NHIA TALK INFUSION WEBINAR

Parenteral Nutrition : A Deep Dive into ILE and the Use of Alternative Lipid Emulsion Formulations in the Adult and Pediatric Population

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Disclosure

No relationships to disclose.

Course Objectives

- Introduction to PN and ILE
- Fatty Acids and their role in inflammation
- Available ILE and their unique properties
- ILE Dosing
- Administration and Best Practices
- Complications of ILE use
- Monitoring PN in the home setting
- Case Study

Parenteral Nutrition Basics

- Intravenous feeding modality that bypasses the GI Tract
- Developed in 1967 by Dr Stanley Dudrick at the University of Pennsylvania Hospital and transformed how we care for patients with feeding complications
- Provides necessary macronutrients, vitamins and minerals
- PN solutions most often contain a combination of Dextrose, AA, Lipids, vitamins, minerals and trace elements

Lipid Injectable Emulsion (ILE)

- The American Society of Parenteral and Enteral Nutrition (ASPEN) and the FDA have adopted this new terminology to decrease risk of potential errors
- Replaces previous terminology Intravenous Fat Emulsion (IVFE) to prevent confusion with IV Iron (IVFe)
- ASPEN announced this change in 2017 and ILE was added to the approved abbreviation list and updated in all publications and presentations[1,2]

Lipids and ILE

- Lipids represent one component of PN solutions that:
  - Provide a calorically dense source of calories
  - Supply essential Fatty Acids
  - Allow for a lower dextrose-load

The Role of Fatty Acids[3]

- Fatty Acids are:
  - A necessary source of cellular energy
  - Important components of cell membranes
  - Precursors to modulators important in immune function, inflammatory response, platelet aggregation and neurotransmitter release
  - Pro-inflammatory, inflammatory neutral or anti-inflammatory

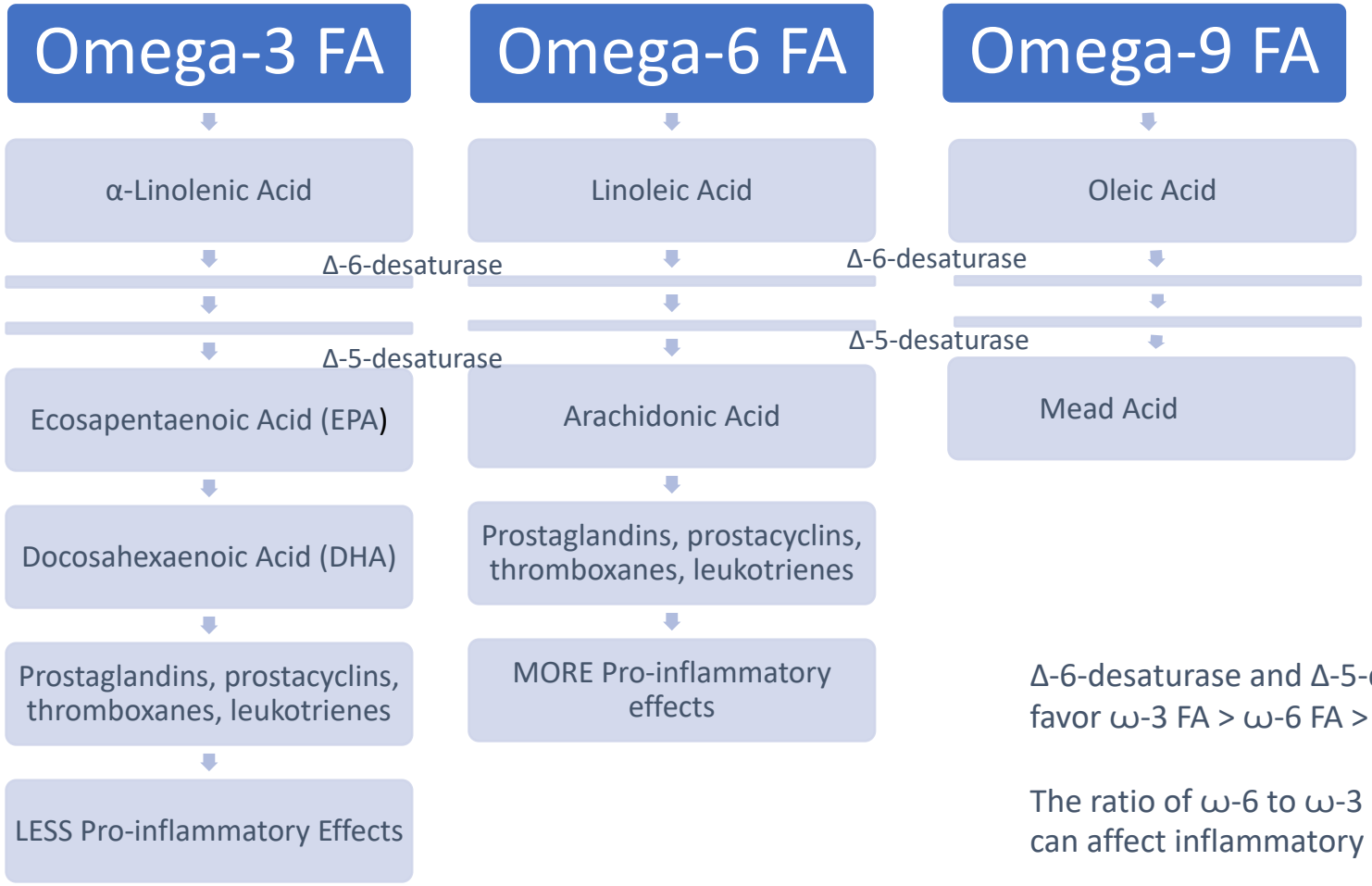
Fatty Acids: Classification[4,5]

