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OLIVE OIL BASED LIPID EMULSIONS

THE EUROPEAN EXPERIENCE

Program Disclosures

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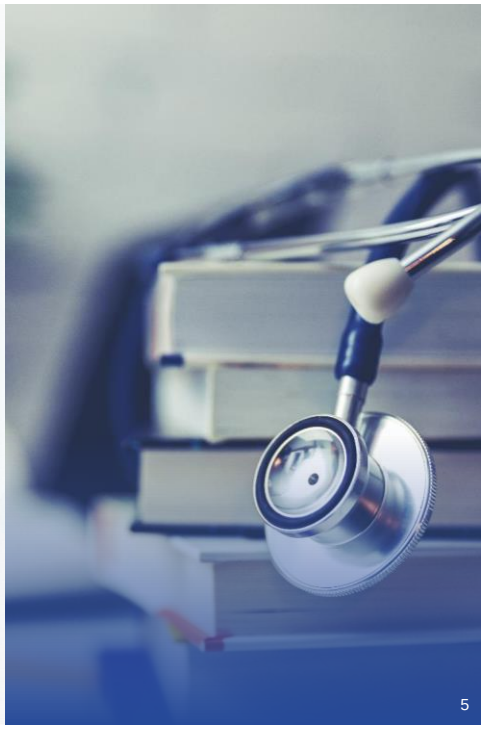
No Disclosures

Learning Objectives

01 Understand SCCM/ASPEN Covid-19 guidance for ILEs

02 Highlight the value of the Olive Oil-based lipid emulsion in PN prescriptions across the continuum of patient care

03 Explain why olive oil-based lipid could be considered as your standard lipid emulsion



SCCM/ASPEN COVID-19 RECOMMENDATIONS

SCCM/ASPEN Guidance for Treatment of COVID-19

Society of Critical Care Medicine
The Intensive Care Professionals

aspen LEADING THE SCIENCE AND PRACTICE OF CLINICAL NUTRITION
American Society for Parenteral and Enteral Nutrition

Nutrition Therapy in the Patient with COVID-19 Disease Requiring ICU Care

Updated April 1, 2020

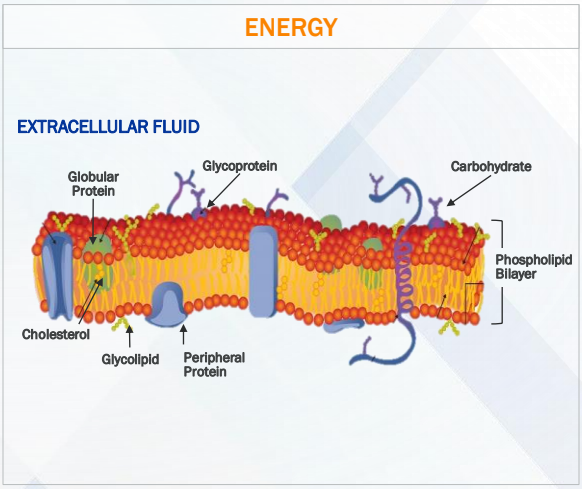
Recommendation 5: Formula Selection

If PN is required in the first week of ICU stay during the acute inflammatory phase of COVID-19, **limiting steps should be taken for use of pure soybean lipid emulsions** as outlined in published guidelines.[3] This can be accomplished **by withholding soybean lipids or using alternative mixed lipid emulsions**.

Why Are Lipids Important?

Why Do We Need Lipids?

- Meet caloric intake requirements with limited volume[1]
- Fulfill provision of essential fatty acids and components of cell membrane structure and fluidity[2]
- Regulate gene expression[2]
- Provide other non-essential fatty acids important to immune and other biological functions[2]



1. Schneider SM. Mediterr J Nutr Metab. 2011;4:87-91;
2. Hise M, Brown JC. *The ASPEN Adult Nutrition Support Core Curriculum*. 2nd Edition, 2012; Silver Springs, MD: American Society for Parenteral and Enteral Nutrition.

