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Neonatal Guidelines

Chapter 3: Fluid, Electrolytes and Nutrition v2015.11

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Directorate of Women & Child Health

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Significant additions / Changes to the revised guideline

- 1. Update on enteral guideline -**
 - a. Emphasis on early feeds**
 - b. breast milk use**
 - c. use of donor milk to initiate feeds**
- 2. Changes in composition of commonly used formulas / fortifiers**
- 3. Changes to Vitamin and Iron supplementation policy**
- 4. Intravenous fluid prescription and TPN section rewritten to reflect changes related to introduction of new TPN**
 - a. Improved guidance on assessment of fluid balance and treatment**
 - b. Single TPN for peripheral and central line use**
 - c. Changes to the composition of TPN**

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Enteral feeding and supplementation guidelines for preterm babies

The aim of this document is to agree a feeding strategy based on available evidence and common sense practice. The document addresses only a limited number of clinical issues and the professional judgement of the clinician should be paramount in deciding the best strategy in complex cases.

The document addresses feeding practices for preterm and growth restricted babies admitted to the neonatal unit for non-surgical conditions. The strategy was discussed in detail at multidisciplinary meetings held on 11/03/2010 and 01/07/2010 and has been successfully implemented in practice.

Definitions:

Preterm: Less than 37 weeks gestation

Small for dates (SFD) and intrauterine growth restriction (IUGR): Although they are distinct entities and have different risk profile and prognosis, these terms are often used synonymously in practice. SFD babies with evidence of IUGR are at higher risk of NEC than those without and babies could have suffered intrauterine growth restriction without being SFD. The definition of IUGR is often based on serial antenatal ultrasound findings of restricted / falling growth parameters with or without Doppler evidence of poor placental perfusion. However, such information is not always available. In the absence of such information the clinician may decide to treat these infants as IUGR. For the purpose of this document we will regard SFD as birth weight below the 2nd centile.

Risk factors:

Necrotising enterocolitis is multifactorial and even seen in babies with minimal risk factors. However, its occurrence in babies not fed enterally is extremely rare and therefore focus on practices of enteral feeding in at-risk babies is justified. Overall incidence in babies <1500 gms is 2-5%

1. Prematurity: Babies under 32 weeks gestation has the highest risk and is more extensively studied. The lower the gestation the greater the risk for NEC.

2: Evidence of IUGR and placental insufficiency

- Reduced / Absent or Reversed end diastolic flow in umbilical artery Dopplers (AREDF)
- Evidence of redistribution of blood flow (High velocity in Middle cerebral artery or abnormal ductus venosus flow)
- Oligohydramnios
- Persistent echogenic bowel
- Falling abdominal circumference

Nutritional goal:

Early weight loss is inevitable and desirable in babies with RDS. Despite attempts at improving nutrition in the early weeks, replication of intrauterine growth rate is impossible to achieve in the first two weeks of life. A fall of two centiles lines below the original birth centile maybe acceptable and subsequent growth should aim at tracking along this new centile. Not all babies show catch up growth. There is now considerable evidence that too rapid catch up growth is associated with long term adverse effects, particularly in the growth restricted babies. Therefore catch up growth should be aimed over a period of months rather than weeks.

A reasonable goal could be

Weight – Not to exceed 10-15gms/Kg/d

Length – 1cm/week (or as per centile chart)

Head circumference 0.7cm/week

The aim is to achieve lean body mass and not fat!

Some general principles on initiation of enteral feeding:

It is expected that all ELBW babies and high-risk VLBW babies will be supported by parenteral nutrition while enteral feeding is established. Our current TPN provides adequate nutrition for the short term (10-14 days) – For details see TPN section Chapter 3, ABM Neonatal guidelines)

1. Start enteral feeds early, preferably on day 1 in haemodynamically stable babies.(Unstable babies are those who are hypoxic despite ventilation, hypotensive requiring high dose inotropes or septic).There is some evidence that early enteral feeding is associated with better tolerance and lesser time to full enteral feeds. This is important as reduced time on TPN / long line reduces the chance of developing nosocomial sepsis - a major cause of neonatal mortality and morbidity.
2. Trophic feeding (up to 1ml/kg/hr) may be beneficial in gut priming and may help establish enteral feeds quicker
3. Mothers milk is always preferable particularly in growth restricted or preterm babies under 32 weeks
4. For babies under 32 weeks and those with growth restriction, our unit policy is to **start breast milk feed on Day 1**. This should ideally be maternal colostrum but **feeding must not be delayed** if this is not available. Donor breast milk should be used unless contraindicated or consent is withdrawn by parents. **Consent for using donor milk in high-risk babies should be part of the antenatal counselling.** As mother's milk volume increases the donor milk could be replaced by mother's milk. It is expected that full enteral feeds will be achieved earlier with this approach without the need for prolonged periods on TPN. Remember, **the role of donor milk is really to facilitate early feeding** and not maintaining nutrition in breast feeding failure and should be used with that purpose in mind.
5. Babies <34 weeks gestation and/or with birth weight <1800 gms who are fed formula milk entirely or as a supplement to mother's milk should be started on Nutriprem 1. Babies <34 weeks but with birth weight >1800gms where mother wishes to formula feed should be started on Nutriprem 2.
6. Presence of umbilical lines, PDA, treatment with indomethacin or blood transfusion are not contraindication to enteral feeding

Progression of enteral feeding - babies less than 32 weeks:

Trophic Feeding: Trophic feeding describes the practice of early enteral feeding of small volumes of milk, in order to stimulate the functional development of the

preterm baby's gastrointestinal tract. A smooth transition to the enteral route of feeding is the ultimate goal.

(The conclusions of meta-analysis of studies on benefits of trophic feeding have frequently changed over the years. The most recent meta-analysis on benefits of trophic feeding on NEC was inconclusive). The principle appears logical and in our unit we normally start trophic feeding as early as possible, preferably on Day 1. Day 1 volumes should commence at 10-15mls/kg/day in divided aliquots at 2 hrly intervals and excluded from the total fluids calculation. If tolerated, feeding intervals should be reduced to hrly on Day 2.

Feed progression: The approach to enteral feed progression should balance the risk of NEC on one hand with slow growth, risks of nosocomial infection and parenteral nutrition related complications with the other. The rate of progression is usually dictated by tolerance but should not exceed 25-30mls/Kg/day. *(Current evidence does not suggest an increased risk of NEC with faster progression as compared to slow progression of enteral feeds. However, even the Cochrane review is underpowered to answer the question. The 'fast progression' in majority of the studies was limited to 25-30mls/Kg/day. Therefore it is prudent not to exceed this rate of progression of enteral feeds)*

The following table gives you a guide on the **initial** rate of progression. For severe IUGR babies consider slower progression –e.g. one step slower than their weight category.

Birth weight	Suggested rate of progression
500- 749 gms	0.5 mls 24 hourly
750 – 999gms	0.5mls 12 hourly
1000 – 1499	0.5 mls 8hrly
1500 - 1750	0.5mls 6hrly
1750-2000	1ml 8hrly

Since enteral feeding is dependant on many other systemic factors, the clinician looking after the baby will often have to modify the feeding approach taking into consideration such complex information.

Except for babies in the lowest birth weight category, enteral feeds are usually taken into account in the total fluid calculation, when a volume of 1 ml/hr is consistently tolerated. **To maximise nutrition in our babies, we will only reduce the volume of TPN as enteral feed volume increases when the total volume (enteral feed +TPN) exceeds 180 mls/Kg/day.**

Breast milk by itself rarely has enough protein to sustain growth in the very preterm baby. Breast milk fortifiers should be added routinely to breast milk in babies less than 34 weeks gestation when they have reached a volume of 150mls/Kg/day. It could be added earlier if babies are fluid restricted and have reached their intended enteral volume. They are normally discontinued when babies are fully established on sucking breast feed.

Feed intolerance:

The quality and volume of gastric aspirate is used as a tool to determine early feeding tolerance. The NG tube should only be aspirated every 4 hours. The signs of poor feed tolerance in a premature baby –

1. Large gastric residue (>50% of the 4hourly amount)
2. Bilious vomiting
3. Abdominal distention and tenderness (Late and serious sign)

In the presence of above – stop enteral feeds, evaluate for possible NEC and manage accordingly.

However, small volume bile stained aspirates in isolation is common in preterm babies. This should prompt a thorough physical examination. Check NG tube position to rule out that the tube hasn't advanced beyond the pylorus. Check for other signs of feed intolerance including abdominal distension and tenderness. In the absence of any other signs of feed intolerance, continue enteral feeds cautiously.

Aspirates less than 50% of the feed volume should be replaced and remaining volume of feed given. Gastric emptying may also be affected by the baby's position. The prone or right lateral decubitus position promotes gastric emptying.

