



Parenteral nutrition manual for adults in health care facilities

April 2009

FOREWORD

The DAA Nutrition Support Interest Group has developed this manual for dietitians and other health care professionals who need a practical resource for managing adult parenteral nutrition support in acute settings. The information in this manual cannot be extrapolated to infant or paediatric patients and is not intended to replace adequate nutrition support training or evidence-based practice guidelines. It should be used in consultation with an appropriately qualified Accredited Practising Dietitian.



This information has been independently reviewed by the Dietitians Association of Australia. For expert nutrition and dietary advice contact an Accredited Practising Dietitian (APD). Visit 'Find an Accredited Practising Dietitian' at www.daa.asn.au or call 1800 812 942.

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A subset of this group met face-to-face six-weekly over 14 months to develop the content of the manual, with various sections divided between small groups which were then incorporated into the whole document under the oversight of the full committee and selected reviewers including new-graduate dietitians. A modified Delphi approach was used to resolve any areas of controversy. After the whole manual was completed, it was examined in detail by reviewers from a variety of clinical backgrounds including medical, nursing and pharmacy as well as dietetics. The reviewers included representatives from all Australian states and territories, and New Zealand.

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TABLE OF CONTENTS

<u>Foreword</u>	2
<u>Introduction</u>	7
<u>What is parenteral nutrition support?</u>	7
<u>When is parenteral nutrition used?</u>	7
<u>When is parenteral nutrition not used?</u>	7
<u>Why is nutritional assessment necessary?</u>	8
<u>What is the role of a TPN team?</u>	8
<u>Planning for Nutrition support</u>	9
<u>Indications for parenteral nutrition</u>	9
<u>Contraindications to parenteral nutrition</u>	9
<u>Flowsheet for nutrition support planning</u>	10
<u>Parenteral nutrition formulations</u>	11
<u>Macronutrients</u>	11
<u>Protein</u>	13
<u>Carbohydrate</u>	13
<u>Fat</u>	14
<u>Comparison of lipid emulsions (typical approximate proportions)</u>	14
<u>Micronutrients</u>	16
<u>Recommended daily doses for vitamins and trace elements</u>	16
<u>Water-soluble vitamins</u>	16
<u>Lipid-soluble vitamins</u>	16
<u>Trace Elements</u>	16
<u>Contaminants in parenteral nutrition solutions</u>	16
<u>Issues concerning some individual micronutrients</u>	17
<u>Iron</u>	17
<u>Vitamin K</u>	17
<u>Choline</u>	17
<u>Carnitine</u>	17
<u>Situations in which individual requirements are altered</u>	18
<u>Increased gastrointestinal losses</u>	18
<u>Burns</u>	18
<u>Pregnancy</u>	18
<u>Renal failure</u>	18
<u>Liver disease</u>	19
<u>Refeeding Syndrome</u>	19
<u>Long-term parenteral nutrition</u>	19
<u>Micronutrient additive products</u>	19
<u>Prescribing micronutrients when requirements are altered</u>	20
<u>Micronutrient administration regimens</u>	20
<u>Advantages and disadvantages of adding micronutrients to the parenteral nutrition solution</u>	20
<u>Advantages and disadvantages of administering micronutrients as a separate infusion</u>	20
<u>Electrolytes</u>	21
<u>Considerations in choosing a parenteral nutrition formulation</u> ..	22
<u>Osmolality</u>	22
<u>Hang-time</u>	22
<u>Stability</u>	22
<u>Specialty parenteral formulations</u>	22
<u>Other alternatives</u>	23
<u>Additives to parenteral nutrition</u>	23
<u>Propofol</u>	23

<u>Intravenous access for parenteral nutrition</u>	24
<u>Blood vessels commonly used as parenteral nutrition access sites</u>	24
<u>Sites of delivery</u>	25
<u>Equipment</u>	27
<u>Intravenous access</u>	27
<u>Central venous access</u>	27
<u>Comparison of central venous access devices</u>	27
<u>Peripheral venous access</u>	30
<u>Situations that may be indications for peripheral parenteral nutrition</u>	30
<u>Confirming correct placement of venous access devices</u>	32
<u>Care of the venous access device⁶⁴</u>	32
<u>Intravenous giving set</u>	32
<u>Administration reservoir</u>	33
<u>Light-protective covering</u>	33
<u>Parenteral nutrition pumps</u>	33
<u>Regimens for parenteral nutrition</u>	34
<u>Choice of nutrition regimen</u>	34
<u>Continuous parenteral nutrition</u>	34
<u>Advantages:</u>	34
<u>Disadvantages:</u>	34
<u>Cyclic / intermittent nutrition</u>	34
<u>Advantages:</u>	34
<u>Disadvantages:</u>	35
<u>Starting parenteral nutrition</u>	35
<u>Parenteral nutrition infusion rate</u>	35
<u>Stopping parenteral nutrition</u>	35
<u>Flushing the line</u>	36
<u>Dual feeding</u>	36
<u>Monitoring of nutrition support</u>	37
<u>Anthropometry</u>	37
<u>Biochemistry / haematology</u>	38
<u>'EUC' and 'CMP' tests (Electrolytes /Urea /Creatinine and Ca²⁺/ Mg²⁺/ PO₄²⁻)</u>	38
<u>Liver tests</u>	40
<u>Iron studies</u>	41
<u>Lipid studies</u>	42
<u>Vitamins, minerals and trace elements</u>	43
<u>Indicators of protein status</u>	47
<u>Clinical assessment and monitoring</u>	49
<u>Nutritional assessment</u>	49
<u>Nutrition support management</u>	50
<u>Dietary intake</u>	51
<u>Adequacy of nutrition support</u>	51
<u>Issues in long-term parenteral nutrition</u>	52
<u>Complications of long-term parenteral nutrition</u>	52
<u>Home parenteral nutrition</u>	53
<u>Transitional feeding</u>	53
<u>Options for transitional feeding</u>	53
<u>Dual feeding</u>	54
<u>Cyclic parenteral nutrition</u>	54
<u>Monitoring during transitional nutrition</u>	54
<u>Oral/enteral intake</u>	54
<u>Fluid balance</u>	54

Discontinuing parenteral nutrition	54
Stopping the parenteral nutrition infusion	54
Removing the intravenous access device	55
Discharge/transfer of the parenterally-nourished patient	55
Trouble Shooting Guide	56
Line problems	56
Blocked intravenous line	56
Suspected line infection	57
Blood vessel problems	58
Phlebitis	58
Thrombosis	59
Line displacement	59
Formulation problems	60
Stability problems	60
Drugs related to parenteral nutrition	60
Intolerance	61
Allergic reaction to parenteral nutrition infusion	61
Nausea	62
Appetite problems	62
Constipation	63
Metabolic abnormalities	63
Refeeding syndrome	63
Overfeeding	64
Dehydration	67
Fluid overload	67
Abnormal biochemical parameters	68
Appendix 1: Glossary of Terms	73
References	76

INTRODUCTION

What is parenteral nutrition support?

Parenteral nutrition support refers to the infusion of an intravenous nutrition formula into the bloodstream. Total Parenteral Nutrition, or TPN, means that the infusion is providing a patient's complete nutritional requirements. Parenteral nutrition can be delivered either centrally, into the superior vena cava, or peripherally, that is into other veins, subject to additional limitations. Peripheral parenteral nutrition is less commonly used in Australian hospitals.

When is parenteral nutrition used?

Parenteral nutrition should be considered only when it is not possible to meet an individual's nutritional requirements by the enteral or oral route. In such cases it may be necessary to bypass the gut and deliver nutrients directly into the bloodstream. Gut failure, intestinal obstruction, or a complete inability to gain enteral access, are examples of situations in which parenteral nutrition is necessary to meet a patient's nutritional needs. Sometimes parenteral nutrition may also be needed to *supplement* an inadequate oral or enteral intake, where this falls far short of requirements. This may occur where there is malabsorption (such as in short bowel syndrome or inflammatory bowel diseases) or where nutritional needs are high (such as in burns).

Adequate nutrition support is important for the following reasons:

- * malnutrition has been found to affect around 40% of patients in major Australian hospitals.^{1,2}
- * patients with chronic or debilitating disease processes are often already malnourished on admission to hospital/health care facilities
- * without appropriate nutrition support, malnourished patients continue to deteriorate in their nutritional status during their hospitalisation, especially if repeatedly placed 'nil by mouth' for investigations and surgical interventions.
- * if not addressed, malnutrition may result in a prolonged and complicated recovery from illness or surgery, due to impaired wound healing and increased risk of infection. This, in turn, leads to a longer hospital stay with an associated increase in cost.^{1,2}

When is parenteral nutrition not used?

Parenteral nutrition should not be used if the patient's nutritional needs could be met via enteral or oral nutrition. Enteral and oral nutrition are more compatible with the body's normal processes, helping to maintain the functioning, structural integrity and immune benefits of the gut.^{3,4,5} Early enteral or oral nutrition is associated with better outcomes after surgery,^{6,7} even with major procedures involving the abdomen and/or gastrointestinal tract.^{8,9}

Enteral and oral nutrition are generally considered to be safer and more cost-effective than parenteral nutrition which is a complex therapy with the potential for serious adverse events.¹⁰ Increased infectious complications are associated with the use of parenteral nutrition, even in cases where clear nutritional benefits are obtained.¹¹ These complications occur independently of blood glucose control.¹² This means that, in most patients, the risks of parenteral nutrition outweigh the benefits if it will be used for only a short period (such as less than five days). In malnourished critically ill patients, however, starting parenteral

nutrition promptly (within 24 hours of ICU admission when it is clear that enteral nutrition is not possible) may perhaps be associated with a decrease in mortality.¹¹ Aggressive nutrition support is not always appropriate in the care of palliative or elderly patients, and careful consideration should be given to patient and family wishes concerning the appropriateness of initiating or continuing nutrition support in such cases. Potential benefits, including quality of life; and possible complications and expected outcomes should be considered.¹³

Why is nutritional assessment necessary?

When providing nutrition support to patients it is important to assess their nutritional status. A formal assessment based on anthropometry, biochemistry, clinical and diet history should be carried out by the dietitian. Nutritional assessment is beyond the scope of this document, but it is important to note that the method of estimating energy, protein and fluid requirements is the same as for enteral/oral nutrition. (While historically it was common to consider only 'non-protein calories' in meeting energy needs, there is no metabolic basis for this.) The nutrition assessment is used to determine priorities of nutritional management, to estimate the patient's nutritional requirements, and to provide a baseline measure for monitoring the effectiveness of intervention. Based on this assessment, a treatment goal can be set and a nutrition care plan developed. This care plan will change over time, particularly for patients on long-term parenteral nutrition (longer than three to six months).

What is the role of a TPN team?

Parenteral nutrition is a complex form of nutritional care that ideally involves medical, nursing and pharmacy staff as well as the dietitian. When these staff work as a team, it is more cost-effective and efficient, and may be associated with a reduction in infectious complications and more appropriate use of parenteral nutrition,¹⁴ perhaps because it facilitates better communication and training, and a more consensual approach to patient care.¹⁵ Possible definitions of members' roles in a TPN team include:

DIETITIAN performs nutritional assessment and monitoring of the patient, estimates requirements, chooses appropriate formulation/nutrition prescription and infusion rate in consultation with other team members

DOCTOR oversees/consults on medical management of the patient, may insert vascular access device, may be responsible for signing off all nutrition prescriptions

NURSE oversees care of the vascular access site, physical management of the parenteral nutrition infusion and related equipment, training for home parenteral nutrition. May be responsible for insertion of some vascular access devices and/or loading of additives

PHARMACIST oversees/consults on the choice of formulation and additives, may be involved with nutrition prescription and compounding of solutions and/or loading of additives

PLANNING FOR NUTRITION SUPPORT

The flowsheet opposite provides a guide to decision-making when parenteral nutrition is being considered.

Indications for parenteral nutrition

The main indication for parenteral nutrition is when the gut is not *functional* or *accessible*. Examples of inadequate gut function might include:

- bowel obstruction or suspected gut ischaemia
- some types/locations of gastrointestinal fistula
- short bowel syndrome
- persistent severe diarrhoea or significant malabsorption
- persistent signs of significant gut dysmotility (a distended and/or painful abdomen, persistent large gastric aspirates, no bowel output)

The gut is not accessible when oral intake is not possible, or an enteral feeding tube cannot be inserted, due to:

- facial injuries/surgery or malformation
- upper gastrointestinal tract obstruction or malformation
- risk of upper gastrointestinal tract bleeding (eg presence of oesophageal varices)

Contraindications to parenteral nutrition

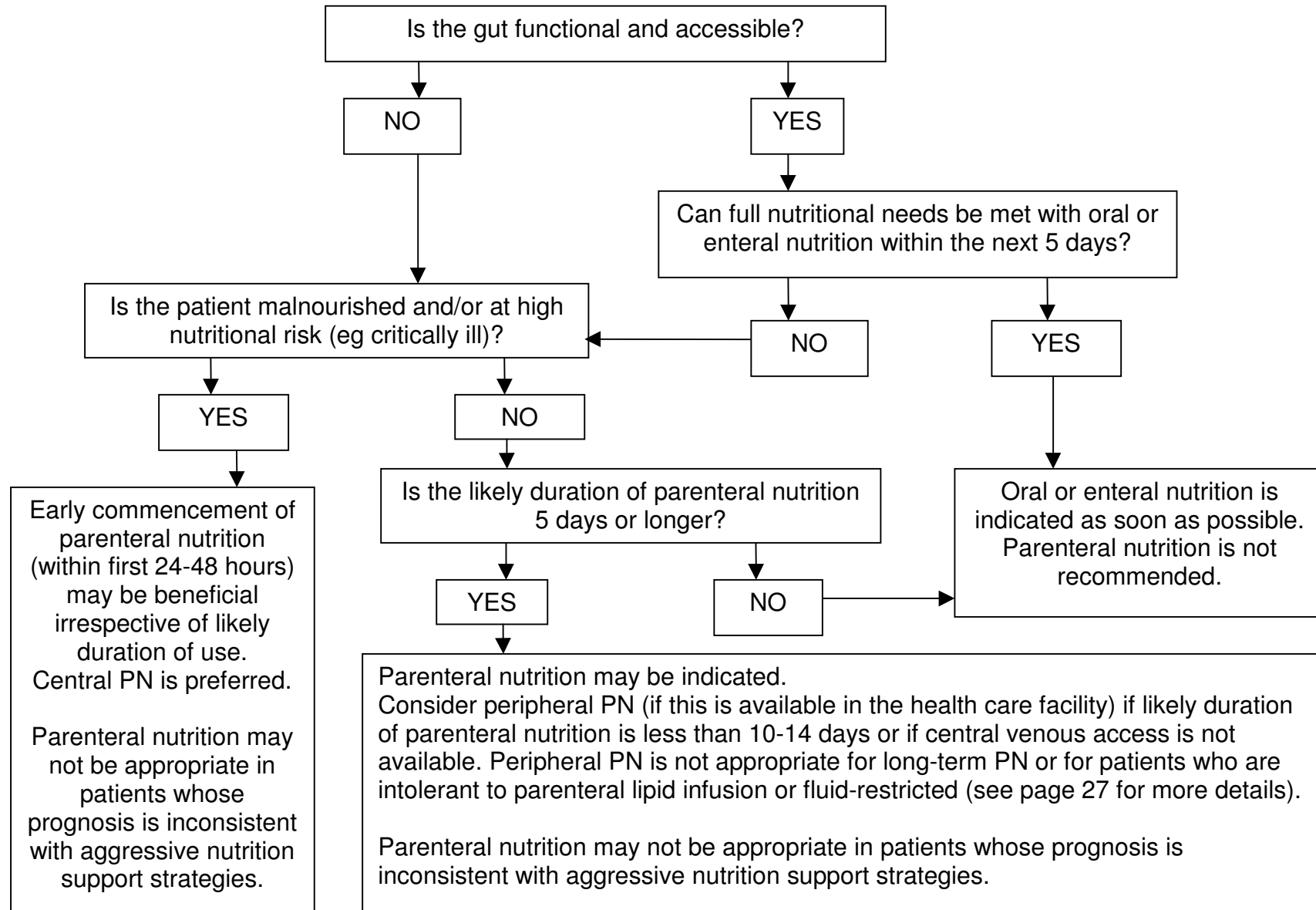
Parenteral nutrition is not usually indicated in normally-nourished patients if full nutritional needs could be met orally or enterally within the next five days (as gut function is expected to improve), or if the likely duration of the parenteral nutrition is less than five days (such as when the only parenteral access available is short-term, or the current line is due to be removed and replacement might be difficult). While it is often very difficult to predict, examples of such situations might include:

- a normally-nourished patient who is currently Nil By Mouth after surgery but will likely be allowed to eat, without expected problems, in the next few days (with a total fasting period of no more than five days)
- a normally-nourished patient who has postoperative gut dysmotility but this is not severe and is expected to resolve in the next few days
- a patient awaiting a surgical procedure in the next few days that will improve gut function and/or accessibility (eg obstruction will be resected, or jejunal tube will be placed for enteral feeding)

These considerations are somewhat different if the patient has poor nutritional status (eg is malnourished, or suspected of malnutrition) or is at high nutritional risk (eg in critical illness, burns, trauma, severe gastrointestinal disease or malignancy). In such cases, there may be significant benefits if parenteral nutrition is started promptly (within 24-48 hours of identifying that oral/enteral nutrition is not possible) even if the likely duration is less than five days or enteral/oral nutrition may be starting in the next few days.

Note that providing even a small amount of enteral or oral nutrition, wherever possible, may be beneficial for patients who are receiving parenteral nutrition, by stimulating normal intestinal functioning (including motility, secretions, gut barrier against bacteria and endotoxin, and immune function of the gut).^{3,4,5}

Flowsheet for nutrition support planning



PARENTERAL NUTRITION FORMULATIONS

Many different parenteral formulations are available, through several different companies. The dietitian selects an appropriate solution based on an individual nutrition assessment of the patient. Standard parenteral solutions are available in ready-to-hang bags, and typical macronutrient compositions for these are shown below; further information on individual products is available from the manufacturer. More expensive non-standard solutions are also available to meet the special needs of individual patients. These are either compounded individually in a hospital pharmacy or supplied to order by the manufacturer. The possibilities for these are limited only by the stability of individual solution components, but availability may be limited by the individual facility's pharmacy service, and by budgetary constraints.

Macronutrients

		Description	ENERGY kcal/mL	PROTEIN %energy	FAT %energy	CARBOHYDRATE %energy	OSMOLALITY mOsm/kg
STANDARD BAG Three-in-one solutions	Higher-glucose solutions	Shelf-life up to two years at room temperature (when there are separate compartments, not yet combined) or one month refrigerated (if all-in-one format) May be available in 1.0, 1.5, 2.0, 2.5 litre bags	0.6-1.2	10-15%	30-35%	45-55%	750 – 1500 depending on electrolyte content
	Lower-glucose solutions				35-45%	35-45%	
STANDARD BAG Two-in-one solutions		Shelf-life one to six months, refrigerated May be available in 1.0, 1.5, 2.0 litre bags.	0.6-1.2	15-25%	0% (fat given separately)	75-85%	1000-2000 depending on electrolyte content
MODULAR PRODUCTS	Amino acids	Available as 500mL of solution with 8-20 g nitrogen per litre, ie 50-125g protein per litre (see below), with or without glucose and/or electrolytes already included. Amino acid profiles may differ.					
	Glucose	Available as 100mL, 500mL, 1000mL of 5%, 10%, 25%, 50%, 70% dextrose solutions (see below)					
	Lipids	Available as 100mL or 500mL of 10%, 20% and 30% emulsions of soybean, soy+olive, fish, multi-oil (see below)					

All of the macronutrients vary considerably, in type and amount, between different parenteral nutrition formulations.

Protein

Protein in parenteral nutrition is delivered in the form of free amino acids. The concentration of amino acids in a parenteral solution is often expressed in terms of the nitrogen content. For example, a solution that is called something like 'Protein 24' will contain 24 g/L nitrogen. The ratio of nitrogen to total molecular weight varies between amino acids, but an average calculation is [nitrogen x 6.25 = total weight of protein]. This means that our 'Protein 24' solution will contain about 24 x 6.25 = about 150g amino acids per litre. (This is only an average – actual amount will vary depending on the amino acid profile of the solution. Check product labelling, which usually gives the total amino acid content as well as the nitrogen.)

Standard parenteral nutrition solutions are relatively low in protein as this has stability advantages. In general, most patients will receive protein at around 1.0 – 1.2 g/kg body weight if their energy needs are fully met with a standard parenteral nutrition solution. This may not be adequate for some patients with increased protein requirements. Note, however, that high protein intake cannot prevent catabolism in the critically ill or septic patient,¹⁶ and increasing protein does not cause albumin levels to improve during the acute phase response (see *Monitoring* section for more detail). Other than in some particular patients (such as those with burns or increased losses), there is no benefit to providing protein in amounts greater than about 1.5 – 2.0 g/kg body weight.^{17,18,19} Manufacturer information generally recommends limiting the infusion rate of an amino acid solution to less than 0.1g/hour/kg body weight.

