

# MedNut Mail

The How, When, Where, Which and Why of pharmacotnutrition

## Warfarin and Vitamin K

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<https://medicationsandnutrition.online>

## Commentary

Vitamin K encompasses several compounds that have similar structures and physiological functions

–

- vitamin K3 - the basic, simplest form with metabolic intermediary roles; not available in the diet;
- vitamin K1 – aka phylloquinone, available from plant sources; low bioavailability which is improved with the addition of lipids; relatively heat stable; light sensitive;
- vitamin K2 variants – aka menaquinone, available from animal and fermented sources, and the gut microbiome.

Vitamin K is an antioxidant, an integral membrane enzyme, an extracellular matrix protein, and a transmembrane receptor.

Vitamin K functions include - anticoagulation, glycaemic control, bone homeostasis, cell differentiation and proliferation, signal transduction, anti-inflammatory, promoter of cognition, inhibition of tumour progression, transcriptional regulator of osteoblastic genes, synthesis of sphingolipids, immune system regulation, inhibition of calcium renal stones formation, influences the

growth and repair of connective tissues, modulation of tissue calcification, transthyretin transport of retinol and the thyroid hormone thyroxine, stimulating insulin release; inhibiting mineralisation of arteries, cartilage and smooth muscle.

Vitamin K deficiency has been linked to cardiovascular diseases, chronic kidney disease, diabetes, osteoarthritis, rheumatoid arthritis, osteoporosis, cancer, dementia, some skin pathologies, functional decline, disability, pathological calcification and inflammation.

Vitamin K is transported by chylomicrons; lipoproteins, and its carriers in the blood are the lipoproteins.

The recommended minimum vitamin K intake for men is 120 mcg/day and for women is 90 mcg/day.

Warfarin is an anticoagulant for which there is a well-known coagulation interaction with vitamin K.

Warfarin transporters are the OAT1/2 (which it also inhibits), and its carriers in the blood are albumin and alpha-1 acid glycoprotein.

Hypoalbuminaemia results in increased availability of free warfarin and consequent elevated INR.

## Warfarin and Vitamin K

Although there is a formal recommendation for a stable vitamin K intake when warfarin is prescribed, most consumers seem to minimize intake

(<http://dx.doi.org/10.1016/j.jand.2015.12.023>). There now seems to be some awareness that it is advisable to check vitamin K status if coagulation control is brittle.

Stability of vitamin K is similarly as important as quantity of intake therefore it is important to monitor both adequacy of intake and stability of intake quantity.

My experience within the residential Aged Care sector in managing a stable vitamin K intake whilst warfarin is prescribed is best described as “very casual”.

What actions will you initiate when you see someone prescribed warfarin – will you -

- check the adequacy of their vitamin K intake (food intake and blood test)?
- ensure there is a stable day-to-day vitamin K intake?
- recommend checking albumin status if there is loss of weight and/or elevated INR?

### Conclusions

The warfarin-vitamin K interaction is important in optimizing the consumer outcome however there seems to be a well-entrenched and casual approach to ensuring both adequacy of intake and stability of vitamin K intake quantity.