Nutrition monitoring:

All babies in ITU/ HDU should be weighed daily for the first week of life. Babies in SCBU and stable ITU babies beyond the first week should be weighed at least twice a week (usually Wednesday and Sunday). ***Presence or absence of oedema should be documented to interpret the appropriateness of weight gain.***

Length should be measured within the first week and then ideally once every week (Sundays)

Head circumference should be measured at birth and then routinely every week

Appropriate weight gain is usually achieved by (EPSGHAN guideline 2009)

Enteral Energy intake of 130 – 135 Kcal/Kg/d

Protein intake of 4-4.5 gms/kg/d

(Protein free calorie intake is not beneficial as it will be simply deposited as fat)

This is the equivalent of 160-180mls/kg per day of a LBW formula and 180mls/kg/day of fortified breast milk. Fortified breast milk may be increased to a total of 200mls/kg/day should the above parameters of growth not be achieved. If high fluid volume is required for growth, careful monitoring of evidence of fluid retention must be in place.

If the above measures do not result in weight gain in a stable baby, look for causes of growth failure

- a) **Excessive work of breathing** – aggressive weaning off CPAP, Heart failure
- b) **Low total body sodium** (*Sodium is necessary for DNA synthesis and growth*)
 - This is difficult to measure. Low serum sodium (<132 mmol / litre) is a late sign of total body sodium depletion and must be treated. Urinary sodium excretion is extremely variable and has a wide normal range and therefore not easily interpretable.

As all infants under 28 weeks have a low body pool of sodium and increased urinary loss and the best approach is to **routinely supplement babies < 28 weeks with 4mmol/kg/d of NaCl as soon as full enteral feeds established and TPN discontinued. Do not wait for them to develop hyponatraemia.** Babies under 26 weeks may need 6-8mmol/Kg of sodium supplements. **These supplements need to be continued for at least 3-4 weeks even if the serum sodium is normal and then re-evaluated.** Reduce supplements if serum sodium > 145 mmol/litre.

If further energy supplementation is required: (For e.g. babies with severe CLD or heart failure)

Involve the dietician. This should be provided using a balanced supplement. Energy supplements such as Duocal (Fat and Carbohydrate), Calogen (Fat only) are not appropriate for this purpose. In breast fed baby, one strategy could be to replace limited number of feeds with low birth weight formula. In formula fed babies, high energy formula (Infatrini / SMA High energy) may be considered for short periods (Note that these high energy formulas are not designed for premature babies).

Vitamin and mineral supplementation: Quick guide

For preterm infants

Notes:

- All preterm infants will need to be assessed for consideration of vitamin and mineral supplementation depending on their gestation and type of enteral feeds
- Vitamin and minerals are supplemented in TPN and therefore consider supplementation as soon as the infant is on full enteral feeds
- Routine Iron supplementation starts at 28 days of life
- The guidance is based on an average intake of 180mls/Kg/d of milk at preterm gestation and 150mls/Kg for near term infants
- It ensures an approximate daily intake of at least 400IU of Vit D, 400µg of Vit A & 2mg/Kg/d of elemental iron without reaching toxic levels of other elements.

- For mixed feeding – change supplementation only if > 75% of feed volume on the new allocation
- When this specific guidance ends - consider for all children until their 5th birthday - the DoH guidance on multivitamin supplementation (see below).

For details - see flow chart - 'Vitamin and Minerals supplementation policy 2014 for preterm infants' (page 14)

Easy to remember guide: The dose of Abidec is 0.3 mls for formula fed babies to be discontinued 1 month post discharge. The dose of Abidec is 0.6 mls for breast fed babies not on fortifiers.

Term Infants:

- The Department of Health recommends that all babies and young children aged six months to five years should take a daily supplement containing vitamin D.
- Term formula milk contains supplemental vitamins and should be sufficient as long as the infant has an average milk intake of 500 mls / day.
- Breast fed infants whose mothers did not receive Vitamin D supplements during pregnancy should also receive multivitamin supplements from 1 months of age. The GP should take care of this during routine check ups.

However, the following **exclusively breast fed** infants are at particular risk of vitamin deficiencies and should be prescribed Vitamin supplements from birth with advice given to GP to continue this throughout childhood.

- Infants in Asian households and other non-white ethnic groups are prone to Vitamin D deficiency
- Breast-fed term infants whose mothers are on restricted diets e.g. vegetarians.

These groups should also receive **Abidec 0.6 mls** per day until one year of age or until they are on a well balanced diet. Infants of vegans who are breast-fed also need Vitamin B12 supplements.

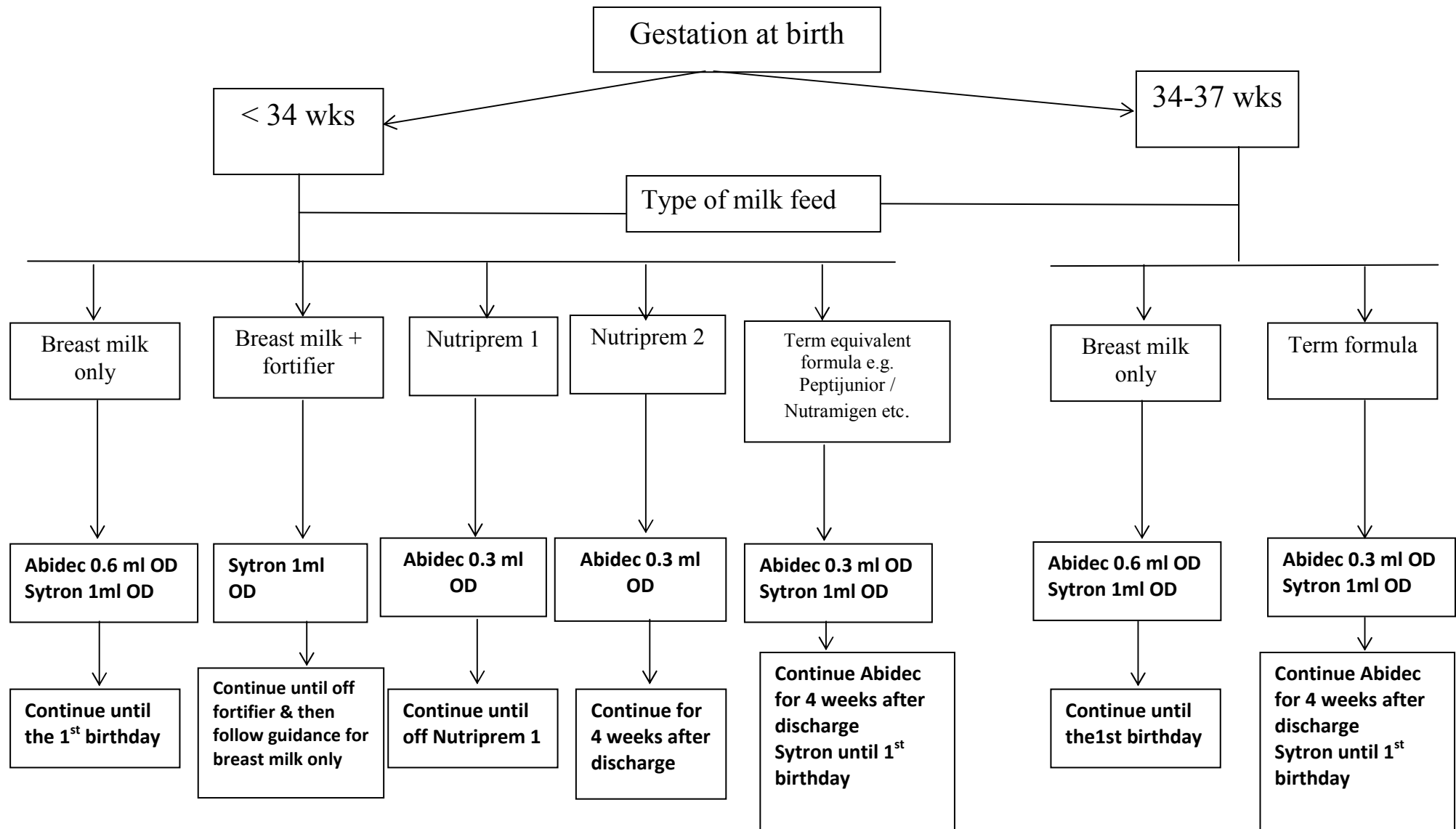
Post Discharge:

Several post discharge formulae are available that have composition intermediate between a term and a preterm formula (e.g. Nutriprem 2). They provide extra protein and energy in addition to calcium, phosphate and vitamins.

