)	mg/100 g
Milk	1 cup	0.93	0.36
Natural yogurt	200 g	1.22	0.61
Cheddar cheese	1 slice	0.25	3.61
Vanilla ice cream	1 scoop	0.15	0.23
Vanilla custard	100g	0.39	0.39
Chicken breast (no skin)	100g	6.21	6.21
Beef mince	100g	0.92	0.92
Salmon	100g	0.46	0.46
Oysters	4 oysters	3.53	14.7
Lobster	1/2 lobster	3.52	3.4
Prawns	6 prawns	2.6	1.5
Barley	1 cup	1.76	0.9
Mixed grain bread	1 slice	0.52	52
Almond	10 nuts	0.41	3.4
Brazil nuts	10 nuts	1.35	4.1
Mussels	4 mussels	1.09	3.4

Table 9n. Recommended Dietary Intake of zinc for people in Australia and NZ, mg/day [43].
Available at https://www.nrv.gov.au/nutrients/zinc

Recommended Dietary Intake (RDI*) for Zinc		
	Males (mg/d)	**Females** (mg/d)
Infants		
0-6 months	2*	2*
7-12 month	3	3
Young children		
1-3 years	3	3
4-8 years	4	4
Children & adolescents		
9-13 years	6	6
14-18 years	13	7
Adults		
19-30 years	14	8
31-50 years	14	8
51-70 years	14	8
>70 years	14	8

* Adequate Intake (AI)

Special attention should be given to those at increased risk of deficiency:

- Vegetarians consuming diets high in phytates. Requirements for zinc may be up to 50% greater for strict vegetarians with a high phytate intake [43,464-466].
- Infants exclusively breastfed from six months of age and not receiving dietary sources of high bioavailable zinc such as meat or fortified cereals.

Adequacy of intake of essential fatty acids and protein should also be considered, as deficiencies in these nutrients may manifest clinically similar to zinc deficiency.

CLINICAL

Zinc deficiency results in non-specific signs and symptoms that may include [43,251,462,464]:

- Growth retardation
- Delayed sexual maturation
- Anorexia
- Mental lethargy
- Alopecia
- Diarrhoea
- High rates of infection, skin lesions and impaired wound healing due to immune dysfunction

A number of disorders may present with signs and symptoms similar to zinc deficiency and differential diagnosis needs to be considered [473].

Medications and supplements may interfere with zinc absorption [462,463]:

- High dose iron supplements ≥60mg elemental iron impairs zinc absorption [473]
- Calcium supplementation does not impair zinc absorption [473]
- The oral contraceptive pill, oestrogen and corticosteroids may impair zinc absorption [463,464]

Zinc may also interfere with copper absorption when zinc intakes are high ≥50mg/d [473].

Both acute and chronic forms of zinc toxicity exist. Acute effects include nausea, vomiting, loss of appetite, abdominal cramps, epigastric pain, diarrhoea, light headedness and headaches[43]. Symptoms of chronic toxicity include a reduction in immune function, decreased HDL cholesterol, and low serum copper concentrations [462,463,473].

Important synergies exist between vitamin A and zinc [475] and correlations have been shown between plasma zinc and retinol in CF [106,108,110]. Zinc is important in vitamin A transport as a component of retinol binding protein (RBP) [464]. A case report has shown that zinc therapy was effective in the treatment of night blindness in a person with CF and vitamin A deficiency, suggesting that the normalisation of zinc levels may be important in maintaining vitamin A status [372,476].

BIOCHEMICAL AND LABORATORY DATA

Serum or plasma zinc is the most widely used index of zinc status though sensitivity and specificity are poor particularly as a measure of marginal zinc deficiency. Plasma zinc is only 0.1% of total body pool and its concentration is tightly regulated [464]. Levels will usually be low in severe zinc deficiency, however are likely to be normal in marginal zinc deficiency states [202,251,463,477].

Serum zinc levels are affected by the following:

- Stress, trauma, infection and inflammation which may lead to falsely low levels [43,251]
- Disease states with low albumin i.e. protein energy malnutrition may result in low zinc as 80% of zinc circulates bound to albumin [463]
- Fasting status and time of day [108,251,464]
- Individual variations due to a high biological variation in serum zinc [464]
- Retinol deficiency (refractory to retinol supplementation) [372,462]

Overall, there is no evidence of benefit for routine annual assessment of plasma zinc levels and this practice is not currently recommended in recent consensus guidelines for CF [78]. Zinc levels in red blood cells are considered by some to be a more accurate measure of zinc [362], however this test is not routinely performed and evidence of its use in CF is limited to one more recent study [103].

