College of Pharmacy
University of Sargodha

M.Phil. Pharmaceutics

Total Parenteral Nutrition (TPN) and its Calculations

Clinical Pharmacy & Therapeutics

Table of Contents

Total Parenteral Nutrition (TPN)

1. History:

- Until the early 1960s, the use of IV nutrition was restricted to high concentrations of dextrose and electrolytes.
- In 1962, Wretlind & Colleagues developed lipid infusion as the principal source of calories for parenteral feeding.
- In 1966, Dudrick & Rhoads developed parenteral nutrition for patients who had lost their small bowel.
- In 1976 Solassol and Joyeux developed the three in one mixture by putting sugars, amino acids and lipids in a single bag.
- In 1976 Shils and colleagues & J.J. Bhoy and colleagues developed home PN to reduce Costs.

2. Nutrition:

Human nutrition is the provision to obtain the essential nutrients necessary to support life and health.

2.1. Nutrients:

Nutrients are the substances that are not synthesized in the human body ---- Must be supplied through diet.

- Macronutrients (Carbs, Proteins, Fats, Fibers & Water)
- Micronutrients (Vitamins, Minerals & Trace elements)

2.2. Nutrients Requirement per Day

Calories- 25kcal/kg

- Proteins: 0.8 – 2 kg/day
- Carbohydrates: Min 75-100 g/day
- Fats: Min 500 mL of 20% lipid emulsion per week to prevent EFA deficiency
- Water: 30-40 mL/kg/day + extra for any fluid loss+ 500ml/day/degree Celcius rise in temperature.
- Electrolytes
  - ✓ Na-60-80 mEq/day
  - ✓ K- 30-60 mEq/day
  - ✓ Cl- 80-100 mEq/day
  - ✓ Ca- 15-20 mEq/day
  - ✓ Mg- 15-25 mEq/day
  - ✓ PO_4^{-3} – 12-24 mEq/day
- Vitamins & micronutrients – Traces

3. Definition of Total Parenteral Nutrition

Total Parenteral Nutrition is a formulation of nutritional components for intravenous delivery. Included are carbohydrates, amino acids, fats including essential fatty acids, electrolytes, vitamins, minerals, trace elements, water and other additives.

4. Aims:

- To provide nutritional support via intravenous route when oral or enteral routes are inadequate, in accessible or non-functional.
- To minimize the potential catheter related, metabolic and infectious complications associated with TPN.

5. Indications:

The golden rule of nutrition is *"If the gut works, use it."*

However, if the gut is unable to perform its functions then we move towards TPN.

5.1. General Indications

- ❖ Patients who can't eat
- ❖ Patients who won't eat
- ❖ Patients who shouldn't eat
- ❖ Patients who can't eat enough

5.2. Specific Indications

- Documented inability to absorb inadequate nutrients via the GIT
- Complete bowel obstruction or intestinal pseudo-obstruction
- Severe catabolism with/without malnutrition when GIT is not usable within 5-7 days.
- Inability to obtain enteral access to provide sufficient nutrients
- Moderate to severe pancreatitis
- Persistent GI hemorrhage
- High output enterocutaneous fistula
- Trauma requiring repeated surgical procedures
- IBD not responding to any medical therapy
- Hyperemesis gravidarum
- Intractable vomiting
- Partial small bowel obstruction
- Intensive chemotherapy
- Major surgery where enteral nutrition is not expected to resume in 7-10 days
- Chylous ascites
- Anorexia nervosa • Contraindications:
- Functional GI tract
- Inability to obtain venous access
- A prognosis that does not warrant aggressive nutrition support
- When the risks of parenteral nutrition are judged to exceed the potential benefits.

6. Contraindications

- Functional GI tract
- Inability to obtain venous access
- A prognosis that does not warrant aggressive nutrition support
- When the risks of parenteral nutrition are judged to exceed the potential benefits.

7. Planning a TPN

1. Calculate Energy/Caloric Requirements
2. Determine Macronutrients
3. Determine Micronutrients
4. Monitoring
5. Complications

7.1. Energy/Caloric Requirements

Kcal is unit used in metabolism studies

"It is the amount of heat required to raise the temperature of 1kg of water by 1°C."