Some solutions are available with specific amino acid profiles, although strong evidence to support such products is lacking. For example, solutions with extra glutamine are available. Glutamine, as the main fuel for gut enterocytes and immune cells, is thought to help reduce catabolism if provided in larger amounts during illnesses that increase the turnover of these cells (such as critical illness, trauma and gastrointestinal disease). Supplemental glutamine has therefore been recommended for these patient groups^{20,21} but evidence of the likely benefits may not yet be adequate to justify the additional expense.²²

Carbohydrate

Glucose (D-glucose, also called dextrose) provides the carbohydrate content of parenteral nutrition, up to 75% of the total energy of the solution. Glucose is the body's main source of energy, and a daily minimum of about 2g/kg body weight is required to meet the needs of those cells (eg brain, kidney, erythrocytes) that cannot readily use other fuels. There is also a maximum rate of glucose oxidation and utilization, about 4-7 mg/minute/kg body weight (5-10 g/kg per day),²³ and exceeding this can increase the risk of complications such as hyperglycaemia, fatty liver, and respiratory problems²⁴ although many patients will tolerate higher glucose infusion rates during cyclic parenteral nutrition. The rate of clearance from the blood does not indicate the rate of oxidation, so normal blood glucose levels do not guarantee that the glucose infusion rate is appropriate.²³ See *Troubleshooting* section on *Overfeeding* for more details.

In parenteral nutrition formulations, the glucose/dextrose component is a water solution, usually expressed as a percentage (weight per volume of total solution). For example, a 5% dextrose solution contains 5g dextrose per 100mL solution, so 1 litre of 5% dextrose provides 50g carbohydrate.

Fat

Lipid emulsion is a soluble form of fat that allows it to be infused safely into the blood. Providing some energy as fat enables the patient's energy needs to be met without exceeding the recommended amounts of glucose. Lipid emulsion also provides essential fatty acids (EFA). Lipid emulsion has a low osmolality,¹⁰ so adding it to a parenteral nutrition formulation will lower the osmolality of the resulting solution; this is important when the solution is to be given peripherally, which requires a limited osmolality of <900mOsm/kg. Peripheral formulations are therefore high in fat.

Parenteral lipid consists of oil stabilised in an emulsion with egg yolk lecithin. The first successful parenteral lipid emulsion was based on soybean oil and this is still the most widely-available type worldwide. Alternative lipid emulsions are now available, including olive-soybean oil mixture (in a ratio 80:20); and less commonly-used types such as fish oil emulsion and other multi-lipids (eg a mixture of soy, MCT, olive, and fish oil in a ratio 30:30:30:10). A wider variety of emulsions have also been used experimentally, such as structured lipids (triglycerides with different fatty acids attached). Strong evidence for the optimal lipid emulsion is lacking at present, and it remains highly controversial whether the risk of lipid-related complications differs significantly between products when they are given in a continuous 24-hour infusion at a rate lower than the recommended limits. Some of the differences between them might include: sterol content (may be associated with liver dysfunction) and omega-6 long-chain polyunsaturated fatty acid content (may be associated with immune dysfunction). A reduced omega-6 fatty long-chain fatty acid content is a common reason why alternative lipid emulsions are used in practice.

Comparison of lipid emulsions (typical approximate proportions)

	omega-3 poly	omega-6 poly	omega-9 mono	saturated	MCT
soybean oil emulsion	5%	60%	20%	15%	
olive-soybean oil mixture	3%	20%	60%	17%	
fish oil emulsion	60%	10%	10%	20%	
soy/MCT/olive/fish multi-oil emulsion	10%	20%	30%	10%	30%

There appears to be no clinical benefit to giving fat in amounts greater than about 30% of total energy,^{25,26} and smaller amounts than this have been recommended for some groups such as the critically ill;²¹ however fat (unlike glucose) does not appear to have a clear, measurable limit to its utilisation. It is thought that excessive parenteral lipid infusion rates are associated with impaired immune function, liver dysfunction, coagulopathy, abnormal lung function, increased vascular resistance, and blood lipid abnormalities, and as a result a general recommendation has been made to keep lipid infusion rates to less than 0.03-0.05g/hour/kg body weight, or around 1g/kg per day.²⁷ Such recommendations for limiting fat are based on studies of soybean oil emulsions, observing the levels at which reported complications have occurred (above 0.11g/hour/kg body weight or 2-3g/kg per day);²⁷ this does not mean that every patient will experience complications above the recommended level, or with other types of oil. In particular, rates faster than this may sometimes be used in cyclic parenteral nutrition. Note that the rate of clearance from the blood does not indicate the rate of oxidation, so normal serum triglyceride levels do not guarantee that the lipid

infusion rate is appropriate.²⁸ Utilisation appears to be better if the lipid is given continuously (over 24 hours) rather than intermittently (over a few hours, several times per week) as is typical in some facilities.^{29,30}

The lipid content of the emulsion is usually expressed as a percentage (weight per volume) and available as 10%, 20% or 30% emulsions. For example, a 10% lipid emulsion contains 10g fat per 100mL solution, so a litre contains 100g fat. The solution also contains glycerol and lecithin, so the energy content is slightly higher than would be calculated from the fat alone, providing 2 Cal/mL for 20% emulsion and 1.1 Cal/mL for 10% emulsion. The ratio of lipid to phospholipid (from the lecithin) differs for the different emulsions, with the 20% emulsion having a ratio closest to the ratio found in chylomicrons. It has been suggested that the risk of lipid abnormalities is therefore lowest when 20% emulsion is used,^{31,32} however the risk appears to be low with a continuous infusion below the recommended limits irrespective of which emulsion is used.

Micronutrients

Parenteral nutrition solutions generally contain macronutrients and electrolytes but not micronutrients. TPN stands for 'Total Parenteral Nutrition', but is not 'total' unless it provides complete nutrition, so micronutrients (vitamins, minerals and trace elements) must be added.

It is highly likely that most patients commencing on parenteral nutrition will have had prior poor nutrition intake and hence have suboptimal stores of micronutrients in addition to high demands and losses. Micronutrients should be a standard inclusion in parenteral nutrition from the first day, as any delay risks depleting a compromised patient's micronutrient reserves and impairing the patient's ability to utilise the nutrition fully (as micronutrients are cofactors for utilisation). Patients on long-term parenteral nutrition (longer than three to six months) need close monitoring of micronutrient status as body stores may become depleted, even with supplementation, due to ongoing increased demands.

Recommended daily doses for vitamins and trace elements

The Australasian Society for Parenteral & Enteral Nutrition has published Guidelines for intravenous trace elements and vitamins.³³ These are now under review but currently recommend the following daily amounts

Water-soluble vitamins

Thiamine	3 mg
Riboflavin	3.6 mg
Niacin	40 mg
Pantothenic acid	7.5 mg
Pyridoxine	4 mg
Vitamin B12	5 µg
Folic Acid	400 µg
Vitamin C	100 mg
Biotin	60 µg

Lipid-soluble vitamins

Vitamin A	1000 µg
Vitamin D	5 µg
Vitamin E	10 mg
Vitamin K	no recommendation made

Trace Elements

Chromium	0.2-0.4 µmol	(10-20 µg)	Molybdenum	0.4 umol	(38 µg)
Copper	5-20 µmol	(0.3-1.2 mg)	Selenium	0.4-1.5 µmol	(31.6-118 µg)
Iodide	1.0 µmol	(0.13 mg)	Zinc	50-100 µmol	(3.3-6.6 mg)
Iron	20 µmol	(1 mg)	Fluoride	no recommendation made	
Manganese	5 µmol	(275 µg)			

Contaminants in parenteral nutrition solutions

Many components of the parenteral nutrition formulation have been shown to be contaminated with micronutrients (such as manganese). It should therefore not be assumed that parenteral nutrition formulations are completely free of all micronutrients. However, the level of contamination is not controlled and may be very variable between batches, and therefore contamination cannot be relied upon to provide necessary requirements. Conversely, contamination can be a cause of micronutrient toxicity (for example, aluminium).

Issues concerning some individual micronutrients

Iron

There has been some controversy regarding routine supplementation of iron. It is thought that the diversion of plasma iron to the storage form in the acute phase response is a protective mechanism, withholding iron from bacteria to reduce infection risk.³⁴ IV iron (particularly the iron dextran form) has been associated with serious side-effects including cramping, hypotension, malaise and even anaphylaxis, and an initial test dose (5-20% of the full dose) is recommended before use.³⁵ ASPEN recommends that parenteral supplementation of iron should be limited to conditions of iron deficiency.¹⁰ However, evidence of side-effects when iron is administered in low concentrations (ie, a basal supply) is lacking, hence others recommend routine supplementation³⁶ and iron is included in the AuSPEN guidelines above. Practice differs in Australian hospitals – some hospitals withhold iron supplementation in acutely unwell patients – but it is common practice to supplement iron in patients who require long-term parenteral nutrition.

Vitamin K

Vitamin K occurs naturally in soybean oil, which is present in most currently-available lipid emulsions.³⁷ However, the exact vitamin K content of lipid emulsions can be variable and unreliable, so it cannot be assumed that vitamin K supplementation is therefore unnecessary. Recommendations vary widely: ASPEN recommends 1mg vitamin K daily,³⁸ whereas the American Food and Drug Administration has recommended 150ug vitamin K per day.³⁹ Some hospitals prescribe vitamin K only as needed to maintain coagulation status; others may give a regular dose of 1-10 mg parenteral vitamin K, once or more per week in all patients unless they are on anti-coagulant therapy when it may be omitted. Vitamin K is not added to three-in-one emulsions due to stability concerns.

Choline

The 2007 Nutrient Reference Values for Australia and New Zealand now include recommendations for choline (recommendations were not previously made).⁴⁰ These recommendations are for healthy people who are enterally-fed, and there are no specific recommendations for parenteral nutrition. However, choline deficiency has been reported as a significant contributor to the development of TPN-associated liver disease (steatosis) in long-term patients⁴¹ and the data suggest that choline is a required nutrient for long-term home TPN patients. However, choline is not included in currently available parenteral vitamin mixtures and IV choline is not available for use outside of the research setting. A trial of orally-administered lecithin (which is 13% choline by weight, available in oral soybean suspension) may be beneficial, however gastrointestinal tolerance and absorption of this supplement may be a limiting factor.⁴²

Carnitine

Carnitine can be synthesized endogenously, however it has been suggested that in the absence of dietary (oral or enteral) carnitine intake this synthesis may be inadequate.^{43,44} Carnitine deficiency has been reported rarely in adults, but more commonly in premature infants, who have limited stores and smaller synthesis. Recommendations for intravenous carnitine supplementation in long-term parenteral nutrition have varied from 2-5mg/kg/day to 15mg/kg/day or a daily dose of 40mg^{43,45} but it remains an uncommon practice in adult patients. However, it is worthwhile testing carnitine levels in cases of otherwise unexplained hypertriglyceridaemia.

Situations in which individual requirements are altered

Individual micronutrient requirements may vary from the above recommendations. Extra care needs to be taken in situations of increased losses (eg GI losses, dialysis) and reduced excretion (eg liver disease, renal disease) which will impact on requirements, increasing risk of deficiency and toxicity respectively. Patients receiving parenteral nutrition are at greater risk of toxicity than those enterally fed. As parenteral nutrition infusions bypass the gastrointestinal tract it removes the body's ability to self-regulate levels of some micronutrients. For example, gastrointestinal absorption of iron is usually reduced when body stores are adequate. Hence close monitoring to assess for potential toxicity is essential (see *Monitoring* section).

Increased gastrointestinal losses

Patients with persistent/ongoing increased gastrointestinal losses (diarrhoea, fistulae or stomas) will have increased requirements for many of the minerals, in particular zinc, copper and selenium. Pancreatic and intestinal fluids are major routes for zinc excretion.⁴⁶ Hence, increased supplementation may be required in chronic intestinal disease (eg Crohn's disease), diarrhoea or increased losses from an intestinal fistula or stoma.⁴⁷ Wolman and co-workers estimated zinc losses of 12mg per kg of small bowel output and 17mg per kg of diarrhoea or ileostomy output,⁴⁸ so an extra 5-15mg/day has been recommended for patients with such losses.⁴⁶ Copper and manganese are primarily excreted in bile, hence patients with excessive bile losses (eg biliary drains, high-output stomas) may be at risk of deficiency and so levels should be closely monitored. Excessive zinc intake can cause a competitive interaction with copper that may result in copper deficiency.⁴⁹ Selenium levels can also be diminished in gastrointestinal disease and with increased losses.

Burns

Zinc, copper and selenium (trace elements important in wound healing, immunity and antioxidant defence) are lost in burn exudate, hence, requirements are increased. There is evidence that provision of increased amounts of zinc, copper and selenium may improve outcome of severe burns.^{50,51} Other vitamins and minerals may also be needed in increased amounts⁵² but there are no set recommended doses for parenteral micronutrients in burns.

Pregnancy

There are no set recommended doses for parenteral micronutrients in pregnancy or lactation. These therefore need to be extrapolated from the enteral Nutrient Reference Values for pregnant or lactating women, with consideration given to impact of intravenous infusion (bypassing digestion and absorption).⁵³ Whilst vitamin A toxicity can cause foetal defects, this does not mean that vitamin A should be completely excluded from supplementation during pregnancy, care should be taken in ensuring appropriate supplementation.

A case has been reported of an infant suffering an in-utero subdural haematoma attributed to vitamin K deficiency, despite the mother's vitamin K status being almost normal (no parenteral vitamin K had been given). It was concluded that it is wise to be generous regarding vitamin K provision in pregnancy to take account of the additional needs of the foetus.⁵⁴

Renal failure

Caution is required in patients with impaired renal function when the excretion of some trace elements normally excreted in the urine (zinc, selenium, fluoride, chromium and molybdenum) may be significantly decreased. Hence, close monitoring of these levels is prudent. Evidence is lacking for the practice of restricting chromium intake in renal failure.⁴⁶ Caution should also be

given to vitamin A supplementation as toxicity is often noted in end stage renal failure. Intermittent haemodialysis causes increased losses of water soluble vitamins⁵⁵ and some minerals⁵⁶ therefore increased supplementation is required. However, as patients with renal failure have decreased excretion of vitamin A, it may not be appropriate to achieve this by simply increasing the dose of a standard parenteral multivitamin.⁵⁵ Intradialytic parenteral nutrition (when the solution is infused during haemodialysis, see *Sites of Delivery*, below) normally uses a standard solution but it is important to check the electrolyte content (particularly potassium) to ensure that it does not exceed the patient's usual restrictions. A solution with a high energy-density is preferred for this purpose, to maximise nutrition input during the short period of infusion (only 3-5 hours).

Liver disease

Patients with alcoholic liver disease are particularly likely to be depleted in folate, vitamin C, thiamine and other B group vitamins. It is essential that supplementary thiamine is provided prior to TPN commencement to prevent Wernicke-Korsakoff syndrome.⁵⁷ Copper and manganese are primarily excreted via bile so caution is required to prevent toxicity in patients with compromised biliary drainage (eg biliary obstruction, cholestasis).⁵⁸ Blood levels of these minerals and liver function should be monitored regularly in such patients and these nutrients should be omitted from the solution if levels are elevated.⁵⁹ Some facilities monitor bilirubin and stop manganese supplementation if bilirubin is elevated⁶⁰ (eg conjugated bilirubin is greater than 3 µmol/L or if total bilirubin is greater than 12 µmol/L). However, hypermanganesaemia may also occur in the absence of cholestasis, suggesting that requirements may be less than previously thought, or that contamination may be contributing extra manganese. It may be more advisable to monitor serum levels of manganese and/or copper and reduce or stop supplementation if they become elevated (see *Monitoring* section).

Refeeding Syndrome

As with oral and enteral nutrition, patients with malnutrition, malabsorption, wasting syndromes such as cancer, prolonged fasting, or chronic alcoholism will require additional supplementation of thiamine, electrolytes and zinc on commencement of parenteral nutrition to reduce the risk of developing refeeding syndrome. Close monitoring, slow refeeding and intravenous (rather than enteral) supplementation is essential. See *Refeeding Syndrome* in the *Troubleshooting* section for more details.

Long-term parenteral nutrition

The body has significant stores of trace elements and fat-soluble vitamins, but patients who are wholly dependent upon parenteral nutrition may experience gradual depletion of these stores over time if their parenteral nutrition regimen does not meet their full needs. Patients on long-term sole parenteral nutrition are therefore at greatest risk of micronutrient deficiencies. See *Issues in long-term parenteral nutrition* section for further details.

Micronutrient additive products

There are pre-mixed products available containing various combinations of vitamins and minerals. By nature, these multiple micronutrient formulations come in a fixed dose, meaning it is not possible to alter the ratio of micronutrients. This poses a problem if the requirements for one micronutrient are lower than the others. In this instance it may be necessary to cease use of the multiple formulation and supplement each micronutrient individually (for example omitting manganese and copper in cholestasis). Likewise, caution needs to be taken if increasing the dose of a multiple formulation to avoid toxicity of some nutrients.

Not all vitamins and trace elements are available individually, and in some cases it may be easier to provide micronutrients via the enteral route. This option will be limited if enteral absorption is affected by the disease process, but can otherwise be very effective. Common examples include iron (where the patient has an intact duodenum and/or proximal jejunum) and vitamin D (where the patient has an intact distal ileum).

Prescribing micronutrients when requirements are altered

If micronutrient depletion is suspected (for example, if serum levels are low), it is usually appropriate to provide specific supplementation (usually 150-300% of 'normal' maintenance quantities); similarly, elevated serum levels may require a reduction in the dose (by 25-75%, depending on the degree of elevation).⁶¹ In either case, the serum level should be checked again in 7-14 days.

Micronutrient administration regimens

Trace elements and vitamins can be administered in two ways:

- * added to the parenteral nutrition solution (either in pharmacy or on the ward)
- * delivered as an infusion (or, in some cases, injection) separately from the parenteral nutrition solution

Advantages and disadvantages of adding micronutrients to the parenteral nutrition solution

If micronutrients are to be added to the parenteral nutrition solution, ideally this should be done under special sterile conditions ('laminar flow') by a pharmacy service. This method minimises compounding errors, solution instability, and possible contamination.⁶¹ However, such a service is expensive and is not available in all facilities. If micronutrients are added to the solution at ward level (not recommended due to the higher risk of error and contamination), aseptic technique should be used.

Advantages:

- Nutrients run over the same time-period as the parenteral nutrition infusion (eg 24 hours) are likely to be utilised better as nutritional co-factors
- Uses only one lumen of the venous access device
- Least risk of errors and contaminants (if added in pharmacy)
- Convenient and less error-prone if micronutrients can be ordered together with the parenteral nutrition

Disadvantages:

- Requires the parenteral nutrition solution to be prepared in advance of use: may mean a delay in obtaining the solution, or limited availability outside normal hours
- Increased contamination/infection risk from the additional manipulation of the bag (especially if added at ward level)
- Increased risk of solution instability and nutrient interactions
- Full daily micronutrient dose is not received if the patient does not use the whole bag (such as when commencing parenteral nutrition at a reduced rate, or with patients whose requirements are small). This could be addressed by increasing the dose of additives but this raises issues of stability and cost.

Advantages and disadvantages of administering micronutrients as a separate infusion

If micronutrients are to be administered as a separate infusion, it is recommended that they be infused slowly over as long a period as possible. For example, all the micronutrient additives can be given over 10-12 hours in 100mL saline⁶² or see manufacturer's recommendations for

administration of individual micronutrients. Rapid injection or bolus is an acceptable method for administering some micronutrients (such as water-soluble vitamins), however cellular absorption and utilisation of trace elements is quickly saturated and significant amounts of the dose may be lost in the urine if infusion is too rapid.⁶²

Advantages:

- Reduced dependence on pharmacy service; increased flexibility in ordering/commencing parenteral nutrition
- Patient receives full daily micronutrient dose independently of parenteral nutrition infusion rate
- Better accountability and data management, as the micronutrients are signed for and checked individually as medications

Disadvantages:

- May require additional lumen of the venous access device, increases infection risk due to the additional manipulations of the line
- Increased nursing labour
- Reduced utilisation/increased excretion if given over short time-period
- Risk of being omitted altogether if prescribing system is different for medications vs nutrition

Electrolytes

Standard parenteral nutrition solutions usually contain electrolytes. Normal electrolyte requirements have been estimated for maintenance nutritional support (assuming normal organ function without abnormal losses).^{10,63} Recommended amounts per day:

Sodium	40-100 mmol or 1-2 mmol/kg
Potassium	60-150 mmol or 1-2 mmol/kg
Calcium	2.5-5 mmol
Magnesium	4-12 mmol
Phosphorus	10-30 mmol
Chloride	As needed to maintain acid-base balance with acetate

As with trace elements and vitamins, close monitoring of inputs and losses must be made to prevent electrolyte deficiencies and overloads. Potassium, phosphate and magnesium excretion are reduced in renal disease, hence restrictions may be required. Reduced-electrolyte parenteral nutrition formulations exist but may not be readily available in all facilities. Requirements for electrolytes may also be increased, if the patient has increased losses, intracellular shifts or increased demand. In such cases, electrolyte supplementation may be managed by additions to the parenteral nutrition solution or via separate infusions (discuss with medical officer, TPN nurse and/or pharmacist). Addition of phosphate, magnesium and calcium to the parenteral admixture is limited due to stability issues. Large increases in requirements must therefore be managed via separate infusions. Note that different forms of electrolyte supplementation will have different effects on acid-base balance (for example potassium chloride versus potassium acetate).⁶³

CONSIDERATIONS IN CHOOSING A PARENTERAL NUTRITION FORMULATION

Osmolality

Delivering parenteral nutrition centrally (into the vena cava) allows extremely high osmolality solutions to be used, as the fast bloodflow (~2-5 litres/minute, through the 2cm wide bloodvessel) instantly dilutes the solution thousandfold. A solution that is to be delivered peripherally should have an osmolality below 900mOsm/kg to avoid irritation to the blood vessels. In the case of intradialytic parenteral nutrition (see *Sites of Delivery*, below), the osmolality is not restricted in this way as the solution is infused along with the blood, which dilutes it. Lipid has a much lower osmolality than amino acids, glucose or electrolytes,¹⁰ so peripheral solutions are high in fat.