Characteristics	Linoleic Acid	α-linolenic Acid	Oleic Acid
Number of Carbon Atoms: • Short chain (2-4 carbons) • Medium chain (6-12 carbons) • Long chain (14-18 carbons) • Very long chain (20+ carbons)	Long Chain 18 carbons	Long Chain 18 carbons	Long Chain 18 carbons
Number of double bonds: • Saturated (no double bonds) • Mono-unsaturated (one double bond) • Poly-unsaturated (2 or more double bonds)	PUFA	PUFA	MUFA
Position of double bonds: Location of the first double bond from the methyl end is the omega (ω) carbon	**ω-6**	**ω-3**	**ω-9**

Fatty Acids in ILE

- Different oils provide varying amounts of omega-3, omega-6 and omega-9 fatty acids.
- Inflammatory properties of the eicosanoids produced by FA metabolism differ between omega-3, omega-6 and omega-9 fatty acids.[6,7]
- The development of novel ILE have addressed the type of fatty acids and ratio of fatty acids present to promote the therapeutic effects of regulation of the inflammatory response and modulation of immunity.[8]

Fatty Acid Metabolism[4,6,7]



Δ-6-desaturase and Δ-5-desaturase favor ω-3 FA > ω-6 FA > ω-9 FA

The ratio of ω-6 to ω-3 FA present can affect inflammatory status

Other Components of ILE

- Phytosterols[9]
  - Plant sterols naturally present in plant oils in differing amounts
  - Minimal oral absorption
  - Hepatobiliary clearance
  - Association with PNALD
- Alpha-tocopherol[10]
  - Antioxidant properties
  - Prevents lipid peroxidation
  - Amount of natural α-tocopherol in ILE varies with oil type

Available ILE Formulations

- 1st Generation: Soy Oil ILE – Rich in □-6 linoleic acid
- 2nd Generation: Soy:MCT ILE (Not available in US) – attempt to decrease □-6 load
- 3rd Generation: Olive Oil containing ILE- High in □-9 Oleic Acid and still supplies sufficient □-6
- 4th Generation: Fish Oil containing ILE (either alone or in combination with other oils) – Rich in α-tocopherol and □-3 DHA and EPA