# Case study

## Medical History with Nutritional Aspect

Amputation	<input type="checkbox"/>	Constipation	<input type="checkbox"/>	Dysphagia	<input checked="" type="checkbox"/>	MND	<input type="checkbox"/>
Anaemia	<input type="checkbox"/>	CVA	<input type="checkbox"/>	Enteral Feed	<input type="checkbox"/>	MS	<input type="checkbox"/>
Arthritis	<input checked="" type="checkbox"/>	CVD	<input type="checkbox"/>	Falls	<input checked="" type="checkbox"/>	Osteoporosis	<input type="checkbox"/>
Cancer	<input type="checkbox"/>	Dementia	<input checked="" type="checkbox"/>	Fracture	<input type="checkbox"/>	PD	<input type="checkbox"/>
CCF	<input type="checkbox"/>	Dentures	<input type="checkbox"/>	Frailty	<input type="checkbox"/>	Pressure Area	<input checked="" type="checkbox"/>
Chest Infection	<input type="checkbox"/>	Depression	<input type="checkbox"/>	Gout	<input checked="" type="checkbox"/>	Renal	<input checked="" type="checkbox"/>
COAD	<input type="checkbox"/>	DM Type 1	<input type="checkbox"/>	Hypertension	<input type="checkbox"/>	Ulcer	<input type="checkbox"/>
Confusion	<input type="checkbox"/>	DM Type 2	<input type="checkbox"/>	Incontinent	<input checked="" type="checkbox"/>	UTI	<input type="checkbox"/>
Food Allergies	<input type="text"/>						
Other:	deafness, ETOH, hypernatraemia, CKD, PA sacral						

## Biochemistry with Pharmaconutritional Consequences

Na:	<input type="text" value="140"/>	mmol/l	Hb:	<input type="text" value="123"/>	g/L	Albumin:	<input type="text"/>	g/L	BSL:	<input type="text"/>	mmol/l
K:	<input type="text" value="5.4"/>	mmol/l	Lymph:	<input type="text" value="2.5"/>		Total Protein:	<input type="text"/>	g/L	HbA1C:	<input type="text"/>	
Urea:	<input type="text" value="16.7"/>	mmol/l	MCV:	<input type="text" value="100"/>	mmol/l	B12:	<input type="text" value="210"/>	pmol/L	INR:	<input type="text"/>	
Creatinine:	<input type="text" value="0.155"/>	mmol/l	Zn:	<input type="text"/>	umol/l	Folate:	<input type="text" value="26.6"/>	nmol/L	TSH:	<input type="text"/>	mIU/L
Other:	eGFR 34, Fe 6, TRF 2.4, satn 10%, ferritin 217, vit D 95, holotranscobalamin 21										

## Medications That May Adversely Affect Nutritional Status

Drug	Vits + Mins	bpp >90%	N/V	C/D	Wt	App	Tst	Thir	Sal	Drlg	d m	Dys	BSL
Allopurinol		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cholecalciferol	(25 mcg/day)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ferrous Sulfate	Ca, Mg, Zn	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
NEO-B12	1 mg weekly	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Paracetamol		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## Summary of medications, nutrients and transporters

Allopurinol is a substrate for OAT2/3 which means likely competition for uptake with vitamin C (OAT2), B6 (OAT3) and folate (OAT2/3).

**Comments – medication and nutrition impacts (direct and indirect) only**

**Data summary**

**Biochemistry**

Recent relevant, available biochemistry indicates -

- elevated urea + creatinine - typically indicates renal function; also indicates loss of lean body mass;
- elevated MCV + low B12 + low holocobalamin - intervention recommended;
- vitamin D status within acceptable range – advisable to continue with this intervention as Mr ACF has limited exposure to sunlight.

**Pharmaconutrition**

Currently prescribed 3 medications that include nausea, vomiting and diarrhoea as side effects.

B12 intervention commenced 4 months ago. Evidence indicates elevated B12 levels diminish cognitive function therefore advisable to check B12 levels and clarify current status.

B12 administration will result in increased red cell production and consequently increase iron requirements - advisable to monitor iron status and correct iron deficiency.

Iron intervention commenced 4 months ago therefore advisable to check SIS levels and clarify current status.

Ferrous sulfate decreases zinc absorption.

Concurrent ingestion of paracetamol and iron resulted increased rate of iron

absorption and decreased extent of drug absorption; the authors advise drug and iron to be administered at different times from each other.

Dietary levels of caffeine intake in conjunction paracetamol drug inhibit antinociception.

**Bowel management**

- no regular intervention prescribed,
- oral PRN interventions prescribed; administered 1 x Jan,
- no Nurse Initiated interventions administered.

**Staff comments**

Staff advise Mr ACF's appetite has improved since return from hospital and that he is currently eating well.

