MEDNUT MAG

PHARMACONUTRITION MATTERS

2023 Issue 1

How it all began

Drug interactions and pharmaconutrition

Falls and pharmaconutrition

Deafness and pharmaconutrition

Should we have nutrient budgets?

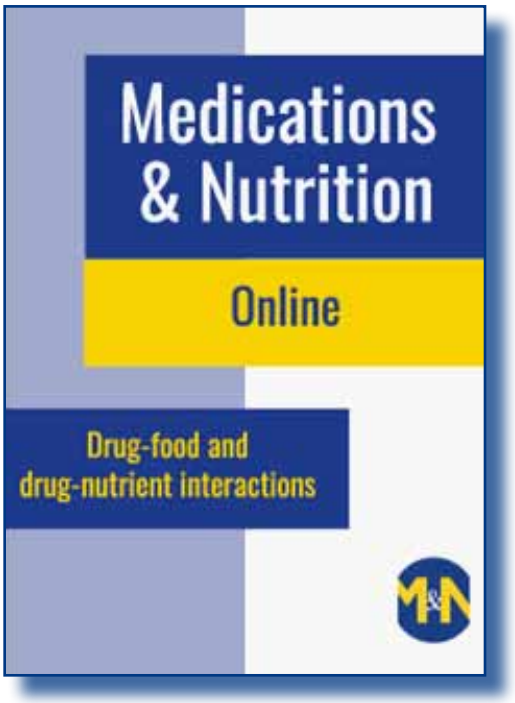
Case study 1

Contents

Welcome Letter from the Founder	6
How it all began	7
Drug interactions and pharmaconutrition	11
Falls and pharmaconutrition	14
Deafness and pharmaconutrition	17
Should we have nutrient budgets?	21
Case study 1	25
Acknowledgements	33

Medications have profoundly and positively changed health outcomes. However, they can come with some nutritional harms. By identifying and addressing the nutritional harms, optimal health outcomes are closer to being achieved.

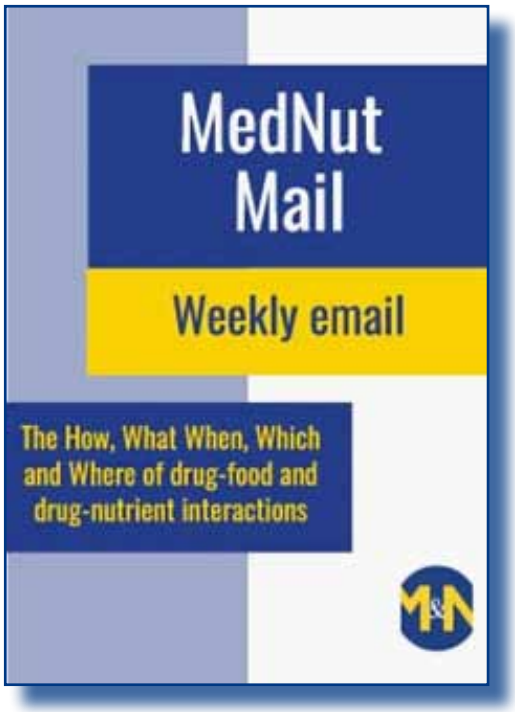
You may be interested in some of our products . . .



You have noted the prescribed medicines in your data collection — do you also note nutritional side effects, identify nutrients that may be impacted, consider whether transporters may be impacting blood test results? How long does it take you to find this information … for each person you see?

Join the increasing number of innovative, busy Health Professionals who integrate pharmaconutrition into their daily clinical practice.

Buy now



MedNut Mail is a free weekly email that consists of two components:

- an editorial, based on some aspect of pharmaconutrition, and
- a case study, difficult, simple, all real-life (and not identifiable).

Content includes examples of how to integrate this information into your clinical assessments.

Subscribe now

Dear Reader,

Welcome, and thank you for your curiosity in pharmaconutrition, a field that encompasses drug-nutrient and drug-food interactions.

Because of the ability of membrane transporters to transfer substances such as nutrients from one area to another, the pharmaceutical sector is hoping to manipulate them to transfer their compounds throughout the body and into currently-inaccessible areas. As a consequence the research is also identifying new mechanisms of action for drug-nutrient and drug-food interactions.

'How do we present the information in a clinically meaningful manner in our reports?' with the underlying question being 'Is it also accessible and useful to all the other clinicians involved in the care of this person?' These questions have guided our development of resources, such as the publication of our weekly email **MedNut Mail** which includes both an Editorial and a Case Study. In the Case Study we demonstrate how to include pharmaconutrition in clinical reports through its impacts on blood test results, glycaemia, side effects with nutritional consequences, and many top-level diagnoses such as bone health, coagulation, etc.

In this our first edition of **MedNut Mag**, we present several aspects of pharmaconutrition including -

- drug interactions — with other drugs, nutrients, and foods,
- impacts on falls and deafness,
- questioning whether there should be nutrient budgets,
- a case study.

If you are interested in learning more about pharmaconutrition but are not sure whether it is relevant to your clinical practice then sign up to **MedNut Mail** which will provide free, useful information.

If you can see the relevance and benefit of this information in your clinical practice then purchase a subscription to our online platform **Medications and Nutrition**.

In being curious about this topic, and hopefully finding a way to apply it in your clinical practice, you are that rare person, an innovative clinician who is also a leader!

We hope you enjoy our first edition of **MedNut Mag**.

