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ESPEN LLL Course
Topic 18 - Nutritional Support in Intensive Care Unit Patients

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Lifelong Learning Programme

Lipids and Carbohydrates: How to Prescribe

Module 18.3

Elisabeth De Waele MD PhD

Dept of Nutrition/ICU
Universitair Ziekenhuis Brussel – Vrije Universiteit Brussel, Belgium

Learning objectives

1. Obtain knowledge of different lipids used in medical nutrition: specific metabolic and immune effects of fatty acids.
2. The role of carbohydrates
3. Fat as substrates and fatty acid classification and main functions
4. Potential indications and controversies around the omega-3 PUFA and the various IV fat emulsions
5. To be able to incorporate lipids and carbohydrates in a nutritional prescription.

Contents

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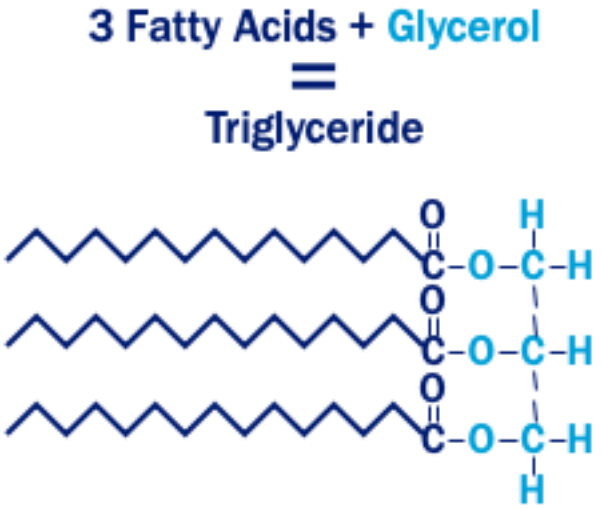
What Is a Lipid?

- Important source of energy[1]
- Provide structural and metabolically functional components of biological membranes[1]
- The lipids used in parenteral nutrition (PN) contain fatty acids in the form of triglycerides[2]
- A triglyceride consists of 3 fatty acid molecules bonded to a glycerol molecule[1]



1. Hise M, Brown JC. *The ASPEN Adult Nutrition Support Core Curriculum*. 2nd Edition, 2012. Silver Springs, MD: American Society for Parenteral and Enteral Nutrition; 2. Wanten GJA, Calder PC. *Am J Clin Nutr*. 2007;85:1171-1184.

What Is a Fatty Acid?

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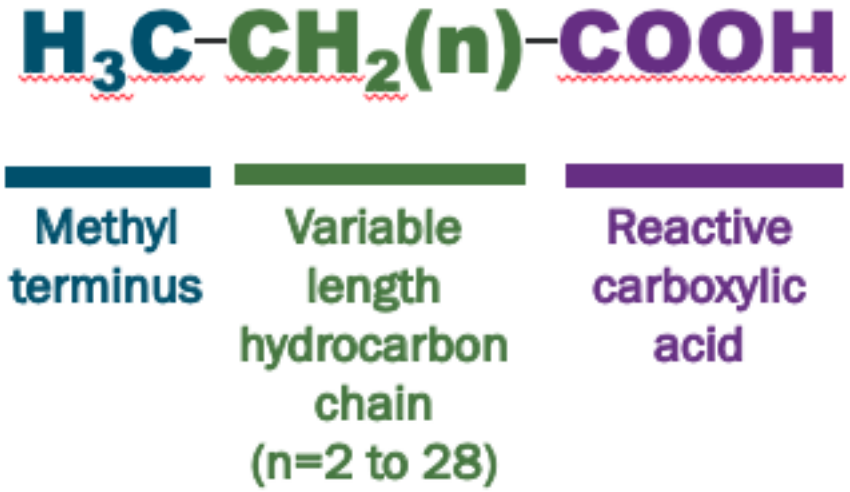
- hydrocarbon chains with methyl group at one end of the chain