**Observations**

Mr ACF was asleep in bed and I did not disturb him however his family was visiting and commented on his improved appetite both in hospital and since return.

**Assessment**

Mr ACF's diagnoses include arthritis for which he is prescribed paracetamol therefore chronic pain is likely- nutritional factors that may be useful to consider in pain management include -

- vitamin D - current intervention may not be adequate to maintain status. Evidence indicates increasingly brittle pain control with decreasing vitamin D levels;

## Warfarin and Vitamin K

- vitamin C - pain increases the reactive substances (formerly Reactive Oxygen Species) within cells. Vitamin C is important in quenching reactive substances and if there is insufficient vitamin C then cell status becomes compromised and the cells typically die which also causes pain. Advisable to consider a vitamin C intervention - the optimal intervention is 500 mg vitamin C/day (if more than 500 mg vitamin C administered at a time then the excess above 500 mg is not absorbed as the vitamin C transporters are overloaded). Vitamin C is not considered part of the pain management armament however it won't cause harm and evidence suggests it may confer benefit. Currently prescribed allopurinol which competes with vitamin C for uptake;

- low B12 exacerbates elevated TNF- $\alpha$  which is an inflammatory response marker; elevation of the inflammatory response can include a pain response and currently prescribed a B12 intervention therefore advisable to monitor B12 status.

Mr ACF's diagnoses include falls - nutritional factors that may be useful to consider in falls management include -

- vitamin D – associated with muscle weakness and consequently falls; currently prescribed an intervention therefore advisable to clarify vitamin D status;

- low B12 - is important in the righting reflex when a person stumbles; currently prescribed an intervention therefore advisable to monitor status;

- low iron – currently prescribed and intervention therefore advisable to check status;

- low zinc – can decrease food intake through altered sense of taste and poor appetite, and consequently reduced muscle mass; currently prescribed an iron intervention therefore advisable to clarify status.

Mr ACF's diagnoses include a pressure area - nutritional factors that contribute to healing include -

- adequate vitamin D status - evidence indicates low vitamin D status is associated with delayed wound healing; currently prescribed a vitamin D intervention;

- adequate vitamin C - important in collagen formation and the strength of the collagen; currently prescribed allopurinol which competes with vitamin C for uptake.

Mr ACF's diagnoses include deafness - nutritional factors that may be useful to consider in deafness management include -

- folate - associated with deafness; currently prescribed allopurinol therefore advisable to monitor folate status and if low then intervention recommended;

## Warfarin and Vitamin K

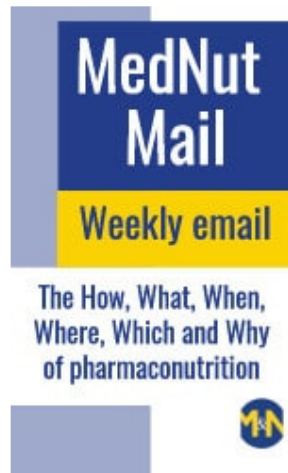
- vitamin C - inadequate dietary intake associated with deafness; currently prescribed allopurinol which competes with vitamin C for uptake;
- vitamin D - associated with low-frequency and speech-frequency hearing loss; currently prescribed an intervention therefore advisable to monitor status;
- zinc - inadequate zinc status has been associated with impaired hearing; currently prescribed ferrous sulfate which decreases zinc absorption therefore advisable to check zinc status and if low then intervention recommended.

What else would you include?

## Warfarin and Vitamin K

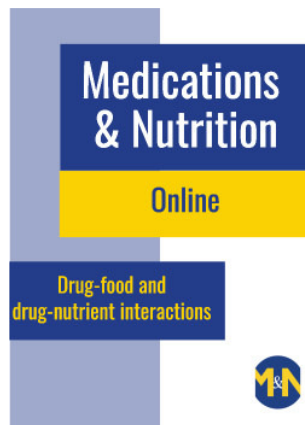
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