(A Cochrane meta-analysis did not show any significant benefit on growth or neurodevelopment at 18 months post term of babies fed on preterm discharge formula when compared to term formula. However the data was limited and somewhat difficult to interpret due to methodological differences).

- Babies with birth weight <1800 gms and who are not breast fed are traditionally sent home on Nutriprem 2. They need Abidec 0.3 mls for 1 month post discharge. After that the large milk volume intake (~ 500mls) provide adequate Iron, Vitamin A and D. However if the baby is taking small volumes of milk on follow up or belongs to high-risk category (dark skinned, prolonged poor nutrition on NICU, poor socioeconomic status), then consideration should be given to supplement Iron and Abidec (Vitamin A and D). *(Vitamin supplementation at this stage is safer, as babies are larger and thereby increasing the margin of safety).*
- The risk of potential oxidative injury with iron overload should be balanced against the risk of worse neurodevelopmental outcome with prolonged iron deficiency. Treatment may need to be individualised in high risk babies following discharge on preterm formula milk. A serum ferritin <50mcg/l at 2 months is suggestive of iron deficiency in preterm babies.
- The department of Health recommends a multivitamin supplement for all children aged between 6 months and 5 years.

Multivitamins and Mineral Supplementation Policy for preterm infants



- Consider vitamin and mineral supplementation when infant on full enteral feeds
- Start Sytron at 28 days of life
- The guidance is based on an average intake of 180mls/Kg/d of milk at preterm gestation and 150mls/Kg at term
- Aims to ensure an approximate daily intake of at least 400IU of Vit D, 400µg of Vit A & 2mg/Kg/d of elemental iron without reaching toxic levels of other elements.
- For mixed feeding – change supplementation only if > 75% of feed volume on the new allocation
- When this specific guidance ends - consider for all children until their 5th birthday - the DoH guidance on multivitamin supplementation.

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Donor Breast Milk policy for clinical use (Revised May 2013)

Donor breast milk may be indicated for preterm babies < 32 weeks gestation. Sometimes senior medical staff may request donor milk for other babies. The reasons must be clearly documented. Examples might be severe growth retardation with documented absent /reversed end diastolic flow where the baby is thought to be at risk of NEC and mother's milk not yet available

The use of donor breast milk is not an alternative to mother expressing her milk. Mother's milk is superior to donor milk as donor milk has been pasteurized and some of the protective factors may be reduced or destroyed. Donor milk is thought to reduce the risk of NEC when compared with formula milk.

Senior medical staff must give approval for donor milk to be used.

Ensure mother is given a parent information sheet entitled "Donor breast milk, your questions answered". Ensure informed verbal consent is obtained from the mother. The discussion and consent must be recorded in the baby notes.

The batch number on the blue lid of the donor milk must be clearly recorded in the baby notes and in the donor Breast Milk Record kept on the fridge door, along with the baby's name, hospital number and date of birth. Please check that donor milk is used in date order and within 3 months of the date that is on the lid. The donor record must be kept for 6 years. A copy of this record is sent to UKAMB (United Kingdom Association of Milk Banking).

Start donor breast-milk as soon as is medically indicated after birth. Give mother's milk as it becomes available and then top up with donor breast milk as required.

Mother's should be encouraged to express 8 – 10 times in 24 hours as per unit policy. The importance of giving mother's own breast milk must be emphasised

Donor breast-milk will be used for a limited period, until mother's own milk is readily available or a decision to use formula milk has been made.

The baby can have more than one batch of donor breast-milk, and more than one baby can share the same bottle of donor breast milk. Defrosted milk is to be used within 24 hours.

For guidelines on safe use of donor milk – see operational guidelines

Table 1: Nutritional content of premature breast milk and different formula
(Per 100 mls of milk)

	Preterm milk	Nutriprem BMF 2.2 g sachet	Nutriprem 1	Nutriprem 2	Term formula C&G
Energy Kcal	65	8	80	75	66
protein g	1.5	0.6	2.6	2	1.3
Fat g	3.5	0	3.9	4	3.3
carbohydrate g	6.9	1.4	8.4	7.4	7.4
Minerals					
Calcium mg	25.4	33	100	94	57
Phosphorus mg	14	19	50	50	32
Magnesium mg		2.5	10	7	5.1
Na mmol	1	0.8	3	1.2	0.74
Cl mmol		0.37	2.17	1.5	1.8
K mmol		0.1	2	2	1.7
Iron mg	0.13	0	0.9	1.2	0.53
Zinc mcg		300	700	900	520
Copper mcg		18	80	60	40
Manganese mcg		4.1	10	6.9	7.8
Vitamins					
Vitamin A mcg/RE	13-33	116	361	100	55
Vitamin E mg	0.3-1.45	1.3	3.5	2.2	1.1
Vitamin K1 mcg		3.2	6	5.9	4.4
Vitamin D3 mcg	0.1	2.5	3	1.7	1.2
Vitamin C mg		6	17	12	9.2
Thiamine mcg		66	140	90	51
Riboflavin mcg		87	200	150	121
Vitamin B6 mcg		56	120	80	35-60
Vitamin B12 mcg		0.1	0.24	0.28	0.18
Niacin mg		1.2	3.2	1.8	0.43
Folic acid mcg		15	35	20	13
Biotin mcg		1.3	3.5	3	1.4
Pantothenic Acid mg		0.38	0.88	0.6	0.34
Osmolality Mosm/Kg/H ₂ O			375	310	343

Table 2: Nutritional content of standard volumes of fortified breast milk and preterm formula & recommended vitamin intakes and vitamin content of multivitamin preparations

	NP1 180mls /Kg/d	Fortifier in EBM 180mls /kg/day	NP2 180mls /kg/day	EPSGHAN 2010 / Tsang 2005 Recommendations <36 weeks 1000-1800g	<1000gm	Abidec 0.6 mls
Energy Kcal	144	144	135	110-135	130-150	
protein g	4.7	4.68	3.6	3.5-4	3.8-4.4	
Fat g	7.0	6.3	7.2	4.8-6.6		
Carbohydrate g	15.1	17.3	13.3	11.6-13.2		
Minerals						
Calcium mg	180	164.5	169.2	120-140	100 -220	
Phosphorus mg	90	94	90	60-90	63-141	
Magnesium mg	18	*14.6	12.6	8-15		
Na mmol	5.4	5	2.2	3-5	3-5	
Cl mmol	3.9	4.2	2.7	3-5		
K mmol	3.6	*0.6	3.6	1.7-3.4	2-3	
Iron mg	1.6		2.2	2-3		
Zinc mcg	1260	1620	1620	1100 – 2000		
Copper mcg	144	*136.8	108	100-132		
Manganese mcg	18	*15.4	12.4	<27.5		
Vitamins						
Vitamin A mcg	650	567	180	400-1000		399.9
Vitamin E mg	6.3	*5.1	4	2.2-11		
Vitamin K1 mcg	10.8	*13	10.6	4.4-28		
Vitamin D mcg	5.4	9.3	3	10-25 /day		10
Vitamin C mg	30.6	*29.7	21.6	11-46		40
Thiamine mcg	252	*255.6	162	140-300		400
Riboflavin mcg	360	*365.4	270	200-400		800
Vitamin B6 mcg	216	*217.8	144	45-300		800
Vitamin B12 mcg	0.4	*0.41	0.5			
Niacin mg	5.8	*4.5	3.2			8
Folic acid mcg	63	*63.2	36	35-100		
Biotin mcg	6.3	*5.2	5.4	1.7-16.5		
Pantothenic Acid mg	1.6	*1.8	10.8	0.33-2.1		

* Mean values found in Tsang 2005.

Intravenous Fluid Prescription

Type of fluids available:

A. Crystalloids:

Fluids are prescribed individually for each baby. Sick babies may need to be assessed several times per day and adjustments made depending on the condition.

Crystalloids available for infusion are:

- a) 10% Dextrose
- b) 10% Dextrose plus electrolytes
- c) 12½% Dextrose, 15% and 20%

The composition of 10% Dextrose plus electrolytes is as follows:

In a 500 ml bag

10% Dextrose	500 mls
NaCl	15 mmols (30 mmol/L)
KCl	8 mmols (16 mmol/L)
Calcium	3 mmols (6 mmol/L)

B. Total Parenteral Nutrition (TPN)

Our TPN solutions are compatible for both central and peripheral infusion. ELBW babies, fluid restricted babies and those who need long term TPN should ideally have parenteral nutrition through central lines. More mature and low risk VLBW infants and those needing short term parenteral nutrition by peripheral route.

We have two types of bags -

- **Starter bags** – Higher dextrose concentration but free of sodium, potassium and phosphate.
- **Maintenance bags** – Contains extra sodium, potassium and phosphate.

Only the maintenance bags contain water soluble vitamins and trace elements.

