MedNut Mail

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

What do physiological transporters have in common with bus services?

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https://medicationsandnutrition.online

Commentary

What do physiological transporters aka drug transporters and bus services have in common?

Networks, hubs, defined load capacities and probably defined turnaround times.

When we travel by bus, we have timetables, designated stops and hubs or stations where we can connect with the next bus to go to wherever we're going.

Seemingly the physiological transporters operate similarly. Most nutrients have one or more designated transporters that will carry them from the gastrointestinal tract to the epithelium (gut wall) where they change transporters to travel to their next destination (liver, kidney, elsewhere), and once they are ready to depart that site then another transporter typically carries them to their next site.

What we still don't know includes -

- **What is the maximum capacity of each transporter?** For example, we know that the Sodium Vitamin C Transporter 1 that transfers vitamin C out of the gut, has a maximum capacity of about 500 mg. That effectively means that if a person takes a 1,000 mg tab vitamin C then the first 500 mg hops on the transporter and the remainder passes out in the pooh.
- **How long does it take for the transporter to carry the nutrient or substrate from the gut to the epithelium hub/station?** For example, we know it takes about an hour for most of the metformin dose to travel from gut, via liver to kidney.
- **How long does it take for the transporter to return to its starting point ready for its next load?** For example, in order to maximize the absorption of 1,000 mg vitamin C it should be administered as 2 x 500 mg doses however what is the minimum period of time until the transporters are back at the starting site and ready for their next load?
- **Does the transporter always return empty or does it "backfill" (to use a trucking term)?** Two-way transporters are common between the cell wall and either inside or outside the cell for many substrates.
- **What determines which transporter is chosen to carry the load to the next destination?** For example, once absorbed from the gut, thiamine

has a choice of transporters – OCT1 to travel to the liver, OCT2 to travel to the kidneys, OCT3 to travel to the ear, muscles, etc. What factors determine the destination, is it the frequency of service, the next transporter in the line, some other factor?

- **How flexible are the transporters with the shape and size of their loads?** For example, many of the thiamine transporters can carry metformin and also the toxic metal cadmium.

Drug companies are spending serious money on research into the physiological transporters so they can design drugs to access currently inaccessible bits of the body. The focus of the drug companies is on utilizing the physiological transporters, and there seems to be limited concern about the nutritional consequences of sustained utilization of these transporters.

Because most drugs are administered prior to meals to maximize drug effect, the drugs have first access to the transporters and there seems to be consequent minimal capacity available to carry the nutrients.

Where are our nutrition scientists? We need the nutrition research so that when the submissions are made to the Clinical Practice Guidelines, that the nutrition component is integrated into the care process and therefore well-managed.

So, what clinical actions should we be initiating/recommending to address some of these issues? Will you be advising -

- administration of nutrient supplements at a different time from any prescribed medications to minimize competitive inhibition?
- administration of nutrient supplements on an empty stomach to maximize absorption?

Conclusions

Drug transporter research is providing a lot of answers and a lot of new questions. It is likely we shall be applying first principles to a number of issues until they are fully addressed, and modifying our clinical practice to accommodate these changes as we learn more.

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Case study

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	☐	DM Type 2	☐	Incontinent	☐	UTI	☐

Food Allergies: decreased sense of smell and taste

Other: altered thyroid function

Biochemistry with Pharmaconutritional Consequences

No recent relevant data available

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
NEO-MERCAZOLE	(5 mg/day) A, Fe, Iodine, Li, S		☐	NV				☑				☐	☐	☑
Olanzapine			☑		C	↑	↑	☐				☑	☐	☐
			▩					▩				▩	▩	▩

What do physiological transporters have in common with bus services?

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

No recent relevant biochemistry available. Advisable to check plasma proteins (albumin, total proteins) as markers of nutritional status. The plasma proteins are the primary transporters for one of the prescribed drugs and hypoproteinaemia may alter its effects including expression of side effects.

Mrs AAI remained relatively weight stable from admission until mid 2019 at which time there was an apparent loss of weight; staff advise Mrs AAI mostly eats well.

Mrs AAI's diagnoses include altered thyroid function therefore given the recent apparent significant weight loss advisable to check thyroid function.

Carbimazole (Neo-mercazole) dose is based on weight stability therefore any reasonable loss of weight increases risk of overmedication and any reasonable gain in weight increases risk of undermedication.

Micronutrients, mostly iodine and selenium, are required for thyroid hormone synthesis and function, therefore advisable to check Mrs AAI's thyroid function. If results are not within acceptable range then consider checking selenium status. There is evidence that if both iodine and selenium levels are low then best to address iodine status first.

Carbimazole can function as a vitamin K antagonist (reduces blood clotting by reducing vitamin K action) therefore advisable to either -

- monitor for evidence of frequent bruising and if present then check vitamin K status, or
- monitor vitamin K status on a regular basis ie at least annually.

Olanzapine is associated with increased risk of insulin resistance, glucose intolerance and diabetes therefore advisable to monitor BSLs and/or HbA1c on a regular basis ie at least 6-monthly.

Olanzapine inhibits thiamine transporters OCT1 (liver) and OCT2 (kidneys) therefore outcome is decreased thiamine uptake by these organs. Advisable to monitor thiamine status and if low then interventions recommended, and advisable to administer either one hour before or 2 hours after olanzapine administration.

What else would you include?

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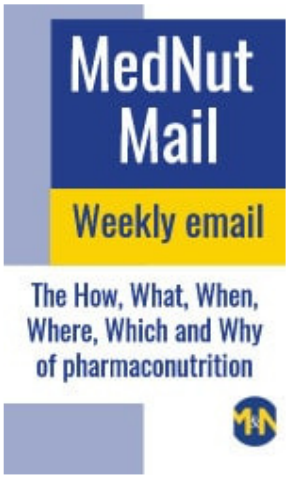

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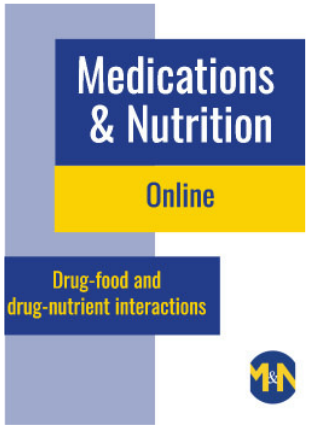

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