1Kcal=1000cal

Caloric demand varies in terms upon physical state and medical condition. This is calculated by Harris-Benedict equation

Harris-Benedict equation

This is usually used to measure basal energy expenditure (BEE) requirements for non-protein calories. It is also referred as,

- RME= Resting metabolic energy
- REE= Resting energy expenditure

For Male:

BEE=66.67+ [13.75 x Wt (kgs)] + [5 x height (cm)] –[6.76 x age(yrs)] For Female:

BEE=655.1+ [9.56 x Wt (kgs)] + [1.86 x height (cm)] –[4.68 x age(yrs)]

Total daily expenditure can be calculated and adjusted for activity and stress factor.

TDE= BEE x activity factor x stress factor Activity factor

Confined to bed	1.2
Ambulatory	1.3

Stress factor

Surgery	1.2
Infection	1.4 to 1.6
Trauma	1.3 to 1.5
Burns	1.5 to 2.1

In addition to TDE, the total daily expenditure can also be calculated generally by scale of kcal/kg.

Normal need	25-30kcal/kg/day
Elective surgery	28/30kcal/kg/day
Severe injury	30/40 kcal/kg/day
Extensive trauma/burn	45-55 kcal/kg/day

Example: for a 70 Kg male with elective surgery X 30 Kcal/Kg = 2,100 Kcal/day **Geriatric Nutrition:** In elderly, there is:

- Decreased metabolic rate
- Decline in body mass
- Less physical activity

So,

- Caloric requirements are different in elderly.
- Therefore, equations were developed for individual over age 60 years. For men

REE= (8.8 x weight (kg)) + (1128 x height in m) – 1071

For women

REE= (9.8 x w8 (kg)) + (637 x height in m) -302

Pediatric Nutrition: In children caloric requirement /kg are higher because of their higher BMR (basal metabolic rates)

- BMR is approximately 50-55kcal/kg/day in infancy.
- It declines to about 20-25 kcal/kg/day during adolescence.
- For children less than 3 years old.

A modified version of Harris-Benedict equation has been developed by Coldwell-Kennedy

REE= 22 + (31 x Weight in kg) + (1.2 x height in cm)

7.2. Determination of Macronutrients:

a. Protein needs

Proteins are provided in TPN as protein hydrolysate or amino acids. The purpose of protein support is not to produce energy although energy is produced by protein by a factor of 4kcal/g but rather to build tissues and also body strength. Protein requirements based on Stress & Body Weight. Protein needs are determined by the patients, usually start with 0.83 gm/Kg and add stress and other factors as needed.

Normal requirement	**1-2g protein/kg/day**
Non-stress patient	**0.8g/kg/day**
Mild stress	**1-1.2g/kg/day**
Moderate stress	**1.3-1.75g/kg/day**
Severe stress	**2-2.5g/kg/day**
Renal failure (no dialysis)	**0.6-o.8g/kg/day**
Renal failure (with dialysis)	**1.2-1.5g/kg/day**

Example:

A malnourished 70 Kg man may need 84 gm protein per day (70 Kg X 1.2 gm/Kg).

Note:

Prolonged TPN solution should contain 2 amino acids: Glutamine (most abundant amino acid in the blood that protects the gut epithelia tissue lining. Choline helps protect the liver from hepatic fat deposits that hinder its function.

b. Fluid Requirements

On case by case basis fluid requirements can be change

- It may be increased (dehydrated, burn patients)
- It may be decreased (renal failure, CHF patients) **Daily normal requirement is 2-3 L/day for an adult.**
- For neonates, infants, adolescents and children without abnormal water losses, the approximate daily water requirement may be calculated by:

Based on age:

Adults	**20-50mL/kg/day**
Neonates	**100-150mL/kg/day**

Based on weight:

A factor of 30mL/kg body weight is used to estimate a patients daily fluid requirements. **Based on body surface area**:

= m^2 x 1500mL/day/m^2

Based on caloric requirements

=1.2ml/kcal x kcal/day

Infusion rate:

How to measure ml/min and drops per minute?

Let's suppose,

D5W 1000mL is infused over 8 hours how many ml/min should be infused?

1000ml/8hours= 125ml/hr (hrs is converted into minutes: 1 hr= 60minutes)

125ml/60min= 2.08ml/min

Now we can find drops /min. this can be find out when we know the tubing no. (gtt/ml) by simply multiplying.

If we use tubing that deliver 15gtt/ml

Then, Gtt/min =2.08ml/min x 15gtt/ml

Drops/min= 31gtt/min **Example:**

A 70Kg dehydrated patient requires how many ml of fluid/day?

70 x 36.3ml/kg=2541mL

c. Lipids

Lipids are known to provide energy when body cannot obtain the entire necessary energy requirement from carbohydrate.