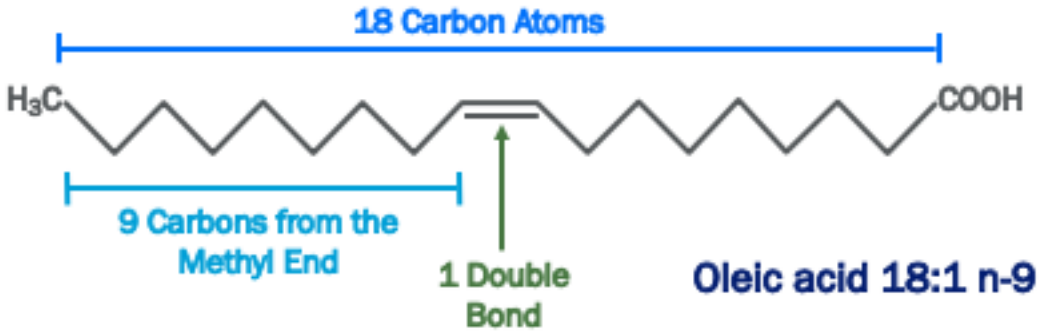
  and reactive carboxyl group at the other end



Wanten GJ, Calder PC. *Am J Clin Nutr*. 2007;85:1171-1184.

Fatty Acid Classification

1. Chain Length
2. Degree of Saturation: Presence and number of double bonds
3. Omega (ω) Classification: Position of the first double bond relative to the methyl end of the carbon chain

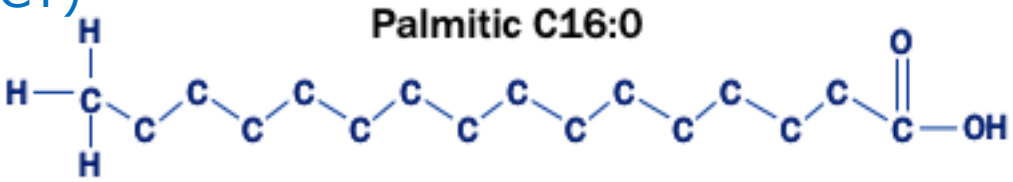


Wanten GJ, Calder PC. *Am J Clin Nutr.* 2007;85:1171-1184.

Fatty Acid Classification

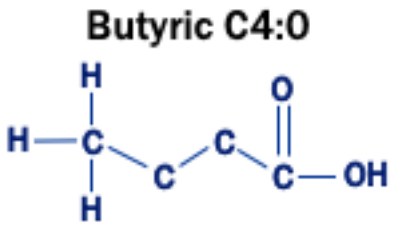
1. Chain Length

Long-chain fatty acids (LCT)
≥14 carbons[1]



Medium-chain fatty acids (MCT)
6-12 carbons[1]

Short-chain fatty acids
2-4 carbons[1]
Not used in PN[2]



Wanten GJ, Calder PC. *Am J Clin Nutr.* 2007;85:1171-1184.

Fatty Acid Classification

1. Chain Length
2. Degree of Saturation: Presence and number of double bonds

Saturated Fatty Acids (SFA):
No double bonds in carbon chain

Monounsaturated Fatty Acids (MUFA):
1 double bond in carbon chain

Polyunsaturated Fatty Acids (PUFA):
≥2 double bonds in carbon chain

Wanten GJ, Calder PC. *Am J Clin Nutr.* 2007;85:1171-1184.

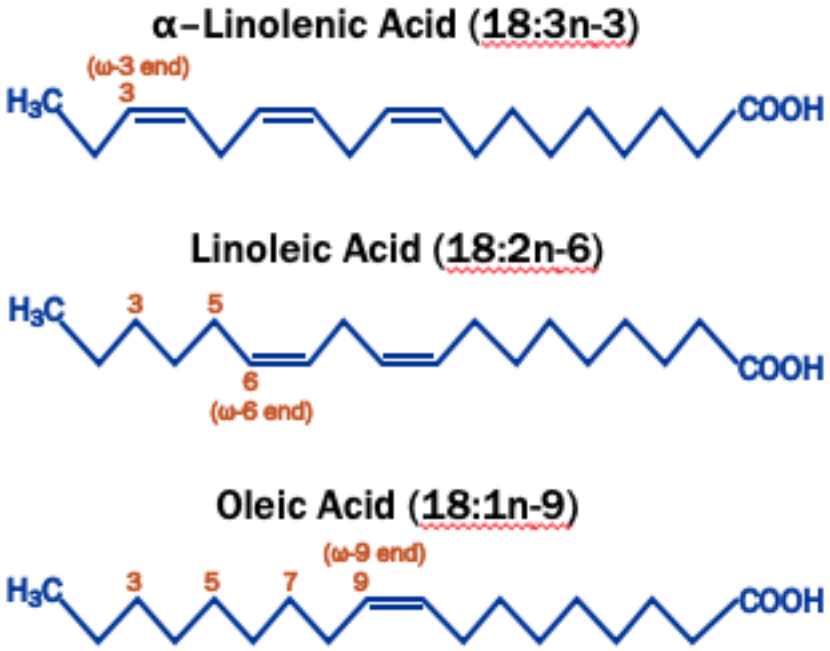
Fatty Acid Classification

1. Chain Length
2. Degree of Saturation: Presence and number of double bonds
3. Omega (ω) Classification: Position of the first double bond relative to the methyl end of the carbon chain

ω-3: First double bond is 3 carbons from the ω end

ω-6: First double bond is 6 carbons from the ω end

ω-9: First double bond is 9 carbons from the ω end



Wanten GJ, Calder PC. *Am J Clin Nutr.* 2007;85:1171-1184.