These have short shelf life of 8 days. They are available on the unit 24 hours and kept in the fridge. In addition, there are maintenance bags without added vitamins with longer shelf life which can be used for a short period, if required.

We add SMOF lipid separately through a syringe infusion.

The starter bag is therefore most suitable for use in -

- The first 48-72 hours of life in a baby with RDS – this time frame is variable and depends on the physiological adaptation of the infant. Change to a maintenance TPN bag only when these conditions are met i.e.
 - Infant has lost ~6% of birth weight
 - Urine output is ~3mls/Kg in very preterm infants OR 2mls/Kg in more mature infants
- Oliguric renal failure with hyperkalemia (Central line TPN is preferred in oliguric infants as it has more concentrated calories and nutrients).
- Severe bruising and hyperkalemia in extreme prematurity

Maintenance TPN is used subsequently in preterm babies for long- term nutrition and a higher protein, sodium, calcium and phosphate intake.

While prescribing TPN on the fluid chart you **must** indicate the **type of bag**, 24 hour volume, hourly rate and the route of infusion.

In babies with complex electrolyte problem special customised bags of TPN can be prepared in the pharmacy which must be prescribed on a separate ‘special’ form by 11 am. These bags will be delivered usually by 5pm on a working day. For weekends, special TPN bags must be requested by 11am on a Friday.

Lipids: The lipid solution is a mixture of SMOF lipid and fat soluble vitamin solution.

**** Note: Do not exceed 120 mls/Kg/d on TPN solution for central line use and 21.6 mls/Kg on SMOF lipid solution.**

General principles of fluid and electrolyte management in preterm babies:

The management of fluid and electrolyte is crucial in managing extremely preterm infants. This is because -

- 1) Water is a major constituent of the body in preterm infants accounting for >90% in the extremely preterm infants
- 2) Massive changes occur as part of adaptation following birth -
 - a. Large insensible losses through skin and respiratory tract in the first week of life until skin cornification begins
 - b. The kidneys shift gears from a state of fluid and electrolyte retention in the first few days to massive urinary losses of fluid and electrolyte in the subsequent days. This is due to immaturity of the renal tubular system and the medullary matrix accentuated by complex interaction of the ANP and the AVP/ RAS axis
- 3) Fluid is the only medium to provide energy to the baby and this consideration further complicates fluid electrolyte balance.

Therefore, fluid electrolyte management in the preterm infants have two important facets –

- prevention of insensible loss
- adequate replacement of incurred loss
- providing adequate protein and energy for preventing catabolism and promoting growth
- maintaining an adequate electrolyte milieu for cellular function to continue efficiently

Prevention of excessive fluid losses and further adjustments:

- Nurse the infant in a fully humidified double walled incubator for 1st two weeks of life to minimise insensible water loss. (See humidification guidelines). Very preterm infants have extremely thin skin and high insensible losses, especially in the first few days. Humidity should be maintained around 90% in premature babies less than 28 weeks gestation in the first week of life and then gradually weaned in the second week. These losses decrease once the epidermis thickens at around 5–7 days. Insensible losses could be reduced by 50% in babies nursed in 90% humidity as compared to 50% only

- **Keep the baby in the plastic bag following admission within the humidified incubator until all initial invasive procedures are completed and the incubator delivers the desired humidity level.** This maintains the micro-environment of high humidity while the incubator windows are opened frequently for procedures. Any clinical procedure must be performed by taking out the limbs through small holes in the plastic bag and immediately replacing it back into the bag after the procedure is completed. The same principle should apply for the umbilical lines. Once all procedures are completed, allow the incubator humidity to build up by closing the windows and doors and only then remove the plastic bag.
- If the baby is on respiratory support, ensure that the humidifier is switched on, filled with fluid and the temperature is set at 37°C
- Review fluid requirements at least 12 hourly in babies under 28 weeks (8 hourly in extremely preterm i.e. 23- 25 weeks , very sick or unstable babies)
 - Measure daily weight using incubator scales. It is good practice to take away the standard weights of equipments such as IV cannula, splints, NG tube etc. so that small differences in weight become apparent.
 - Serum Na, Urea , Creatinine (8-12 hrly). Pay careful attention to electrolyte trends on the blood gases and this will allow quicker fine adjustments
 - Measure urine output by weighing nappies. Avoid catheterisation if possible. Calculate intake output balance for every shift

How much fluid should a baby be started on?

Infant characteristics	Initial volume of fluids
≥32 weeks to term AGA	60 mls/ Kg/day
<32 weeks Small for gestation baby Infant of diabetic mother	90 mls/ Kg/ day

However, this is only an initial guide and will need to be tailored to individual requirements based on the guide below. The composition and volume of fluid that needs to be prescribed is dependant on

1. Change in weight
2. Serum electrolytes trend (most important – Na)
3. Urine output trend
4. Presence or absence of oedema OR third spacing due to capillary leak as in severe sepsis or NEC
5. Blood sugar concentration and glucose infusion rates (GIR)

In the first few days of life and in the absence of severe capillary leak syndrome the following table provides a good guide to the state of fluid and electrolyte status

<u>Weight</u>	<u>Serum Na</u>	<u>Urine output</u>	<u>Inference</u>	<u>Expected action</u>
Increased	Low	Low	Water retention	*Reduce total fluid intake Avoid adding Na in the fluids
Increased	High	Low / Normal	Salt and water retention	Reduce Na intake
Reduced	High	Low / Normal	Pure water loss – usually insensible loss from skin	Check humidity *Replace water loss Avoid excess Na intake
Reduced	Low	High	Salt and water loss – usually from the kidneys	*Replace excess water loss + increase Na intake

* Increments or reduction of fluid volume is usually 20-30mls /Kg but larger changes may be required in extremely preterm infants. If in doubt, discuss with more experienced clinicians

Tips for further adjustments to fluid type and volume:

- In a preterm baby with RDS, a weight loss of 2-3% per day is expected in the first 72-96 hours. A static phase for a couple of days is then followed by gradual regaining of birth weight often completed by 10-14 days. Weight trends deviant from this pattern suggests abnormal fluid balance. **NB:** Severe IUGR babies may not have the initial weight loss due to lack of interstitial fluid.
- Prior to diuresis, a premature infant with RDS has no sodium or potassium requirement. The water loss through the skin is salt poor due to lack of Na / K ATPase and sweat glands. Beware of hyperkalemia in bruised babies!
- **Change to an infusion containing electrolytes (either maintenance TPN or glucose plus electrolytes solution) only when -**
 - there is demonstrable weight loss of least of 6% from birth weight **AND**
 - diuresis is established (~3 mls/kg/day IN very preterm and ~2 mls Kg in more mature babies).
 - Once diuresis is established a VLBW baby would need nearly 4mmol/Kg/day of Na supplements to keep up with renal losses. For infants under 26 weeks the losses may be as high as 6-8mmol/kg/day and replacements should reflect this. Serum Na is a poor indicator of total body sodium and hence routine replacement in babies under 28 weeks is advisable.
 - Potassium requirements are usually 2-3 mmols/Kg/d
- This usually happens between day 3-5 after birth and precedes the improvement in respiratory status. Introducing too much Na before diuresis is established prevents the physiological contraction of ECF and is associated with increased neonatal morbidities such as CLD, NEC, IVH and PVL.
- Calculate glucose requirements separately (mg/Kg/minute) from water requirements to determine % strength of glucose solution to be administered. For e.g. If there is high glucose requirement but low fluid volume requirement you will need to prescribe a higher concentration of glucose solution either on its own or as part of the TPN (12½% Dextrose or 15% Dextrose – **see fluid calculator on SharePoint and Appendix 1)**

- IUGR babies often need more glucose to maintain normoglycaemia. A glucose level less than 2.6 mmol/l on PCX should be corrected. Avoid a dextrose bolus unless the infant is symptomatic and correct using higher GIR. If a bolus is required in symptomatic babies, 2.5 mls/kg of 10% dextrose should be sufficient and **must** be followed by an infusion of higher GIR than before (See glucose infusion table). Do not assume that this will correct hypoglycaemia and blood glucose must be checked within the hour.
- **Hyponatraemia in the 1st few days of life is usually dilutional and associated with weight gain.** Do not add sodium in such situations as it will make the situation worse!! It is an indication to restrict total fluids by 10-20% in the next **8-12 hour cycle period** during which the monitoring process is repeated. The aim is to maintain weight loss within the acceptable range and keep the serum Na in the normal range of 135-145 mmols/L.
- **Hypernatraemia (Serum sodium >145mmol/litre) secondary to dehydration must be accompanied by weight loss.**
 - If urine output has not increased, this is usually pure water loss from skin and should be replaced as such.
 - If there is a concomitant increase in urine output it is usually a mixture of insensible and renal losses and requires replacement of water and electrolytes.
- A spontaneous rise in haemoglobin or albumin in the first few days suggests dehydration
- Urea levels are not a sensitive guide to fluid balance in the first few days in the VLBW infant as it is affected by concurrent catabolism, severe bruising and pooled bleeding, commonly seen in these group of infants. It is also raised in protein intolerance.
- After the first few days the baby's skin cornifies and thickens, transepidermal losses fall, and the baby may require less fluid. Hydration status can usually be maintained with volumes of 120-150 mls/Kg/day.
- As crystalloid solutions provide negligible nutrition, in well hydrated infants, there is little point to exceed 120mls /Kg/d of intravenous crystalloid fluids such as dextrose and electrolytes. Higher volumes may be required to correct dehydration.