Biologic Effects of Fatty Acids

	N-6 PUFA	N-3 PUFA	N-9 MUFA
Fatty Acids	Linoleic, arachidonic	DHA, EPA (ALA)	Oleic
Inflammation	Stimulation (1,4,5) and Suppression (2,15)	Suppression (1,5,6,13)	Neutral (1,2)
Cellular immune functions	Suppression (1-3,7,16,17)	Suppression (12,13,16-18)	Neutral (1-3,16)
Oxidation potential (double bonds)	Moderate (2,8-11,14)	High (8,9,11,14)	Low (2,8-11,14)

Fatty Acid Effects are Dose Dependent

Fatty Acid Effects are Class Dependent
(PUFA, MUFA, n-6, n-3, n-9)

1. Calder PC et al, ICM (2010) 36:735;
2. Buenestado A et al, JPEN (2006) 30: 286;
3. Granato D et al, JPEN (2000) 24: 113;
4. Furukawa K et al, Nutrition (2002) 18:235;
5. Mayer K et al, Am J Resp Crit Care Med (2003) 167:1321;
6. Caughey GE et al, Am J Clin Nutr (1996) 63: 116;
7. Cury-Boaventura MF et al, JPEN (2006) 30: 115;
8. Watkins SM et al, J Lip Res (1998) 39: 1583;
9. Fuhrman B et al, Nutr (2006) 22: 922;
10. Goulet O et al, AJCN (1999) 70:338;
11. Xu Z et al, JPEN (2016) 40: 672;
12. Tull SP et al, PLoSBIOL (2009) 7:e1000177;
13. Hecker M et al, Crit Care (2015) 19: 226;
14. Bruna E et al, Lipids (1989) 24: 970;
15. Loo LS et al, J Infect Dis (1982) 146: 64;
16. Soyland E et al, Eur J Clin Invest (1993) 23: 112;
17. Calder PC et al, Clin Nutr (1994) 13: 69;
18. Miles EA et al, Proc Nutr Soc (1998) 57: 277

ω-6 (Soy) PUFAs: Immunosuppressive Effects

***In vitro* and *in vivo* impairment of**

- Lymphocyte proliferation[1]
- Lymphokine-activated killer cell generation[2] and activities[1]
- Chemotaxis and phagocytosis of neutrophilic granulocytes[3]
- Monocyte chemotaxis and phagocytosis[4]

Prolongation of graft survival in an animal transplant model[5]

These effects were dosage dependent[1,3,4]

1. Sedman PC, et al. JPEN J Parenter Enteral Nutr. 1990;14:12-17;
2. Sedman PC, et al. Br J Surg. 1991:78:1396-1399;
3. Wiernik A, et al. Am J Clin Nutr. 1983;37:256-261;
4. Fraser I, et al. Clin Nutr. 1983;2:37-40;
5. Grimm H, et al. Transpl Immunol. 1995;3:62-67.

ω-9 MUFA: Immune Function Neutral and May Interfere Less with Normal Inflammatory Responses [1,2]

- Omega-9 fatty acids (i.e., oleic acid within olive oil) influences the metabolic effects of lipids but does not produce eicosanoids[1]
- Studies have demonstrated a reduced lipid peroxidation, immune function impairment, and an inflammatory neutral effect of olive oil-based emulsions[1-4]

MUFA=monounsaturated fatty acids.