Importance of 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.

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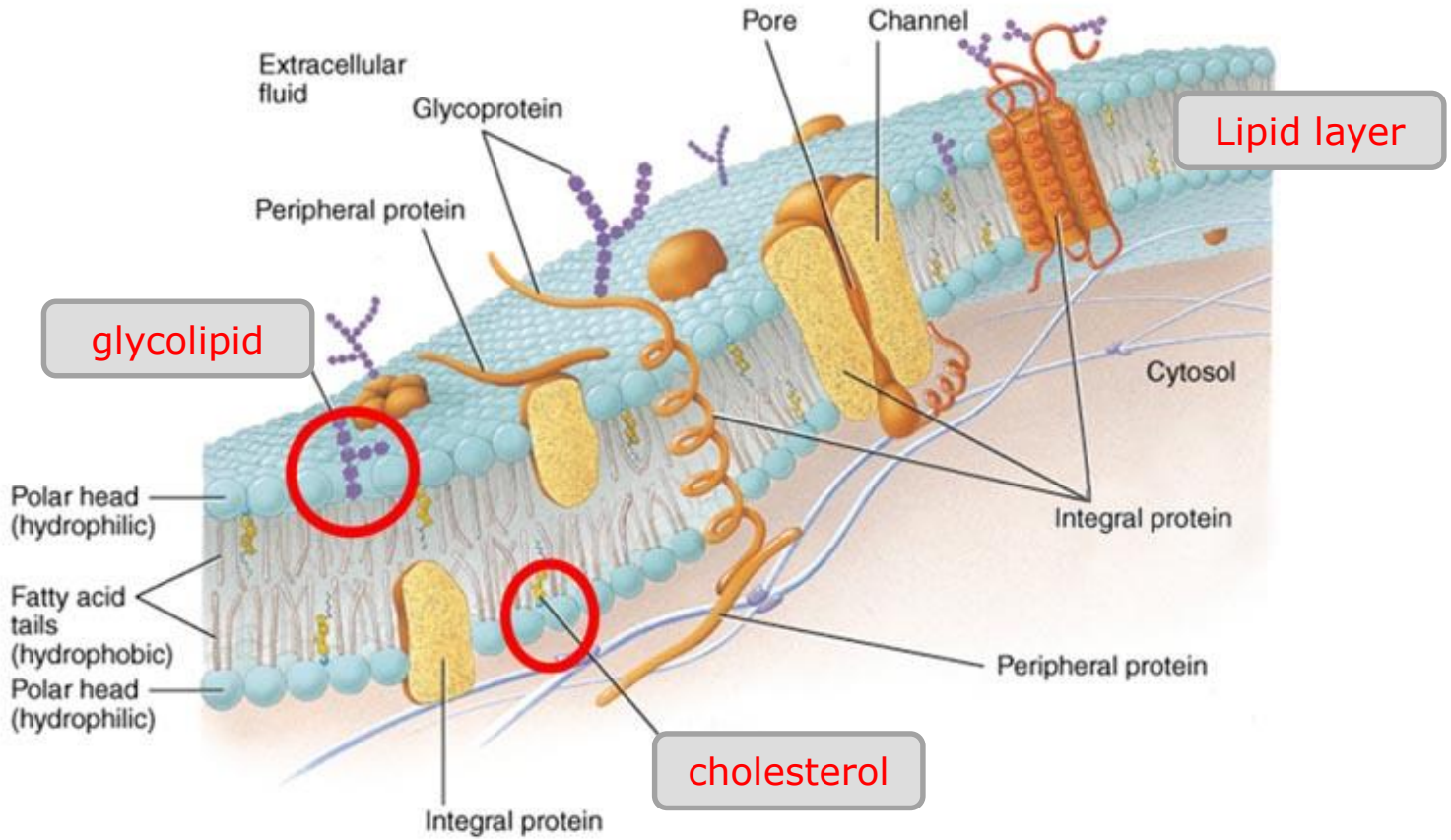
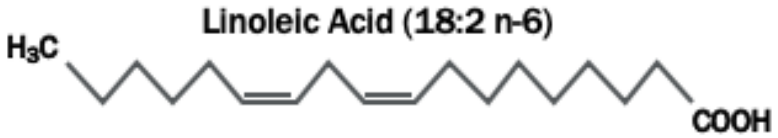