Hang-time

Official (American CDC)⁶⁴ and manufacturer guidelines are available for the safe hang-time of parenteral nutrition products. Several different factors affect the shelf-life and hang-time of parenteral nutrition solutions. Firstly, interaction between the macronutrients and/or micronutrients reduces the availability of the nutrients and the stability of the solution. Shelf-life is prolonged by keeping macronutrients separate (as in a multi-chamber bag) and/or by loading micronutrients into the solution as close as possible to the time of starting the infusion. Secondly, different solutions may vary markedly in how readily they support bacterial growth.⁶⁵ For example, lipid solutions have a lower osmolality and acidity than amino acids or glucose solutions, and therefore form a better growth medium for bacteria. Consequently the hang-time for lipid on its own is shorter (usually 12 hours) than for three-in-one or two-in-one solutions (24 hours).⁶⁴

Stability

Loss of stability (eg where the lipid ceases to be fully emulsified or where compounds precipitate out of solution) can make the parenteral nutrition formula unsafe for infusion. Several factors can have an impact on the stability of a parenteral nutrition solution. Multi-chamber bags usually have a long shelf-life at room temperature because their reactive components are kept separate; individually-compounded bags, and those with the micronutrients already added, usually need to be kept refrigerated and have only a short shelf-life. In general, stability is maximised by storing the solution correctly (check manufacturer recommendations for temperature, light protection and shelf-life) and by avoiding adding anything to the solution (consult pharmacist and check manufacturer's stability information on maximum levels of additives).

Specialty parenteral formulations

Specialty formulae are available in addition to the ones listed above. These may be more expensive than standard parenteral formulations, especially if they are made to order, but allow an individual patient's specific requirements to be met. Standard solutions are appropriate for the majority of patients, but they are relatively low in protein and contain a standard amount of electrolytes. Therefore, particular groups who might benefit from an individualised formulation include: patients with increased protein or electrolyte requirements (such as with burns, critical illness, trauma, post major surgery or where there are increased losses such as with fistula or intestinal failure); patients requiring restricted fluid or electrolytes (such as renal patients); and home parenteral nutrition patients who will benefit from having their full daily fluid and nutrient requirements provided by one bag of the correct volume.

Other alternatives

Instead of using expensive individualised formulations, it may be possible to increase protein or electrolyte input separately from the parenteral nutrition. For example, additional electrolytes can be given as separate infusions. Additional protein can be given in the form of protein modular solution, using another lumen of the central line or (less desirably, because of infection risk) by piggybacking it onto the same lumen as the parenteral nutrition infusion. Note that these methods do provide additional fluid, which needs to be taken into consideration.

Additives to parenteral nutrition

Each solution has an upper limit for nutritional additives, such as electrolytes or micronutrients, and these additives should be discussed with a pharmacist to ensure that the resulting solution will be stable. In general, because parenteral nutrition solutions are so complex (containing a large number of different substances, many of which are reactive), it is not recommended to mix any medications with parenteral nutrition or infuse them through the same lumen.¹⁰ The most common exceptions to this rule are ranitidine (for gastric acid suppression) and insulin, both of which are added to parenteral nutrition solutions in some facilities. Adding insulin to parenteral nutrition can be a convenient way to provide a continuous insulin infusion to provide baseline requirements, with the advantage that it is automatically stopped when the parenteral nutrition is stopped. Note this is not suitable if the patient's insulin requirements are likely to change, and it is essential to monitor closely (as for an insulin infusion). Also note that some of the insulin will be lost via adsorption to the bag surface, so the patient will require a dose that is slightly different from that in a separate infusion or injection. If insulin is added to the parenteral nutrition bag, frequent blood glucose monitoring is essential for the entire time that the parenteral nutrition is infusing.

Propofol

Propofol is a short-acting sedative delivered in a 10% lipid solution, ie providing 1.1 Cal/mL. Sometimes patients are receiving a continuous infusion of propofol for several days and this adds to the amount of intravenous lipid that the patient is receiving. The fat and energy contribution of this infusion need to be taken into account in planning the patient's nutrition support regimen to avoid overfeeding, as it can be a significant proportion of the patient's needs (eg a rate of 15mL/h for 24 hours provides 1655kJ (almost 400Cal) as fat). See *Drug-Nutrient Interactions* in the *Troubleshooting* section for more details on Propofol.

INTRAVENOUS ACCESS FOR PARENTERAL NUTRITION

Intravenous lines for parenteral nutrition may be inserted into a number of different veins (see Figure 1) although the *tip* (inner end) of the line will usually be located in the vena cava or the axillary or subclavian veins. From there, the solution is carried in the blood to the heart for immediate circulation around the body. The choice of parenteral nutrition route depends on several factors, such as the intended duration of nutrition support, the patient's condition, the osmolality of available solutions, and any limitations to access (such as trauma or obstructions).¹⁰

Central venous access means the fluids are delivered to the superior vena cava or right atrium, or less commonly the inferior vena cava (from a femorally-inserted line). The line will usually enter the body at another location (so a central line might not look 'central'). The central position of the line tip is always confirmed by chest x-ray (unless the line was placed under fluoroscopy/x-ray in the first place). In *peripheral venous access*, the tip of the line is usually in the axillary or subclavian veins. Intradialytic parenteral nutrition is another form of peripheral access (see *Sites of Delivery*, below).

Blood vessels commonly used as parenteral nutrition access sites

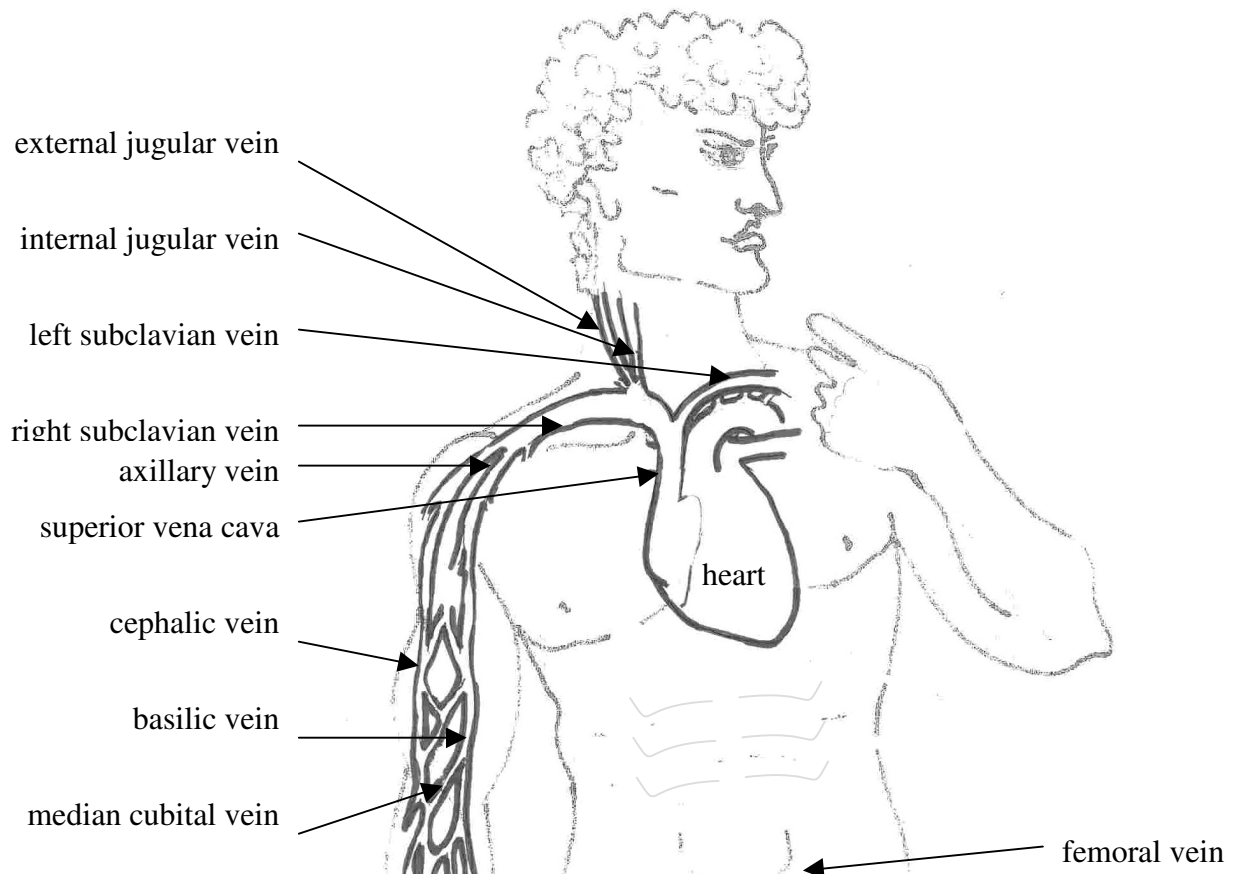


Figure 1: Blood vessels commonly used as sites of insertion for parenteral nutrition access. See below for details of the different types of lines used.

SITES OF DELIVERY

Parenteral nutrition can be delivered, via a variety of different access devices, either centrally or peripherally. There are advantages and disadvantages to each.

SITE	ACCESS	INDICATIONS	ADVANTAGES	DISADVANTAGES
Central (superior vena cava, right atrium, or inferior vena cava)	<ul style="list-style-type: none"> percutaneous central catheter Hickman line Broviac line Groshong line PICC line portacath (see below for more detail on types of access) 	<ul style="list-style-type: none"> longer-term use short-term use when peripheral solution cannot meet full nutritional needs or if peripheral route not available 	<ul style="list-style-type: none"> no limit to osmolality, pH or volume of infusion device can have multiple lumens allow simultaneous delivery of different incompatible infusions (drugs, nutrition etc) 	<ul style="list-style-type: none"> complex insertion, requiring specialised facilities, equipment and training higher cost of lines more complex site care requirements greater risk of infection possible complications include: bloodstream infection; thrombosis; perforation to major blood vessels,⁶⁶ heart or gut; deep chest wound if line is misplaced ('extravasation')
Peripheral (any other vein)	<ul style="list-style-type: none"> peripheral cannula midline catheter midclavicular catheter 	short-term use (<10-14 days)	<ul style="list-style-type: none"> insertion is safer and easier than for central access, less training required lower risk of infection than central access 	<ul style="list-style-type: none"> peripheral cannula remains in place for several days only – recommendation is usually to resite after 48-72 hours; midline and midclavicular catheters may remain in place for up to several weeks devices are single lumen only more vulnerable to being bumped or knocked, may have more mechanical problems⁶⁷ difficult or impossible in patients with poor vascular access infusion osmolality limited to <900mOsm/L which may mean a larger volume of infusion, with higher fat content (lower glucose and protein) possible complications include: phlebitis (inflammation of the blood vessel), local infection, damage to hand and/or arm if line is misplaced ('extravasation')
Intra-dialytic administered during haemodialysis	<ul style="list-style-type: none"> venous port of haemodialysis tubing (into AV shunt) 	malnourished haemodialysis patients who are unable to maintain weight <u>and</u> oral / enteral nutrition is <u>not possible</u> or has <u>failed</u> ⁶⁸	<ul style="list-style-type: none"> safe^{69,70} convenient not usually limited by the patient's fluid restriction (as the extra fluid infused can be removed during the dialysis) 	<ul style="list-style-type: none"> can provide only a modest proportion of the patient's nutritional needs, (only about 800-1200Cal per treatment, ie standard three-in-one solution at ~150mL/h for 3-5 hours during each dialysis) so <u>not recommended</u> for patients with grossly inadequate oral intake (eg <20Cal/kg) for whom it would be more appropriate to organise full TPN instead, if enteral nutrition not possible may require special solution in some patients, to limit electrolyte input not always well-tolerated only weak evidence of improved outcomes with ongoing therapy^{69,70,71}

For more details about the differences between parenteral nutrition formulations used for central or peripheral delivery, see *Parenteral Nutrition Formulations* section

EQUIPMENT

Equipment involved in parenteral nutrition may include the following:

- intravenous access device
- intravenous giving set
- administration reservoir (fluid bag, bottle, etc) containing parenteral nutrition solution
- infusion delivery device (IV pump)
- syringes for additives

Intravenous access

Parenteral nutrition is given into an intravenous access device, a fine silicon or polyurethane tube that is inserted into a vein. Some intravenous lines contain multiple lumens – tiny separate tubes within the line – enabling several different incompatible solutions to be delivered at the same time. Parenteral nutrition must be given into a lumen that is dedicated for that purpose – that is, that lumen should not be used to give medications or anything other than nutrition.

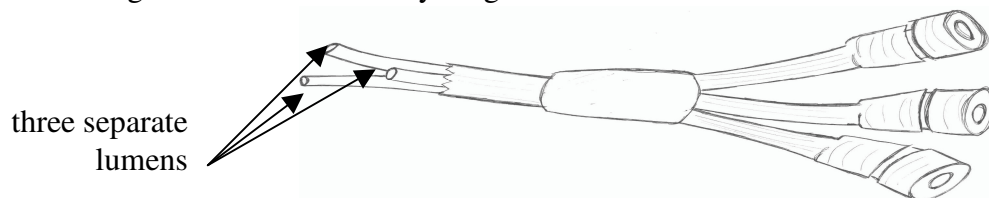


Figure 2: triple-lumen line, showing cut-away view of the lumens within it

Intravenous access must be obtained before parenteral nutrition can be commenced, and it may not be a simple process. Access problems are the most common barrier to successfully establishing and maintaining parenteral nutrition. If the patient has existing intravenous access, it is important to check whether the device is suitable for parenteral nutrition, is placed centrally, and has a lumen available that can be dedicated for nutrition: it may be the case that the current line is fully occupied and an extra line must be inserted before nutrition can commence. A line that has become infected is not suitable for parenteral nutrition and has to be removed. IV lines need to be changed regularly and this may also cause a delay: there is little point in starting parenteral nutrition using a line that is due to be removed shortly.

Central venous access

Whilst all central venous access devices, by definition, have their delivery tip in the vena cava or right atrium, different types will be inserted via different sites on the body and vary in how long they can be used, and how complicated the insertion and removal methods are.

Comparison of central venous access devices

The most common types of venous access line include:

- * polyurethane short-term central line (also called ‘percutaneous non-tunnelled catheter’)
- * PICC line (peripherally-inserted central venous catheter)
- * tunnelled central venous catheter (also called Hickman line or Broviac or Groshong)
- * Portacath (also called ‘implanted catheter’)

Short-term central lines are available as single, double, triple or quadruple (‘quad’) lumen lines. PICCs and Hickmans are generally available as single or double lumen lines. More lumens make the line thicker, stiffer, and more complicated to insert, increasing infection risk but allowing simultaneous infusion of multiple solutions.

Figure 3. Polyurethane short-term central line (also called ‘percutaneous non-tunnelled catheter’)

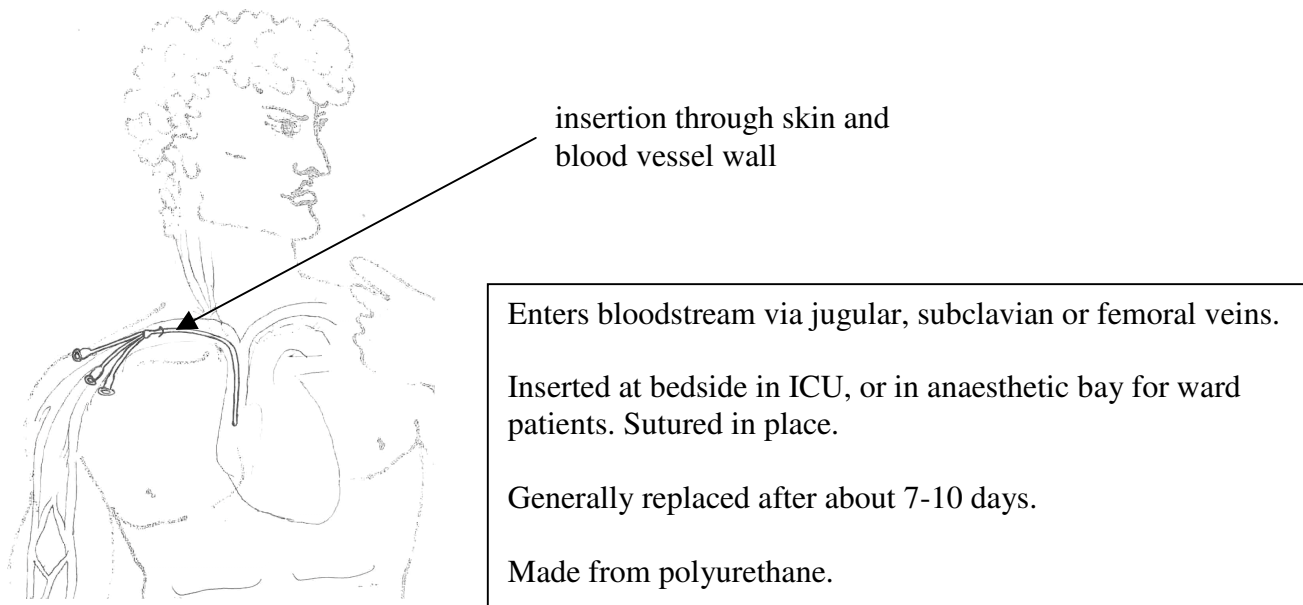


Figure 4. PICC line (peripherally-inserted central venous catheter)

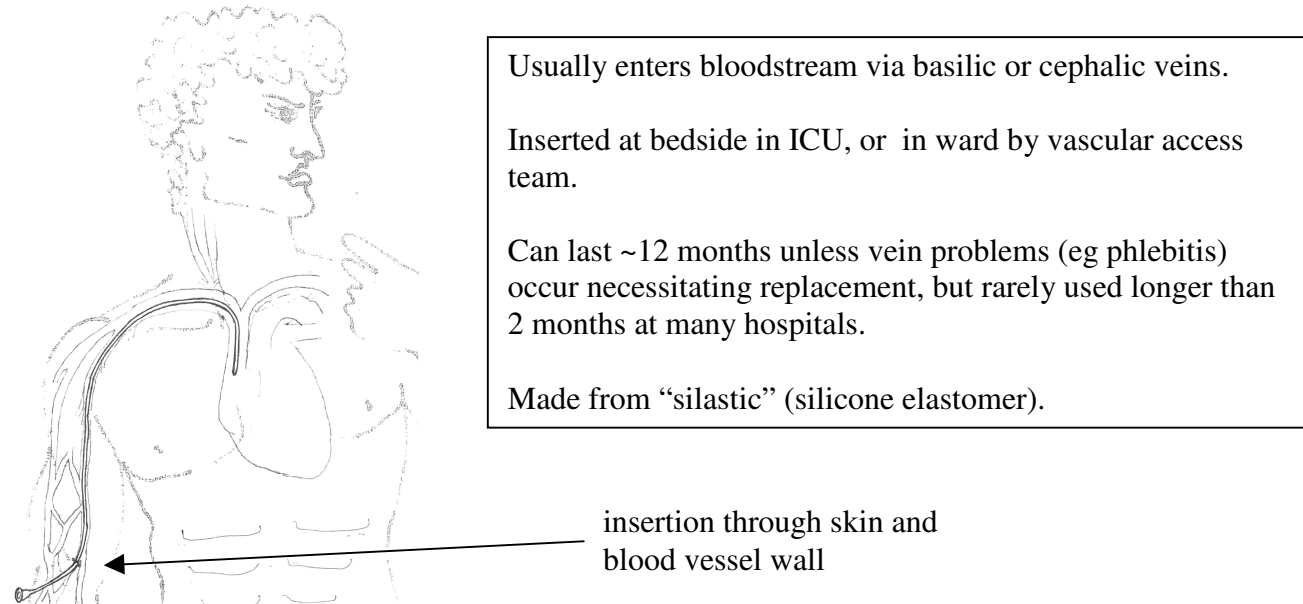


Figure 5. Hickman catheter (also called “tunnelled central venous catheter”)