Regards,

Yvonne Coleman,

Founder

How it all began

Working in a post-Acute, Rehabilitation and transition Aged Care facility in the 1990s, we frequently saw elderly people prescribed 12+ different medicines – never mind the number of tabs they consumed on a daily basis, and for some of these people it may have been 30+ tabs per day. The elderly people were often frail, dealing with many losses, were often losing weight, had poor appetites, and were not always responding well to rehabilitation interventions. What is the impact of all those different medicines on their nutritional health and how much is it impacting their responses? were questions I often asked.

Access to information on the impact of prescribed medicines on nutrition factors was extremely difficult in the 1990s due to factors such as:

- no Internet;
- long delays between request for research articles and their receipt;
- limited research;
- finding the articles as the published research was scattered through a broad range of publications.

Out of curiosity and frustration I started to pull together the research, summarised it, and organised it into a table for quick access. I then told my staff that we would now include this information in all our clinical assessments and they asked "how". More work was required, and twenty plus years later the "how" has mostly been sorted out.

The impact of prescribed medicines on nutrition factors is overlooked by doctors and pharmacists — mostly because nutrition is not included in their training. This is surprising given 80+% of western ill-health has an underlying negative nutrition component.

However, some of this oversight is likely to change, primarily because there is a lot of research into the use of physiological transporters to deliver drugs to currently inaccessible bits of the body; the primary role of these transporters is to deliver nutrients to required areas. The early research shows that many of the currently researched drugs either inhibit the transporters or can be transported by them – both these scenarios mean nutrient displacement. Until this recent research there was no awareness of this degree of pharmaceutical interference with nutritional factors.

Nutrients are typically absorbed during the meal as food is digested and nutrients released, whilst drugs are commonly administered before meals to improve their absorption, therefore drugs access the transporters before the nutrients and it is unlikely this nutrient deficit will be compensated.

Chronic, sustained medication intake can be for years and decades, therefore a sustained interference with nutrient availability will result in malnutrition and cascading consequences including poor responses to treatment (which we probably already see and don't recognise as such).

As most of the research is conducted by pharmaceutical companies, and published in pharmaceutical journals, it is likely pharmacists will become aware of the implications of this research and have the potential to become significant drivers of change, primarily through advising

the prescribing doctors of negative interactions. However, given their lack of nutrition knowledge it is also likely this negative impact on nutritional factors will be overlooked. Therefore the most likely drivers of change will be the nutrition clinicians i.e. those with a degree and/or a post-graduate degree in nutrition.

Currently, farsighted, visionary clinicians are already integrating this evidence into their clinical practice.

There are two components to medications and nutrition interactions:

- accessing the information; and
- presenting the findings in a clinically meaningful format.

Accessing the information

The online platform Medications & Nutrition provides a comprehensive range of clinically-useful research evidence, that is updated on a regular basis, and is summarised to dot points, to improve the accessibility to the latest research in this important area of care for busy clinicians.

Presenting the findings in a clinically meaningful format. So how does one present the information in a clinically meaningful format? Through trial and error we have found that:

- a table is great for presenting summary information such as the various side effects (nausea, vomiting, etc) and nutrients affected (B12, Mg, Ca, Fe, etc);
- actually identifying individual impacts. For example, wound healing requires an increased nutrient intake to support the increased nutrient demands for healing purposes. If a number of drugs are prescribed that negatively impact the status of one or more nutrients, then healing can be delayed.

Ultimately this magazine is about addressing both of the above-identified components by providing resources to both easily access information and how to apply it in a clinically-meaningful format.

The final question to be asked is: what is the qualification behind the person promoting awareness of this oversight in healthcare? And the answer is:

- Bachelor of Applied Science (Food Science & Nutrition),
- Graduate Diploma in Dietetics,
- Graduate Diploma in Health Education & Promotion,
- Thirty plus years clinical experience in both the Public Health system (Australia and overseas) and the residential Aged Care sector — where one sees and learns a lot.

Our philosophy is to provide as much of the accessible credible research, in one place, to increase ease of use for clinicians, and thereby improve outcomes for those in their care. With that aim in mind, the information is presented in dot points and then referenced so the source can also be easily accessed.

It is perhaps time to share some of our expertise!

If you have read this far then you must be a curious (and probably visionary) clinician. We hope you find our resources to be useful to your practice.

Yvonne Coleman

Drug interactions and pharmaconutrition

The terms 'medications', 'medicines', 'drugs' are used interchangeably to describe chemical substances that are administered to confer therapeutic benefit; they interact with 3 key groups:

- Other medicines — referred to as drug-drug interactions,
- Nutrients — referred to as drug-nutrient interactions,
- Foods — referred to as drug-food interactions.

Drug-drug interactions are well researched, and many facets of these interactions are included in the drug discovery process. The combination of the FDA (Food and Drug Administration) policy to reduce drug-drug interactions and the desire of the pharmaceutical companies to access currently inaccessible body areas has resulted in extensive research in "drug" transporters, i.e., physiological transporters that are utilised by nutrients.

Until the early 1990s the pharmaceutical sector considered food to be "benign" and their issue was whether to administer their drugs prior to food in order to maximise therapeutic benefit or with food to minimise side-effects. Then in the early 1990s a Canadian research team investigating *felodipine/nifedipine* interactions with alcohol discovered the grapefruit effect — subsequent research identified the key mechanism to be *cytochrome* (CYP) *P450 isoform 3A4,* and interactions with it are now part of the drug discovery process.