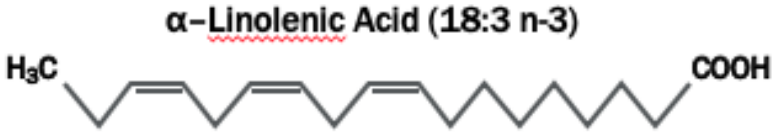
Essential Fatty Acids

- Can not be manufactured in the body and must come from our diet[1]
- Linoleic acid and α-linolenic acid are considered EFAs in humans[1,2]
- To prevent EFA deficiency: recommend intake:
  2.5% of total energy intake as linoleic acid
  0.5% of total energy intake as α-linolenic acid

Linoleic Acid:
An omega-6 (ω-6) fatty acid

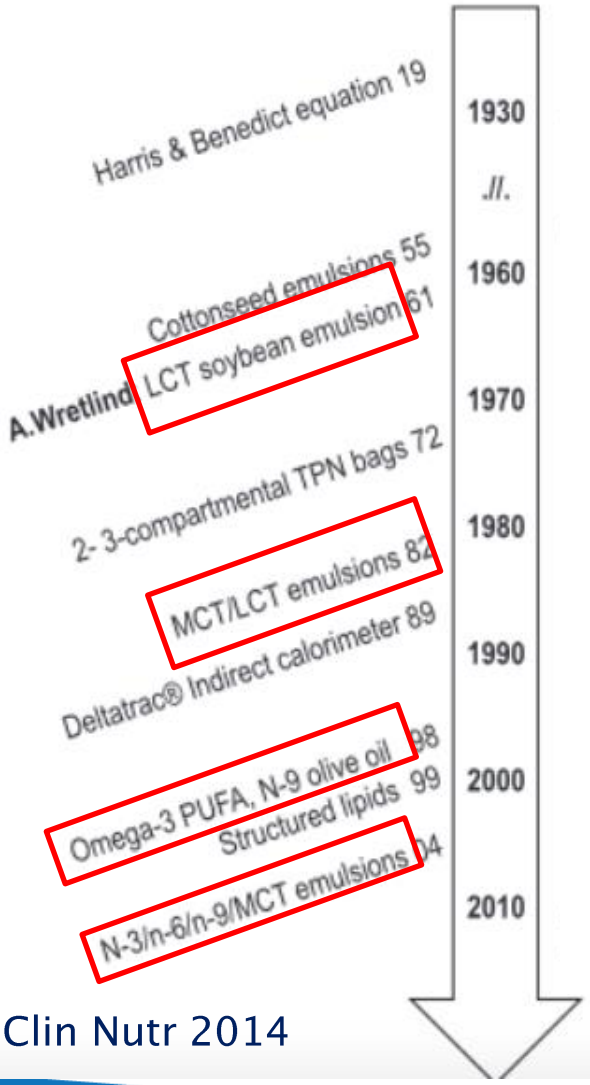


α-linolenic Acid:
An omega-3 (ω-3) fatty acid

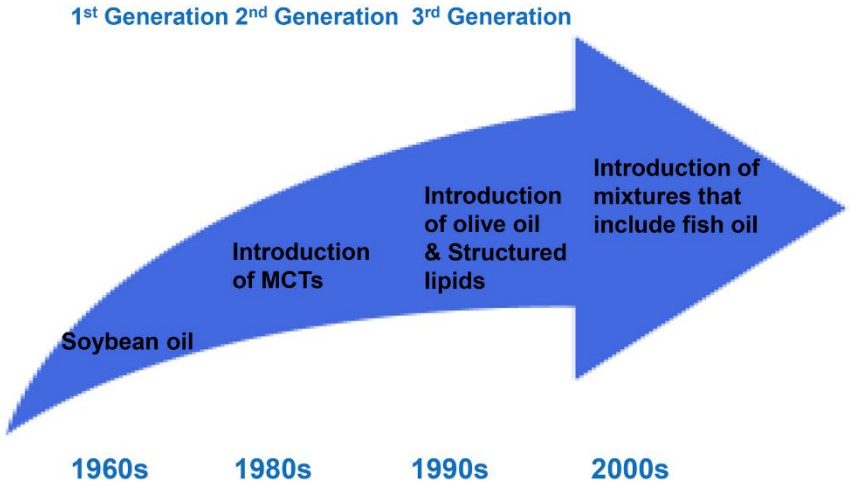


1. Wanten GJ, Calder PC. *Am J Clin Nutr.* 2007;85:1171-1184; 2. Fats and fatty acids in human nutrition. Report of an expert consultation, FAO Food and Nutrition Paper 91, FAO, Rome, 2010. (Final report). http://www.fao.org/3/a-i1953e.pdf.