Available ILE Formulations

More Proinflammatory

Soybean Oil

↓

MCT Oil

↓

Olive Oil

↓

Less Proinflammatory

Fish Oil

Available ILE Formulations-FA Content

ILE Lipid Source (%)	Linoleic Acid Content (ω-6)	α-linolenic Acid Content (ω-3)	DHA Content (ω-3)	EPA Content (ω-3)	Oleic Acid Content (ω-9)	ω-6:ω-3 FA Ratio	α-tocopherol Content
Soybean oil 100%[11-12]	44-62%	4-11%	0	0	24.5%	7:1	35-38mg/dL
Soybean 20%: Olive Oil 80%[13]	13.8-22%	0.5-4.2%	0	0	44-79.5%	9:1	32mg/dL
Soybean oil 30%: MCT 30%: Olive Oil 25%: Fish Oil 15%[14]	14-25%	1.5-3.5%	1-3.5%	1-3.5%	23-45%	2.5:1	~200mg/dL
Fish Oil 100%[15]	1.5%	1.1%	14-27%	13-26%	4-11%	1:8	150-296 mg/dL

Contraindications for the use of ILE

- Allergy to any ingredient of the ILE
  - Soy, olive oil, coconut, fish, shellfish, eggs, peanuts
- Lipid Disorders
  - Serum TG > 1000mg/dL
- Fish oil is contraindicated in patients with severe hemorrhagic disorders[15]

Available ILE for Adult Use in U.S.

- Soybean Oil ILE
- Soybean : Olive Oil ILE
- Multi-Oil ILE
- Approved indications for use:
  - Source of calories and essential fatty acids when oral or enteral nutrition is not possible, insufficient or contraindicated[11-14]

ILE – Adult Dosing

ILE Lipid Source	kCal /mL (% solution)	Manufacturer's dosing guidelines	Max dosing guidelines
Soybean oil[11,12] *Intralipid® (Baxter) Nutrilipid® (B. Braun Medical)	2kcal/mL (20%)	1 to 1.5g/kg/day	2.5gm/kg/day
Soybean: olive oil[13] Clinolipid® (Baxter)	2kCal/mL 20%	1 to 1.5g/kg/day	2.5gm/kg/day
Multi-oil[14] SMOF® (Fresenius Kabi)	2kCal/mL 20%	1 to 2g/kg/day	2.5g/kg/day
Fish oil[15] Omegaven® (Fresenius Kabi	10kCal/mL 10%	Not currently approved for adult use in U.S.	Not currently approved for adult use in U.S.

Available ILE for Pediatric Use

- Soybean Oil and Fish Oil are approved for Pediatric use

- Approved indications for use:
  - Soy ILE: source of calories and EFA
  - Fish ILE: source of calories and EFAs specifically in pediatric patients with PN-associated cholestasis.[15]

ILE – Pediatric Dosing

ILE Lipid Source	kCal/mL (% Solution)	Mfg. Dosing Guidelines	Max Dosing Guidelines	Rate of infusion Guidelines
Soybean oil[11,12] Intralipid® (Baxter) Nutrilipid® (B. Braun Medical)	2kCal/mL 20%	Preterm and term infants up to 1 yrs: 1-2g/kg/day	3gm/kg/day	0.05mL/min x 15-30min, then gradual increase to max 0.75mL/kg/hour
		11 to <17 yrs: 1g/kg/day	2.5gm/kg/day	0.05mL/min x 15-30min, then gradual increase to max 0.5mL/kg/hour
Soybean: olive oil [13] Clinolipid® (Baxter)	2kCal/mL 20%	Not currently indicated for use in Pediatric population in the US		
Multi-oil[14] SMOF®	2kCal/mL 20%	Not currently indicated for use in Pediatric population in the US		
Fish Oil (Omegaven)[15]	10kCal/mL 10%	1g/kg/day	1g/kg/day	0.05mL/min x 15 to 30 min then increase to max 1.5mL/kg/hour (0.15g/kg/hour)

Administration of ILE

- Parenteral Nutrition is a high risk “medication”
- Guidelines exist for all facets of PN from ordering and prescribing to administration[16,17]
  - ASPEN
  - Infusion Nurses Society