Intervention

What are the recommendations for zinc supplementation in people with CF? PICO 9.5.2

[Grade D] There is insufficient evidence to make recommendations for routine supplementation or supplementation for suspected zinc deficiency in CF. Until further evidence is available, it is suggested that zinc supplementation be guided by recommendations in CF consensus guidelines. As per the 2016 ESPEN-ESPGHAN-ECFS CF nutrition guidelines[78], CF people at high risk of deficiency should receive the following supplementation doses for 6 months; infants (1mg/kg/d), children (15mg/d), adults (25mg/d). [103-110]

Summary of current consensus based guidelines suggest the following in terms of zinc supplementation in CF:

- Infants under 2 years of age with persistent failure to thrive despite adequate caloric intake and PERT and/or those with severe steatorrhoea, an empiric trial of zinc supplementation of 1mg elemental zinc/kg/d in divided doses for 6 months (max 15mg/day) should be considered [78,87]
- Children at high risk of zinc deficiency should trial 15mg/day of zinc for 6 months [78]
- Adults at high risk of zinc deficiency should trial 25mg/day for 6 months [78]
- A cross sectional study in adults reported routine supplementation for low plasma zinc of 50mg zinc for 3 months without evidence of excess zinc levels or adverse effects [108]

The clinical significance of marginal zinc deficiency and improvement with zinc supplementation is unclear, however positive effects have been shown on nutritional status, pulmonary function, infection rates and inflammation in children and adolescents with CF [105-107,110].

Supplemental zinc is available in CF-specific and general multi-vitamin and mineral preparations, in some cold and flu supplements and in zinc only supplements (usually 25mg).

- The CF multivitamin VitABDECK® contains 7.5mg zinc
- Elemental zinc composition of readily available zinc supplements include: [463]
  - Zinc oxide (80% elemental zinc)
  - Zinc acetate (30% elemental zinc)
  - Zinc sulfate (23% elemental zinc)
  - Zinc gluconate (14% elemental zinc)
- Readily available zinc supplements in Australia and New Zealand are outlined in table 9o

Table 9o. Readily available zinc supplements

Supplement	Tablet/Liquid (Dose)	Elemental Zinc (mg)
Liquid Zinc	10ml	13.5
Zinc Drops	1 dose (5 drops)	5.76
Blackmores Bio Zinc	1 capsule	25.0
Zincaps	1 capsule	50.0

What is the safe upper limit for zinc supplementation in CF? PICO 9.5.3

[Ungraded] There is insufficient evidence available to make a recommendation.

The upper limits established for the healthy population applies to total zinc intake from food and supplements [43]. It has been suggested that the upper limit particularly in children aged 2-3 years, is too low and should be reviewed [462,473]. Zinc is considered relatively non-toxic with supplemental intakes <50mg/d, however chronic toxicity has been observed with intakes ranging from 150 to 450mg/d in adults [473]. The impact of chronically exceeding the upper limit of zinc intake in patients with CF requires further investigation.

Monitoring & Evaluation

There is no evidence as to how often zinc levels should be assessed and how supplementation should be monitored. Only one paediatric CF Guideline provides any guidance, recommending that zinc levels should not be measured and the adequacy of supplementation be assessed by monitoring functional changes in clinical outcomes [202].

Practice Points PICO 9.5.1

Assess zinc status and monitor empiric trials of zinc supplementation using a combination of dietary, biochemical and clinical/functional indicators.

Serum/Plasma Zinc

- Measure using the local laboratory reference ranges.
- Analyse levels in the context of dietary and clinical information. Consider;
  - Zinc is an insensitive marker of deficiency however may be helpful diagnostically in severe zinc deficiency
  - Levels are best measured when person with CF is clinically stable. Where acute phase response and inflammation is suspected, check CPR.
  - There is high individual biological variation in zinc levels
  - There is diurnal variation in zinc levels and levels may reflect recent dietary intake. Recommend where possible to measure fasting levels.

...table continued overleaf

Clinical Indicators

- Marginal zinc deficiency may be diagnosed in some patients via a positive response to zinc supplementation e.g. improved growth.
- Evaluate differential diagnoses as other conditions may present with similar signs and symptoms of zinc deficiency.

Diet

- Attention should be given to those at high risk of inadequate zinc intakes/absorption;
  - Strict vegetarian diets with high intake of phytates
  - Infants older than 6 months exclusively breastfed or consuming limited high bioavailable zinc foods such as fortified cereals or meat
  - High iron supplementation

Assess adequacy of protein and essential fatty acids because deficiency may manifest similarly to zinc deficiency.

Practice Points PICO 9.5.2 and 9.5.3

Suggested supplementation doses.

- Infants (<2yrs) with persistent failure to thrive and/or those with severe steatorrhoea:
  - Consider a trial of zinc supplementation
  - 1mg elemental zinc/kg/d in divided doses for 6 months (max 15mg/day).
- Children with suspected zinc deficiency:
  - 15mg/d for 6 months
- Adults with suspected zinc deficiency:
  - 25mg/day for 6 months
- In vitamin A deficiency refractory to Vitamin A supplementation, consider an empiric trial of zinc supplementation.
- The amount of zinc in the CF-specific multivitamin, VitABDECK®, is not adequate to correct zinc deficiency and additional zinc is likely required.
- The main dietary source of zinc are animal foods as well as zinc fortified cereals
- Where practical, zinc is best tolerated if given in divided doses

Translating into Practice

The following conversions exist for zinc:

- 1mmol zinc = 65.4mg
- 1 µg/dL = 6.54µmol/L