Evolution intra venous lipid emulsion Parenteral Nutrition



Berger M, Clin Nutr 2014



Calder, Clin Nutr 2018

Specific fatty acids

1. LCT
   - Mainly n-6 fatty acids
   - Correlated with pro-inflammatory profile
2. LCT/MCT
   - Less pro-inflammatory
   - Fewer clinical infections
   - Favourable effect protein metabolism

Berger M, Clin Nutr 2014

Specific fatty acids

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3. Olive oil

- Preserve immune, hepatobiliary, endothelial cell function
- May reduce lipid peroxidation and plasma lipid levels

Little Impact on Lymphocyte Function Independent of the Dose

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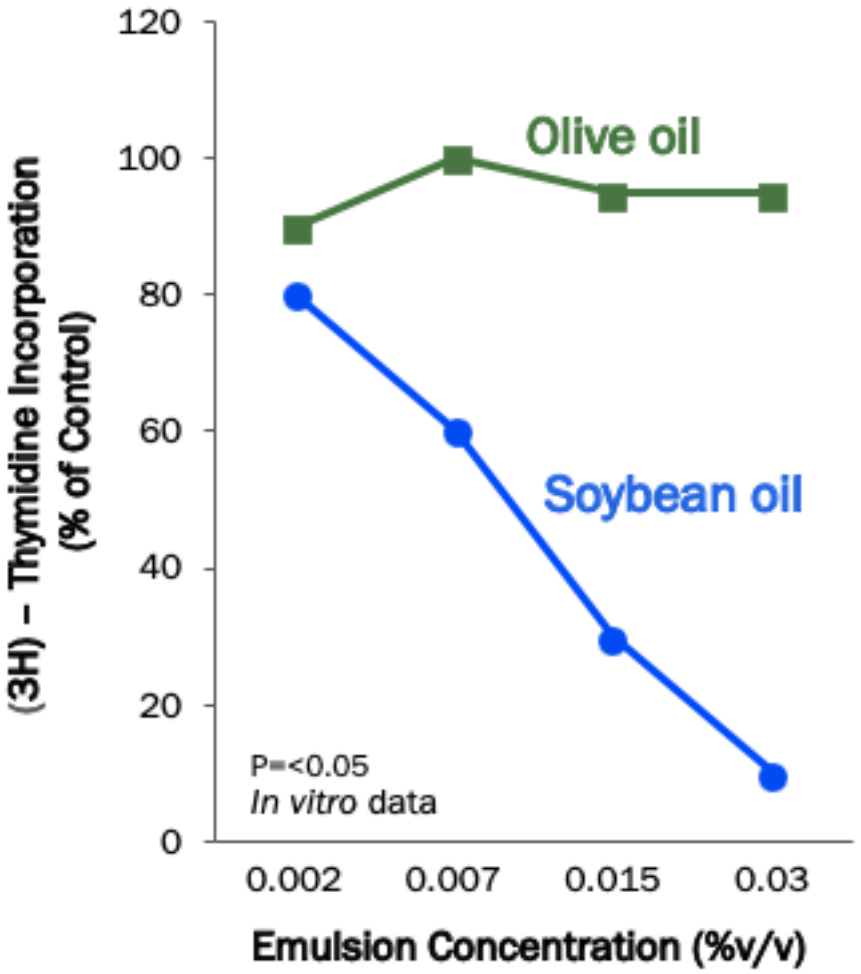
Human Lymphocytes