The proportion of lipid calories provided is restricted to 30% of total daily calories. Lipids are generally provided in the form of emulsions that contain carbohydrate bas emulsifying agent which also contribute to caloric content.

% of fat emulsion	Kcal/cc
10%	1.1
20%	2.0
30%	3.0

Fat emulsions are commonly available in 250 and 500cc bottles.

Example: How much fat required by a 70kg man if 1.3g fat/kg required? 500cc?

Ans: 70 Kg X 1.3 = 91 gm fat

From calculation,

500 cc of 10% lipid emulsion provides 61 grams fat and 550 kcal as:

500 x 1.1 = 550/9kcal/g = 61g

So if you give 750 cc (1.5 bottle of 500 cc bottle) of lipid you will be adding: 61g/bottle X 1.5 bottle = 91.5 g of fat /day and 550 kcal/bottle X 1.5 bottle = 825 Kcal/day from fat.

d. Carbohydrates

Carbohydrates are the primary source of cellular energy.

Carbohydrate requirement=3-5g/kg/day.

In formulas for parenteral nutrition, dextrose provide 3.4kcal of energy/g.

How many Kcal required of crabs can be determined by:

Total kcal-fat kcal= carbohydrate

Example: As mentioned above in first step total caloric requirement of patient weighing 70kg is 2100kcal and 825 kcal of fat per day. So how many kcal of carbohydrate required?

Ans: using the formula,

2100-825=1275kcal

1275 kcal of carbohydrates is required. To see how many gram of dextrose is this?

1275 Kcal/3.4 Kcal/gm = 375 g dextrose needed

If we use D50W as starting solution, we will need to use X ml of this solution:

375 g / X ml = 500g/1000 m

X=375000 / 500 = 750 ml

7.3. Determination of Micronutrients

- Electrolytes
- Vitamins
- Trace elements **Electrolytes:**

Sodium	1-2mEq/kg
Potassium	1-2mEq/kg
Chloride	Based on acid base balance
Acetate	Based on acid base balance
Calcium	5-15mEq
Magnesium	8-20mEq
Phosphorus	15/50mmol

Vitamins:

1 amp multivitamin per bag of TPN is added but does not include vit-K.

1mg	Per day
5-10mg	Per week

Trace elements:

Trace elements like Zn, Cr, Cu, and Mn may also be added.

TPN solutions may be contaminated with aluminium and chromium. Patients with cholestatic jaundice should be closely monitored for copper toxicity. Patients with renal impairment may not be able to excrete selenium, molybdenum, zinc and chromium. Trace elements Zinc, Selenium and Iodine are added to TPN infusion bags at the following rates:

Zinc 440 µg/kg/day at 135 ml/kg/day Selenium
2.7 µg/kg /day at 135 ml/kg/day Iodine 1.08
µg/kg /day at 135 ml/kg/day.

Final Volume of TPN

Since the fluid needs are 2,100 – 3,600 cc/day, with protein needs of 84 gm/day: your formulation for your 70 Kg patient will be:

- 10% amino acids 840 cc
- D50W dextrose 750 cc
- 10% lipid 750cc
- Total volume: 2,440 cc/day

You need to add 70-150 cc fluid for electrolytes, vitamins, and additives to give a final volume of say 2490 ml/day.

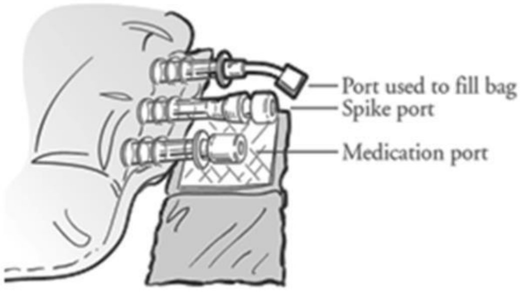
Administration

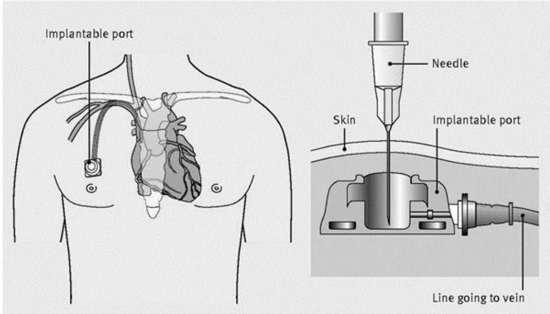
First, TPN is administered through a needle or catheter that is placed in a large vein that goes directly to the heart called a central venous catheter.