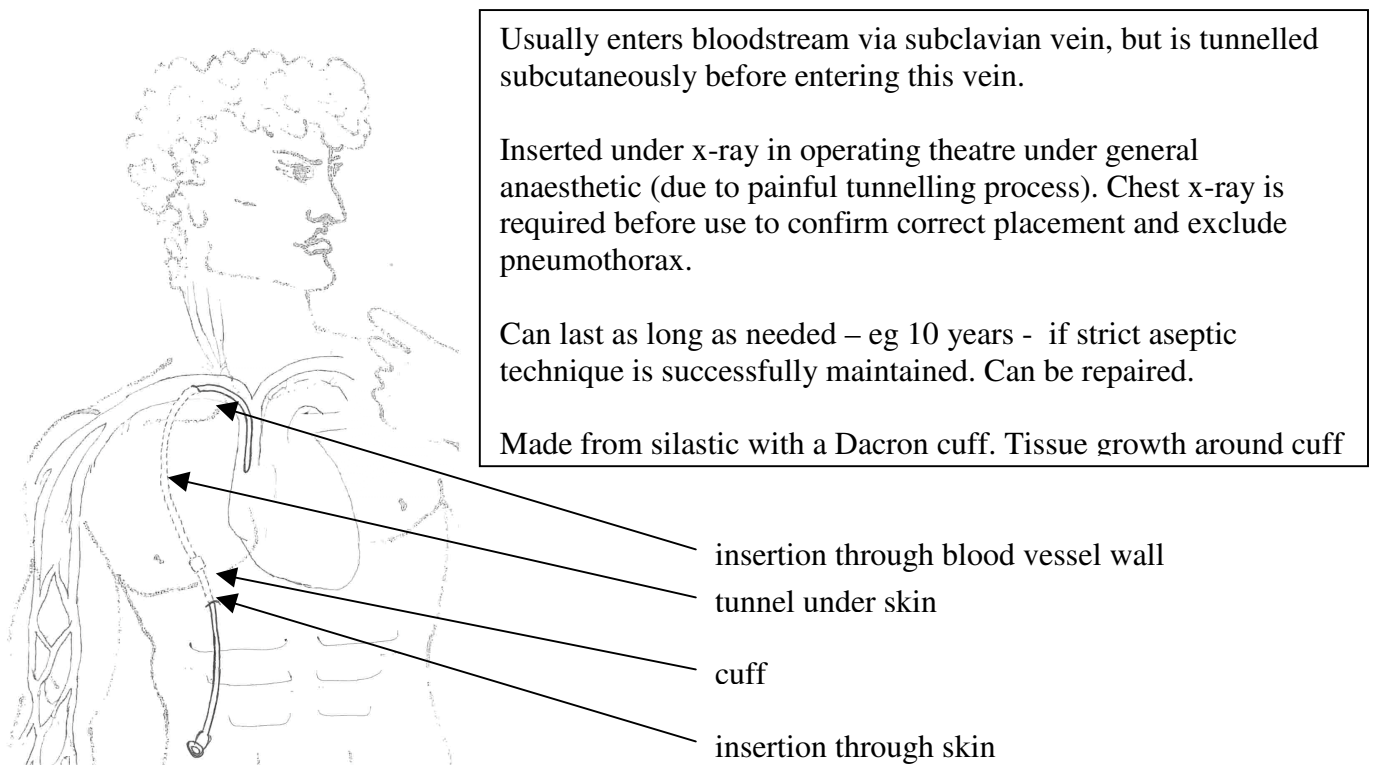
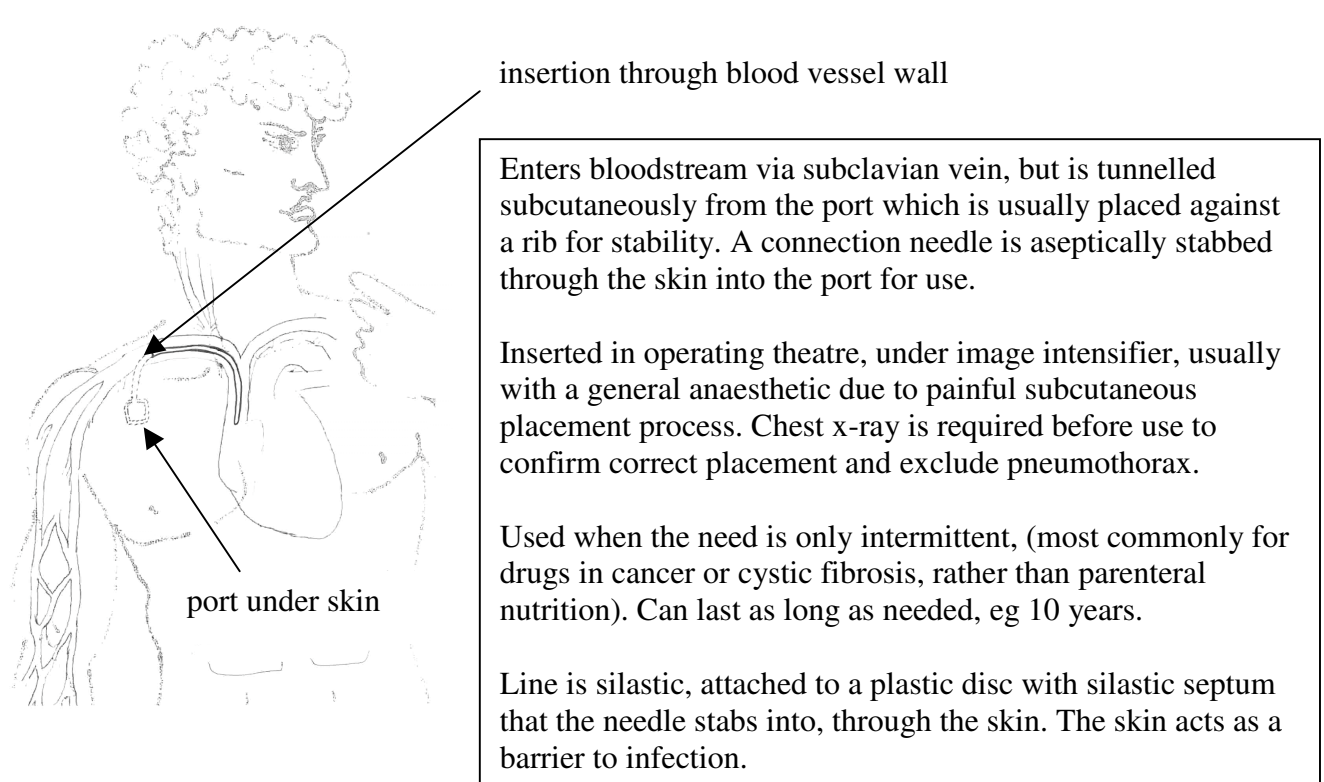


Figure 6. Portacath (also called “implanted catheter”)



Peripheral venous access

Peripheral lines are those that have their delivery tip outside the vena cava; the tip may lie in the subclavian or axillary veins (midclavicular catheters) or somewhere in the upper arm (midline catheters) or be a standard peripheral cannula in the basilic or cephalic veins of the lower arm. Many hospitals in Australia do not offer peripheral parenteral nutrition at all. It may be indicated in a limited range of situations but requires a high level of expertise in placing the access device and caring for the site in order to maintain access and spare the patient from frequent repeated cannula insertions: it is not just a matter of infusing a parenteral nutrition solution into any existing cannula!

Situations that may be indications for peripheral parenteral nutrition

Peripheral parenteral nutrition may be indicated if:

- * parenteral nutrition is indicated but the likely duration of use is less than two weeks
- * patient is malnourished, has been on central parenteral nutrition and central access has been lost (eg due to line displacement or infection) or is not yet available, where it is undesirable for them to receive no nutrition while waiting for their new central line to be placed

Solutions that can be used peripherally must usually be limited to less than 900mOsm/kg to minimise blood vessel damage. This means that peripheral parenteral nutrition solutions are a larger volume, more dilute solution, with a higher proportion of fat (eg 40-60% of total energy) because fat has lower tonicity. Peripheral parenteral nutrition is therefore not usually recommended for patients who are fluid-restricted, who have high protein requirements, who are intolerant to IV lipid infusion or who have high serum triglyceride levels. These limitations may mean that it is difficult to meet a patient's full nutritional needs.

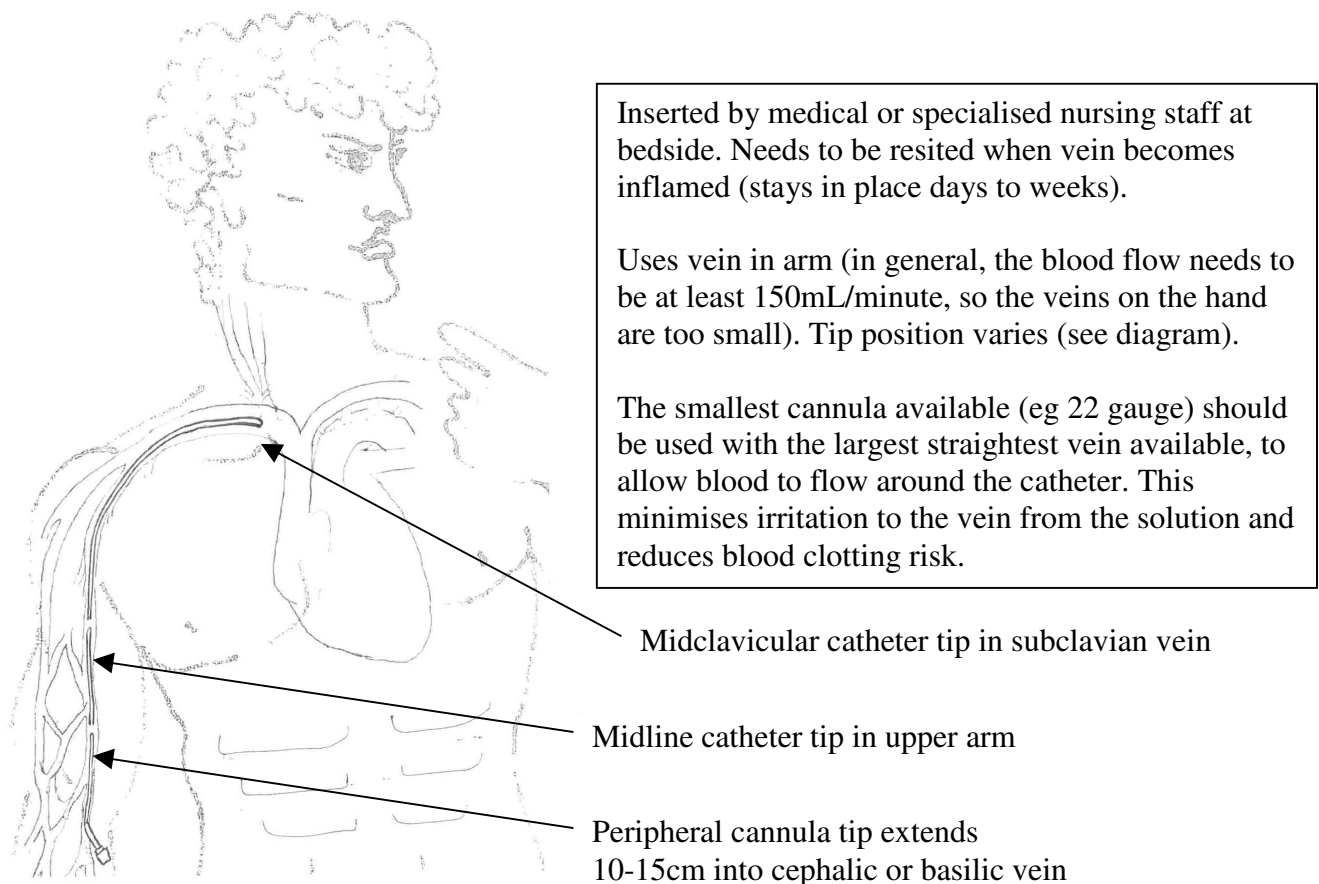


Figure 7: features of peripheral lines

Advantages and disadvantages of different lines

TYPE OF LINE	ADVANTAGES	DISADVANTAGES
Polyurethane short-term central line	<ul style="list-style-type: none"> • quick and easy to insert and remove, even if triple or quad lumen • relatively cheap 	<ul style="list-style-type: none"> • need to be changed every 7 days • higher infection risk
PICC line	<ul style="list-style-type: none"> • fairly quick and easy to insert and remove • relatively cheap • can last 12 months • infection risk lower than for short-term central line 	<ul style="list-style-type: none"> • difficult for patient to provide self-care of site due to arm position of insertion • single-lumen lines much easier to insert
Hickman line	<ul style="list-style-type: none"> • very long-lasting, can be repaired • easy self-care by patient • leaves arms free, hidden by clothing • very low infection risk 	<ul style="list-style-type: none"> • complicated insertion and removal • expensive • multi-lumen tubes are rarely used as they are very thick and stiff (risk of pneumothorax during insertion)
Portacath	<ul style="list-style-type: none"> • very long-lasting (limit is in terms of number of uses, not timespan) • easiest self-care by patient and least maintenance needed • hidden under skin • minimal infection risk 	<ul style="list-style-type: none"> • complicated insertion and removal • only suitable for intermittent use Requires needlestick into skin • expensive • risk of misplacement of needle (eg into edge of port septum) • usually only one lumen
Peripheral line	<ul style="list-style-type: none"> • quick and easy to insert, with minimal training • cheap • very low infection risk 	<ul style="list-style-type: none"> • usually requires site rotation about every 3 days due to vein inflammation (this will vary according to line care expertise) • peripheral delivery limits the type of solution that can be used – see <i>Parenteral Nutrition Formulations</i> section

Confirming correct placement of venous access devices

Ensuring the correct position of the device, with x-ray or fluoroscopy, is essential prior to commencing parenteral nutrition infusion. If the tube is incorrectly positioned, the infusion fluid may cause serious damage to the blood vessel or surrounding tissue.

Care of the venous access device^{64,72,73}

Central lines are an invasive therapy that increases the risk of a major bloodstream infection, so four-hourly temperature and pulse should be monitored, and meticulous infection control procedures maintained at all times. Everything that goes near or into a venous catheter must be prepared aseptically.

Apart from portacaths that are not currently being used (where the intact skin covering protects against infection once the incision is healed), central lines require careful attention to the exit site, the insertion site and the hub. To reduce infection risk, the exit site (the area where the device enters the skin) is usually covered with a breathable transparent dressing that needs to be kept dry, ie protected from water with plastic when showering. Tunneled cuffed catheters can often be managed without a dressing once the incision is healed, as the subcutaneous tunnel and cuff are sufficiently protective against infection, however in hospital a dressing would still normally be used. The site should be disinfected regularly with chlorhexidine – weekly if the dressing is intact, or more frequently if the dressing needs to be changed sooner than this (if it is loose or has become soggy).

The insertion site (the place where the line enters the blood vessel) should be examined daily for any possible signs of infection such as tenderness, redness, pus – but note that in many cases there will be no visible local signs when infection does occur, even though the patient may be experiencing general unwellness, fever, chills, shivering. See *Troubleshooting Guide* for details on managing an infected line.

The hub (the port or stopper at the end of the device which receives the infusion) is the other major source of potential infection. Risk increases when there are more manipulations of the hub (such as connecting and disconnecting bags of solution, flushing) so it is good to minimise these as far as possible. The hub is wiped with 70% alcohol before and after anything is connected or disconnected.

In general, one lumen of the venous access device should be reserved for parenteral nutrition only, and other substances should not be administered using that lumen. This reduces the risk of blocking or contaminating the line. While not recommended, if other substances *are* to be given into that lumen, the line should be flushed with 5mL normal saline before and after they are given. Additionally, central lines are sometimes flushed with a solution of heparin to prevent them blocking with blood-clot or fibrin. Flushing usually occurs daily, although portacaths need to be flushed only once per month. (Flush with saline before and after heparin, to avoid interaction with the parenteral nutrition solution.) All venous access devices need to be locked with heparin if not in use, or otherwise need fluids to be running through them at a minimum of 10mL/h to avoid blocking. Again, it is important to flush with saline before and after the heparin.

Intravenous giving set

In enteral nutrition, frequently changing the giving set (every 24 hours) is recommended for preventing contamination. In parenteral nutrition, in contrast, any manipulations of the line or giving set will *increase* contamination risk and therefore for infusions without lipid it is recommended not to change the giving set more frequently than 72 hours unless infection is suspected. Infusions containing lipid may need more frequent changes and every 24 hours is usually recommended.⁶⁴

Any extension sets or filters should be changed at the same time.¹⁰ Filters are commonly used in many countries overseas but less often in Australia. The small-sized filters that stop bacteria cannot be used with lipid as they do not allow lipid droplets to pass intact, and thus destabilise the emulsion. Filters therefore tend not to be used in places where three-in-one solutions are in wide use.

Administration reservoir

Administration reservoirs are available as either bags or bottles, in a range of sizes. Bottles are the traditional way by which modular parenteral nutrition is provided: that is, separate bottles of amino acid solution, glucose, and lipid emulsion are hung, either consecutively or simultaneously (in separate lumens or ‘piggy-backed’ onto one lumen). Increasingly, this bottle system has been replaced by combination 1000mL, 1500mL or 2000mL bags. These bags may have separate sections or ‘chambers’ containing all three macronutrients (‘three-in-one’ solution or Total Nutrient Admixture (TNA)) which are mixed before hanging; or may contain just the amino acid and glucose (‘two-in-one’ solution) with bottles of lipid still given separately. (Note that macronutrient utilisation is improved with continuous infusion of all three macronutrients, rather than alternating or intermittent infusion.)^{29,30} The recommended hang-times differ: lipid hanging on its own should be changed every 12 hours, while two-in-one and three-in-one solutions can safely hang for 24 hours at room temperature,⁶⁴ due to their higher tonicity and acidity (which make them less susceptible to bacterial growth).⁶⁵ See section on ‘Hang-time’ in *Considerations in choosing a parenteral nutrition formulation*.

Light-protective covering

It is recommended to cover the parenteral nutrition solution with an opaque cover to prevent deterioration due to UV light, particularly if the solution is a transparent (two-in-one) formulation. Sturdy plastic light-protective cover bags are provided with most parenteral nutrition products, but sometimes need to be ordered separately. An opaque plastic shopping bag or brown-paper medications bag, or aluminium foil, are all reasonable alternatives if the covers are temporarily unavailable. Any covering should be folded or taped closed at the bottom for maximum protection. Opaque giving sets are also available for ambulatory patients who will regularly be outside in direct sunshine during infusion.

Parenteral nutrition pumps

Parenteral nutrition is usually delivered using an ordinary intravenous therapy (IV) pump such as the ones used for other IV fluids in the hospital setting. Many different types of IV pump are available, including lightweight, compact pumps for ambulatory patients. IV pumps require a power source although some have battery back-up; other useful features of the pump include portability, simplicity of use and ease of cleaning, alarm sound, quiet operation, excess pressure cut-out, a hold facility for administration of medications and a method of attaching the pump to the bed/IV pole/other location. Pumps should be kept clean by wiping daily with a cloth moistened in mild detergent and water.

Some companies provide pumps for hire in addition to selling them, but in general, IV pumps are a very expensive part of parenteral nutrition therapy and can be a major obstacle to home parenteral nutrition for some patients. Check that the supplier provides maintenance service as this can be another cause of nutrition interruptions for home patients.

REGIMENS FOR PARENTERAL NUTRITION

The choice of parenteral nutrition regimen is based on assessment of the individual needs of the patient. The goal is to provide safe parenteral nutrition and hydration appropriate to the clinical status of the patient, taking quality of life issues into consideration.

Note that each facility will normally have its own standard parenteral nutrition formulations and typical regimens. There may also be limitations on ordering, dispensing or delivery, set by the facility's pharmacy or stores, which affect the availability of parenteral nutrition solutions at particular times. There may be nursing procedures that set out what time parenteral nutrition bags are changed, and which staff have the authority to order or hang the bags or add vitamin and trace element additives to them. All of these factors need to be considered when planning a patient's parenteral nutrition regimen as they will limit the available options. Consult the facility's procedures for details on managing parenteral nutrition within that particular setting.

Choice of nutrition regimen

Parenteral nutrition infusions can be: continuous (running 24 hours a day), cyclic (running for a period of between 8 and 18 hours each day) or intermittent (on some days only).

Continuous parenteral nutrition

Parenteral nutrition infuses for 24 hours continuously. This is the most common type of regimen in the hospital setting. Infusion rates usually range between 40-150mL/h.

Advantages:

- Allows the lowest possible hourly infusion rate to meet nutrient requirements
- Better control of blood glucose levels due to continuous carbohydrate input
- May result in better utilisation of nutrients^{29,30}

Disadvantages:

- Physical attachment to the pump (may affect quality of life)
- Higher risk of biliary stasis (if no oral/enteral intake)
- Promotes continuous high insulin levels, which may increase risk of fatty liver

Cyclic / intermittent nutrition

Parenteral nutrition is run over a shorter period and then stopped. The shorter the period of nutrition, the higher the rate may need to be in order to meet the patient's requirements. Cyclic infusions are commonly used in long-term parenteral nutrition, especially for home patients who may receive infusions overnight only, or only on some days of the week. The infusion rate may be as high as 200-300mL/h. (For example, a typical overnight regimen might infuse a 2000mL three-in-one bag over eleven hours as follows: 200mL/h from 9pm to 6am, then two hours at 100mL/h before stopping for the day.)

Advantages:

- Allows greater patient mobility (may improve quality of life)
- Mimics physiological feeding/fasting pattern, which may help to prevent accumulation of fat in the liver and sludge in the biliary system

Disadvantages:

Compared with continuous nutrition, a higher infusion rate is required to provide the same volume of feed. This may be less well-tolerated, with a higher risk of problems such as:

- Fluid overload (and frequent urination during infusion, inconvenient especially at night)
- Electrolyte fluctuations
- Unstable blood glucose levels

Starting parenteral nutrition

Where there is no obvious risk of refeeding syndrome or other metabolic issues, there is little evidence to support the practice of gradually initiating parenteral nutrition, and it can usually be commenced at the goal infusion rate as long as measures have been taken to minimise metabolic complications and appropriate monitoring (including hourly blood glucose monitoring for the first few hours) is in place.^{74,75,76,77} The availability of close monitoring is usually the factor that determines whether it is safe to start at the goal rate in a particular setting. Starting parenteral nutrition infusions abruptly can (rarely^{74,75}) cause temporary hyperglycaemia, particularly if the solution is high in glucose. Starting the infusion with a lower-glucose solution or at half the goal rate for an hour or two, before increasing to goal rate, can prevent this, and may be recommended in patients with known glucose intolerance. It is not necessary to increase the rate more slowly than this, and a slow initiation regimen may significantly delay the patient receiving his or her full nutritional requirements. The main exception is in the case of patients who are at risk of refeeding syndrome as the risk is highest with parenteral nutrition unless precautions are taken. These may include patients who have been nil-by-mouth for a prolonged period, who are critically ill or who have previous significant weight loss, or where heavy or chronic alcohol misuse may be involved – see *Refeeding Syndrome* in Troubleshooting section for details.