- If on TPN, all parenteral nutritional requirements are covered by 120mls/Kg/day and must not be exceeded to avoid toxic levels of constituents. If extra fluid is required for hydration, add in crystalloid solutions in the prescription or correct with additional enteral feeds. Additionally, a maximum of 21.6 mls / Kg of SMOF lipid solution could be given. (See TPN guide).
- In very sick babies and in those paralysed, it may be necessary to restrict fluids to a maximum of 100-120mls/kg/day to avoid interstitial tissue fluid retention and oedema. However, such babies may be depleted intravascularly and frequent fluid boluses may be required to maintain tissue perfusion until the primary disease recovers. A classic example is severe sepsis / NEC. Heart rate trend and Echocardiographic assessment of systemic filling may be a good guide in such cases.

Appendix 1: The amount of glucose provided by different dextrose solutions at different infusion rates are -

Infusion volume (mls/kg/day)	10% Dextrose (Glucose mg/kg/min)	12.5% D (Glucose mg/kg/min)	15%Dextrose (Glucose mg/kg/min)	20% Dextrose (Glucose mg/kg/min)
30	2.1	2.6	3.1	4.2
40	2.8	3.5	4.2	5.6
50	3.5	4.4	5.2	6.9
60	4.2	5.2	6.2	8.3
70	4.9	6.1	7.3	9.7
80	5.6	7.0	8.3	11.1
90	6.3	7.8	9.4	12.5
100	7.0	8.7	10.4	13.9
110	7.7	9.6	11.5	15.3
120	8.4	10.4	12.5	16.7
130	9.1	11.3	13.5	18.0
140	9.8	12.2	14.6	19.4
150	10.5	13.0	15.6	20.8

Neonatal Parenteral Nutrition

Introduction:

The best nutrition for all babies is breast milk and this should be given whenever possible. However, very premature / VLBW babies are not able to tolerate full enteral feeds from the start and require a number of days before the premature gut matures and adapts to tolerate enough milk to sustain growth. If adequate parenteral nutritional support is not provided during this period of adaptation, the infant starts breaking down its own body protein and energy stores and enters into a catabolic state. Most babies will not survive if left in this state for several days and will suffer irreparable organ injuries including the brain.

Parenteral nutritional support is designed to bridge this gap. It is a mixture of protein, carbohydrate and lipids supplemented with essential vitamins and minerals to provide balanced nutrition. It can be provided by both central and peripheral venous route. Other babies who will benefit from parenteral nutritional support include those with NEC, septic paralytic ileus, congenital bowel malformations requiring surgery etc.

Nutritional Physiology in VLBW infants - *important to understand goals of TPN*

The gold standard for post-natal growth is to achieve the same rate of growth as in utero. This is rarely achieved in practice with TPN only but adhering to sound principles of nutrition ensures the most optimal outcomes related to growth and development.

Energy:

The ideal energy requirement of growing VLBW infants is between 110-135cal/Kg/day. Extremely preterm infants and those with increased work of breathing such as CLD may require higher energy for growth

- Around 40-50% of this energy required in a growing healthy infant is spent in maintaining basal metabolic rate (BMR)
- ~ 25% is utilised for growth
- 12% for physical activity
- 5-8% for excretion
- 5% for absorbing food – the specific dynamic action

To prevent catabolism, a baby should be provided with at least the amount of energy spent in maintaining the BMR i.e. ~ 40-55 Kcal along with optimal protein. In the short term, where a very ill septic baby cannot tolerate full TPN, the goal of energy delivery may need to be adjusted to maintain essential functions while waiting recovery. Higher energy will be required to sustain growth

Protein metabolism

- Until 28 weeks gestation, the fetus relies on glucose and amino acids as the main energy sources. Approximately half of the amino acids taken up by the fetus are oxidised to energy, the other half being used for growth.
- If a preterm infant born weighing 1,000 grams is provided with glucose only, that baby will lose approximately 1.5 gm/kg/day of its body protein stores. (Endogenous protein catabolism). Within one week, the baby will have lost approximately 10% of its total body protein stores, and also will have failed to accrue another 10% body protein had the infant remained in utero. Therefore, the baby will have a greater than 20% protein deficit or negative nitrogen balance compared to a fetus of comparable gestational age. New protein synthesis will cease and impair tissue repair.
- Endogenous protein catabolism may result in hypoalbuminaemia, render the baby more prone to infection, impair tissue repair and have long term effects on neurodevelopmental outcome, growth and future health.
- **Therefore, 1.5 gms/kg of amino acid must be given per day to prevent protein catabolism.** An amino acid intake of greater than 2 gms/kg/day is necessary for any growth and 3.5-4 gms /Kg/d achieved optimum growth.
- It is difficult for the baby to catch up and make good the protein loss. Improving protein intake from day 1 leads to larger babies with better head growth i.e. larger OFC at term. 3 g/kg/day of amino acid can be provided on the first day safely and without any adverse effects.
- Adrenaline infusions and Dexamethasone lead to increased protein breakdown in VLBW infants but it is not clear how sepsis and stress affect protein metabolism in this group

Lipid metabolism:

- There is little lipid uptake in-utero in preterm gestation.
- Essential fatty acids are important for brain and vascular growth throughout pregnancy and beyond and are preferentially transferred across the placenta from the mother to the fetus.
- Lipids are energy dense substrates which spare protein degradation. Imlof SMOF lipid provides 2 Kcal.
- **Infusing amino acid solution without TPN will not provide enough calories for growth**
- Very ill or premature infants may not be able to tolerate high lipid content and could become lipaemic. In such cases, the lipid infusion rate may need to be reduced with consequent effect on supplied calories.
- Infants on prolonged TPN support should have their TG levels checked every month.
- If lipaemia is a problem for blood sample analysis (bilirubin, creatinine) stop lipid infusion 30 minutes prior to sampling.
- We currently use SMOF lipid routinely in our unit as it has been reported to have better tolerance and cause less hepatotoxicity

Carbohydrate metabolism:

- Glucose is the main energy substrate for the fetus and the neonate. A baby born of less than 1.5 kg has very little energy stores and will quickly become hypoglycaemic without additional exogenous glucose supply.
- The normal glucose requirement of a VLBW infant is 4-6 mgs /kg/min.
- Very low birth weight infants often develop insulin resistance and hyperglycaemia when the glucose delivery exceeds 8-10mg/kg/min. This is less likely to develop if amino acids are commenced on day one in adequate amounts. For management of hyperglycaemia and insulin therapy - see Section 9 (Endocrine).
- In order to support protein deposition adequate calories must be provided along with amino acids as otherwise the amino acids are converted to glucose by gluconeogenesis.

Electrolyte requirements:

- Na – (after diuresis)
 - Term – 2-3 mmol/Kg/d
 - very preterm 4 mmol/Kg/d
 - extreme preterm 6-8mmol/Kg/d
- K – (after diuresis) 2-3 mmol/Kg/day
- Calcium – 2.5-5.5.mmol/Kg/d
- Phosphate – 1-3mmol/Kg/d

Neonatal TPN in ABMU – Practice points

In ABMU we now have a single neonatal TPN suitable for both central and peripheral use. There are two amino acid formulations –

- Starter TPN – Higher protein and dextrose concentration to provide more protein and calories at smaller volumes. It is free of Na , K and phosphate
- Maintenance TPN – Has reduced dextrose concentration (10%) to improve glucose tolerance and the calorific disadvantage is compensated by greater volumes usually used during this period. It has appropriate Na , K and phosphate supplements

Both bags are clearly labelled and must be kept in the fridge. Each bag will contain 200 mls and can be infused for a maximum of 48 hours. It must be given via a 0.2 µm IV filter.

Supplemental vitamins are added aseptically to the generic bags in the pharmacy lab. Once vitamins have been added the shelf life is 8 days. TPN bags without the vitamins can be infused in the short term if required i.e. nights and weekends.