No-one investigated which other foods also alter drug effect and 30 years later we still do not have a comprehensive database on drug-food interactions.

Drug-nutrient interactions were also disregarded until 2012 when early clinical trials found that within several months of administration the then new drug *fedratinib* caused Wernicke's Syndrome, as it inhibited all the thiamine transporters, i.e., absorption, distribution and excretion, and so it was not released. For some reason the *metformin*-B12 interaction remains "ignored" even with 60 years of evidence.

As the "drug" transporters research progresses, it is likely many currently unrecognised drug-nutrient interactions will be identified. In order to modify the negative impact of prescribed medications we do require our nutrition scientists to be clarifying issues such as:

- the degree of negative impact on nutrients of each prescribed medicine;
- the best time to administer nutrient interventions; and
- the optimal nutrient dose to be administered.

Drug-food interactions have continued to be disregarded, even with the grapefruit findings and it is worthwhile pondering "why?". Pharmaceutical research is based on many knowns — the amount of the therapeutic substance, and the functions and effects of the excipients (ingredients) associated with the therapeutic substance — their main unknown is individual physiological response which is governed by genetic and environmental factors.

Food research starts from a very complex base that is influenced by:

- geographic location, which influences nutrient content;
- localised climate, which influences protein content;
- foodstuff genetics, which influence responses to their environment and their uptake of nutrients;
- cultural and social factors, which influence food choices and meal combinations.

So, when food intake is associated with an altered response to a pharmaceutical intervention, then the question is: is it caused by a pharmaceutical factor or a food factor? and how do we clarify the cause?

We do know about some single drug-food interactions — with alcoholic beverages, with grapefruit, and some related to caffeine. Perhaps the starting point is identifying interactions with a comprehensive range of single foodstuffs, and then as the expertise increases, we could consider more complex foodstuffs. Doing nothing because it is too difficult is unacceptable.

In order to encourage increased research in the areas of drug-nutrient and drug-food interactions, will you write to:

- the FDA (US regulatory body) and TGA (Australian regulatory body) to comment on the paucity of research in relation to these areas of significant interactions and request they be moved up the priority ladder?
- your professional body and suggest these areas be prioritised in student projects?
- your local Members of Parliament (House of Representatives and Senate, State and Federal) and request these areas be prioritised?

Conclusion

Although there are three pharmaceutical interaction categories, being **drug-drug** interactions, **drug-nutrient** interactions and **drug-food** interactions, only drug-drug interactions attract significant research interest. Seemingly, drug-food interactions are far more difficult than, for example, landing a man on the moon!

Falls and pharmaconutrition

A fall is defined as an event in which a person inadvertently comes to rest on the ground or other lower level. A fall can result in physical harm such as broken skin and bones, emotional and mental harm such as loss of confidence, and damaged ego as falling is quite inelegant.

Falls are the largest single cause of injury mortality in the elderly and are also an independent indicator of the functional decline that results in 40% of all nursing home admissions.

Pharmaconutritional factors that may be contributing to an increased risk of falls include:

- **high vitamin B3**. High doses (≥1000 mg/d) can be associated with low blood pressure.
- **high pyridoxine**. High doses (≥500 mg/d) associated with neurological symptoms, including ataxia, neuropathy, and decreased muscle tone.
- **high homocysteine**. High doses can permanently degrade the molecular structural integrity of collagen, elastin and proteoglycans, and cause an increased risk of muscular-skeletal mechanical instability. Can be due to low riboflavin and/or low pyridoxine and/or low B12 and/or low folate.

- **low B12**. Can cause neuropathy that can lead to impaired balance, proprioception, amyotrophy and depressed psychomotor retardation, which is important in the righting reflex when a person stumbles.
- **Folate**. Is important in neurotransmitter synthesis, myelination, synthesis of DNA and protein, DNA methylation and epigenetic regulation. Low levels increase risk.
- **Vitamin D**. Protects bone mineral density and improves muscle function and strength. Low levels increase risk.
- **Calcium**. Can affect muscle function. More likely to be low if potassium or magnesium is low. Low levels increase risk.
- **Potassium**. Maintains nerve and muscle function, bone health and insulin sensitivity, and muscle mass. Low levels increase risk.
- **Iron**. Important in a range of functions including muscle function. Low levels increase risk.
- **Magnesium**. Important in muscle function, and is an intracellular ion, which means difficulty in detecting early depletion. Low levels increase risk..
- **Zinc.** Important in a range of functions, including muscle function; more likely to be low if associated with loss of weight. Low levels increase risk.
- **Carnitine**. Is both absorbed and produced de novo, and is important in a range of muscle functions; magnesium is important in de novo carnitine production. Low levels increase risk.
- **Hb**. If Serum Iron Studies are within acceptable range and Hb is low, then this may indicate reduced biotin availability, as biotin is important in five stages of Hb formation. Low levels increase risk.
- **loss of weight**. Typically results in reduced muscle mass and strength, and can be due to multiple factors.

What actions will you initiate when you see someone whose diagnoses include falls, will you:

- ensure identified nutritional factors are well within acceptable ranges?
- review prescribed medications that may negatively impact nutritional factors that have been associated with the risk of falls?
- include pharmaconutrition impacts on falls risk in your report to colleagues?

Conclusions

The research into risk factors for falls causation and outcomes remains limited as the consequences to health and productivity continue to be underestimated.

Prescribed medications that impact nutritional factors that are associated with falls risk are likely to further exacerbate that falls risk.