Parenteral nutrition infusion rate

All patients require individual assessment for determining the rate of delivery of nutritional support, which depends on the patient's nutritional requirements and medical condition. Typical infusion rates vary between 40-150mL/h, but cyclic infusions may be delivered at rates as high as 300mL/h.

Stopping parenteral nutrition

It is important to continue monitoring closely, with hourly blood glucose testing, for several hours after stopping a parenteral nutrition infusion, as the metabolic effects of the infusion do not cease immediately. Abruptly stopping parenteral nutrition when there is no other nutrition input can (rarely^{74,75}) cause a rebound hypoglycaemia in some patients due to ongoing action of insulin (infusion, injection or even the patient's own endogenous secretion), particularly if the solution was high in glucose or if blood glucose levels have been difficult to control. Depleted patients, lacking an adequate glycogen store, may also be at risk if the infusion is stopped shortly after starting, before their stores have been replenished. For patients with normal blood glucose levels who have not been receiving insulin, the infusion can usually just be stopped. Other patients may benefit from a brief tapering regimen: ensure that insulin infusions are ceased, that other insulin dosage is reviewed, and then decrease the parenteral nutrition infusion rate by half for an hour. Alternatively the parenteral nutrition can be replaced with a 10% dextrose infusion at the same rate for an hour, before stopping completely. There is no evidence to support ceasing parenteral nutrition if a patient is having surgery, however it is usual practice to minimise the number of different infusions that have to be transported to surgery with the patient, so it is normally stopped.

Flushing the line

In general, one lumen of the venous access device should be reserved for parenteral nutrition only, and other substances should not be administered using that lumen. This reduces the risk of blocking or contaminating the line. If other substances *are* to be given into that lumen, the line should be flushed with 5mL normal saline before and after they are given. If the parenteral nutrition solution is stopped, the line should be flushed with 5mL normal saline before the line is locked with a heparin solution.

Dual feeding

If a patient is transitioning to tube feeding, or if a low rate of enteral nutrition is being administered for gut benefits,^{3,4,5} the patient will be receiving both parenteral and enteral nutrition at the same time: this is called dual feeding. Dual feeding allows gut functioning to be maintained during parenteral nutrition, and can also ensure that a patient's full nutritional needs are met in cases where only a low rate of enteral feeding is tolerated. If the enteral feed rate is increasing, the parenteral nutrition rate should be decreased to maintain a constant (goal) energy input. It is important to check that the rates are being titrated against one another correctly, as it is very easy to overfeed a patient who is having dual feeding.⁷⁸ A simple way to avoid significant overfeeding is to set a total for the two rates (enteral + parenteral), and keep the total the same while the parenteral rate decreases and the enteral rate increases. Typically this total will be the goal rate for the tube feeds, but may differ if the two solutions have different energy concentrations or if enteral absorption is inadequate.

MONITORING OF NUTRITION SUPPORT

Once parenteral nutrition has been initiated, ongoing monitoring is essential to ensure that the patient receives adequate nutrition, to identify and manage potential complications, and to ensure safety.

What should be monitored, and the frequency of monitoring, will depend on factors such as:

- the expected duration of treatment
- the health care setting
- the patient's disease state
- the presence (and severity) of any abnormal results
- whether the patient is stable (ie the parenteral nutrition solution is running at goal rate, fluid and blood glucose are being managed without difficulty, there are no major new procedures or treatments occurring, test results (while these may still be abnormal) are not raising new unsolved questions or requiring large changes in management, etc.)

Care must be taken in the interpretation of any of these measures in isolation. Results should be interpreted in the light of the patient's condition and any previous results available.

Anthropometry

MEASURE	APPLICATION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Weight	Unstable fluid balance (including large fistula or stoma output)	- whether fluid input is meeting needs - whether it should be restricted or increased	Baseline then daily
	Patients in first 1-2 weeks of parenteral nutrition	- whether fluid input is meeting needs	Baseline and then second-daily
	Patients in first 3-6 weeks of parenteral nutrition	- whether energy input is meeting needs -interpret in the light of fluid changes	Baseline and then weekly
	Continuation of long term parenteral nutrition	- whether energy input is appropriate	Baseline and then monthly
Height	Use in conjunction with weight to assess BMI	May be difficult to obtain in acute setting. Demispan or knee height can be used for estimating height until a more accurate measure can be obtained.	Baseline
Mid-arm circumference (at midpoint on back of arm, halfway between acromial surface of scapula and olecranon process of elbow)	Long term parenteral nutrition	- whether energy and protein input are appropriate - interpret in the light of changes in patient's activity level	Baseline and then monthly. (Serial measures are more informative than comparing single measures to percentile charts.)
Calf circumference (at widest point)		- acute changes in fluid balance may confound this measure in trauma and critical illness	

Biochemistry / haematology

Check with your laboratory for the normal range for each parameter as some of these will vary between sites. Only a basic survey of each test is given here. For more details of each test and its interpretation, refer to a clinical chemistry text or your laboratory's handbook, and discuss with medical team.^{79,80} Refer to *Troubleshooting* section for management of abnormal biochemical results.

'EUC' and 'CMP' tests (Electrolytes /Urea /Creatinine and Ca^{2+} / Mg^{2+} / PO_4^{2-})

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Sodium	Major extracellular electrolyte, plays an important role in fluid balance. Also involved in nerve conduction and membrane transport	INCREASED in dehydration, refeeding syndrome. DECREASED in overhydration, SIADH, and salt-wasting conditions. -consider whether all the other electrolytes are increased or decreased. -check total fluid input, diuretics, sodium content of parenteral solution, and whether any additional IV fluids are saline or dextrose -serum osmolality can help determine fluid status -urinary sodium and osmolality can help identify SIADH or salt wasting.	Daily or second-daily in the acute setting depending on patient stability. Monthly if possible, for long term parenteral nutrition.
Potassium	Major intracellular electrolyte, influences fluid balance. Also involved in nerve conduction and muscle contraction (esp. cardiac)	INCREASED in dehydration, renal failure (acute, or serious chronic), or when K ⁺ shifts out of the cell (as in acidosis or insulin deficiency) DECREASED by increased losses (vomiting, diarrhoea) or when K ⁺ shifts into cell (as in refeeding syndrome, reversal of acidosis, administration of insulin) -consider effect of diuretics (may cause K ⁺ wasting or retention) -consider possible losses	Daily or second-daily in the acute setting depending on patient stability. Monthly, if possible, for long term parenteral nutrition
Magnesium	Intracellular; cofactor for enzymes in nearly every stage of aerobic metabolism. Required in muscle and nerve function	INCREASED in renal failure or high intake (eg magnesium antacids) DECREASED by some diuretics, malnutrition and muscle loss, malabsorption, and when Mg ²⁺ shifts into cell (as in refeeding syndrome)	Daily or second-daily in the acute setting depending on patient stability. Monthly, if possible, in long term parenteral nutrition
Phosphate	Intracellular; part of ATP, so involved in all energy production / storage processes. Found in bone and muscle	INCREASED in renal failure, hypoparathyroidism, laxatives DECREASED in muscle loss and malnutrition, malabsorption, vitamin D deficiency, hyperparathyroidism and refeeding syndrome.	Daily or second-daily in the acute setting depending on patient stability. Monthly, if possible, in long term parenteral nutrition.

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Urea (note is <i>not</i> the same as 'Blood Urea Nitrogen' (BUN))	End product of protein metabolism, formed by liver to detoxify ammonia. Excreted in urine, rate depends on GFR (glomerular filtration rate) and urine output.	INCREASED in renal failure, dehydration, high protein intake (from diet, or GI bleed), renal obstruction DECREASED with reduced muscle turnover (small muscle mass, low protein intake, low activity) or severe liver dysfunction - Urea:Creatinine ratio >1:10 can indicate dehydration or GI bleed.	Daily or second-daily in the acute setting depending on patient stability. Monthly, if possible, in long term parenteral nutrition.
Creatinine	Produced by body muscle, also small amounts come from meat in the diet. Excreted in urine, rate depends on GFR <i>and</i> tubular secretion. Proportional to muscle mass	INCREASED in renal failure, fever, large meat meal, large muscle mass (bodybuilder, acromegaly) some medications DECREASED with loss of muscle, low protein intake	Daily or second-daily in the acute setting depending on patient stability. Monthly, if possible, in long term parenteral nutrition.

Liver tests

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
ALT, AST (alanine aminotransferase, aspartate aminotransferase) also known as SGPT and SGOT (esp. in USA)	‘Transaminases’, released in cell damage (ALT in liver cells; AST in liver, muscle and red blood cells)	INCREASED in liver damage ALT only: mild liver damage AST only: chronic liver disease with tissue destruction, or damage to other body muscle Both ALT and AST raised: major damage; can indicate overfeeding, esp. with excessive carbohydrate.	Daily/second-daily in the acute setting Monthly if possible, for long term parenteral nutrition
GGT, ALP (gamma glutamyl transferase, alkaline phosphatase)	‘Cholestatic enzymes’, found in bile duct cells, produced by liver in increased quantities during biliary obstruction. GGT also induced by some medications, alcohol and obesity ALP also in bone and placenta	INCREASED in biliary obstruction GGT only: drugs, alcohol, obesity ALP only: bone activity including fractures, growth including metastasis, pregnancy, childhood Both GGT and ALP: cholestasis (may occur due to lack of enteral stimulation in longer-term parenteral nutrition); will increase in overfeeding, esp. with excessive carbohydrate, but not usually to abnormal level.	Daily/second-daily in the acute setting Monthly, if possible, for long term parenteral nutrition
Bilirubin	Breakdown product of haem molecule. WBC in spleen produce bilirubin; liver makes bilirubin soluble and secretes it into bile	INCREASED in internal bleeding or haemolysis, liver dysfunction, biliary obstruction, also many drugs. Transient rise may occur in first few weeks of parenteral nutrition and then normalise after 4-5 weeks, mechanism is poorly understood. May DECREASE in overfeeding.	Daily/second-daily in the acute setting Monthly, if possible, in long term parenteral nutrition
INR or PTT (prothrombin time)	Measures blood clotting time	INCREASED with liver dysfunction or with anticoagulant therapy DECREASED with coagulant therapy	Daily/second-daily in the acute setting Monthly, if possible, in long term parenteral nutrition

Iron studies

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Haemoglobin	Iron-containing portion of the RBC which binds oxygen for transport throughout the body	INCREASED in haemochromatosis DECREASED with blood loss, acute phase response and in all types of anaemia	Daily to weekly in the acute setting Monthly, if possible, in long term parenteral nutrition
Ferritin	Storage form of iron	INCREASED in acute phase, malignancy, sepsis (to reduce availability to bacteria), iron overload. DECREASED in iron deficiency (diagnosis of iron deficiency anemia if haemoglobin also low). More sensitive and specific than other iron tests.	As required to assist in interpretation of abnormal iron studies.
Transferrin	Transport form of iron	INCREASED in iron deficiency DECREASED in acute phase response, malnutrition, iron overload, liver disease Not a sensitive measure of protein status due to wide normal range and unpredictable response to nutrition support.	As required to assist in interpretation of abnormal iron studies.
Iron	Free iron in the serum	DECREASED in iron deficiency, acute phase. Not very sensitive or specific. Significant diurnal changes and wide normal range.	Monthly to three-monthly, particularly in long-term parenteral nutrition.
Haematocrit (also known as Packed Cell Volume or PCV)	Volume of red cells in relation to the total volume of blood	INCREASED with dehydration DECREASED in anaemia and other blood abnormalities, blood loss, nutritional iron deficiency.	Does not provide additional information if haemoglobin result already available as relationship with Hb is linear.
Mean corpuscular volume (MCV)	Reflects RBC size, to classify type of anaemia	INCREASED in macrocytic anaemia NORMAL in normocytic anaemia DECREASED in microcytic anaemia	As needed to assist in interpretation of abnormal iron studies.

Lipid studies

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Triglycerides	Storage form of fat in the body. Consumed in diet, or made by the liver. Need fasting blood sample for accurate assessment, however it is not usually necessary to stop parenteral lipid infusion for the test unless investigating a previous abnormal result (note higher allowed normal range – up to ~4.5mmol/L).	INCREASED in overfeeding, glucose intolerance, hyperlipidaemias, hypothyroidism, pancreatitis, poor tolerance of exogenous (parenteral) lipid, carnitine deficiency. Allowed ‘normal’ range is doubled if bloods were taken during lipid infusion. DECREASED in malabsorption or very low fat intake, hyperthyroidism.	May be useful to obtain baseline level prior to commencement of lipid-containing parenteral nutrition (to exclude pre-existing hyperlipidaemia). Weekly in the acute setting Monthly, if possible, in long term parenteral nutrition
Cholesterol	Made in the liver, needed for production of hormones, bile acid and vitamin D.	INCREASED in acute phase and sepsis (to reduce availability to bacteria) as well as hyperlipidaemia and increased dietary intake. DECREASED with malnutrition, liver disease, hyperthyroidism	As needed Refer to Vitamin E monitoring as this may affect level.
Essential fatty acids (‘triene:tetraene ratio’ is test for deficiency)	Fatty acids (linoleic, and alpha-linolenic) that the body cannot itself synthesise and must obtain from the diet or parenteral lipid emulsion.	Triene:tetraene ratio >0.4 indicates essential fatty acid deficiency. Symptoms of deficiency include scaly dermatitis, alopecia, delayed wound healing, platelet dysfunction, fatty liver.	If deficiency is suspected, ie see symptoms (in a patient who is not receiving lipid).

Vitamins, minerals and trace elements

The availability of laboratory tests varies between facilities. Some will be able to test for a wide range of vitamins, minerals and trace elements; others may be using a remote laboratory service which will mean a delay in receiving results. Even if this is the case, baseline measurements should ideally be obtained for all patients who are likely to require long term parenteral nutrition, with follow-up monitoring as required.

Note: interpretation of many of these tests is difficult. Blood levels may not reflect total body stores, due to varying distribution of vitamins/minerals in body tissues. Levels may not be indicative of nutrition due to the effects of the acute phase response. For these reasons, sequential monitoring is generally more meaningful than a single result.

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Vitamin A	Retinol and carotenoids; essential for vision, growth, iron metabolism. Deficiency signs include night blindness, anaemia, immune impairment, follicular hyperkeratosis.)	INCREASED in renal failure (due to decreased losses) or excessive dosing. Renal retention is not associated with toxicity, but excessive dosing can cause liver damage. ⁸¹ DECREASED in fat malabsorption (such as with ileal resection, pancreatic insufficiency, or excess bile salt loss) and in acute phase response.	On commencement of long-term parenteral nutrition, and then annually or as needed. Note blood samples for retinol testing should be wrapped (in foil/paper) after collection to avoid light exposure.
Vitamin D	Active form is 1,25-dihydroxyvitamin D; controls calcium utilisation, has immune function, interacts with serum calcium and phosphorus, and parathyroid hormone. Deficiency signs include bone abnormalities, low serum phosphate, raised ALP.)	INCREASED in excessive dosing, excess parathyroid hormone, some disease conditions (eg sarcoidosis, lymphomas) DECREASED in lack of sun exposure, malabsorption (esp. in elderly), chronic kidney and liver disease. Some drugs (eg phenytoin) can interfere with liver production of precursor.	On commencement of long-term parenteral nutrition, and then three-monthly or as needed. Note usually test serum level of precursor form (25-hydroxyvitamin D) as this is the major circulating form and a more sensitive test than 1,25 form.
Vitamin E	Tocopherols, expressed as alpha-tocopherol equivalents; act as anti-oxidant in the lipid phase of cell membranes to protect cell structure. Deficiency signs include peripheral neuropathy, myopathy, ataxia.	INCREASED in hyperlipidaemia (test result can be corrected for cholesterol level). DECREASED in fat malabsorption, genetic abnormalities, malnutrition.	On commencement of long-term parenteral nutrition, and then three-monthly or as needed. Test is plasma alpha-tocopherol

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Vitamin K	<p>Phytomenadione and quinones; involved in blood coagulation and bone metabolism. Mostly obtained from gut bacteria, needs bile and pancreatic secretions for optimum absorption.</p> <p>Deficiency signs include poor clotting and bone malformation.</p>	<p>DECREASED in fat malabsorption, biliary obstruction, pancreatic insufficiency, liver cirrhosis, destruction of intestinal flora (by broad-spectrum antibiotics).</p> <p>Excessive dosing can interfere with concurrent anticoagulant therapies.</p>	<p>Coagulation is assessed by monitoring the INR (International Normalised Ratio), at least weekly in the acute setting and monthly in long-term parenteral nutrition. Vitamin K levels are not usually tested.</p>
Vitamin B12	<p>Cyanocobalamin and other cobalamins; act as cofactor in fat metabolism and DNA synthesis. Stored in liver. Deficiency signs include neurologic symptoms (fatigue, weakness, depression), glossitis, stomatitis, pallor, gut dysfunction, megaloblastic anaemia.</p>	<p>INCREASED in acute phase and sepsis, and some malignancies (esp liver)</p> <p>DECREASED if relying on enteral/oral intake with loss of stomach or ileum function, malabsorption (eg in coeliac disease or pancreatic insufficiency), vegan diets, old age, pernicious anaemia, nitrous oxide anaesthesia (oxidises the B12). Many of these patients will need regular B12 injection.</p>	<p>On commencement of long-term parenteral nutrition, then three-monthly or as needed.</p> <p>Serum cobalamin assay checks B12 level, levels are low in deficiency. Serum methylmalonic acid is elevated in B12 deficiency but not in folate deficiency. Unstable, so blood sample should be frozen after collection.</p>
Folate	<p>Folic acid and related compounds, involved in coenzymes of many metabolic processes, esp. amino acid interconversions and DNA synthesis. Deficiency signs include neurologic symptoms (weakness, depression), glossitis, stomatitis, megaloblastic anaemia.</p>	<p>May be INCREASED in cases of small bowel bacterial overgrowth. DECREASED in smokers and in alcoholism. Low levels associated with higher cardiovascular risk but cause/effect unclear.</p>	<p>On commencement of long-term parenteral nutrition, then annually or as needed.</p> <p><u>Erythrocyte</u> (not serum) folate is best test. Unstable, so blood sample should be frozen after collection.</p>
Copper	<p>Essential trace mineral present in all body tissues and cofactor in many metabolic pathways. Mainly excreted in the bile.</p>	<p>INCREASED in biliary obstruction, pregnancy, Wilson's disease, acute phase response. DECREASED where there are high losses (wound, ileostomy), malabsorption, corticosteroids, and with excessive zinc or iron supplementation.</p>	<p>Weekly to monthly in the acute setting if available, then three-monthly or as needed in long-term parenteral nutrition. Monitoring essential in patients with liver disease (eg if total bilirubin >60 or conjugated bili >12) to identify high level and prevent toxicity. Test is serum copper.</p>

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Manganese	Essential trace mineral involved in formation of bone, as well as cofactor in many metabolic pathways. Mainly excreted in the bile.	INCREASED in long-term parenteral nutrition patients, in anaemia, and in biliary obstruction. Toxicity symptoms including tremor, gait disturbance, confusion/headache. No known reports of deficiency in parenteral nutrition patients.	Monitoring for toxicity essential in long-term patients and those with liver disease (eg if total bilirubin >60 or conjugated bili >12) to identify high level and prevent toxicity. Test is whole blood or erythrocyte manganese.
Chromium	Essential trace element, required for normal glucose metabolism and peripheral nerve function. Deficiency signs include impaired glucose tolerance, peripheral neuropathy, ataxia, confusion. Mainly excreted in urine.	DECREASED only in severe deficiency: serum levels remain normal for a time while body stores are depleting. INCREASED in anuric renal failure. However, no known reports of chromium toxicity.	Only as needed. Monitoring may be indicated in renal failure. Test is plasma chromium.
Selenium	Antioxidant, interacts with thyroid hormones. Absorbed in duodenum. Deficiency signs include muscle weakness, cardiomyopathy.	DECREASED in pregnancy, alcoholism, malabsorption burns, and in immunocompromised patients.	Weekly to monthly in the acute setting if available, then three-monthly or as needed in long-term parenteral nutrition. Measured by testing serum selenium level or glutathione peroxidase activity.
Zinc	Important cofactor for many enzymes, role in immune function. Deficiency signs include impaired taste and smell functions, skin rash/lesions, alopecia, glossitis, stomatitis, diarrhoea, depression.	DECREASED in acute phase response, malabsorption, chronic renal failure or loss of skin tissue (as in burns or psoriasis). Folate supplementation may interfere with zinc absorption.	Weekly to monthly in the acute setting, then three- to six-monthly or as required in long-term parenteral nutrition. Serum value should be corrected for low albumin level. Test should be done promptly after blood collection as zinc leaks out of blood cells over time, increasing the serum result.
Molybdenum	Essential trace element, required as cofactor for metabolic enzymes. Deficiency signs include tachycardia, tachypnoea, headache/ confusion.	DECREASED in long-term parenteral nutrition or with molybdenum cofactor abnormality.	Only if deficiency is suspected. Test is plasma molybdenum.