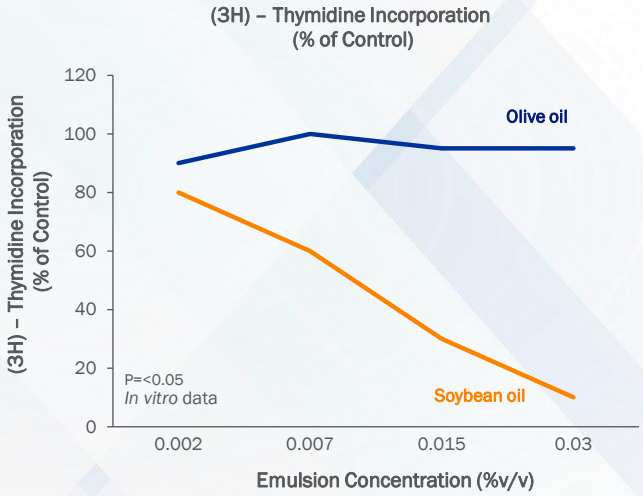
1. Pontes-Arruda A. *Clin Nutr Suppl.* 2009;4:19-23;
2. Waitzberg DL, et al. *JPEN J Parenter Enteral Nutr.* 2006;30:351-367;
3. Calder PC, et al. *Intensive Care Med.* 2010;36:735-749;
4. Reimund JM, et al. *Clin Nutr.* 2004;23:1324-1332.

Olive Oil has Little Impact on Lymphocyte Function Independent of the Dose

Human Lymphocytes

Olive oil–based ILE vs
Soybean oil–based ILE

Thymidine Incorporation
(% of control)



IVLE=intravenous lipid emulsions.
Adapted from Granato D, et al. *JPEN J Parenter Enteral Nutr.* 2000;24:113.

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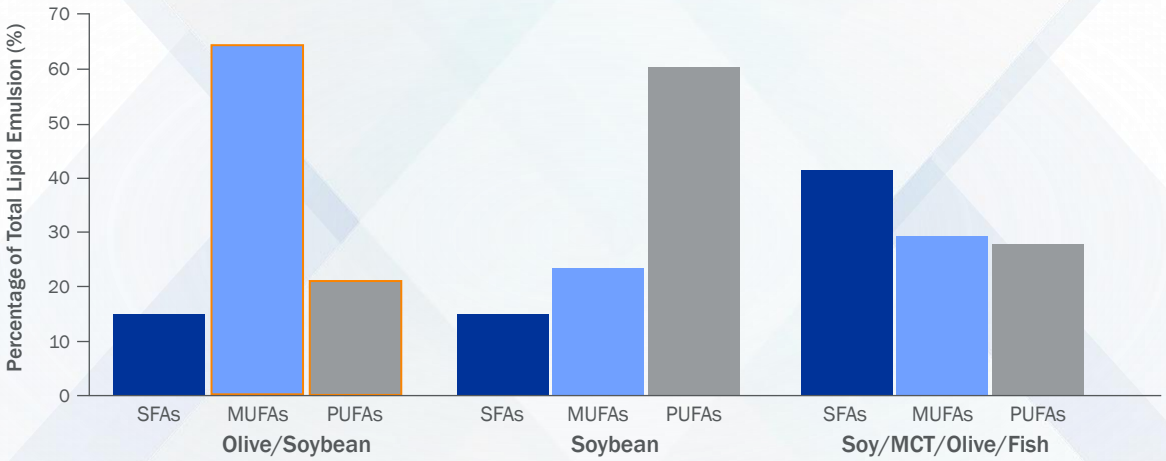
Fatty Acid Composition of Lipid Emulsions



SFA-saturated fatty acid; MUFA=monounsaturated fatty acids; PUFA= polyunsaturated fatty acids; LCT=long-chain triglycerides.
These IV Fat Emulsions are not approved or marketed in the U.S.A.
Adapted from Calder PC, et al. *Intensive Care Med.* 2010;36:735-749.