Under no circumstances should any additives be added directly to the TPN bag on the ward

Lipids are provided in a separate syringe as 20% SMOF lipids and its rate can be adjusted independent of the amino acid solution. Lipid syringes will need changing every 24 hours

Who should have parenteral nutrition through central lines?

This is a matter of clinical judgment and if in doubt consult with an experienced clinician. Commonly the following babies often have central lines inserted.

1. ELBW babies (i.e. birth weight <1000 gms)
2. Sick infants where central line is inserted for continuous monitoring or to facilitate administration of drugs such as inotropes
3. Confirmed NEC
4. Infants where it is anticipated that enteral feeding will take long time to establish— gastroschisis, short gut syndrome etc.
5. Infants where it is anticipated that pronged peripheral access could not be sustained

When should parenteral nutrition through peripheral line be considered?

1. Infants unlikely to establish enteral feeds by Day 5 of life and where a central line PN may not provide a significant advantage. For e.g.
 - a. Infants with birth weight 1000-1500grams
 - b. Infants born between 30-32 weeks gestation
2. As a transient nutritional bridge
 - a. where a central line was removed for concerns related to catheter sepsis and unlikely to have replacement within the next 24-48 hours
 - b. Transient feeding intolerance where no firm decision has been taken for enteral rest
 - c. Where a central line was removed for other reasons i.e. blockage and the infant is likely to establish full enteral feeds within the next few days

Composition of Neonatal TPN:

Designed to provide full nutrition at volumes of 120 mls/Kg/day along with 21.6 mls/Kg of SMOF lipid

Nutrition parameter	*Starter TPN At volumes of 120mls/kg	Maintenance TPN At volumes of 120mls/kg
Nitrogen (g)	0.63	0.57
Amino acid (g)	4.5	3.97
Glucose (g)	13.2 (11%)	12 (10%)
Non-protein calories	52.9	48
Total calories (Protein + Non -protein)	69.4	62.6
Sodium (mmol)	0	4.39
Potassium (mmol)	0	2
Calcium (mmol)	1.42	1.47
Magnesium (mmol)	0.31	0.3
Phosphate (mmol)	0	1.49
Acetate (mmol)	0	3.39
Chloride (mmol)	0	0
Osmolality mosm/Kg	1010	1020

*** Starter TPN will rarely be used in its full volume as it is likely to be replaced by maintenance TPN and therefore in reality will deliver less nutrients than shown in the table**

**** Note each 200mls bag contain 1.6 mls of Peditrace (trace elements) and 0.16 vial of Solvito N (vitamins)**

The maximum volume is restricted to 120mls/Kg to allow for maximum nutrition in fluid restricted sick babies who are usually on such volumes of infusion

- Start TPN infusion with the **Starter Bag** as soon as reliable IV access is obtained. TPN bags used on a peripheral line cannot be swapped to a central line. For babies where a central line will be inserted on D1 , crystalloids could be started through the peripheral line for a couple of hours to avoid wasting a TPN bag.
- Start at an appropriate volume – usually 60-90mls/Kg/day along with SMOF at 6mls/Kg/day. This will give a GIR of 4.5 -6.8 mgs/kg/min, a protein intake of 2.25 -3.37gms/Kg/d and 46.7-63.9 calories/Kg/d (lipids included). This should be adequate to prevent catabolism

- In sick infants, the actual volume of TPN is often eaten away by other infusions such as inotropes, morphine and heparinised saline. Try to use these as concentrated solutions to reduce the impact on TPN volume. Try not to reduce TPN infusion rates below 60 mls/kg/day as this will reduce calories and protein.
- Try not to restrict fluids unnecessarily as it will have impact on nutritional quality. There is now evidence that CLD is associated with amounts of sodium infused before diuresis and physiological weight loss rather than the actual amounts of infused fluid. Increments in amino acid solutions are usually in 20-30mls /Kg/day but may be adjusted as per clinician's judgment.
- Once diuresis and or loss of weight (6%) is achieved (see previous section), sodium/ potassium and phosphate intake could be liberalised by changing to **Maintenance TPN Bag**.
- If baby is oedematous or in renal failure, can restrict to 40-60 mls/kg/day
- On subsequent days increase to a **maximum** of 120 mls /kg/day, which will provide ~4 gms amino acid/kg and a GIR of 8.3 mg/kg/min.
- If baby needs extra fluids above this give as water or 5-10% glucose as appropriate
- **Once enteral feeds are introduced build up the total fluid to 180 mls /Kg /day before starting to cut down on TPN volume to maximise nutrition**
- Extra sodium may be needed in some babies. Most VLBW babies require 5-6 mmols/kg/day. Give the sodium via a separate infusion where possible.

SMOF Lipid

	Day 1	Day 2	Day 3	Day 4
SMOF lipid 20% (200 mgs/ml or 2 Kcals/ml)	5 mls/kg	10 mls/kg	15 mls/kg	18 mls/kg
Vitlipid	1 mls/kg	2 mls/kg	3 mls/kg	3.6 mls/kg
Total	6mls/kg	12mls/Kg	18mls/kg	21.6mls/kg

- Start on day 1
- Start with 6mls/kg/day and increase as above to a maximum of 21.6 mls/kg/day as tolerated
- Do not exceed an infusion rate of 0.75 mls /kg/hour
- Protect the lipid from ultraviolet light to prevent generation of free radicals
- Do not give more than 10 mls Vitlipid per day (caution with babies >2.8 kg!)
- If serum becomes lipaemic, reduce the rate of infusion by 50% and try and increase again the next day.

Work out daily the calorie intake of the baby on all babies on TPN.

Monitoring babies on TPN :

Site:

- Secure intravenous site (central or peripheral) with a clear dressing so that the entry and local site is clearly visible at all times. Apply splint as appropriate
- Observation of the intravenous site on the VIP scale and the infusion pump pressures should be documented every hour on the nursing chart and action taken to review / replace site as appropriate
- Report any significant tissue damage through extravasation injury via the online Incident reporting system. Follow our extravasation injury management guidance in the clinical procedures chapter.
- At all times review and encourage early establishment of enteral nutrition using human milk to reduce the duration of parenteral nutrition through any route

Bloods:

- Daily U&E, calcium, phosphate.
- Twice weekly LFT's, Alkaline phosphatase.
- Head circumference weekly.
- Weight at least twice weekly.

If on TPN for over a month, consider checking

- Lipid profile
- Trace elements

**Appendix 2: Starter TPN in 11% Dextrose (1010 mosm/Kg)-
Nutritional parameter as per prescribed volume**

Nutrition parameter	60mls/Kg	75mls/Kg	90mls/Kg	100mls/Kg	120mls/kg
Nitrogen (g)	0.32	0.40	0.48	0.53	0.64
Amino acid (g)	2.2	2.8	3.3	3.67	4.4
Glucose (g)	6.6	8.25	9.9	11	13.2
GIR	4.58	5.72	6.87	7.6	9.16
Non protein energy(kcal)	26.45	33.06	39.60	44	52.90
AA Energy (kcal)	8.25	10.3	12.3	13.75	16.5
Total Aqueous TPN Energy(kcal)	34.7	43.36	51.9	57.75	69.4
Total Energy with lipids at 6-12 mls/Kg/d	46.7-58.7	55.36-67.36	63.9-75.9	69.75-81.75	81.4-93.4
Sodium (mmol)	0	0	0	0	0
Potassium (mmol)	0	0	0	0	0
Calcium (mmol)	0.71	0.89	1.1	1.2	1.42
Magnesium (mmol)	0.15	0.19	0.23	0.25	0.3
Phosphate (mmol)	0	0	0	0	0
Acetate (mmol)	0	0	0	0	0
Chloride (mmol)	0	0	0	0	0

**Appendix 3: Maintenance TPN with 10% Dextrose –(1020 mosm/Kg)-
Nutritional parameters as per prescribed volume**

Nutrition parameter	75mls/Kg	90mls/Kg	100mls /kg	120mls/kg
Nitrogen (g)	0.35	0.43	0.47	0.57
Amino acid(g)	2.4	2.9	3.3	3.9
Glucose (g)	7.5	9	10	12
GIR	5.2	6.25	6.9	8.3
Non protein (kcal)	30	36	40	48
AA Energy (kcal)	9.14	10.96	12.18	14.62
Total AQUEOUS Energy(kcal)	39.14	46.96	52.18	62.62
With full lipids 21mls/Kg/d	81.14	88.96	94.18	104.62
Sodium (mmol)	2.7	3.3	3.6	4.38
Potassium (mmol)	1.2	1.5	1.6	1.9
Calcium (mmol)	0.9	1.1	1.2	1.4
Magnesium (mmol)	0.19	0.23	0.25	0.3
Phosphate (mmol)	0.93	1.1	1.25	1.49
Acetate (mmol)	2.1	2.53	2.8	3.3
Chloride (mmol)	0	0	0	0