MEASURE	DESCRIPTION	INTERPRETATION	IDEAL FREQUENCY OF MONITORING
Calcium	Essential component of bone (with phosphate).	Bone density is DECREASED in long-term parenteral nutrition due to decreased calcium intake and increased excretion.	Yearly in high-risk patients (see <i>Issues in Long-Term Parenteral Nutrition</i>) for more details. Test is DEXA (dual-energy x-ray absorptiometry) scan of bone density.
Iodine	Essential trace element, involved in synthesis of thyroid hormone which helps regulate metabolic rate and body temperature. Deficiency signs include reduced thyroid hormone level, and/or enlarged thyroid gland (goitre).	DECREASED in long-term parenteral nutrition when iodine is not provided.	Only if deficiency is suspected. Test is serum TSH (thyroid-stimulating hormone) and serum Free Thyroxine ('T4')
Aluminium	An undesirable contaminant found in all components of parenteral nutrition. Toxicity signs include neurological signs (such as confusion). Also thought to increase risk of metabolic bone disease.	INCREASED in impaired renal function, cholestasis, macrocytic anaemia.	Only if toxicity is suspected. Test is plasma aluminium.
Carnitine	A 'vitamin-like' substance, involved in transport of fatty acids into mitochondria. Usually synthesised in the liver and kidneys but this may be decreased in the absence of oral/enteral intake. Deficiency signs include altered lipid metabolism (with raised serum triglycerides) and fatty liver.	DECREASED in haemodialysis, renal and liver disease, long-term parenteral nutrition, malnutrition. Not currently included in standard available adult parenteral nutrition solutions or micronutrient additive products.	Only if deficiency is suspected (such as in long-term parenteral nutrition patients with an unexplained raised serum triglycerides level.) Test is plasma acylcarnitine : free carnitine ratio. Ratio >0.4 may indicate deficiency.
Choline	A 'vitamin-like' substance, precursor for acetyl choline (a neurotransmitter) and a number of important phospholipids, necessary for VLDL synthesis and normal cell membrane structure. Deficiency signs include fatty liver, decreased cholesterol level, and renal abnormalities.	DECREASED in long-term parenteral nutrition, folate or B12 deficiency. Not currently included in available parenteral nutrition solutions or micronutrient additive products.	Unable to be tested in Australian hospital laboratories at time of publication. See <i>Micronutrients</i> section for more information.

Indicators of protein status

Interpreting these indicators can be complex.^{82,83,84,85} Note the effect of the acute phase process (see *Glossary*) on all of these indicators. Acute phase markers (such as C-reactive protein, see below) may be useful in quantifying this.

MEASURE	DESCRIPTION	INTERPRETATION	MONITORING
Albumin	A non-specific carrier protein, plays important role in controlling fluid distribution between tissue compartments. Made in the liver. Half-life 18-20 days.	INCREASED in dehydration or when IV albumin is given. DECREASED in acute phase, liver failure, protein malnutrition, overhydration, loss of body tissue (as in bleeding, burns, surgery, fistula), diarrhoea.	Strong prognostic indicator, ⁸⁶ because it is a measure of disease severity. Cannot be used to assess nutritional status in acute phase situation. Good screening parameter as an indicator of long-term nutritional status in healthy populations only.
Prealbumin, also known as thyroxine-binding protein or transthyretin	Transport protein for thyroxine, also associated with retinol-binding protein transport. Made in the liver, mostly cleared by the kidneys. Half-life 3-5 days.	INCREASED in renal failure, steroid therapy, non-hodgkin's lymphoma, head injury (? via cortisol secretion.) DECREASED in acute phase, liver failure, protein malnutrition, hyperparathyroidism.	Much earlier indicator of patient's clinical improvement, compared to albumin. Correlates with previous 5 days' cumulative nutrition intake in a stable patient (even in acute phase) and should be normal in a stable fed patient after 1-2 weeks.
Retinol-binding protein	Transport protein for retinol. Made in the liver. Half-life 12 hours.	INCREASED in renal failure, vitamin A deficiency. DECREASED in acute phase, liver failure, protein malnutrition.	Extremely sensitive indicator of patient's clinical condition. May fluctuate too much to be a useful measure.
Total protein	Total of serum proteins. Albumin and immunoglobulins are the major components of this total.	DECREASED in acute phase, or any other situation where albumin is decreased.	Severe acute phase may cause a decrease in alb:total protein ratio, due to falling albumin and increasing contribution by acute phase proteins (such as c-reactive protein)
Nitrogen balance	Most direct measurement of actual protein status, by comparing nitrogen output and input. Less accurate with unquantifiable protein losses (such as from wounds/fistulae/dialysis)	Positive nitrogen balance (input > output) indicates anabolism. Negative nitrogen balance indicates lean tissue loss. (Will be negative in acute phase, and improvement may not be possible.)	24-hour urine collection is tested for urea (or, preferably, total nitrogen ⁸⁷) content. Calculation then estimates nitrogen balance: Nitrogen input (g) = protein intake (g) ÷ 6.25 Nitrogen output = 24-hour urinary urea + "insensible losses", usually use 3-5 g but may be more.
Handgrip strength	Squeeze strength using handgrip dynamometer	Direct functional measure of protein status	Weekly for serial measure of protein status. Can also compare to percentile tables.

MEASURE	DESCRIPTION	INTERPRETATION	MONITORING
C-reactive protein (CRP)	An acute phase protein – a non-specific marker of infection and inflammation.	INCREASED very rapidly in acute phase, sensitive correlation with disease severity. NORMAL level is around 0.	Helps in interpretation of other indicators, by quantifying acute phase situation. Should have inverse correlation with prealbumin etc, in an adequately nourished patient.
Erythrocyte sedimentation rate (ESR)	A less specific indicator of acute phase response.	INCREASED in acute phase and inflammation. DECREASED in CCF, sickle cell anaemia and polycythaemia.	C-reactive protein is a better indicator of the acute phase response.
White cell count (WCC)	(= total of lymphocytes, neutrophils, basophils, eosinophils.) A good general indicator of infection and stress.	INCREASED in tissue damage and infection. DECREASED in immunocompromised patients.	Decreases promptly as infection resolves.
Lymphocytes (Total lymphocyte count: TLC)	Marker of bone marrow and immune function. Good predictor of healing. ⁸⁸	DECREASED in the acute phase response and in immunocompromised patients.	Increases as acute phase response is decreasing.
Neutrophils	Immune cell that engulfs and destroys bacteria. A marker of bacterial infection.	INCREASES in infection DECREASES in neutropenic immunocompromised patients.	Decreases promptly as infection resolves.

Clinical assessment and monitoring

Physical examination of the patient is important during the initial assessment, particularly in critical illness when other indicators are affected by the patient's acute condition.

Nutritional assessment

MEASURE	DESCRIPTION	METHOD OF MONITORING	IDEAL FREQUENCY OF MONITORING
Lean tissue stores	= muscle mass Main determinant of resting metabolic rate; decreases in critical illness and immobility. Lost during rapid weight loss, regained only slowly	Assess: <ul style="list-style-type: none"> temporal muscles (should be flat or plump, not hollowed) clavicle (should not be prominent with hollowing; should not be visible at all in men) shoulder (should be rounded, not square looking with prominent bones) scapula (should not be prominent; surrounding ribs should not be prominently visible) quadriceps (should be plump with good tone, and without bone dent or bony prominence at knee) calf (should be plump with good tone) interosseus muscle (between thumb and forefinger, should be plump or flat, not depressed) 	Baseline and then weekly-monthly in longer term care.
Adipose tissue	= fat mass Has minimal metabolic activity at rest, but the added weight increases energy expenditure during activity. Gained particularly with rapid weight gain	Assess: <ul style="list-style-type: none"> fat pads under eyes (should be slightly plump, not hollowed) triceps skin fold (should have substantial fold, not thin or loose) biceps skin fold (should have substantial fold, not thin or loose) 	
Skin condition	Indicator of general nutritional status, also often first sign of micronutrient deficiencies, esp protein, zinc, essential fatty acid, vitamin C and vitamin E nutrition.	Examine skin appearance with particular attention to wound sites, check areas not exposed to sun which should be intact without significant blemishes, soft, dewy. Wounds should look clean and pink, without very red or gummy edges. Sores, bruising, dryness or flaking can all be significant. Breakdown at corners of eyes, nose and mouth (and tongue, gums) are significant in vitamin deficiencies.	Better for initial assessment than for monitoring as changes are often slow and difficult to quantify. Objective tools are useful (such as the PUSH tool for wound healing). ⁸⁹
Hair/nails	Indicator of general nutritional status, also protein, zinc, vitamin C and vitamin E nutrition.	Inspect hair, test pluckability of individual hair. Should be shiny, not coarse / dry. Loss of pigmentation, and easy pluckability may be significant. Fingernails should have a slight gloss, pink nail bed and white lunula. Horizontal ridges,	Good for initial assessment but not for monitoring in most patients, as changes are extremely gradual.

MEASURE	DESCRIPTION	METHOD OF MONITORING	IDEAL FREQUENCY OF MONITORING
Nails cont'd.		yellowing, pale nail bed, loss of lunula, raised nail edges can all be significant.	Indicates long term nutritional status.
Fluid status	Patients who can drink to thirst and have normal renal function and no abnormal losses should maintain normal fluid status. Involuntary nutrition, altered renal function, or increased losses will all increase risk of abnormal fluid status.	<p>Assess dehydration by:</p> <ul style="list-style-type: none"> • dry skin, dry mucosa, reduced skin turgor (turgor not useful indicator in elderly) • reduced urine output • very yellow or dark urine • low blood pressure, increased heart rate <p>Abnormal fluid (such as ascites, oedema) should be taken into consideration. (Dehydrated patients can still be oedematous.)</p> <p>Note: in the critically ill, fluid balance would normally be monitored closely by medical/nursing staff. The dietitian should still be aware of the patient's fluid status and the team's goals for fluid management. On the ward level, the dietitian may need to take an active role in ensuring that the patient's fluid requirements are met.</p>	Daily or more frequently depending on patient stability.

Day-to-day management of a parenterally-nourished patient requires attention to practical aspects of parenteral nutrition. (See *Troubleshooting* section for management of nutrition problems.)

Nutrition support management

MEASURE	DESCRIPTION	METHOD OF MONITORING	IDEAL FREQUENCY OF MONITORING
Nutrition delivered	<ul style="list-style-type: none"> • is the nutrition infusion rate correct? • has the patient received the prescribed parenteral nutrition including micronutrients? • reasons for interruptions to nutrition 	<p>Hospital flowsheet or fluid balance charts</p> <p>Pump with "total volume delivered" function</p> <p>Medical record documentation</p>	Daily in acute care situation; 2-3 times weekly in stable hospital patients; weekly – monthly in long term care.
Care of intravenous access site	<ul style="list-style-type: none"> • regular flushing of the intravenous device • access site care • monitoring patient vital signs (temp, heart rate, BP) for possible sepsis 	<p>Hospital flowsheet/ care plans; medical record documentation.</p> <p>Examination of access site for signs of redness or irritation.</p>	At least daily. Vital signs at least four-hourly in the acute setting.
Tolerance of parenteral nutrition	<ul style="list-style-type: none"> • is the patient metabolically tolerating the required amount of parenteral nutrition? 	<p>Blood glucose levels</p> <p>Serum triglycerides levels</p>	Blood glucose levels usually 4-6 hourly in acute care situation (hourly when starting and stopping); 2-3 times weekly in stable hospital patients and weekly to monthly in long term care. Triglycerides weekly in acute care, and monthly, if possible, in long term care.

Dietary intake

Adequacy of nutrition support

MEASURE	DESCRIPTION	METHOD OF MONITORING	IDEAL FREQUENCY OF MONITORING
Nutritional input	<ul style="list-style-type: none"> • is the patient receiving/tolerating the prescribed amount of parenteral nutrition? • is the type of parenteral nutrition solution appropriate for the patient's needs (energy and protein needs, RDI volume)? • is oral/enteral intake (if applicable) increasing or decreasing? 	Hospital flowsheet or fluid balance charts Pump with "total volume delivered" function Medical record documentation Food charts/observation Patient report of intake	Daily in acute care situation; 2-3 times weekly in stable hospital patients; weekly – monthly in long term care.
	<ul style="list-style-type: none"> • is the patient receiving adequate fluid?⁹⁰ 	Free water input should match fluid output in a stable patient. Input includes: water from parenteral nutrition solution, line flushes, other IV fluids, fluids given with drugs, any oral/enteral fluid intake. Output could include: urine output, stoma/faecal output, losses from wounds/fistulae, discarded gastric aspirates/vomit, insensible losses (perspiration, breath moisture) increased in fever.	
Review of requirements	<ul style="list-style-type: none"> • have requirements changed (due to new infections or surgery, or improvement in condition, or change in activity level)? • is amount of parenteral nutrition still appropriate to meet needs? Has oral/enteral intake (if applicable) changed? • is nutrition regimen still appropriate? 	Patient weight monitoring Biochem/haem Medical record documentation Review estimation/measurement of energy expenditure Clinical progress	Weekly in acute care situation; monthly in stable hospital patients. 1-6 times per year in long term care.

ISSUES IN LONG-TERM PARENTERAL NUTRITION

Parenteral nutrition is a life-saving therapy for many patients. With proper management, patients can live for many years with parenteral nutrition as their sole source of nutrition.⁹¹ However, with prolonged use of parenteral nutrition, new issues arise. These considerations for long-term parenteral nutrition apply to patients who require it for longer than three to six months.

Complications of long-term parenteral nutrition

ISSUE	DESCRIPTION	MANAGEMENT
Metabolic bone disease (osteoporosis and osteomalacia)	Loss of bone mass and structure, due to both the underlying disease state and direct effects of the parenteral nutrition. Common in long-term parenteral nutrition: prevalence of osteoporosis and osteomalacia in patients receiving parenteral nutrition for longer than 3 months is 40% and 80% respectively.	All patients receiving long-term parenteral nutrition should have their bone mineral density screened. Dual energy x-ray absorptiometry (DXA) is recommended yearly in high-risk people and every 2-4 years in low risk groups. ^{92,93} (High risk groups include menopausal females, smokers, history of fractures or those with malabsorption symptoms.) At the same time Vitamin D, phosphate and magnesium levels should be monitored so that deficiencies can be corrected. Reduce risk by encouraging weight-bearing exercise, tapering corticosteroids where possible, encourage smoking cessation, consider hormone replacement therapy in post menopausal women. Ensure parenteral nutrition solution contains sufficient vitamins and minerals for bone health, including calcium, magnesium and phosphorus. Avoid aluminium toxicity (check individual parenteral nutrition formula with pharmacist; minimise IV albumin which is high in aluminium) NOTE: Cyclic parenteral nutrition does not reduce the risk of metabolic bone disease.
Liver dysfunction - cholestasis	Impaired bile secretion or direct biliary obstruction. Characterised by elevated GGT, ALP &/or bilirubin levels.	Reduce total calories and/or glucose infusion rate. ^{42,59,60,96} Keep lipid to less than 1g/kg per day. ⁹⁴ Enteral/oral nutrition (even minimal) reduces risk. Higher risk of gallstones may require a prophylactic cholecystectomy in long-term patients.
Liver dysfunction – steatosis (fatty liver)	Accumulation of fat in the liver, interfering with normal liver functioning. Characterised by elevations in levels of transaminases – AST and ALT.	Reduce total calories (from glucose and lipid) and keep lipid to less than 1g/kg per day. ⁹⁴ Cyclic parenteral nutrition allows mobilisation of fat during fasting, and may reduce fatty liver. ^{42,59,60,96}
Hyper-manganesaemia	Accumulation of manganese in the body, leading to brain and liver complications.	Monitor manganese levels in all long-term parenteral nutrition patients (see <i>Monitoring</i> section). Trace element dosage may need to be reviewed. ⁹⁵

ISSUE	DESCRIPTION	MANAGEMENT
Gut atrophy	Normal intestinal functioning (including motility, secretions, gut barrier against bacteria and endotoxin, and immune function of the gut) is stimulated by the presence of nutrients in the gut. Lack of enteral nutrition may promote gut atrophy, reducing the gut's immune capability, absorptive capacity, and barrier function. ^{3,4,5}	Ideally the patient receiving parenteral nutrition will still have some oral or enteral nutrition to maintain normal gut functioning. Even a low rate of enteral nutrition (10-30mL/h of standard feeding formula) may be adequate to achieve this. When recommencing oral or enteral nutrition in a patient who has been receiving sole parenteral nutrition for some time, it may be necessary to start and increase intake slowly to reduce the risk of malabsorption.
Renal dysfunction	Gradual decline in renal function not associated with known pre-existing renal impairment.	Ensure that fluid requirements are fully met. Check with pharmacist regarding possible nephrotoxic effects of current medications. Review chromium requirements as excess can affect renal tubules. ⁹⁶

Home parenteral nutrition

Patients requiring parenteral nutrition in the long term may, subject to availability and patient suitability, be discharged home with self-managed parenteral nutrition. This is very expensive, and funding options vary widely across different areas. This issue of cost needs to be considered carefully at the beginning of the planning process. Patients who are to go home on parenteral nutrition are trained for several weeks before discharge, usually by a TPN nurse, in how to hang and administer their parenteral nutrition. Patients need to be stable on their home regimen (which is often a cyclic regimen) before discharge, and be competent in maintaining aseptic technique, caring for their dressing, storing/handling their parenteral nutrition products correctly and recognising/managing problems that may occur.⁹⁷ It is important that the patient has appropriate facilities and support at home, and continues to receive close health monitoring and support, ideally by a multi-disciplinary team. See *Monitoring* section for details.

Transitional feeding

Transitional feeding describes the process by which a parenterally-fed patient changes over to enteral or oral nutrition and ceases parenteral nutrition. The ultimate goal of transitional feeding is that the patient's full nutritional needs will be met with oral/enteral intake alone. Ideally, the transition will be a smooth process, which may take a few days or several weeks. Abrupt cessation of parenteral nutrition is not recommended, as nutritional status may be compromised if the patient then fails to establish adequate oral/enteral intake. Reductions in the parenteral nutrition infusion should be made in proportion to increases in oral/enteral intake.

Options for transitional feeding

Satiety and lack of appetite are common barriers to achieving an adequate oral/enteral intake. Transitional feeding strategies aim to promote the patient's normal appetite and encourage an increase in oral/enteral intake, so that reliance on the parenteral nutrition is gradually reduced.

Dual feeding

When enteral tube feeds are started, the patient may be receiving both parenteral and enteral nutrition simultaneously for a time: this is called dual feeding. Typically the parenteral nutrition rate is decreased as the enteral nutrition rate is increased, maintaining a constant (goal) energy input. See *Regimens for Parenteral Nutrition* section for more details on dual feeding. In general, supplemental parenteral nutrition is still indicated when the patient is tolerating less than about 75% of goal enteral feeds.

Cyclic parenteral nutrition

Infusing the parenteral nutrition cyclically (for example only overnight – for 8-16 hours) encourages oral/enteral intake during the day. The length of the overnight parenteral nutrition cycle can be adjusted depending on the oral/enteral intake during the day, but will also depend upon the patient's tolerance of the higher parenteral infusion rates needed. See *Regimens for Parenteral Nutrition* section for more details on cyclic parenteral nutrition.

Monitoring during transitional nutrition

Refer also to *Monitoring* section.

During transitional feeding, supplemental parenteral nutrition will be needed until oral or enteral intake is adequate. Requirements for supplemental parenteral nutrition should be calculated carefully, based on oral/enteral *absorption*, not just total *intake*. Any losses need to be monitored carefully.

Oral/enteral intake

Food/fluid charts can be used to record the patient's oral/enteral intake. Energy, protein and fluid intakes can then be monitored by the dietitian and compared with the patient's requirements (for example by calculating the percentage of requirements being met by oral/enteral intake). The parenteral nutrition regimen should be adjusted accordingly, decreasing infusion rate or infusion time as the oral/enteral intake increases.

Fluid balance

When the rate or volume of parenteral nutrition is reduced, it is important to monitor the patient's fluid input to ensure that requirements are still being met. This is particularly important if there are ongoing high output losses, or when the oral diet has a modified texture and/or fluids are thickened (as fluid intake will often be less than with thin fluids). If oral fluid intake remains inadequate, an additional source of fluid may be needed and feeding tube insertion may be indicated.

Discontinuing parenteral nutrition

The goal of transitional feeding is the eventual cessation of the parenteral nutrition, but it is important that this occurs at the appropriate time.

Stopping the parenteral nutrition infusion

In general, parenteral nutrition may be ceased once the patient is able to maintain an adequate oral/enteral intake. This may require improvement in their gut function or their general wellbeing, and the time required for this will differ between individual patients.

If the patient is able to consume around 75% of their nutritional requirements orally/enterally, it may be appropriate to discontinue the parenteral nutrition and use oral supplements or supplemental tube

feeding to meet the remainder of the patient's requirements. In long term patients it is important to be sure that they can maintain their nutritional status with oral/enteral nutrition before parenteral nutrition is ceased and the device removed.⁹⁸ Some patients may need to continue some form of parenteral nutrition support (such as periods of full parenteral nutrition, or just periodic IV 'top-ups' of fluid and electrolytes) to maintain nutritional status.

For some patients, additional fluids, electrolytes, or medications, may be easier to give intravenously and this may continue for some time after parenteral nutrition has ceased.

Removing the intravenous access device

The time frame for removing intravenous access will vary greatly between patients and the reason for the original line insertion. In particular, it is important to make clear to the team any concerns about the patient's gut function, oral/enteral intake or nutritional status, where the patient might benefit from a longer period of parenteral nutrition support. This is also an opportunity for the team to discuss the patient's possible future needs for parenteral nutrition support (such as planned surgery or other treatments which might compromise oral/enteral intake or nutritional status).