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Biological and Clinical Aspects of an Olive Oil-based Lipid Emulsion: Literature Review

Method

Medline and Embase databases (inception to 15 September 2017) were searched using the terms (parenteral nutrition or PN) AND olive AND (lipid* OR oil* OR emulsion* OR ILE OR ILE)

References identified in search (N=386)

- References excluded (n=271)
- Not relevant (n-115)
- Reviews (n=90*)
- Abstracts (n=52)
- Editorials/letters/comments (n=10)
- Case reports/case studies (n=5)

References included (n=115)

*Bibliographies of review articles were searched by hand to identify additional relevant articles. Cai W, et al. *Nutrients*. 2018; 2018;10(6), 776; https://doi.org/10.3390/nu10060776

Characteristics of Olive Oil-based Lipid Emulsions

Immune Function[1]

- Has beneficial effects on immune cell proliferation and function and/or immune cell death
- Appeared to be more neutral in its effect on inflammatory eicosanoid or cytokine production compared with other ILEs

Lipid Peroxidation[1]

Was associated with less lipid peroxidation compared with other ILEs, most likely due to its high MUFA and low PUFA content

Hepatobiliary Markers and Plasma Lipid Levels[1]

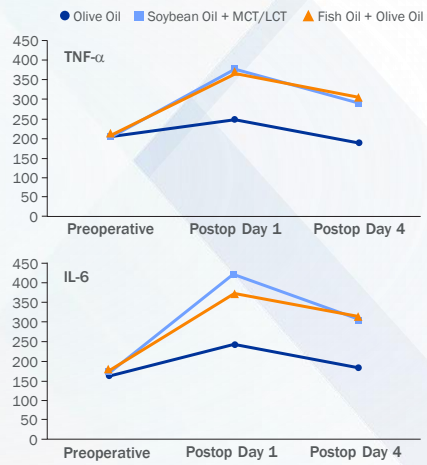
Was not associated with increased hepatobiliary and lipid disturbances

TNF=tumor necrosis factor; IL=interleukin.
Group I, soybean oil + medium chain triglycerides; group II, soybean oil + olive oil; group III, soybean oil + olive oil + fish oil.

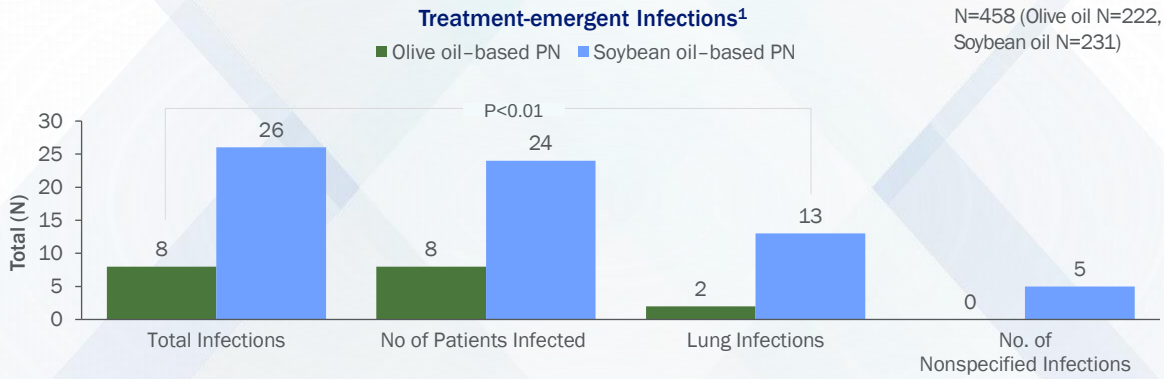
1. Cai W, et al. *Nutrients*. 2018;10(6), 776; https://doi.org/10.3390/nu10060776;
2. Demirer S, et al. *Ann Surg Treat Res*. 2016;91(6):309-315.

TNF-α and IL-6 Levels in Adult Patients Undergoing Major Abdominal Surgery[1,2]

(N=52)



IV Impact of Soybean Oil and Olive Oil-based Lipid Emulsions on Infections



In a large randomized controlled trial (N=458), olive oil-based PN was clearly associated with fewer infections compared to a soybean oil-based PN.

Adapted from Jia ZY, et al. *Nutr J.* 2015;14:119:1-15.

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What Do the Latest Guidelines Say?