An approach to hyponatraemia in newborn

- Normal serum sodium is 135-145 mmol/L
- Serum sodium is determined by the ratio of sodium to water in the blood and not by the absolute amount of either
- Clinical features vary from totally asymptomatic state to severe neurological dysfunction
- Hyponatraemia can cause apnoea, hypotonia, ileus, hypotension, bradycardia, in severe cases, seizures. Factors that contribute to CNS symptoms are
 - i. rate at which serum Na levels change
 - ii. serum Na level
 - iii. duration of the abnormal serum Na level
 - iv. presence of risk factors
- Chronic hyponatraemia can cause poor weight gain

Hyponatraemia – Causes:

Primary water excess

- Excess intake - mother or baby
- Impaired excretion - Intrinsic renal failure, Indomethacin, SIADH

Primary sodium depletion

- Insufficient intake – Maternal laxative or diuretic abuse, use of breast milk in pre-term infant
- Excessive loss - Renal tubular dysfunction, diuretics including xanthenes, pyelonephritis, nephrotoxic agents, obstructive uropathies
- Endocrine -Salt losing congenital adrenal hyperplasia, hypoaldosteroidism, adrenal hypoplasia
- Gastrointestinal - External or sequestered – such as vomiting, Ileostomy / colostomy loss, diarrhoea, Ileus, obstruction, NEC
- CNS - following repeated drainage of CSF in PHH

Mixed:

- Water excess and sodium depletion - Chronic lung disease on diuretics
- Water excess disproportionate to whole body sodium excess - Congestive heart failure, nephrotic syndrome

Evaluation:

History -

- Type, volume and frequency of input and output
- **Weight trends** : very important
- Hyponatraemia in the first 48 hours is almost always associated with fluid retention and gain in weight. Fluid restriction or onset of diuresis usually results in improvement
- Post -diuresis – hyponatraemia is usually due to loss of excess sodium in the urine and associated with weight loss or poor weight gain.

Investigations:

- **Bloods for**
Plasma electrolytes, creatinine, urea, glucose, albumin, osmolality
- **Urine for**
 - Osmolality., electrolytes, creatinine
- **Other tests in refractory hyponatraemia**
 - TFT, cortisol, aldosterone
 - MRI Brain

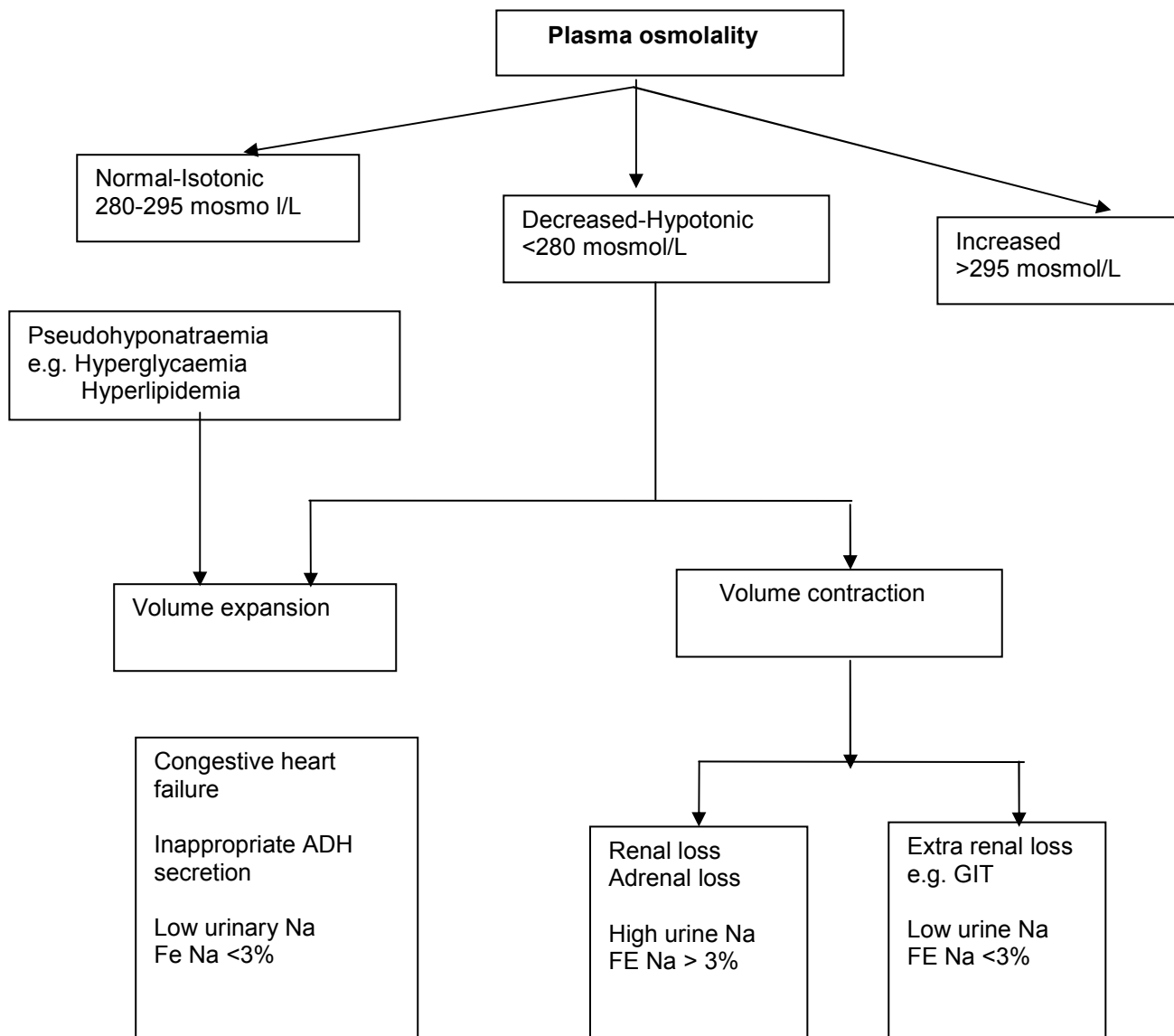
To calculate Fractional excretion of sodium

$$FE\{Na\} = \frac{U \{Na\} \times P \{Cr\}}{U \{Cr\} \times P \{Na\}} \times \frac{100}{1000} \%$$

U Na: Urinary Sodium (mmol/l) U Cr: Urinary creatinine (mmol/l)

P Cr: Plasma creatinine (umol/l) P Na: Plasma sodium (mmol/l)

Approach to diagnosis:



Treatment:

- Consider treatment if serum sodium is approaching 132mmol/l
- **Treatment of the underlying condition is the most important approach**
- In most cases anticipation of the problem can avoid complicated IV correction at later stage. For e.g. routine supplementation in babies under 28 weeks once diuresis established, fluid restriction in oedematous babies or those with impending renal failure
- In SIADH - fluid restriction with judicious use of sodium

- Optimal treatment of hypotonic hyponatremia requires balancing the risks associated with treatment and preventing cerebral edema while avoiding osmotic demyelination. Given the risk of demyelinating lesions, the recommended rate of correction should not exceed 8 mEq/L/24 hours.

To calculate the amount of sodium, **add up the deficit, the ongoing loss and maintenance requirements.**

- Find sodium deficit
(Desired Na – Present Na) X 0.8 X body wt
- Symptomatic hyponatremia: Calculate deficit to 125 and correct it over 3-6 hrs.
The remaining deficit over next 24 hrs
- Asymptomatic hyponatraemia
 - Calculate the deficit and correct ½ deficit over 6-8 hrs and the rest over next 24-48 hrs
 - Avoid hypotonic solutions

In most cases make a solution of 1 mmol/ml of sodium e.g. 5 mls of 30% NaCl (5mmol/ml of NaCl) made up to 25 mls with Dextrose and infuse at 0.5 – 1 mmol/hour. Check Na⁺ again in 6 hours.

Hypokalemia

The normal serum potassium levels¹:

Preterm - 0 to 7 days - 3.5 – 6.7mmol/l

Term - 0 to 7 days - 3.2 – 5.5mmol/l

Preterm & Term - 8 – 28 days - 3.4 – 6.0mmol/l

Causes & features:

Excess GI loss - Vomiting, NG aspiration, pyloric stenosis, diarrhoea

Renal loss -congenital adrenal hyperplasia, renal disorders.

Intracellular shift – Therapeutic hypothermia

Drugs - Diuretics, Corticosteroids, Amphotericin B, Gentamicin, Salbutamol, Insulin,

Acute hypokalaemia is associated with muscle weakness, urine retention and ECG changes of prominent 'U' wave, prolonged Q-T interval, flattening of 'T' wave⁴.