Discharge/transfer of the parenterally-nourished patient

When the patient is transferred from one health care facility to another, or discharged home under the care of their local doctor, it is important to provide adequate information to enable continuity of nutritional care. For the nutrition support patient, particular information that is useful to include in a handover/discharge summary would include:

1. Date when the intravenous access device was inserted, type of device (brand, size, type)
2. Date when parenteral nutrition commenced
3. Indication for parenteral nutrition
4. Nutrition route (central or peripheral)
5. Name and manufacturer of parenteral nutrition solution, and composition details if solution is not a standard formulation
6. Types and compositions of current parenteral micronutrient additives
7. Reason for choice of the particular nutrition solution and additives
8. Parenteral nutrition regimen, including rate, hours of infusion, and tapering procedure if applicable; dosing schedule for micronutrient additives if applicable
9. Total volume of parenteral solution per day; amount of energy, protein, fat, glucose, electrolytes and fluid provided
10. Type of oral/enteral intake (if relevant), or reason why patient is kept NBM
11. Other relevant information (such as nutritional assessment data, estimated requirements and how these were calculated)
12. Other recommendations (such as weight monitoring)
13. Follow-up plan

TROUBLE SHOOTING GUIDE

Line problems

Blocked intravenous line

PROBLEM: BLOCKED INTRAVENOUS LINE		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Insufficient flushing, allowing clot or coagulation to build up	Check connections and line for visible blockage. Attempt to aspirate catheter and then flush with normal saline. Flush with an anti-coagulant if a blood clot is suspected.	Prevent by regular flushing of the line. Flush before and after administration of the parenteral nutrition solution.
Thrombosis due to blood flowing back down the line (when blood is taken, or due to line being disconnected, patient coughing/straining or pump failing to exert adequate pressure)	Flush with an anti-coagulant.	Ideally do not use parenteral nutrition line for taking blood. Ensure line is flushed with saline if blood is taken from the line. Some lines have a valve to prevent blood flowing back down the line and reduce blockage risk.
Line is incorrectly positioned (eg peripheral line tip is too near to a pair of vein valves, or central line is kinked or compressed by a bone or by the sutures holding it in place)	Adjust line position if possible Line may need to be removed and resited	Prevent by careful selection of site prior to insertion. Ultrasound or angio check of the intended insertion site can help to identify existing vein problems (such as scar tissue, thrombosis or unusual anatomy) that may make correct insertion difficult or inappropriate for that site.
Precipitated lipid or medication	Dispose of the giving set and attempt to aspirate from the blocked lumen. If blood is able to be aspirated, flush the line well with normal saline and resume parenteral nutrition infusion. In desperate cases the line can sometimes be saved by dissolving the blockage (with dilute HCl if calcium-phosphate is suspected; sodium	Prevent by thorough flushing with saline in between administering different substances or sampling blood. In general, one lumen of the line should be isolated for parenteral nutrition and not used for anything else. Review all additives being used with pharmacist: these may need modification to prevent future blockage. Always check with pharmacist for compatibility before adding anything to a parenteral nutrition solution. Common problems are due to calcium and

PROBLEM: BLOCKED INTRAVENOUS LINE

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Precipitated lipid or medication, cont'd.	bicarbonate if heparin or antibiotics are suspected; ethyl alcohol if lipid clot is suspected.) ⁹⁹ This is not recommended practice, however.	phosphate interaction, antibiotics, and lipid. Always inspect solution before starting infusion and do not use a solution that looks 'wrong' (eg emulsion has separated, or particles are visible in the solution)

Suspected line infection

PROBLEM: SUSPECTED LINE INFECTION

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Contamination of the line (eg with skin bacteria) or colonisation of the line with existing blood-borne pathogens	<p>Obtain blood samples from all lumens of the venous access device as well as peripherally and send for culturing to establish whether the line is the source of bloodstream infection (ie if the culture count is higher for the line than for the peripheral site). Consider other sources of infection.</p> <p>Best treatment is removal of the line, particularly if the patient is immunocompromised, has endocarditis, or the infection is fungal rather than bacterial. However, in patients requiring long-term access, particularly when access was difficult, an attempt may be made to avoid line removal. (Each new line insertion can create scarring and promote thrombosis, making future access more difficult.) Cease infusion and consider systemic antibiotic treatment or use an 'antibiotic lock' (every 24 hours for 7-10 days, fill the infected lumen with concentrated vancomycin solution and leave for 12 hours, flush through or withdraw before resuming nutrition infusion – cyclic parenteral nutrition can still proceed.</p>	<p>Prevent by close attention to hygiene: during insertion of catheter, strict sterile technique and full barrier precautions should be used. Aseptic technique should be used for preparation of parenteral nutrition solutions/additives and all manipulations of the venous access line. Care for the site appropriately (see <i>Care of the venous access device</i>). As far as possible, minimise the number of lumens and line manipulations.</p> <p>Antibiotic-impregnated lines are available which may reduce infection risk.</p>
Prolonged use of venous access device	Venous access device should be changed regularly, according to recommendations (time period differs for different devices and sites).	Monitor the line for discharge at the insertion site, pain, redness. Monitor the patient for any increase in temperature, or rigors. May need to change the line and obtain alternative IV access in a different location

PROBLEM: SUSPECTED LINE INFECTION

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Contaminated parenteral nutrition solution	Cease infusion and investigate. Take specimen of solution for microbiological testing. Identify batch number of the suspected solution and remove from the hospital supply all bags from same batch until investigation is complete. Keep a sample of the solution in case testing is required. Inform the parenteral nutrition supplier.	Adhere to recommended hang-times for solutions. ⁶⁴ The date, time and batch number (on the parenteral solution bag) should be recorded in the patient's medical record each time a new bag is hung, to enable tracing of suspected contamination.

Blood vessel problems

Phlebitis

PROBLEM: PHLEBITIS (irritation of peripheral blood vessel)

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Leaving catheter in too long	Change the catheter promptly when indicated	
Using a catheter that is too large for the vein	Use the smallest gauge catheter available	
Traumatic insertion of the catheter	Ideally peripheral parenteral nutrition catheters should be inserted only by specialised staff, particularly when the patient has poor venous access.	
Chemical irritation from medications	Ideally isolate one lumen for parenteral nutrition only. Consult pharmacist.	
Infusing excessively high-concentration solution	Resite peripheral cannula. Soothing anti-phlebitis dressings are available for site care.	
		Prevent by ensuring that peripheral solutions are <900mOsm/kg and that an appropriate vein is being used

Thrombosis

PROBLEM: THROMBOSIS		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Coagulation is activated by damage to the vein wall or other inflammation, and the line interferes with normal blood flow, allowing clot to form.	Flush with an anti-coagulant if line is blocked. Venogram or ultrasound is used if thrombosis of the blood vessel is suspected. The parenteral nutrition infusion is stopped; catheter may need to be removed.	Prevent by regular flushing of the device and appropriate selection of catheter site. For peripheral parenteral nutrition, use the smallest gauge catheter available. Some lines have a valve to prevent blood flowing back down the line and reduce blockage risk. Ideally peripheral parenteral nutrition catheters should be inserted only by specialised staff, particularly when the patient has poor venous access.
Fibrin sheath formation (a 'sleeve' of clot surrounding the outer surface of the catheter tip in the blood vessel)	Anticoagulant/antithrombolytic therapy may be used. Venogram or ultrasound is used if thrombosis of the blood vessel is suspected. The parenteral nutrition infusion is stopped; catheter may need to be removed.	

Line displacement

PROBLEM: LINE DISPLACEMENT		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Accidental bumping or pulling of the device or administration tubing	Cease infusion and monitor the patient for adverse events. Check catheter placement with x-ray or fluoroscopy. Device may need to be resited.	Appropriate dressing can help protect against accidental dislodgement. See <i>Care of the venous access device</i>
Inappropriate site selection	(Access device is not removed unless absolutely necessary as each new line insertion can create scarring and promote thrombosis, making future access more difficult.)	Ultrasound or angio check of the intended insertion site can help to identify existing vein problems (such as scar tissue, thrombosis or unusual anatomy) that may make correct insertion difficult or inappropriate.

Formulation problems

Stability problems

PROBLEM: SUSPECTED STABILITY PROBLEMS ('looks wrong')		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Inappropriate storage or handling (ie high temperature, addition of incompatible substances, manufacturing error) causing precipitate, or separation of the emulsion, or solution discolouration etc	Do not administer the infusion. Keep the solution to show manufacturer. The date, time and batch number (on the parenteral solution bag) should be recorded in the patient's medical record each time a new bag is hung, to enable tracing of problems with the solution.	Ensure that manufacturer's advice is followed regarding correct storage of parenteral nutrition products. Always check compatibility before adding anything to a parenteral nutrition solution.

Drugs related to parenteral nutrition

This section discusses basic information for a few selected medications only. Drug-nutrient handbooks, and your pharmacist, can provide more details.

PROBLEM: DRUG-NUTRIENT INTERACTIONS		
DRUG	ISSUE	INTERVENTION / REMARKS
Phosphate and calcium interaction	Both calcium and phosphate are needed by the body. Calcium phosphate is an insoluble compound and will precipitate if formed in the parenteral nutrition solution. Adjustments to the dose or timing of calcium and phosphate supplementation may be needed.	Check with pharmacist if the patient requires additional phosphate or calcium, as it may be necessary to calculate the dose limits, and/or separate the doses by 2 hours, to avoid precipitation.
Propofol a short-acting sedative that is water-insoluble and delivered in the form of a 10% lipid emulsion (just like the type used in parenteral nutrition)	If the patient is continuing on a significant rate of propofol, its contribution to total energy and fat intake needs to be considered. A high-protein fat-free parenteral nutrition solution is ideal in this situation, to ensure that the patient's needs are met while propofol is providing significant fat. If this is not available, it may be necessary to reduce parenteral nutrition infusion rate to avoid overfeeding but this can compromise protein intake. If this is the case, discuss with medical team: sometimes an alternative sedative can be used.	10% lipid provides 1.1 Cal/mL (0.1g fat/mL) 10% lipid emulsion has a less physiological (chylomicron-like) ratio of phospholipid to triglycerides in the lipid droplets, compared to the 20% lipid usually used in parenteral nutrition formulations, and so may be less well utilised.
Vitamins and minerals	Vitamins and minerals are required by the human body and are usually added to the parenteral nutrition solution. Excessive amounts of some of these can destabilise the solution.	Check with pharmacist. Product information for parenteral nutrition formulations usually gives the dose limits for various micronutrient additives.

PROBLEM: DRUG-NUTRIENT INTERACTIONS

DRUG	ISSUE	INTERVENTION / REMARKS
Insulin an analog of the pancreas's secretion	In some facilities, insulin is added to the parenteral nutrition bag. Advantages include: ensures continuous insulin, which is provided only when patient is receiving glucose and stops if the parenteral nutrition stops; reduces need for other insulin. Disadvantages include: insulin adsorbs to the plastic of the bag so the actual delivered dose is uncertain; cannot remove the insulin from the bag (so if insulin requirements change, the whole bag may be wasted)	Discuss with medical team and pharmacist.

Intolerance

Allergic reaction to parenteral nutrition infusion

PROBLEM: ALLERGIC REACTION TO THE INFUSION

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Allergy to egg yolk (egg lecithin is used as the emulsifier in parenteral lipid)	Cease lipid infusion and confirm the reaction with a controlled trial of lipid. Essential fatty acid (EFA) requirements could be met orally if possible (preferable) or by rubbing EFA-containing oil such as sunflower/safflower into the forearms daily (a pleasant lotion can be made up by a pharmacist for this purpose. ¹⁰⁰) This may not be adequate to reverse an existing deficiency, however, and it has also been suggested that this skin treatment may address only the skin symptoms of EFA deficiency.	Low-rate or intermittent lipid may still be tolerated by patients whose symptoms are not life-threatening (eg headache, nausea, dizziness). Otherwise, lipid must be avoided. Use a lipid-free parenteral nutrition formulation, with oral lipid as tolerated.
Allergy to soy (parenteral lipid contains soybean oil) or fish (if fish oil is being used)		
Allergy to components of the micronutrient additives	Cease use of all additives and confirm the reaction with a controlled trial of each additive one at a time. A trial of an alternative product may be indicated, or alternatively micronutrient requirements could be met orally.	Low-rate or intermittent use of the additive may still be tolerated by patients whose symptoms are not life-threatening (eg headache, nausea, dizziness). Otherwise, the additive must be avoided.

Nausea

If the patient experiences nausea, assess the cause and treat appropriately. Nausea is associated with many different medical conditions and medications, unrelated to parenteral nutrition. It is usually not necessary to cease the parenteral nutrition infusion.

PROBLEM: NAUSEA OR VOMITING		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Response to metabolic signals stimulated by intravenous nutrition infusion (IV lipid emulsion can reduce gastric emptying, causing ‘full’ feeling or even nausea)	In general, it is important not to compromise the patient’s nutrition if there is another way that the problem can be managed. Anti-nausea medications may be needed. Try cyclic parenteral nutrition. In contrast, some patients feel worse with a higher rate of infusion and temporarily reducing infusion rate, and running the parenteral nutrition continuously (24 hours) or omitting the lipid may help.	Ensure blood glucose levels are well-controlled. Monitor triglycerides. Pleasant distractions such as activities and visitors, encouraging the patient to relax etc may also help reduce the effects of nausea.
Allergy or infection	Nausea/vomiting may be a symptom of allergic reaction or an infected line. Refer to appropriate sections of this Troubleshooting Guide (above).	
Medications (eg opioids)	Review medications and cease non-essential medications. Consider prokinetic agent (eg: metoclopramide, erythromycin) if the patient is also having any oral/enteral intake.	

Appetite problems

If the patient is receiving an oral diet in addition to parenteral nutrition, a poor intake is often attributed to the parenteral nutrition having a detrimental effect on appetite, however it is important to consider that the underlying medical condition is a likely cause. Look for other possible causes such as medications before altering nutrition regimen.

PROBLEM: APPETITE PROBLEMS		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Feedback signals caused by raised blood glucose or lipid levels, or abnormal electrolytes	In general, it is important not to compromise the patient’s nutrition if there is another way that the problem can be managed. Try cyclic parenteral nutrition. In contrast, some patients feel more full with a higher rate of infusion and temporarily reducing infusion rate, and running the parenteral nutrition continuously (24 hours) may help.	Ensure blood glucose and electrolyte levels are well-controlled. Monitor triglycerides.
Medications (eg opioids)	Review medications and cease non-essential medications. Consider prokinetic agent (eg: metoclopramide, erythromycin) which may help the patient feel less ‘full’.	

Constipation

Patients receiving only parenteral nutrition will usually still pass a small stool every 3-7 days which will often not have a normal consistency due to lack of enteral/oral intake. Constipation can still occur and may be uncomfortable for the patient.

PROBLEM: CONSTIPATION		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Medications	Review medications for possible causes of constipation (eg opioids)	
Inadequate fluid	Ensure adequate fluid. Review requirements and monitor intake and output.	Discuss with team. Additional IV fluids may be needed if requirements are increased.
Lack of normal food and activity, lack of toileting privacy	Discuss issues with team. Mobilising where possible, and attention to privacy, may help.	

Metabolic abnormalities

Refeeding syndrome

PROBLEM: REFEEDING SYNDROME^{101,102,103}		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Resumption of nutrition in a patient who is severely malnourished or who has adapted to a state of starvation	<p>Recognise the risk - patients who have:</p> <ul style="list-style-type: none"> • Alcoholism • Malnutrition • Anorexia nervosa • Loss of >10% of body weight within 3 months (including obese patients) • Low serum levels of phosphate, potassium, magnesium (however, patients with normal levels may still be at risk) • 7-10 days of fasting and evidence of physiological stress/depletion (weakness, shortness of breath, bradycardia, peripheral numbness) <p>Discuss with team. In high-risk patients may need to give IV thiamine, multivitamin and supplement electrolytes, then retest levels, before commencing nutrition support.</p> <p>Start parenteral nutrition infusion at 50% of the patient's <i>basal</i> requirement (eg 5-10Cal/kg) and increase gradually. In a high-risk patient it may be appropriate to increase the rate only every second</p>	<p>Refeeding syndrome can occur with oral, enteral or parenteral nutrition. It may emerge as late as a week after nutrition support starts.</p> <p>When electrolyte levels are stable within the normal range, and the patient is tolerating parenteral nutrition at the goal infusion rate, electrolyte supplementation can be ceased.</p>

PROBLEM: REFEEDING SYNDROME^{101,102,103}

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
<p>Refeeding syndrome, cont'd.</p>	<p>day, aiming to reach goal over a week or more. Fluid balance should be monitored as refeeding can cause fluid overload due to sodium shift. Fluid and/or sodium restriction may be required.</p> <p>Check electrolytes within 6 hours of commencing nutrition support and then at least daily during first week. Supplement as needed. Stop parenteral nutrition infusion and supplement if any electrolyte level drops to critically low level.</p> <p>Check electrolyte levels for three days after stopping supplementation.</p>	

Overfeeding

Refer to *Monitoring* section for details on estimation of energy requirements.

PROBLEM: SUSPECTED OVERFEEDING

SIGN	ACTION	OTHER INTERVENTION / REMARKS
<p>Increased blood glucose levels or insulin requirements</p>	<p>Check glucose infusion rate. Glucose infused at more than about 5mg/minute/kg body weight will exceed the cell's glucose oxidation capacity and may not be tolerated in critically ill patients. A higher-lipid, lower-glucose formulation may help here. However, healthy ambulant patients (such as those on home parenteral nutrition) may receive 5-10mg/min/kg and may tolerate more than 20mg/min/kg when cyclic parenteral nutrition is used. Discuss with medical team. In general, nutrition provision should not be compromised in order to control blood sugar levels. The patient's need for insulin should be reviewed. Very high blood glucose levels (such as >20mmol/L when the patient is already receiving insulin) may need temporary stopping or reduction of parenteral nutrition infusion rate, to gain control. Consider possibility of undiagnosed diabetes.</p>	<p>Blood glucose level rises in stress and sepsis and hyperglycaemia is associated with poor outcomes.^{104,105} Moderate control of blood glucose level (6-10mmol/L) in this situation appears to improve outcomes and can be achieved by increasing insulin rather than altering nutrition input)^{106,107} as long as hypoglycaemia is avoided.¹⁰⁸ Chromium deficiency can reduce glucose tolerance. If deficiency is suspected, ensure that chromium needs are being met adequately. Starting parenteral nutrition infusions abruptly can (rarely^{74,75}) cause temporary hyperglycaemia, particularly with glucose rates above 5mg/min/kg and running the infusion at half the goal rate for an hour or two can prevent this.</p>
<p>Increased serum triglycerides</p>	<p>Check both fat and glucose infusion rates. Overfeeding with either fat <i>or</i> glucose can contribute to serum triglycerides²⁴ (fat</p>	<p>Giving parenteral lipid continuously along with the rest of the nutrition rather than</p>

PROBLEM: SUSPECTED OVERFEEDING

SIGN	ACTION	OTHER INTERVENTION / REMARKS
<p>Increased triglycerides, cont'd.</p>	<p>infused at more than about 0.11g/hour/kg has been associated with complications; glucose infused at more than about 5mg/minute/kg body weight will exceed the cell's glucose oxidation capacity. However, healthy ambulant patients (such as those on home parenteral nutrition) may receive glucose at 5-10mg/min/kg and may tolerate more than 20mg/min/kg when cyclic parenteral nutrition is used.) Discuss with medical team. Higher triglyceride levels (up to about 4.5mmol/L) are acceptable if the blood was drawn while parenteral lipid was infusing.^{38,109} If triglycerides are persistently above this level, or rising, then usually the parenteral nutrition infusion would be reduced or stopped for a period to see if this helps.</p>	<p>intermittently (such as twice per week) has been shown to lead to improved metabolism of the lipid.^{29,30} Also, using a 20% lipid emulsion is better utilised than 10% emulsion due to the more physiological (chylomicron-like) ratio of phospholipid to triglycerides in the lipid droplets. Check for pre-existing high triglycerides (prior to starting on parenteral nutrition). Retrospective laboratory testing is sometimes available for this.</p>
<p>Increased transaminases</p> <p>AST and ALT = liver enzymes aspartate aminotransferase and alanine aminotransferase</p> <p>also known as SGOT and SGPT (esp. in USA)</p>	<p>Check glucose infusion rate. Glucose infused at more than about 5mg/minute/kg body weight will exceed the cell's glucose oxidation rate. (However, healthy ambulant patients (such as those on home parenteral nutrition) may receive glucose at 5-10mg/min/kg and may tolerate more than 20mg/min/kg when cyclic parenteral nutrition is used.) Overnutrition, especially with excessive carbohydrate, can lead to fatty liver (abnormal liver function tests, esp. AST and ALT) and/or high triglycerides.²⁴</p>	<p>AST and ALT are found inside cells - ALT is mostly found in liver cells but AST is found in cells and in the mitochondria of skeletal muscle, heart, pancreas as well as the liver, so may be increased in general trauma. Chronic cholestasis can eventually lead to liver damage (from bile backflow) and raise transaminase levels. Poorly-perfused liver (= 'shock liver') due to ischaemia or blood loss/surgery/trauma, can also cause increased transaminases. No action is required other than to ensure patient is not being overfed. Liver damage due to choline deficiency can be another cause of increased transaminases.</p>
<p>Respiratory problems or difficulty weaning ventilation</p>	<p>Review requirements. Overfeeding can cause increased respiratory demand.²⁴ Although it has been claimed that a higher fat content is best for minimising respiratory quotient, the difference is not clinically significant as long as overfeeding is avoided.¹¹⁰</p>	
<p>Fluid overload</p>	<p>Review volume received, consider other fluid sources (other IV fluids, medications, line flushing)</p>	<p>Consider changing to a more concentrated parenteral formulation if available. Check with medical team re: other sources of fluid that could be reduced (eg</p>

PROBLEM: SUSPECTED OVERFEEDING

SIGN	ACTION	OTHER INTERVENTION / REMARKS
		unnecessary IV fluids).