Administration of ILE

- All ILEs can be administered via peripheral or central venous access.
- Can administer alone or mixed with PN as a total nutrient admixture (TNA)
- TNA cannot always be administered peripherally – must check osmolarity

Administration of ILE[16,17]

- All ILE and TNA should be administered via filtered, non-DEHP infusion set.
  - Non-vented unless infusing Fish Oil ILE (Omegaven®) separately from its glass container [15]
- 1.2-micron filter
- Administer via infusion pump with rate control
- Recommendations for hang time
  - 12 hours for ILE alone
  - Max 24 hours for ILE mixed in a TNA

Administration of ILE- TNA Stability Concerns

- ILE mixed in TNA must follow stability and sterility guidelines [18]
- ILE can be destabilized
  - acidic pH (<5)
  - inappropriate electrolyte content (++)
- Follow proper order of mixing to avoid issues with stability

Administration of ILE – TNA Stability Guidelines

- ASPEN recommendations based on Soybean ILE:[19]
  - Dextrose ≥ 10%
  - Amino Acids ≥4%
  - Soybean ILE ≥ 2%

- Beyond Use Date (BUD) assigned to TNA with soybean ILE can be up to 9 days from preparation with proper storage[18]

- Alternative ILE:
  - Manufacturer guidelines should be followed for mixing in TNA
  - Medical information can be consulted for stability information

Multi-Chamber Bag PN (MCB-PN)

- When TNA stability is of concern, MCB-PN may be an option
- Commercially available
- Activated just prior to infusion; no instability or incompatibility concerns
- Long shelf life – room temperature storage prior to activation

Multi-Chamber Bag PN (MCB-PN)

- Currently two manufacturers market MCB-PN in the U.S.
- Two Chamber and Three Chamber Options
- Various volumes and concentrations
- With and without electrolytes
- Products with alternative Lipid sources in development

MCB-PN (Available Options)

	Two Chamber MCB-PN (Clinimix and Clinimix-E Baxter) [20]	Three Chamber MCB-PN (PeriKabiven and Kabiven (Fresenius Kabi) [21]
Patient Population	Pediatric and Adult	Adult Only
Volume Available	1000mL and 2000mL	1026mL, 1540mL, 2053mL, 2566mL
Lipid Emulsion	Not included	39g per Liter Soybean Oil
Dextrose concentration	5 to 25%	9.8%
Amino Acid Concentration	2.75% to 5%	3.31%
Standard Electrolytes	With or without	with

