

Micronutrients

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Micronutrients Deficiency and more

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Conclusions

Too little

About right

Too much



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Too little

About right

Too much

Problems

diagnostic uncertainties
lack of therapeutic flexibility



Spontaneous Nutrition

Micronutrients not a major issue for most people

Vitamin D is an exception

Many micronutrients have limited stores but vitamin and trace elements are generally well maintained

Maintained in starvation and most illnesses

Deficiency rarely conveyed to the fetus (nb folate)



Spontaneous Nutrition

Iodine deficiency mainly historic

Selenium deficiency rare

but relative deficiency when dominant cereal
grown in soil with low Se

Disease-related deficiency

Usually only in gastrointestinal disease

Special case of refeeding syndrome

Non-specific effects of illness/anorexia may
provoke specific micronutrient deficiency

Usually a global picture of disease-related
malnutrition

Gastrointestinal disease-related micronutrient deficiency

Site / type

Deficiency state

Gastric or ileal

Vitamin B12

Pancreatobiliary

All fat-soluble vitamins

Small intestine

Usually a global defect but
sometimes asymmetrical

Bariatric surgery

Unpredictable

Enteral Nutrition

Micronutrients not a major issue in most cases

Standard enteral feeds all contain a balanced range of vitamins and trace elements

European law requires manufacturers to include RDA for all micronutrients in the volume of feed that provides 1500kcal

Where additional supplements are needed it is because of underlying disease/prior deficit

Enteral Nutrition - Cautions

Smokers

Severe diarrhoea

Chronic liver disease (alcoholic)

Prolonged anorexia and social isolation

Risk of refeeding syndrome



What about Parenteral Nutrition ?



PN Background

Much PN used for short periods in relatively healthy people (pre-morbid state) therefore

Trace elements (deficiency or excess) rarely an issue

Vitamin excess unlikely to be a problem

Vitamin deficiency may be a big problem even in short-term care

Approach to the problem

Formal analysis of each individual micronutrient

Each micronutrient is different

- correct ratio - oral/iv often not known

- availability from standard PN mixtures varies

- need is different according to pre-nutrition state
and demands of current illness

- potential for harm variable

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10+ trace elements, 12+ vitamins (134 ASPEN pages)



History of micronutrients in PN

Vitamins

Need always recognized (1972 PN “ineffective”)

1975 US recommendation for addition of vitamins

1985 US refined dosages = more ascorbate,
thiamine, pyridoxine and folate

addition of vitamin K to adult feeds



History of micronutrients in PN

Trace elements

1977 US recommendation for 7 elements

1979 selenium added

1982 copper dose reduced

Much data from 1990s on trace element toxicity but
no change to official recommendations



Micronutrient availability for PN

Some individual components – not all countries

eg: thiamine, folate, zinc, selenium

Mostly administered as fixed combinations

eg: Solivito/Vitlipid vitamins, Additrace trace elements

Big variation in content despite suggested daily amounts



Micronutrient challenges

Not a comprehensive evaluation

Some problems highlighted in ASPEN review

Therefore:

B, Cr, F, Fe, I, Mb and Si

and most vitamins

will be neglected

Zinc

Important in enzyme systems & gene expression

Often low in tissues (not necessarily blood)

Deficiency associated with growth retardation
acrodermatitis and infection risk

Typical adult requirement ~3mg/day

Trace element mixtures contain 1 to 10mg

Available separately (? ee)

Acrodermatitis enteropathica



Zinc in intestinal failure

Poor absorption in intestinal inflammation

Lost ++ in diarrhoea, fistula drainage, etc

Deficiency associated with increased infection risk and acrodermatitis in patients on TPN

Typical adult requirement ~3mg/day

Requirement in diarrhoea >10mg/day or 12mg/L

Measuring leukocyte zinc is better than blood ?

Copper

Component of many enzyme systems

Deficiency is rare other than in diabetes and burns:
provokes anaemia and neurology like B12 deficiency

Excess also associated with neurological features

Assessment of normal levels poorly established

Typical adult requirement ~0.3mg/day

Trace element mixtures contain 0.1 to 1.3mg

Copper and long-term PN

Deposition in brainstem & kidneys

Contributes to Parkinsonian state

Probably reversible if identified early

Gradual reduction in copper in PN

but most widely used trace element mixture in
Europe still contains 1.3mg

Note “balance” with zinc of potential therapeutic value

Copper and digestive disorders

Excreted in bile

Increased losses in diarrhoea

Rises in most cholestatic disease (Wilson's)

Contributes to cholestasis of IF-associated liver disease or is consequence of this?