Special considerations:-

1. Potassium over dose can be fatal.
2. Potassium infusions should not have a concentrations of greater than 40mmol/l (0.04mmol/ml) for peripheral infusion, and an absolute maximum of 80mmol/l(0.08mmol/ml) for central infusion. Infuse potassium, only with ECG control.
3. **Do not infuse potassium infusion faster than 0.2mmol/kg/hour.**

Dose:-

Oral dose²: Preferred method of replacement
1 -2 mmol/ kg/ day in two divided doses. Adjusted according to plasma potassium concentration

Intravenous dose³: **1 – 2mmol/kg/dose.**

It is supplied in prefilled syringes of potassium chloride 4mmol in 50mls of 5% dextrose. Solution must be diluted to 2mmol in 50 ml if given via peripheral line or 4mmol in 50ml via central line.

Preparation for intravenous infusion⁵

Peripheral infusion:

1. Draw up 25 mls of prefilled syringe solution (4mmol in 50mls) and make up to 50mls by adding 25 mls of 5% dextrose
2. This has a concentration of 0.04mmol/ml of potassium.
3. Infuse this at a rate of 1ml/kg/hour (maximum infusion rate is 5ml/kg/hour)

Central infusion:

1. Use prefilled syringes from Pharmacy (4mmol KCL / 50ml of 5% dextrose)
2. This has a concentration of 0.08mmol/ml of potassium.
3. Infuse this at a rate of 0.5ml/kg/hour(maximum infusion rate is 2.5ml/kg/hour)

Compatibilities: Aciclovir, Adrenaline, Dobutamine, Dopamine, Heparin, Insulin, Midazolam, Tazocin.

Incompatibilities : Furosemide.

Availability:

- Prefilled syringe 50mls (4mmol KCL in 50mls)
- The injection is available as (15%) KCL – 10ml ampoule containing **2mmol of K⁺ per ml.**
- An oral solution (Kay -Cee L) is available containing **1 mmol of K⁺ per ml.**

References:

- 1 Roberton's textbook of Neonatology, Fourth edition, page 1304.
- 2 BNF for children page 514
- 3 BNF for children 2007, page 522
- 4 Neonatology; LANGE clinical manual, Fifth edition, page 268
- 5 Handbook of drugs of the Neonatal units of the Gwent Healthcare NHS Trust-2007

Hyperkalemia

Hyperkalemia is defined as serum potassium level more than 6.7mmol/l in a preterm infant and more than 6mmol/l in a term infant².

Excess potassium lowers cell-resting action potential and prevents repolarisation and excites myocardial cells leading to ventricular tachycardia, sinus bradycardia and asystole. It also causes skeletal muscle paralysis.

Causes of Hyperkalemia include increased IV or oral potassium intake, packed cell transfusion, conditions which causes transcellular shift (acidosis, cell necrosis, digitalis toxicity, succinylcholine, beta blocker) and conditions of decreased potassium excretion (acute & chronic renal failure, Addison disease, 21-hydroxylase deficiency, potassium sparing diuretics).

Principles of treating Hyperkalaemia:

- ❖ Stop administration of potassium immediately.
- ❖ Look for ECG changes, such as flattening of 'P' wave, wide QRS complex, tall and tenting of 'T' wave. ECG changes indicate myocardial excitability.
- ❖ Prevent or treat already established myocardial excitability by either calcium gluconate or calcium chloride.
- ❖ Medications to increase cellular uptake of potassium in order of preference:
 - Sodium bicarbonate
 - Glucose –insulin
 - IV Salbutamol
 - More than one medication may need to be given
- ❖ Removal of excess potassium: Sodium polystyrene sulfonate
 - Ca polystyrene sulfonate
- ❖ In refractory conditions:
 - Exchange transfusion
 - Peritoneal dialysis
 - Hemodialysis
 - Hemofiltration

Prevention or treatment of myocardial irritability

- Calcium gluconate: 0.5 – 1mmol/kg to be given over 5 – 10 minutes **OR**
- Calcium chloride: 0.25 – 0.5mmol/kg to be given over 5 – 10 minutes.
- Should be given with ECG monitoring.
- This will not reduce the potassium concentration.
- Print or save the rhythm for evidence.

Medications to increase intracellular shift of potassium²

Glucose –insulin infusion

- Take 100mls of 25% dextrose and add 12 units of soluble insulin.
- From that give 5mls/kg over 30 minutes.
- This gives a insulin concentration of 0.6u/kg, and glucose/ insulin ratio of 2.08.
- This is safer in very extreme preterm.
- Blood glucose before and after the infusion should be measured.

Sodium bicarbonate

- Give 1 -2 mmols/kg of 4.2% sodium bicarbonate over 10-30 minutes intravenously
- It may be given, even when there is no acidosis.
- It is equally effective as glucose-insulin infusion.

IV Salbutamol

- IV Salbutamol 4microgram/kg, over 5 minutes.
- Some times more than one medications need to be given. Continuous ECG monitoring needs to be done.
- Sodium & calcium polystyrene sulfonates- side effects include bowel irritability, concretions and bleeding in preterm infants. It is slow to act as well. Complications outweigh benefits.

Refractory hyperkalemia

- Exchange transfusion with freshly washed packed red cells, re constituted with plasma.
- Peritoneal dialysis, Hemodialysis, Hemofiltration.
- Limited by the time involved in transfer and preparation.

References:

1 Fetal and Neonatal Physiology; WB Saunders, 3rd edition

2 Robertson's text book of Neonatology

3 LANGE clinical manual Neonatology, 5th edition

Appendix 4: Solivito N

One vial (10 mls) of Solivito N has the following composition:

Thiamine Mononitrate	3.1 mg	(Vitamin B1 2.5 mg)
Riboflavine Sodium Phosphate	4.9 mg	(Vitamin B2 3.6 mg)
Nicotinamide	40 mg	
Pyridoxine Hydrochloride	4.9 mg	(Pyridoxine 4 mg)
Sodium Pantothenate	16.5 mg	(Pantothenic acid 15 mg)
Biotin	60 micrograms	
Folic acid	400 micrograms	
Cyanocobalamin	5.0 micrograms	
Sodium Ascorbate	113 mg	(Vitamin C 100 mg)

Other ingredients include Glycine, Disodium edetate, Methylparahydroxy and water. There is $\frac{1}{10}$ vial (1ml) per 120mls TPN

APPENDIX 5 – PEDITRACE:

1 ml of Peditrace trace element concentrate for infusion contains:

Active Ingredients	Quantity
Zinc chloride	521 µg
Copper chloride 2H ₂ O	53.7 µg
Manganese chloride 4H ₂ O	3.60 µg
Sodium selenite 5H ₂ O	6.66 µg
Sodium fluoride	126 µg
Potassium iodide	1.31 µg

The active ingredients in 1 ml correspond to:

Zn	250 µg	3.82 µmol
Cu	20 µg	0.315 µmol
Mn	1 µg	18.2 nmol
Se	2 µg	25.3 nmol
F	57 µg	3.00 µmol
I	1 µg	7.88 nmol

APPENDIX 6 – VAMINOLACT

QUALITATIVE AND QUANTITATIVE COMPOSITION

Amino acids Amount

Alanine Ph Eur 6.3 grams

Arginine Ph Eur 4.1 grams

Aspartic acid Ph Eur 4.1 grams

Cysteine/Cystine 1.0 grams

Glutamic acid Ph Eur 7.1 grams

Glycine BP 2.1 grams

Histidine USP 2.1 grams
Isoleucine Ph Eur 3.1 grams
Leucine Ph Eur 7.0 grams
Lysine 5.6 grams
Methionine Ph Eur 1.3 grams
Phenylalanine Ph Eur 2.7 grams
Proline Ph Eur 5.6 grams
Serine Ph Eur 3.8 grams
Taurine 0.3 grams
Threonine USP 3.6 grams
Tryptophan USP 1.4 grams
Tyrosine USP 0.5 grams
Valine Ph Eur 3.6 grams
in each 1000 ml

Product properties

Amino acids 65.3 g/l

Total nitrogen 9.3 g/l corresponding to 58 g/l protein

Acetate Nil

Energy 240 kcal (1.0 MJ)/l

Osmolality 510 mosmol/kg water

pH 5.2

Free from antioxidant additives, chlorides and other inorganic electrolytes.

APPENDIX 7 - VITLIPID N INFANT:

One ml of Vitlipid N Infant contains the active ingredients:

Retinol palmitate corresponding to retinol	69 micrograms (230 IU)
Ergocalciferol	1.0 micrograms (40 IU)
DL-alpha-tocopherol	0.64 mg (0.7 IU)
Phytomenadione	20 micrograms