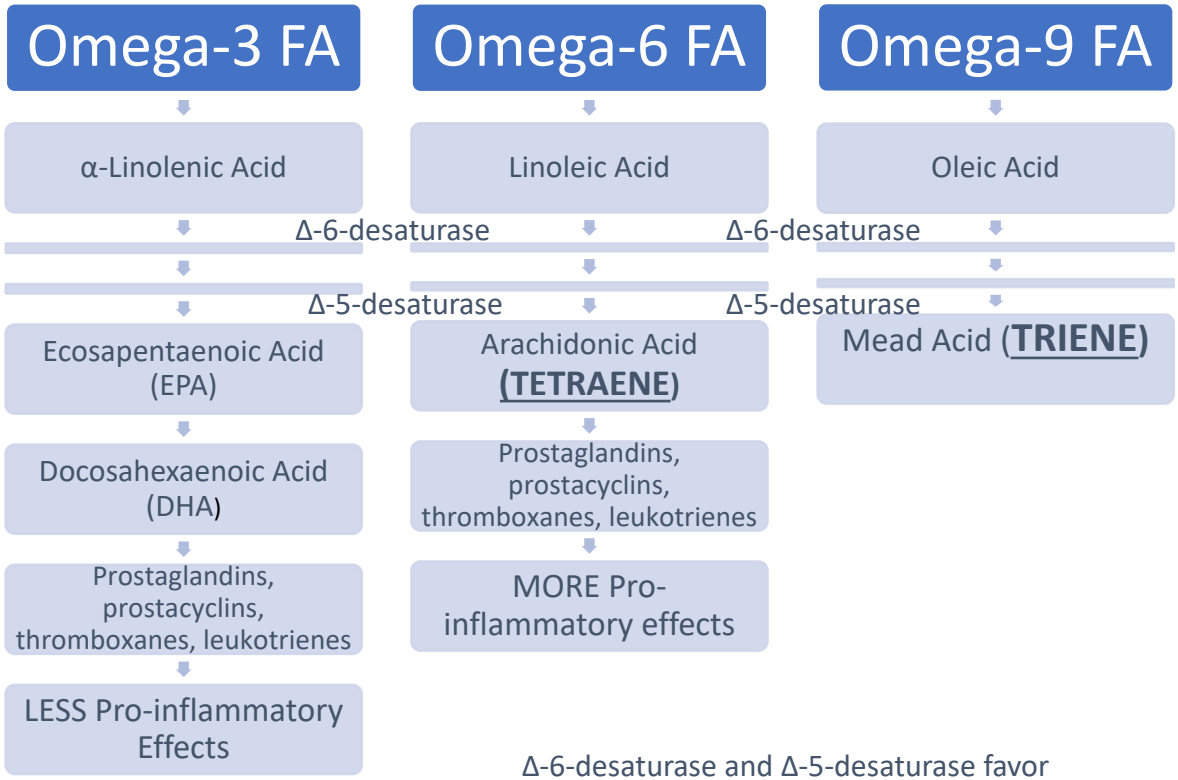
Administration – Additional Concerns

- Repackaging for infant/neonate use[16,22]
- Best practice: infuse from manufacturer's container
- Neonate/infant doses can be very small volumes
- If repackaging is necessary:
  - Aseptically performed
  - Maximum 12-hour infusion time per container

Complications of ILE use

- Adverse Events: hyperlipidemia, hypercoagulability, thrombophlebitis, thrombocytopenia.[11-15]
- Fat Overload Syndrome[22,23]
- Refeeding Syndrome[24]
- Catheter Related Bloodstream Infections[25,26]
- Essential Fatty Acid Deficiency

Fatty Acid Metabolism and EFAD[4,6,7]



Δ-6-desaturase and Δ-5-desaturase favor ω-3 FA > ω-6 FA > ω-9 FA

If essential FAs, linoleic (ω-6) and α-linolenic acid (ω-3), are not available in sufficient quantity, metabolism of *oleic acid (ω-9) increases.*
*Mead Acid (a triene) concentrations increase > Arachi*donic Acid (a tetraene).
This triene-tetraene ratio can be measured and a value >0.2 indicates an essential fatty acid deficiency (EFAD)

Clinical Symptoms: Dry, scaly rash, poor wound healing, hair loss, increased risk of infection, inadequate growth in children

Amount of ILE to Prevent EFAD[27]

ILE Lipid Source	Amount of ILE per day Necessary to prevent EFAD in Adults
Soybean oil Intralipid® (Baxter)[11] Nutrilipid® (B. Braun Medical)[12]	**38mL required/1000 kcals (4% of total energy)**
Soybean: olive oil Clinolipid® (Baxter)[13]	**113mL / 1000 kcals (4% of total energy)**
Multi-oil SMOF® (Fresenius Kabi)[14]	**113mL / 1000 kcals (4% of total energy)**
Fish oil Omegaven® (Fresenius Kabi)[15]	**No data for adults.**

Common Indications for Home Parenteral Nutrition[28]

- Crohn's Disease and other malabsorptive disorders
- Fistulae
- Gastroschisis
- Malignant bowel obstruction or carcinomatosis
- Radiation enteritis
- Motility disorders
- Short bowel syndrome / Intestinal failure
- Neonates in critical care setting when enteral nutrition does not promote adequate growth
- When use of Enteral therapy has been evaluated and deemed to be not feasible
- Preoperative Patients that are severely malnourished and unable to tolerate oral or enteral nutrition

Considerations for Appropriateness of Home PN[29]

- Adequate Financial Coverage
- Ability to perform therapy and availability of caregiver support
- Appropriate vascular access
- Medical stability before initiation of PN