Deafness and pharmaconutrition

Deafness is a multifactorial, global health issue that is commonly inadequately managed in healthcare services; for example, an elderly person who responds inappropriately to a question is automatically labelled as suffering dementia and the alternative is not considered, i.e., deafness.

When a deaf person does not respond appropriately, even when spoken to with a raised voice, then the clinician typically gives up trying to communicate, which leaves the deaf person feeling diminished and not worth any effort, Sadly, this is a very common scenario.

Tip — carry a small portable whiteboard and pen – you write and they can reply verbally — this is a useful strategy for minimising communication confusion, and doesn't take much extra time.

Is there evidence of an association between deafness and nutrition factors? Surprisingly, given the extent of deafness globally, this area has attracted very little research. Outlined as follows are several key nutrition factors for which there is evidence.

B12 and folate

Low B12 and/or folate have been found to be associated with deafness, and in fact some researchers recommend B12 and folate testing be routinely included when evaluating symptomatic hearing loss.

There is some evidence that B12 interventions are therapeutic in tinnitus management.

Vitamin C

Hearing impairment is being related to inadequate dietary intake especially in the elderly, particularly with findings that indicate an adequate dietary intake of vitamin C is associated with better hearing in the older population.

Vitamin D

Low vitamin D status was associated with low-frequency and speech-frequency hearing loss in the elderly. And this indicates that low vitamin D status may be a potential risk factor for age-related hearing impairment.

Early evidence suggests early correction of vitamin D deficiency in newly-diagnosed Meniere's disease reduces the necessity for more extreme interventions.

Calcium

Apoptosis (programmed cell death) is a calcium-dependent process, and is a common theme in many forms of acquired hearing loss.

Iron Deficiency Anaemia (IDA)

Evidence indicates mild maternal IDA during pregnancy and lactation may inhibit cochlear hair cell development in the infant.

Further, latent iron deficiency is associated with abnormal auditory neural maturation in infants at 34 weeks gestational age.

Zinc

Inadequate zinc status has been associated with impaired hearing.

Coffee

Evidence indicates coffee protects against hearing loss and tinnitus.

Polyunsaturated Fatty Acids (PUFAs)

Evidence indicates an inverse association between long-chain n-3 PUFAs intake and hearing impairment.

Thiamine

There is some recent evidence that thiamine deficiency can present as bilateral hearing loss.

Thiamine transporter OCT2 is expressed in the hair cells of the cochlea. Therefore, interruptions to thiamine accessibility are likely to impact cochlear hair cell function.

Dysfunctional mitochondria

The evidence is increasing that diagnoses that include dementia, diabetes, overweight and/or obesity i.e., all diagnoses associated with dysfunctional mitochondria, are associated with increased risk of hearing impairment.

Frailty

There is some evidence of an inverse correlation between hearing impairment and frailty. Further, moderate or greater hearing impairment in older adults is associated with decreased levels of physical activity.

There is some interesting evidence that *fenofibrate* protects against *cisplatin*-induced ototoxicity by maintaining peroxisome and mitochondria number and function, reducing inflammation, and decreasing Reactive Oxygen Species levels.

There is also some interesting evidence that the composition of intestinal microbiota may influence the expression of hearing impairment.

Some authors recommend dietary counselling become an integral component in the strategies to address hearing impairment.

Meniere's disease is a subset of deafness and is partially managed by a very low salt diet. However, it seems likely to me that at some point it will be deemed a neurodegenerative disorder as there is an increasing number of commonalities between Meniere's and neurodegenerative disorders, and consequently management will be changed from "just a low salt diet" to neurodegeneration management.

What actions will you initiate when you see someone whose diagnoses include deafness, will you:

- ensure you have a strategy to maximise communication and minimise a sense of diminishment of the person with deafness?
- review prescribed medications that may impact nutritional factors that have been associated with hearing impairment?
- include pharmaconutrition impacts on hearing impairment in your report to colleagues?

Conclusions

Research into deafness in general is very limited as deafness impacts on health and productivity have been significantly underestimated.

The evidence is increasing that malnutrition contributes to the risk of hearing impairment, throughout life.

By default, prescribed medications that impact nutritional factors associated with hearing impairment are likely to further exacerbate that hearing impairment.

Should we have nutrient budgets?

Money and nutrients have some surprising commonalities:

- similar income/intake on a relatively regular basis;
- other income/intake on an irregular basis;
- regular costs;
- pleasure costs.

Money management typically starts with a budget, with a defined portion of money being allocated to various accounts such as regular bills, mortgage/loan repayments, holidays, savings. What remains, and possibly a bit more, is spent on current pleasures. There is also other income such as interest paid on bank deposits and returns on investments.

Nutrition management typically does not include a "nutrient budget" for defined "spending on energy", and so pleasure costs are prioritised. Regular nutrient costs include the metabolic requirements for the body to function and the long-term prescribed medication impacts on individual nutrients. Unaccounted costs include the stresses and the presumed increases in operating costs due to a long-term chronic diagnosis, and savings would be replenishment of nutrient stores. As neither the long-term prescribed medication impacts have been quantified nor the unaccounted costs relating to stresses and chronic unwellness, it is very difficult to "budget" for them. The "other income" equivalent would be the supply of nutrients from the gut microbiota — this source is not well-researched and so we don't know whether the input is similar to savings account interest, i.e., negligible at this stage or higher as in returns from investments. This income/

intake source is likely to be compromised with sustained long-term consumption of prescribed medications.