SCCM-ASPEN Clinical Guidelines: Critical Care

SCCM-ASPEN suggests **withholding or limiting soybean-based ILE** during the first week following initiation of PN in the critically ill patient unless there's concern for essential fatty acid deficiency[1]

SCCM-ASPEN suggests that **alternative ILEs may provide outcome benefit** over soy-based ILE[1]

"Substitution of an alternative IVFE for PN, particularly an **OO-based preparation**, may improve outcomes when compared with the more standard SO-based product; however, the committee cannot make a recommendation at this time regarding substituting alternative IVFE sources for SO due to lack of availability on the market of these products in the United States" …[1]

ILEs= injectable lipid emulsions; PN=parenteral nutrition.
1. McClave SA, et al. *JPEN J Parenter Enteral Nutr.* 2016;40:159-211;
2. Vanek VW, et al (ASPEN position paper). *Nutr Clin Pract.* 2012;27:150-192.

ESPEN Guidelines: Parenteral Nutrition

ESPEN guideline on clinical nutrition in the intensive care unit

- The administration of ILEs should be generally a part of PN[1]
- Intravenous lipid (including non-nutritional lipid sources) should not exceed 1.5g/kg/day and should be adapted to individual tolerance[1]

Lipids are used in PN primarily due to their high caloric content and are thus a good concentrated source of energy, reducing the amount of carbohydrate that needs to be provided as part of the nutrition support[2]

Lipids provide the building blocks for cell membranes and provide EFAs, thereby preventing EFA deficiency[2]

LCT=long-chain triglycerides; MCT=medium-chain triglycerides.
1. Singer P, et al. Clin Nutr. 2019;38(1):48-79;
2. Calder PC, et al. Clin Nutr. 2018;37(1):1-18.

Case of COVID-19 Critically Ill Patient

Nutritional Management

Case Based on COVID-19 Experience – Privacy Proof

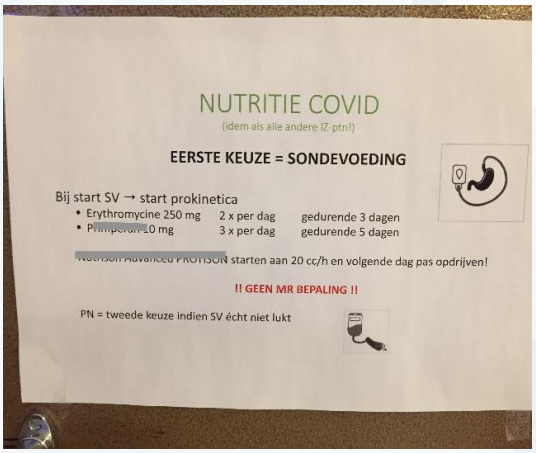
- **Male patient COVID19 >60y**
- **Respiratory failure – intubated ventilated**
- **Day 1 ICU**
- **Nutritional therapy is discussed**
  - No oral intake will be possible

Case Based on COVID-19 Experience – Privacy Proof

- **Gastric tube was inserted at intubation**
- **After stabilisation (low dose noradrenaline, low lactate) enteral nutrition was initiated 20ml/h.**
- **Prokinetics were initiated IV: erythromycin 250mg 2/d and metoclopramide 10mg 3/d**

Nutrition COVID

- First choice = enteral
- Start prokinetics
- Start at 20ml/h until target is known
- NO GASTRIC RV
- PN when EN is insufficient or impossible



Case Based on COVID-19 Experience – Privacy Proof

- **Targets were set:**
  - Protein 65x1.3g = 85 g
  - Calories: indirect calorimetry
- **To be reached by day 3-4**
- **Enteral or combined with Supplemental Parenteral Nutrition**

Case Based on COVID-19 Experience

3067 kcal/24h

- Target 2396 ml/24h is 100ml/h of formula 1.28kcal/ml enteral OR
- Target 1535 ml/24h is 64ml/h of formula 2kcal/ml enteral