Dehydration

Refer to *Monitoring* section for details on assessment of fluid status.

PROBLEM: DEHYDRATION		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Inadequate fluid intake	Review fluid requirements and ensure these are met with current parenteral nutrition formulation and IV fluids. This may need to be supplemented with additional IV fluids. In general, increasing the rate of nutrition infusion is not an appropriate way to increase fluid input as it is likely to result in overfeeding.	Consider changing to a less concentrated parenteral formulation if available. Hypertonic dehydration can occur when excessive protein and inadequate fluid is given to a patient who cannot drink to thirst or whose fluid losses are high, and who cannot concentrate urine (especially the elderly). ²⁴ This is rare with parenteral nutrition, however.
Excessive fluid losses (from diarrhoea / vomiting / diuresis / burns / fever / fistula etc)	Ensure that the patient is receiving adequate fluid to make up for losses. Review fluid requirements and ensure these are met with current parenteral nutrition formulation and IV fluids. (This may need to be supplemented with additional IV fluids if inadequate.)	Discuss with medical team. Address individual conditions as needed

Fluid overload

Refer to *Monitoring* section for details on assessment of fluid status.

PROBLEM: FLUID OVERLOAD		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Excessive fluid intake	Review volume received, consider other fluid sources (other IV fluids, medications, line flushing)	Consider changing to a more concentrated parenteral formulation if available. Check with medical team re: other sources of fluid that could be reduced (eg unnecessary IV fluids).
Compromised renal or cardiac function	Review volume of parenteral nutrition, consider other fluid sources that could be reduced (eg IV fluids). Renal or cardiac infection should be treated, discuss with team.	Consider changing to a more concentrated parenteral formulation if available. Check with medical team regarding appropriate fluid allowance.
Refeeding syndrome	Initiate parenteral nutrition gradually according to a set protocol with careful monitoring of fluid status. (See separate section on <i>Refeeding Syndrome</i> above for more details on this).	

Abnormal biochemical parameters

Refer to *Monitoring* section for details on assessment of biochemical parameters.

PROBLEM: ABNORMAL BIOCHEMISTRY		
CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Sodium – high (hyponatraemia)	Discuss with medical team. Increased fluid may be required, particularly if losses are increased (eg from diarrhoea, fistula)	Changing the sodium concentration of the parenteral nutrition formula rarely makes any difference as hyponatraemia is usually a fluid management problem: sodium input is not the main contributor to serum levels and parenteral nutrition solutions are generally low in sodium.
Sodium – low (hyponatraemia)	Discuss with medical team. Serum osmolality can help to identify the need for fluid restriction (if osmolality is low, check that patient is not receiving excessive fluid) or for extra sodium in the parenteral nutrition solution and/or extra fluids as saline (if osmolality is normal or high).	If sodium losses (in urine or GI output) are high, it may also be necessary to replace these.
Potassium – high (hyperkalaemia)	It may be necessary to reduce potassium content of the parenteral nutrition solution, or change to a low-potassium solution. Discuss with medical team. Some medications cause potassium retention.	Potassium may be raised in situations of metabolic acidosis, when there is anaerobic metabolism (in hypoxic or poorly-perfused or damaged tissue). Dextrose + insulin infusion, or dialysis, may be used for acute management of hyperkalaemia.
Potassium – low (hypokalaemia)	Check that patient is not receiving excessive fluid. Manage causes (eg vomiting, diarrhoea, inadequate intake, Refeeding Syndrome, alkalosis). Discuss with medical team. May need potassium supplementation, either as a separate IV infusion or by increasing potassium content of the parenteral nutrition solution. Close monitoring is required.	Discuss with medical team. Some medications (eg some diuretics) may increase potassium losses.
Calcium – high (hypercalcaemia)	Check that the patient is receiving adequate fluid. Changing the calcium content of the parenteral nutrition solution rarely makes any difference due to large body store in skeleton. Note need for “corrected calcium” calculation if albumin level is abnormal (most labs do this automatically).	Discuss with medical team. Can be due to excess vitamin D, A or calcium supplementation (particularly with poor renal function or alkalosis). There are many other possible causes (eg malignancy, medications).
Calcium – low (hypocalcaemia)	Vitamin D deficiency can cause hypocalcaemia in patients deprived of sun exposure, particularly if inadequate Vitamin D is provided, if the patient is receiving phenytoin (which enhances Vitamin D destruction) or if the patient has renal failure or malnutrition/malabsorption.	Excess IV phosphate supplementation, parathyroid abnormality or hypomagnesaemia can also cause hypocalcaemia. Changing the calcium content of the parenteral nutrition solution rarely makes any difference.

PROBLEM: ABNORMAL BIOCHEMISTRY

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
Phosphate – high (hyper-phosphataemia)	It may be necessary to change to a low-phosphate parenteral nutrition solution. Discuss with medical team.	Can be caused by excess vitamin D supplementation.
Phosphate – low (hypo-phosphataemia)	Discuss with medical team. May need phosphate supplementation. Note risk of interaction between calcium and phosphate in parenteral nutrition if planning to increase phosphate in the solution. Manage causes (vomiting, malabsorption, Refeeding Syndrome, alkalosis).	Discuss with medical team. Some medications increase losses (eg diuretics).
Glucose – high (hyperglycaemia)	Discuss with medical team. In general, nutrition provision should not be compromised in order to control blood sugar levels. The patient’s need for insulin should be reviewed, and endocrinology consulted if needed. Very high BSLs (such as >20mmol/L when the patient is already receiving insulin) may need temporary stopping or reduction of parenteral nutrition infusion rate, to gain control. Check that the patient is not being overfed: glucose infused at more than about 5mg/minute/kg body weight will exceed the cell’s glucose oxidation capacity and may not be tolerated in critically ill patients. ²³ A higher-lipid (lower-glucose) formulation may help here. However, healthy ambulant patients (such as those on home parenteral nutrition) may receive 5-10mg/min/kg and may tolerate more than 20mg/min/kg when cyclic parenteral nutrition is used.	Blood glucose level rises in stress and sepsis and hyperglycaemia is associated with poor outcomes. ^{104,105} Moderate control of blood glucose (6-10mmol/L) in this situation appears to improve outcomes and can be achieved by increasing insulin rather than altering nutrition input) ^{106,107} as long as hypoglycaemia is avoided. ¹⁰⁸ Chromium deficiency can reduce glucose tolerance. If deficiency is suspected, ensure that chromium needs are being met adequately. Starting parenteral nutrition infusions abruptly can (rarely ^{74,75}) cause temporary hyperglycaemia, particularly with glucose rates above 5mg/min/kg and running the infusion at half the goal rate for an hour or two can prevent this.
Glucose – low (hypoglycaemia)	Discuss with medical team. In general, parenteral nutrition should not be used to supplement blood glucose levels beyond the patient’s overall nutrition requirements. It may be necessary to review the patient’s need for insulin.	Abruptly stopping parenteral nutrition can (rarely ^{74,75}) cause a rebound hypoglycaemia in some patients due to ongoing action of insulin (whether from pancreatic action or if patient is receiving insulin), particularly with glucose rates above 5mg/min/kg or where BSLs are generally unstable. This can be prevented by running the infusion at half the goal rate for an hour, or replacing it with 5% or 10% dextrose for an hour, before stopping completely.

PROBLEM: ABNORMAL BIOCHEMISTRY

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
<p>Triglycerides – high (hyper-triglyceridaemia)</p>	<p>Discuss with medical team. Higher triglyceride levels (up to about 4.5mmol/L) are acceptable if the blood was drawn while parenteral lipid was infusing.^{38,109} If triglycerides are persistently above this level, or rising, then usually the parenteral nutrition infusion would be reduced or stopped for a period to see if this helps. Confirm result by repeating the test after parenteral lipid has been stopped for 2 hours. Check that the patient is not being overfed with fat <i>or</i> glucose as either can contribute to serum triglycerides²⁴ (fat infused at more than about 0.11 g/hour/kg has been associated with complications; glucose infused at more than about 5mg/minute/kg body weight will exceed the cell's glucose oxidation capacity.) Giving parenteral lipid continuously along with the rest of the nutrition rather than intermittently (such as twice per week) has been shown to lead to improved metabolism of the lipid.^{29,30}</p>	<p>Overnutrition, especially with excessive carbohydrate (more than about 5mg/minute/kg body weight) can lead to fatty liver (abnormal liver function tests, esp. AST and ALT) and/or high triglycerides.²⁴ Using a 20% lipid emulsion is better utilised than 10% emulsion due to the more physiological (chylomicron-like) ratio of phospholipid to triglycerides in the lipid droplets. Check for pre-existing high triglycerides (prior to starting on parenteral nutrition). Retrospective laboratory testing is sometimes available for this. Consider carnitine deficiency (see <i>Micronutrients</i>).</p>
<p>Urea and creatinine – high</p>	<p>Discuss with medical team. In general, nutrition provision should not be compromised in order to control urea and creatinine levels. It may be necessary to change to a parenteral nutrition solution with a more moderate level of protein. In general, providing about 1.0-1.2g protein per kg body weight is a reasonable restriction unless the patient is not for dialysis.^{111,112}</p>	<p>A urea:creatinine ratio of >1:10 may indicate dehydration or GI bleeding.</p>
<p>Bilirubin - high</p>	<p>Parenteral-nutrition-related liver disease usually causes an increase in bilirubin in the first 1-2 weeks of parenteral nutrition, which resolves within 3-4 weeks. No action is required, apart from ensuring that the patient is not being overfed. Continuous three-in-one parenteral nutrition may be preferred to intermittent lipid.</p> <p>Increased bilirubin also occurs in cholestasis (where there is a biliary obstruction) which is more likely to occur in long-term parenteral nutrition where there is no enteral/oral intake. Try a cyclic parenteral nutrition regimen. Fish-oil based lipid has been suggested to help too.</p> <p>Allow some oral/enteral intake if possible; in particular foods high in fat can stimulate bile flow (eg regular oral/enteral dose of oil; or ice cream!)</p>	<p>Haem is released from red blood cells at the end of their life and recycled by the body. Haem is converted to bilirubin, and carried to the liver where one of the liver's functions is to conjugate it and excrete it in the bile. Haemolysis (eg from abnormal blood cells being destroyed by the spleen) increases bilirubin level by releasing more haem. Jaundice (icterus) occurs when plasma bilirubin exceeds 40µmol/L.</p>

PROBLEM: ABNORMAL BIOCHEMISTRY

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
<p>AST and ALT – high</p> <p>Liver enzymes aspartate aminotransferase and alanine aminotransferase</p> <p>also known as SGOT and SGPT (esp. in USA)</p>	<p>Check that the patient is not being overfed. Glucose infused at more than about 5mg/minute/kg body weight will exceed the cell's glucose oxidation rate. The cell cannot take in more than about 7mg/minute/kg. Overnutrition, especially with excessive carbohydrate, can lead to fatty liver (abnormal liver function tests, esp. AST and ALT) and/or high triglycerides.²⁴</p>	<p>AST and ALT are found inside cells - ALT is mostly found in liver cells but AST is found in cells and in the mitochondria of skeletal muscle, heart, pancreas as well as the liver, so may be increased in general trauma.</p> <p>Chronic cholestasis can eventually lead to liver damage (from bile backflow) and raise transaminase levels.</p> <p>Poorly-perfused liver (=‘shock liver’) due to ischaemia or blood loss/surgery/trauma, can also cause increased transaminases. No action is required other than to ensure patient is not being overfed. Liver damage due to choline deficiency can be another cause of increased transaminases.</p>
<p>ALP and GGT – high</p> <p>Liver enzymes alkaline phosphatase and gamma glutamyl transferase</p>	<p>Try a cyclic parenteral nutrition regimen Allow some oral/enteral intake if possible; in particular foods high in fat can stimulate bile flow (eg regular oral/enteral dose of oil; or ice cream!)</p> <p>High ALP and GGT are not associated with overfeeding.</p>	<p>Increased ALP (>3 times normal) and GGT are characteristic of cholestasis (where there is a biliary obstruction) which is more likely to occur in long-term parenteral nutrition. Many medications also increase ALP and/or GGT. Ursodeoxycholic acid may be a possible treatment for biliary sludge.</p>
<p>trace element levels – high</p>	<p>Repeat test using a trace-element-free test tube for blood collection (available from laboratory) to avoid confounding due to contamination. If high levels are confirmed, dose should be reduced.</p>	<p>Patients with liver disease have impaired excretion of copper and manganese and these may need to be reduced or omitted for some time to avoid toxic levels.</p>
<p>trace element levels – low</p>	<p>Repeat test to confirm a low level before increasing trace element supplementation. Add an extra dose per week, and then repeat the test.</p>	<p>Trace element requirements may be increased with wound losses, diarrhoea, biliary drainage.</p>
<p>suspected choline deficiency</p>	<p>Supplement parenteral nutrition solution with choline if available.</p>	
<p>suspected carnitine deficiency</p>	<p>Carnitine is routinely added to infant parenteral nutrition and can be supplemented for adults if needed. Symptoms include fatty liver and neurological symptoms.</p>	<p>Carnitine is not an essential nutrient in adults as it can be synthesised from lysine and methionine. However, this process requires cofactors niacin, vitamin C, pyridoxine, and iron. Deficiencies in these may also lead to carnitine deficiency.</p>

PROBLEM: ABNORMAL BIOCHEMISTRY

CAUSE	ACTION	OTHER INTERVENTION / REMARKS
<p>suspected essential fatty acid (EFA) deficiency</p>	<p>Without lipid in the parenteral nutrition, adults can develop EFA deficiency within 1-4 weeks.¹⁰ 2-4% of calories should come from linoleic acid, ie at least 500mL of 20%lipid once per week (however, lipid is better tolerated if given continuously).^{29,30} If the patient cannot tolerate IV lipid, oral lipid could be given if possible. Skin (and possibly other) symptoms of EFA deficiency can be prevented by rubbing EFA-containing oil such as sunflower/safflower on the skin (a pleasant lotion can be made up by a pharmacist for this purpose.¹⁰⁰) This may not be adequate to reverse an existing deficiency, however, and it has also been suggested that this skin treatment may address only the skin symptoms of EFA deficiency.</p>	<p>Linoleic acid and possibly alpha-linolenic acid (ALA) are essential. Test for deficiency using a triene:tetraene ratio (should be <0.4)</p> <p>It has been suggested that deliberate underfeeding can prevent EFA deficiency by forcing the body to mobilise the EFA that are held in the body's fat stores, however this is not a reliable way to prevent deficiency.¹¹³</p>
<p>Albumin – low (hypoalbuminaemia)</p>	<p>Check that the patient is receiving adequate nutrition. Review energy and protein requirements to ensure that these are both being met. (Note: nutrition in excess of patient's needs will not cause albumin level to increase more quickly.)</p>	<p>Level will not reach normal range if there is ongoing inflammation or infection (acute phase response). Indicators with a shorter half-life (such as prealbumin) may show faster improvements if reassurance is needed. Trend (over time) may be more informative than any single result. See <i>Monitoring</i> section for more details.</p>

APPENDIX 1: GLOSSARY OF TERMS

Acute phase response

The body's natural response to injury or infection, involving a process of inflammation and alterations in metabolic pathways. In particular, the liver prioritises the manufacture of inflammatory proteins (such as c-reactive protein) and the levels of these are greatly increased. Normal proteins, such as those involved in carrying vitamins and hormones, are downregulated and their levels decrease *independently* of nutritional status or the current level of nutrition. Many of the proteins that are typically seen as 'nutritional indicators' (such as albumin, prealbumin, transferrin, retinol-binding protein, etc) fall into this category. This means that these proteins do *not* indicate nutritional status during the acute phase response. They will decrease, but this does not indicate malnutrition, instead it just reflects the severity of the acute phase response (ie how sick the patient is). This can be useful information when planning the patient's nutrition support or estimating requirements, but it does not indicate nutritional status. Similarly, increasing nutrition support during the acute phase response will not cause an increase in albumin level. Levels of normal proteins will slowly rise on their own as the acute phase response resolves.

Central venous access

Central venous access means that the infused solution is delivered to the superior vena cava, right atrium or less commonly the inferior vena cava. Delivery to any other blood vessels is not considered 'central' access. The venous access device will usually enter the body at another location (so the visible part of a central line might be peripheral on the body) but it is the location of the delivery tip, not the insertion point, that determines whether the access is central or peripheral.

Exit site of venous access device

The point at which a venous access device initially pierces the skin. It may then be tunnelled some distance subcutaneously before entering a vein.

Extravasation

If a venous access device becomes misplaced, solution may leak into body tissue. If the solution is a vesicant (irritating) substance, this leakage is called extravasation. Extravasation of vesicant substances can cause blistering or necrosis, killing tissue and resulting in large deep ulcerated wounds. Some examples of vesicant substances include parenteral nutrition solutions, electrolytes and drugs.

Infiltration

If a venous access device becomes misplaced, solution may leak into body tissue. If the solution is a non-vesicant (non-irritating) substance such as saline, this leakage is called infiltration.

Insertion site of venous access device

The point at which a venous access device pierces the blood vessel (may be some distance from where it entered the skin, when the device is tunnelled subcutaneously).

Lock

A central line is 'locked' when it is filled with a fluid and then clamped. The fluid then remains in the line. Examples include heparin lock, which is used to prevent clotting when the line is not being used; and antibiotic lock, which may be used to treat an infected line.

Lumen

The hollow space inside a tube. In parenteral therapy, the term 'lumen' is used to refer to the miniature separate tubes that may be found within a venous access device. For example, a 'triple lumen central line' is a venous access device which contains three separate inner tubes, each ending in its own connection port. These lumens can be used to infuse solutions that are incompatible with one another, as they remain separate for the entire length of the device.

Osmolality

The concentration of a solution, expressed in terms of the amount of osmotically active solute particles per kilogram of solvent. (For example, a mole of sodium chloride, when in solution will dissociate into a mole of osmotically active sodium ions and a mole of osmotically active chlorine ions, so the solution contains *two* osmoles. A mole of glucose in solution is osmotically active, but does not dissociate into smaller particles, so it will contain *one* osmole.) Units are usually milli-osmoles per kilogram of solvent, or mOsm / kg. The approximate osmolality of a parenteral nutrition solution can be calculated from the components' osmolalities.¹⁰

Osmolarity

The concentration of a solution, expressed in terms of the amount of osmotically active solute per litre of the final formula solution. Units are usually milli-osmoles per litre of final formula, or mOsm / L.

This is a less common way of describing the concentration, because of the way that volume can change with temperature, altering the measurement.

Parenteral Nutrition (PN)

Parenteral nutrition support refers to the infusion of an intravenous nutrition formula into the bloodstream, bypassing the normal (gastrointestinal) route by which nutrition is normally delivered to the body.

Peripheral Parenteral Nutrition (PPN) and Peripheral Venous Access

Peripheral parenteral nutrition support refers to the infusion of an intravenous nutrition formula into a vein other than the vena cava (which would be considered 'central' parenteral nutrition). In peripheral delivery, usually the tip of the venous access device is in the axillary or subclavian veins. The smaller size of the vein and slower blood flow mean that the osmolality of the infusion must be limited, and this affects its nutritional profile: see *Peripheral Venous Access*. Peripheral parenteral nutrition is less commonly used than central parenteral nutrition in Australian hospitals.

Phlebitis

Inflammation of a vein. Phlebitis can be caused by chemical or mechanical irritations (such as highly-concentrated infusions, or infections, or the presence of a venous access device). Pain, tenderness, redness and swelling may occur around the site of the phlebitis. Thrombosis may develop as a result.

Refeeding syndrome

A group of signs and symptoms caused by the metabolic disturbances that occur when nutrition is re-introduced to someone who has metabolically adapted to starvation. Refeeding the starved or semi-starved patient causes acute cellular uptake of phosphate, potassium and magnesium in particular, and the resulting drop in serum levels can cause a variety of problems that can be fatal if not managed appropriately. See *Refeeding Syndrome* section of the *Troubleshooting Guide* for more details.

Thrombosis

Thrombosis means clotting of the blood, and is a problem if the clot occurs within a blood vessel, as it can potentially block blood flow, causing a stroke or a heart attack or ischaemia in a limb. Blood clots can also block the central venous access device. Thrombosis in a vein may occur in connection with inflammation (see Phlebitis, above).

Total Parenteral Nutrition (TPN)

Total Parenteral Nutrition, or TPN, means that a parenteral nutrition infusion is providing a patient's complete nutritional requirements, without any oral or enteral nutrition. That is, the parenteral nutrition solution contains the patient's full needs for macronutrients (water, amino acids, fat, carbohydrate) and micronutrients (all the essential electrolytes, vitamins, minerals and trace elements).

Vesicant

A substance that is harmful to body tissue, causing damage such as blistering or necrosis. In parenteral therapy, a vesicant substance is one that will kill tissue if extravasation occurs.

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