When we have more financial costs than our regular income then we draw on our reserves or savings. Likewise with nutrients, when there is an inadequate availability of all relevant nutrients to metabolise that energy from within the energy source then we draw on our reserves or stores for those that are missing and/or for which there is an inadequate availability.

When we consistently draw on our financial reserves, they become depleted and then there are penalties such as interest, penalty interest, late payment fees, etc. It is similar to the availability of our nutrients, i.e., a lack of adequate availability results in consequences and the well-known example is thiamine deficiency, where sustained short-term inadequate intake results in Wernicke's Syndrome whilst sustained long-term inadequacy results in the irreversible Korsakoff's Psychosis.

When there are insufficient financial reserves, the financial institutions step in rather quickly and encourage us to change our consumption patterns until we again have adequate reserves. This is not the case with nutrients as a sustained nutrient inadequacy may not be blatantly obvious and there is no intermediary or gatekeeper to step in and create an awareness, so nutrient intake inadequacies may result in irreversible changes to body function without any personal awareness, or the unwellness is blamed on other factors.

Many nutrition pleasures increase the nutrient requirements for the metabolism of the energy associated with the pleasure, i.e., many pleasure costs provide energy (kilojoules or calories) without an adequate supply of necessary nutrients to pay for them. This is the same as having a credit card, allowing us to spend at whim without having the money readily available to pay now.

And the truly hidden nutrient cost is the negative impact of toxic metals. How much do toxic metals diminish response to therapeutic

interventions and increase nutrient requirements due to their displacement of therapeutic interventions and nutrients? Toxic metals would be the equivalent of bank fees and government charges on all transactions.

The general belief is that we 'eat adequately to meet our nutritional needs', but do we? Supermarket purchases and the rapid growth in fast food consumption suggest it is likely energy needs are being met, but not the nutrient requirements to metabolise the energy; when energy is not metabolised it is stored as fat.

Further, the recommended intakes for a range of nutrients have been based on people without disease. We don't know the degree of increase in nutrient requirements, due to disease and its associated stresses. What percentage of the recommendation should we factor in to accommodate unwellness? Should we be recommending a doubling of each nutrient's recommendation, a tripling, a quadrupling, perhaps more? Or should there be a ranking similar to that of 'energy consumed' based on the level of exercise?

We have all seen various financial budget models. However, given there aren't any nutrient budget examples, we will have to speculate on what one would look like, and there seem to be two formats:

1. Given that people are familiar with weight charts that state if you are X height then you should weigh Y kgs, energy and nutrient charts could be based on the same concept, i.e., if you weigh Y kgs then you require Z kJ (energy) to maintain weight and you need to consume A amounts of nutrients for this energy to be properly metabolised.

2. For each 1,000 kJ to be metabolised adequately you require A amounts of nutrients. Once you know how much you weigh, calculate the amount of energy you require to meet your metabolic requirements (formula), and multiply by B factor rating to address the increased nutrient demands due to your current diagnosis, prescribed medications, stress due to your chronic unwellness, personal idiosyncratic nutrient requirements.

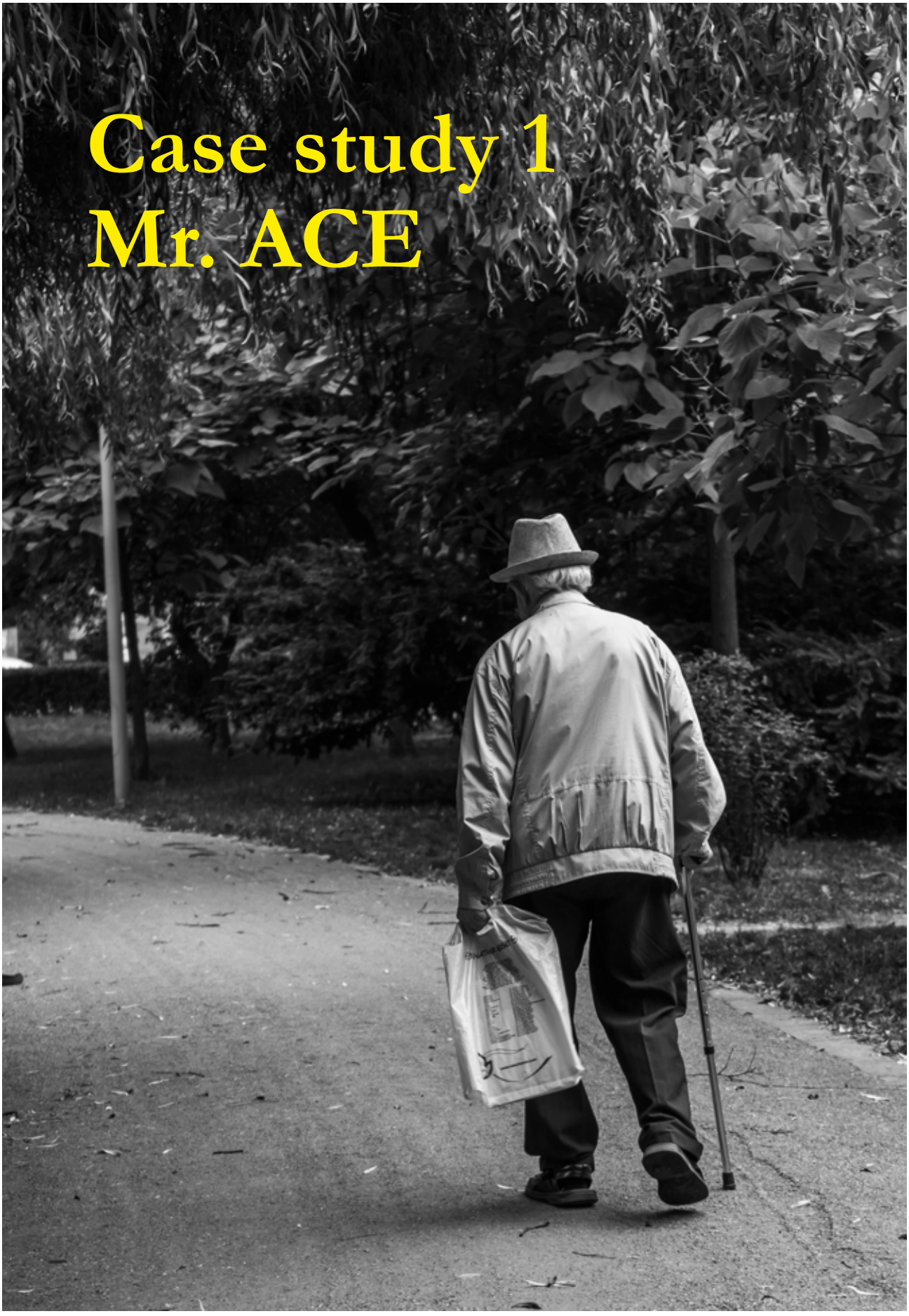
Given that we, as clinicians, mostly consult with people who have chronic health issues, how do you address the lack of a "nutrient budget"? Do you:

- monitor blood test results and aim to maintain nutrient levels in the upper 50% or top 75% of recommended range?
- use the recommended intakes as the minimum amount required and then add a percentage more?
- discuss a nutrient budget?

Conclusions

Many despair at the lack of money management displayed by some, yet no-one despairs at the lack of nutrient management displayed by most. Perhaps applying the money management model to nutrient management may improve nutrient awareness and the need for a "nutrient budget".

Case study 1 Mr. ACE



Medical History with Nutritional Aspect

Amputation	☐	Constipation	☐	Dysphagia	☐	MND	☐
Anaemia	☐	CVA	☐	Enteral Feed	☐	MS	☐
Arthritis	☐	CVD	☐	Falls	☐	Osteoporosis	☐
Cancer	☑	Dementia	☐	Fracture	☐	PD	☐
CCF	☐	Dentures	☐	Frailty	☐	Pressure Area	☐
Chest Infection	☐	Depression	☐	Gout	☐	Renal	☑
COAD	☐	DM Type 1	☐	Hypertension	☑	Ulcer	☐
Confusion	☐	DN Type 2	☑	Incontinent	☐	UTI	☐

Food Allergies	Renal transplant
Other	DVTs, Ca lung + bony mets. deafness

Biochemistry with Nutritional Aspect

Na:	133	mmol/l	Hb:	83	g/L	Albumin:	36	g/L	BSL:		mmol/l
K:	4.8	mmol/l	Lymph:	0.5		Total Protein:	66	g/l	HbA1c:		
Urea:	11.0	mmol/l	MCV:	108	mmol/l	B12:	1193	pmol/L	INR:		
Creatinine:	0.114	mmol/l	Zn:		umol/l	Folate:	48.1	nmol/L	TSH:		mIU/L

Other: eGFR 7, U alb 7, U creat 3.5, U alb:creat 2.0, CRP 118, ESR 95, Fe 10, TRF 1.6, satn 25%, Ferritin 3894, Mg 0.95

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
Amitriptyline	B2	☑	NV	CD	↑	↑	☑		↓		☑	☐	☑
Esomeprazole	(40 mg/day) B1, B12, Ca, Fe,	☑	NV	CD	↑		☑				☑	☐	☐
Frusemide	(60 mg/day) Ca, Cl, K, Mg, Na,	☑	NV	CD		↓	☐				☑	☐	☑
Gliclazide	(08:00)	☑	NV	CD	↑	↕	☑				☐	☐	☑
Prednisolone	(08:00, 17:00) Ca, Cr, D, Iodin	☑	NV	CD	↕	↑	☐				☐	☐	☑
Spironolactone	K, Mg	☑	NV	D			☐				☐	☐	☐
Tacrolimus		☑	NV	CD		↕	☐				☐	☐	☑
TARGIN		☐	NV	CD		↕	☑				☑	☑	☐

Extra drug: linagliptin (08:00), aranesp, enoxaparin

BACK TO CONTENTS

Summary of medications, nutrients and transporter

Organ (transporter)	Thiamine	Choline	Pyridoxine
Inhibitor function			
From gut to epithelium	*Amitriptyline* (THTR2)		
Liver	*Amitriptyline* (OCT1) *Esomeprazole* (OCT1) *Spironolactone* (OCT1)	*Amitriptyline* (OCT1) *Esomeprazole* (OCT1) *Spironolactone* (OCT1)	
Into kidneys	*Amitriptyline* (OCT2) *Prednisolone* (OCT2) *Spironolactone* (OCT2) *Naloxone* (OCT2)	*Prednisolone* (OCT2) *Spironolactone* (OCT2) *Naloxone* (OCT2)	
From kidneys to urine			*Amitriptyline* (THTR2)
Into retina	*Amitriptyline* (OCT1)		
Substrate function			
Into muscles	*Amitriptyline* (OCT3)	*Amitriptyline* (OCT3)	

Comments — medication and nutrition impacts (direct and indirect) only.