More care over copper provision needed

Suggest 0.4-0.5mg/day in short bowel, etc

0.15mg/day in liver disease

Manganese

Component of many enzyme systems - especially in control of oxidative stress (Mn-SOD)

Deficiency “doesn’t” occur (contaminant)

Excess associated with neurological features

Assessment of normal levels poorly established

Typical adult requirement unclear

1.8-2.3 mg/day US Nat Acad Sci

0.06-0.1 mg/day ASPEN/ESPEN

Trace element mixtures contain 0.025 to 0.51mg

Manganese and long-term PN

Deposition in brainstem

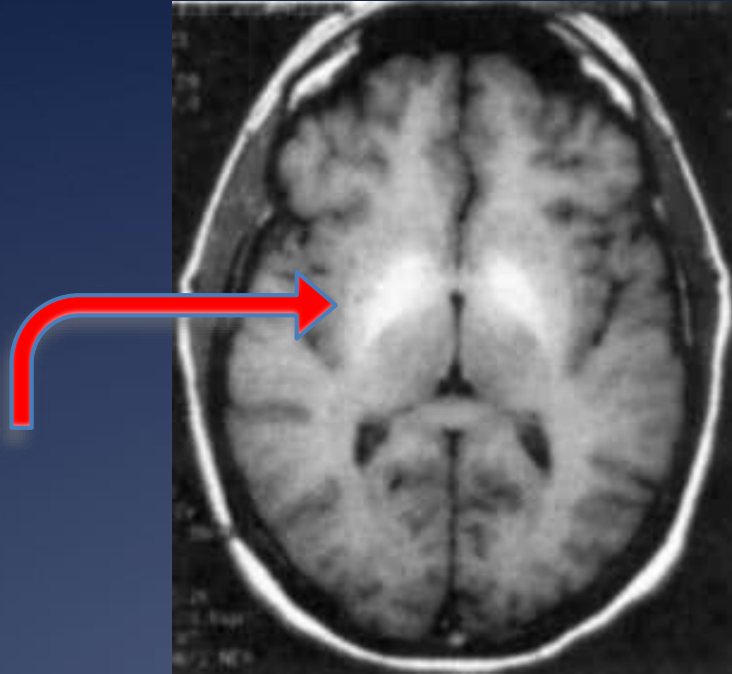
Contributes to Parkinsonian state

Probably reversible if identified early

Gradual reduction in manganese in PN

but trace element mixture most widely used in
Europe still contains 0.2mg

Symmetrical basal deposition of manganese on
T1 MRI scan in long-term PN



Manganese and digestive disorders

Excreted in bile

Rises in most cholestatic disease

Contributes to cholestasis of PN-associated liver disease or is consequence of this?

More care still needed

Recommend maximum of 0.001mg/kg ~0.07mg/d

Not easily possible



Canadian trace element overview

Registry of 135 patients on HPN

Average daily prescriptions (μmol) compared with “recommendations”

Zinc 131 ± 84

Manganese 8.2 ± 3.3

Selenium 1.0 ± 0.6

Chromium 0.2 ± 0.1

Copper 10 ± 5.6



Canadian trace element overview

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But

Canadian trace element overview

One centre measured the levels

Average daily prescriptions (μmol) compared with “recommendations”

Zinc	131 ± 84	XS	90% in NR
Manganese	8.2 ± 3.3	XS	95% XS
Selenium	1.0 ± 0.6	XS	38% Low
Chromium	0.2 ± 0.1	-	96% XS
Copper	10 ± 5.6	XS	23% XS





Vitamins

Multiple deficiencies common

Vitamin D and Vitamin K present special problems
but have their own literature

Rare for excess of any vitamin to pose a problem



Vitamin C – ascorbic acid

Strong antioxidant & cofactor for many enzymes

Hypothetical risks at very high iv doses but 7.5g/day seems safe

Increased demand in smokers

140mg vs 60mg/day

Increased demand in stress

200mg/d in any patient needing PN

up to 3000mg/d?

Vitamin C – ascorbic acid in PN

Light and oxygen sensitive

Oxygen should be excluded from PN bag

Multilayer bags reduce oxygen transfer

In conventional bags <20% remains at end of typical infusion

Multilayer bags and efforts to exclude light and oxygen improve this to >90% at 48 hours

Vitamin C deficiency – scurvy

Still seen in poorly managed PN practice

Sub-clinical deficiency associated with poor wound healing, increase in infections & multi-organ failure

Measurement in blood is unreliable

Most multivitamin preparations provide only 100mg – but it is available separately → action

Vitamin C deficiency – scurvy



From "Fundamentals of Clinical Nutrition" by R. L. Weinstier copyright 1993 by Mosby-Year Books Inc. N.Y.

Fig. 2-5 Periodontal disease seen in scurvy.