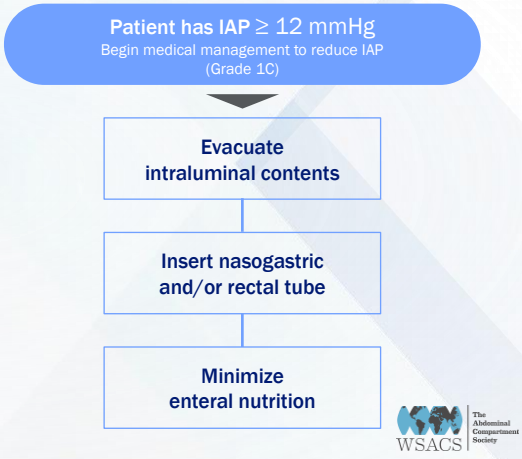
Pump rate was increased

Case Based on COVID-19 Experience – Privacy Proof

- On day 2 high intra-abdominal was pressure was measured and we needed to stop enteral nutrition
- Switch to parenteral
- Repeated IC to know caloric target
- Choice of ready to use bag

Nutrition COVID

- First choice = enteral
- Start prokinetics
- Start at 20ml/h until target is know
- NO GASTRIC RV
- PN when EN is insufficient or impossible



Case Based on COVID-19 Experience – Privacy Proof

- Switch to parenteral
- Repeated IC to know caloric target: 1853 kcal/24h
- Choice of ready to use bag
- 1853 kcal and 85g protein,
  - Vitamins and trace elements are standard order
- Start parenteral nutrition

Case Based on COVID-19 Experience – Privacy Proof

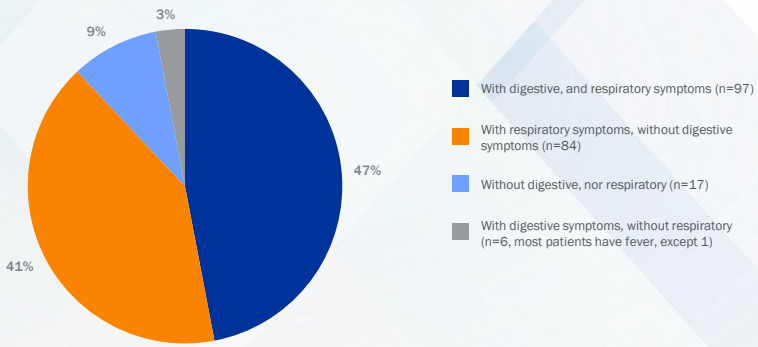
- Male patient COVID19 > 60y
- Respiratory failure – intubated ventilated
- Day 1 ICU
- Nutritional therapy
- Enteral nutrition first
- Parenteral nutrition second
- After stabilisation first combined therapy, then enteral only

Case of COVID-19 Critically Ill Patient Nutritional Management

The American Journal of Gastroenterology
Wolters Kluwer Health

Clinical Characteristics of COVID-19 Patients with Digestive Symptoms in Hubei, China:
A Descriptive, Cross-Sectional, Multicenter Study

Frequency of COVID-19 patients with or without digestive symptoms



Lei Pan, MD, PhD[1,2], Mi Mu, MD[3,4], Pengcheng Yang, MD[5], Yu Sun, MD[6], Runsheng Wangm MS[7], Junhong Yan, MD[8], Pibao Li, MD[9], Baoguang Hu, MD, PhD[10], Jing Wang, MS[1], Chao Hu, MS[7], Yuan Jin, MD[6], Xun Niu, MD[6], Rongyu Ping, MD[2], Yingzhen Du, MD[7], Tianzhi Li, MD[2], Guogang Xu, MD, PhD[2], Qinyong Hu, MD[5], and Lei Tu, MD, PhD[11]

Take Nutritional Therapy Seriously. Act on What You Preach

ICU dietitian Joy and MD Joop:
indirect calorometry on COVID patients

First COVID19 ventilated patient leaves ICU in UZ Brussels

CEO hospital +
Nutrition Nurse Lode

Baxter

Thank you