Since the central venous catheter needs to remain in place to prevent further complications, TPN must be administered in a clean and sterile environment.

For instance, external tubing should be changed every day and dressings should be kept sterile with replacement every two days.

TPN is usually used for 10 to 12 hours a day, five to seven times a week. Most TPN patients administer the TPN infusion on a pump during the night for 12-14 hours so that they are free of administering pumps during the day. TPN can also be used in both the hospital or at home.





7.4. Monitoring

TPN administration requires careful clinical and laboratory monitoring. Adequate growth is best determined by linear growth as weight gain can reflect an increase in total body water rather than tissue accretion. In addition to routine observations the following are required for short term TPN use.

Test	First 3 Days	Thereafter
UEC (Na, K, Cl, HCO3, urea)	Daily	Monday/Thursday
Ca, PO4, bilirubin, albumin	Baseline	Monday
FBC	Baseline	Monday
Triglyceride	With each increase	Monday / When ill
Plasma ammonia	Once on maximum PN AA intake (135 ml/kg/day of PN)	
Clinical		
Blood glucose level	4-6hrly	Twice a day once stable

7.5. Complications

Following complications are commonly associated with TPN

- Mechanical Complications
- Metabolic Complications
- Infectious Complications

a. Mechanical Complications Related
to vascular access technique:

- air embolism
- arterial injury
- bleeding
- brachial plexus injury (A network of nerves formed by cervical and thoracic spinal nerves and supplying the arm and parts of the shoulder)
- catheter mal-placement
- catheter embolism (A coiled worm shaped aggregate of platelets and fibrin)
- thoracic duct injury **Related to catheter In-situ:**
- Venous thrombosis
- Catheter occlusion

b. Metabolic Complications
Abnormalities related to excessive or inadequate administration:

- hyper / hypoglycemia
- electrolyte abnormalities
- acid-base disorders
- hyperlipidemia

Hepatic complications

- Biochemical abnormalities

- Cholestatic jaundice (cholestasis is decrease in bile flow due to impaired secretion of hepatocytes or due to obstruction of bile flow.)
- too much calories (carbohydrate intake)
- too much fat

c. Infectious Complications

- Insertion site contamination
- Catheter contamination
- improper insertion technique
- contaminated TPN solution
- contaminated tubing
- Secondary contamination
- Septicemia (blood poisoning)

8. Stopping a TPN

Stop TPN when enteral feeding can restart. Wean slowly to avoid hypoglycemia. Give IV Dextrose 10% solution at previous infusion rate for at least 4 to 6h. Alternatively, wean TPN while introducing enteral feeding and stop when enteral intake meets TEE (total energy expenditure)

9. Prescription in Infants

Premature infants tolerate TPN from day 1 of post-natal life. Parenteral nutrition can be delivered using standardized or individualized bags. Standardized bags are both easier and cheaper. Some babies, particularly if they are very unstable, may need individualized bags. Individualized prescription should only be done after consultation with the consultant on service. **Starter Parenteral Nutrition** Suitable for:

- preterm infants within the first 24-48 hours of life
- Term infants with fluid restriction and renal impairment.

Starter PN is low sodium and potassium free solution that provides good amount of amino acids at less volume.

Continued usage of these solutions is dependent on the electrolyte status of infant.

Commence as soon as central line access obtained.

Standard Preterm Parenteral Nutrition:

Standard solution for preterm infants after 24-48 hours of age.

10. Recommendations:

Preoperative TPN:

- Only to severely malnourished patients
- 7-10days pre-op **Postoperative TPN:**
- Patients who experience complication resulting in inability to tolerate oral diet for
- 7-10 days in previously well-nourished patients
- 5-7 days in malnourished patients

11. References

- Calculating Parenteral Feedings HSCI 368, D. Chen-Maynard, PhD, RD
- Total parenteral nutrition by mrs.k.shailaja.,m.pharm dept of pharmacy practice, srm college of pharmacy.
- TPN origin and calculations Naureen Iqbal slideshare.com
- Recollections of pioneer in nutrition: Landmark in development of parenteral nutrition. J Am Coll of Nutrition.1992 Aug;11(4):366-73.
- Appropriate protein provision in critical illness: a systematic and narrative review. Am J Clin Nutr 2012. 96. 591-600.
- Total parenteral nutrition in the surgical patient: a meta-analysis. Can J Surg 2001, 44:102-
  11.
- http://health.csusb.edu/dchen/368%20stuff/TPN% 20calculation.htm
- http://clincalc.com/TPN/Macronutrients.aspx