Data summary

Biochemistry

Recent relevant biochemistry indicates:

- low sodium — currently prescribed *esomeprazole*; query SIADH status; advisable to recheck status;
- low Hb — associated with increased risk of falls, and poor appetite; currently prescribed *esomeprazole*;
- elevated B12 — evidence indicates elevated B12 levels diminish cognitive function; currently not prescribed a B12 intervention - prescribed historically;

- elevated ferritin — typically indicates mobilisation of the storage form of iron to the active form due to inadequate iron availability; currently prescribed *esomeprazole*.

Glycaemia

- before breakfast — 5.0-8.2, mostly 5-7; recommended range 4-6;
- tested weekly.

Diabetes drugs

- *gliclazide* has a duration of 18-24 hours;
- *linagliptin* has a duration of 24 hours.

Diabetes drugs coverage

- Before breakfast BSLs — minimal, if any, coverage from previous morning's *gliclazide* or *linagliptin*.
- Before evening meal BSLs — covered by the current morning's *gliclazide* and *linagliptin*.

Currently prescribed four medications that may alter glycaemia, being *amitriptyline*, *frusemide*, *prednisolone* and *tacrolimus*.

Prednisolone induces hyperglycaemia in the afternoon and evening but not overnight, consequently hyperglycaemia management strategies should target the timeframe from midday to midnight.

Pharmaconutrition

Currently prescribed:

- Seven medications that include hyponatraemia as a side effect.
- Six medications that include nausea, vomiting and diarrhoea as side effects.
- Four medications that include altered taste and dry mouth as side effects.

Phenothiazine derivatives such as *amitriptyline* are similar in structure to vitamin B2 (riboflavin) and consequently decrease riboflavin availability.

Esomeprazole decreases B12, vitamin C, magnesium, zinc and iron absorption, may decrease calcium absorption, and decreases thiamine availability.

Frusemide increases urinary excretion of calcium, magnesium, potassium, sodium and thiamine.

Prednisolone is associated with lower vitamin D levels; proposed mechanism steroids may enhance inactivation of vitamin D-2 by upregulating 24-hydroxylase activity.

Spironolactone impairs zinc status.

Urinary **thiamine** losses have been indicated with almost all diuretics including spironolactone.

Tacrolimus reduces intracellular magnesium levels: proposed mechanism — drug-induced suppression of vitamin D receptor expression.

Currently prescribed the trifecta, i.e., three drugs that decrease magnesium availability (*esomeprazole*, *frusemide*, and *tacrolimus*). Magnesium deficiency manifests as confusion, disorientation, personality changes, loss of appetite, depression, muscle cramps, tingling, numbness, hypertension, cardiac dysrhythmia, seizures. Cellular magnesium status is unknown whilst magnesium levels are within the acceptable range. However, if magnesium levels are low then significant cellular depletion is typically indicated and intervention recommended.

Bowel management

- No regular intervention prescribed.
- Oral PRN aperient prescribed.
- No Nurse-initiated interventions administered.

Staff comments

Staff advise Mr. ACE eats well.

Observations

Mr. ACE is a tall, large-framed, pale, breathless man with 'thyroidy' eyes, a large abdomen, and scrawny shoulders — he told me the food has a bitter and/or metallic taste and attributes this to the chemotherapy. Mr. ACE also told me that he wishes to be provided with 'regular' meals as (at home) he was a sympathy-vegetarian to support his wife. Mr. ACE also told me he enjoys milkshakes. Mr. ACE was weight stable at admission and is now losing weight.

Assessment

Mr. ACE has lost weight. Loss of weight is associated with depletion of zinc status and zinc is important in a range of body functions, including sense of taste and release of the hunger hormone Neuropeptide Y. Since Mr. ACE has lost weight, it is advisable to check zinc levels and if inadequate then short-term (90-120 days) intervention and recheck status prior to cessation of the intervention. However, he is currently prescribed *esomeprazole* which may reduce the effectiveness of the zinc intervention.

Mr. ACE's diagnoses include chronic pain — nutritional factors that may be useful to consider in pain management include:

- Vitamin D — current intervention may not be adequate to attain adequate range. Evidence indicates increasingly brittle pain control with decreasing vitamin D levels. Currently prescribed *prednisolone* which decreases vitamin D status. Advisable to check vitamin D levels and if still low then review current vitamin D management strategy.
- 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 maximum intervention is 500 mg vitamin C/dose (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 *esomeprazole* which decreases conversion of vitamin C to its active form.

- Low B12 exacerbates elevated TNF-α which is an inflammatory response marker; elevation of the inflammatory response can include a pain response and currently prescribed *esomeprazole* therefore advisable to check B12 status.
- Magnesium — proposed mechanism magnesium blocks the NMDA receptor channels in the spinal cord and thus limits the influx of calcium, i.e., reduces the risk of excitotoxicity and consequent exacerbation of pain. Currently prescribed *esomeprazole* and *frusemide* which decrease magnesium availability. Advisable to clarify magnesium status.

Mr ACE's diagnoses include deafness — nutritional factors that may be useful to consider in deafness management include:

- B12 and/or folate — associated with deafness; currently prescribed *esomeprazole* therefore advisable to check B12 and folate levels and if low, then intervention(s) recommended.
- vitamin C — inadequate dietary intake associated with deafness; currently prescribed *esomeprazole* which reduces conversion of vitamin C to its active form.