Considerations for Appropriateness of Home PN

- Proper training in the storage, set-up and administration of PN
- Instruction in the areas of aseptic technique, compatibility of additives and medications added to the PN bag
- Ability to recognize complications of parenteral nutrition support
- Ability to visually inspect each bag of PN prior to infusion and recognize unusual appearance of PN / ILE

Safe Home PN Administration

- If prepared in accordance with USP <797>, the TNA:[18]
  - Can be assigned a Beyond Use Date (BUD) of *up to* 9 days from preparation
  - Should be shipped and stored properly under refrigeration
  - Aseptic technique must be followed for all manipulation

Visual Inspection: Signs of PN Instability[31]

- Aggregation (change in droplet size and distribution)
- Color change
- Separation of phases during storage due to degradation of lipid emulsion
- Formation of a film
- Precipitation of insoluble components
- Degree of creaming (a translucent phase that appears at the bottom of the emulsion)
- Evidence of cracking (appearance of a yellow liquid at the surface; may also be marbling or streaking)

Monitoring Home Parenteral Nutrition

- Employing a multidisciplinary approach to care and service can help mitigate the risks associated with administration of PN in the home
- The first Nutrition Support Team (NST) was identified in 1972 when a group of clinicians organized a team to look at the high incidence of sepsis in hospitalized PN patients[32]
- NSTs typically consist of a physician, an RD, a pharmacist and an RN

Attributes of Nutrition Assessment

- Review of the clinical documentation and patient interview
- Evaluation of:
  - Nutrition needs
  - Hydration status
  - Weight trend
  - Routine surveillance of lab indices

Lab Monitoring

- Monitoring labs allows for regular review of:
  - Fluid status
  - Electrolyte abnormalities
  - Metabolic complications
  - Glucose management
- A series of chemistries is identified and evaluated at the start of therapy and tend to decrease in frequency as we see less lability in results

Monitoring Home Parenteral Nutrition

- Lab Monitoring:[33]

	Initial	Weekly
Na, K, Cl, CO_2		
Ca, Phos, Mag		
Glucose		
BUN/Cr		
LFTs		
Triglycerides		
CBC		

Case Study

Patient: JM, 47-year-old male on Home TPN since March 2014

PMH: Presented to hospital in 2013 w/ pain and inability to tolerate an oral diet. Dx presumed to be autoimmune pancreatitis w/ recurrent episodes of acute pancreatitis w/ pseudo-mass in head of pancreas

Ongoing clinical complications: acute mesenteric ischemia w/ necrotic bowel, SMA thrombosis, SMV/portal vein thrombosis, right colectomy, pancreaticojejunostomy, hepaticojejunostomy, gastrojejunostomy; development of fistula

Case Study #1 - Adult

- Baseline Labs

	March 2014	March 2015	March 2016	March 2017	March 2018	March 2019	March 2020
Alk Phos	198	127	131	174	125	143	130
AST	37	36	17	122	19	21	30
ALT	36	48	19	172	23	19	28
TBili	0.9	2.9	0.4	8.1	0.8	0.7	0.8
Wt (kg) / BMI	68 / 23.5	65.9 / 22.7	52.2 / 18.0	50.0 / 17.2	59.0 / 20.4	75.0 / 25.9	76.8 / 26.5

3/2015 – TPN held due to elevated TBili with stable weight.
3/2015 – When TPN resumed, 25g given twice weekly. Permitted to try yogurt and very limited selections for fat.
3/2016 – Receiving 50g three times weekly. Significant weight loss noted with limited ability to increase calories.
3/2017 – Decreased lipid to 50g twice weekly. Further weight loss with limited ability to increase calories.
7/2017 – Initiated SMOF Lipid at 50g daily.
3/2018 – Continues on SMOF Lipid at 50g daily. Weight gain noted.
11/2018 – Placed on Bowel Transplant list at Georgetown.
3/2019 – Further weight gain to healthy BMI.
3/2020 – Sufficient weight gain achieved. Dextrose calories decreased, in conjunction with Georgetown Transplant Dietitian to prevent unwanted weight gain.

Maine Lipid

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Thank You

Any questions?

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