Vitamin C deficiency – scurvy



Thiamine

Major metabolic roles

Especially in handling of carbohydrates

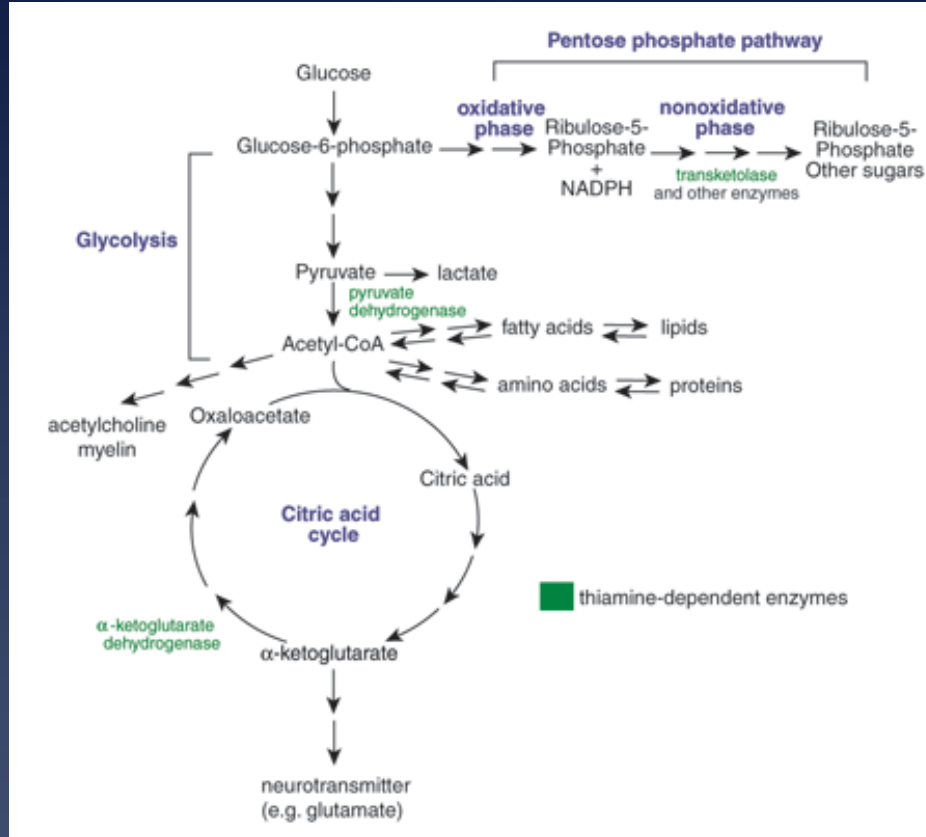
Malnourished patients often thiamine deficient

Glucose load of PN exacerbates problem by
increasing demand

Wernicke/Korsakoff syndrome



Thiamine / vitamin B1



Ophthalmoplegia



At rest

Ophthalmoplegia



At rest



Looking to right

R eye VI nerve palsy

Lactic acidosis

- * Japanese report of 5 cases of PN-associated lactic acidosis $\text{pH} < 7.13$
- * All had severe GI disease & minimal food intake
- * All had post-op PN with no vitamin supplements

Lactic acidosis

- * Japanese report of 5 cases of PN-associated lactic acidosis $\text{pH} < 7.13$
- * All had severe GI disease & minimal food intake
- * All had post-op PN with no vitamin supplements
- * Readily reversed with the right treatment

Lactic acidosis

1996-7 US-wide shortage of iv multivitamins

- * inevitable impact on patients on HPN
- * multiple case reports of lactic acidosis
- * all associated with deficiency of x

Morb Mortal Wk Rep 1997



Lactic acidosis

~~1996-7~~ US-wide shortage of iv multivitamins

- * inevitable impact on patients on HPN

- * ? more case reports of lactic acidosis

associated with deficiency of thiamine ?

Also Jan 2021 !!

Good practice in PN

- * Always consider micronutrients
- * Always give vitamins
 - * always be generous with thiamine & ascorbate
- * Give trace elements
 - * If known to be deficient
 - * If at high risk of being or becoming deficient
 - * If due for longer term PN (>1 week)
 - * but with care not to poison the patient

Therapeutic uses of micronutrients

- * Not just replacement
- * Many unverified reports with commercial bias
- * Pauling – orthomolecular medicine



Therapeutic uses of micronutrients

- * 18g/d vitamin C – nonsense
- * Vitamin D to treat osteoporosis in absence of deficiency ?
- * Possible benefit in infection (C,D,E,Se,Zn)
- * Various COVID trials in progress
- * Zinc useful in Wilson's disease – safer than penicillamine
- * Multiple agents in ICU unhelpful (eg ASPEN 2020)
- * Biotin no help in multiple sclerosis (Cree 2020)
- * C and E possibly even harmful in athletes (Higgins 2020)
- * Antioxidants do not prevent cardiovascular disease
- * Distinction from foods rich in antioxidants

Therapeutic uses of foods

- * Mediterranean diet
- * Rice water-based oral rehydration solution
- * Green bananas - lectin
- * Pineapple – bromelain
- * Mangos – polyphenols, anthocyanins
- * Most berries – anthocyanins
- * Broccoli – sulphoraphane

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- * Most berries – anthocyanins
- * Broccoli – sulphoraphane
- * And many more to come