- vitamin D — associated with low-frequency and speech-frequency hearing loss; currently prescribed *prednisolone,* therefore advisable to clarify status.
- zinc — inadequate zinc status has been associated with impaired hearing; currently prescribed *esomeprazole* therefore advisable to check zinc status and if low then intervention recommended.
- thiamine — associated with bilateral hearing loss and proposed mechanism of action is that thiamine transporter OCT2 is expressed in the hair cells of the cochlea therefore interruptions to thiamine accessibility are likely to impact hair cell function; currently prescribed *esomeprazole* and *frusemide* which decrease thiamine availability both directly and indirectly.

ACKNOWLEDGEMENTS

Photographs

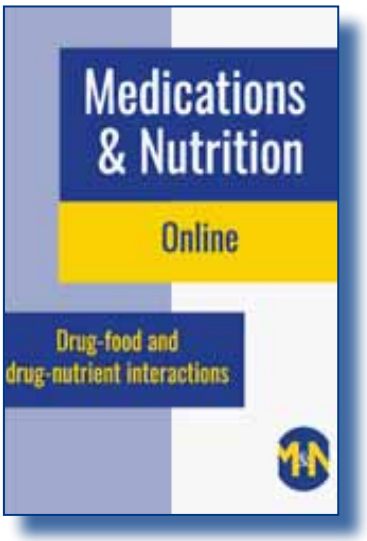
Engin Akyurt *Contents top*, 23
Vlad Chetan 25
Yvonne Coleman *front cover*, 2, 4, 24, 33, *back cover*
Cottonbro Studio 7
Eren Li 15
Mart Production 32
Tima Miroshnichenko 8
Aleksandar Pasaric *Contents bottom*
Pixabay 10, 11
Anna Shvets 16
Matthias Zomer 19

Design and Layout

Michael Birch

This resource is for innovative clinicians looking to expand their expertise so they can continue to provide their best service to the people in their care.

Click here



The following is an example of content available in *Medications & Nutrition.*

SERTRALINE

DRUG DETAILS

Sertraline Antidepressant

NUTRIENTS AFFECTED	ADVERSE REACTIONS		BIOCHEMICAL FACTORS
Na[112]	Nausea[1, 2]	Appetite down[1, 2]	Hypoglycaemia[1]
B1[23, 60]	Vomiting[1, 2]	Appetite up[2]	Hyperglycaemia[2]
	Constipation[1, 2]	Dry Mouth[1, 2]	Hyponatraemia[1, 2, 112, 114, 115 , 139, 397]
	Diarrhoea[1, 2]	Sweating[1, 2]	
	Weight up[2, 113]	Tremor[1, 2]	Hypercholesterolaemia[2]
	Weight down[1, 2]		Hypouricaemia[2]

Pharmacokinetics

- Binding of drug to plasma proteins ~ 98%[1, 2].
- Associated with cytochrome P450 pathway[1], isozyme 2D6[2].
- May alter glycaemic control[1].

Drug-food Interactions

- Tryptophan contra-indicated[2]. Tryptophan food sources include bananas, pineapples, walnuts, milk protein, eggs, white bread, beef, corn[116].
- May interact with tryptophan[1].
- Interacts with grapefruit juice to increase drug availability[111].
- Alcohol contra-indicated[2].

Drug-nutrient Interactions

- Concurrent administration with diuretic has a synergistic effect for hyponatraemia[112].
- Regular measurement of serum sodium levels recommended[112].
- Drug is a THTR2 inhibitor (blocks transporter function)[23, 60]. THTR2 functions as a major thiamine transporter that transports thiamine and pyridoxine[600] from the intestine into enterocytes[62], excretion of thiamine from the kidneys[23], and facilitates thiamine absorption into retinal cells[62]. Therapeutic doses of the drug are likely to inhibit thiamine absorption[23, 60], and renal re-absorption[23], and may contribute to thiamine deficiency[23, 60], especially in at-risk populations[60]; proposed mechanism — inhibition of intestinal THTR2[23, 60]. Drug inhibition of THTR2 is a proposed mechanism for drug-induced lactic acidosis[60].
- Drug is an OCT1 inhibitor (blocks transporter function)[38]. OCT1 functions as a major thiamine transporter[9, 10, 11, 12, 13, 14, 15], that can also transport choline[9, 11, 16, 17], and tyramine[9, 10], from the portal vein into liver hepatocytes[9, 11, 12, 14, 16, 18, 19].
- Drug is an OCT2 inhibitor[39]. OCT2 transports a number of endogenous substances, including choline[10, 11], histamine[10, 11], creatinine[10, 11], and primarily thiamine[10, 21]; a significant function seems to be transfer of thiamine from the blood stream into the kidneys[21].
- Drug is an OCT3 substrate (can be carried by the transporter)[23]. OCT3 is a polyspecific organic cation transporter[22] that transports several endogenous substances, including choline[11, 23], histamine[11, 23], creatinine[11, 23], carnitine[23] and thiamine[10, 21, 24]; albeit thiamine transport is equivocal[25]. OCT3 is predominant in skeletal muscle[10, 26], and strongly expressed in salivary gland[10, 26]; dysfunction or inhibition of salivary glands can lead to dry mouth[26].

Are you going to nurture your budding skills,

allowing them to blossom and expand,

letting them broaden your professional horizons,

producing the fruits of your study and research?

For more information **Click here**

BACK TO CONTENTS