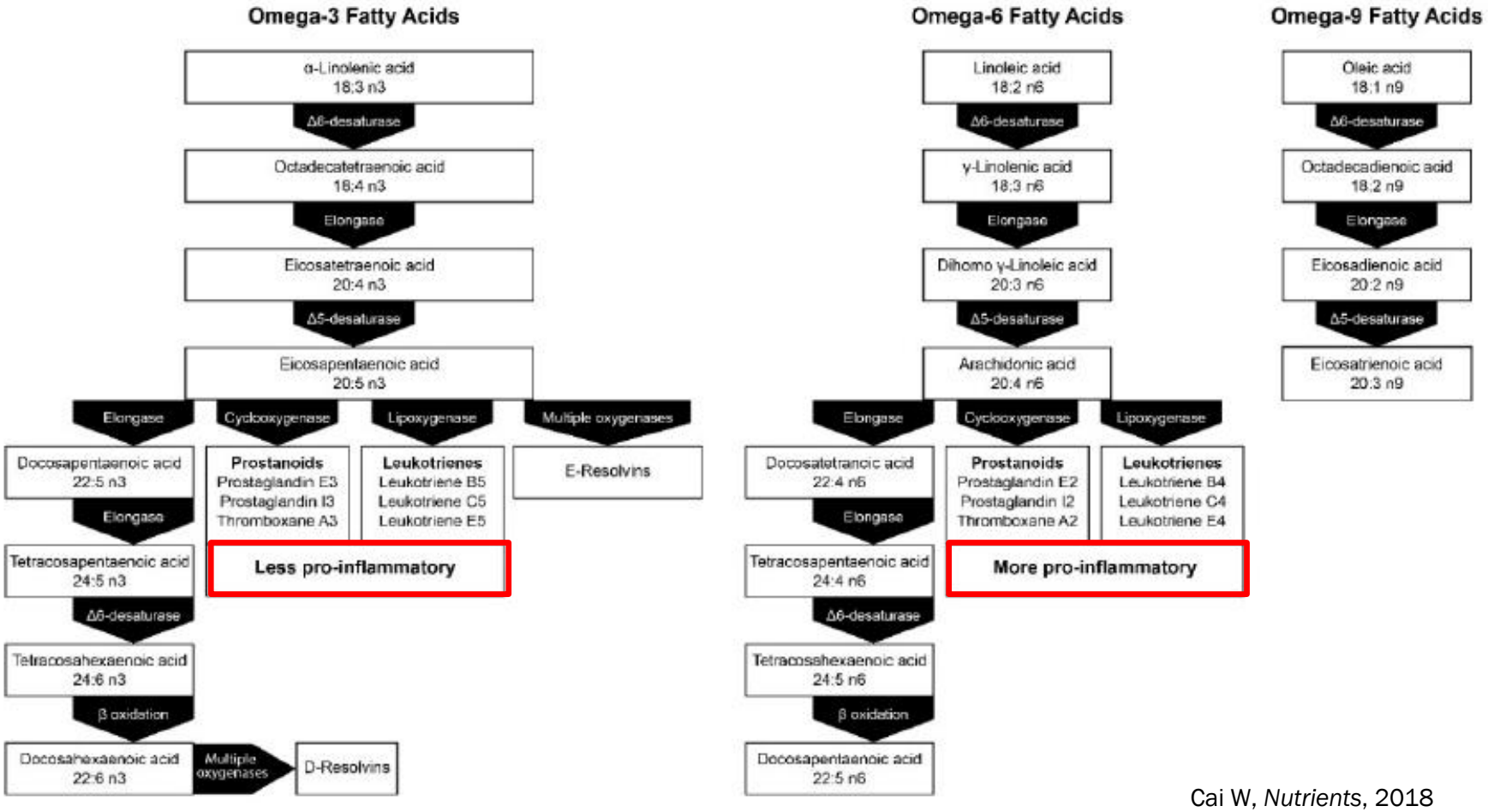
- Olive oil–based IVLE vs Soybean oil–based IVLE
- Thymidine Incorporation (% of control)



Cai W, *Nutrients*, 2018

Specific fatty acids

4. n-3/n-6/n-9/MCT



Cai W, *Nutrients*, 2018

ω-6 PUFAs: possible 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]

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: possible neutral effect on Immune Function[1,2]

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- Omega-9 fatty acids (i.e., oleic acid within olive oil) influences the metabolic effects of lipids but does not produce eicosanoids[1]

- Reduced lipid peroxidation, reduced immune function impairment, and an inflammatory neutral effect of olive oil-based emulsions[1-4]

MUFA=monounsaturated fatty acids.

1. Pontes-Aruda 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.

ω-3 PUFAs: Possible Dose-dependent Antiinflammatory Effects[1,2]

- EPA and DHA: different effects on immune cell functions and gene expression[3]
  - May decrease immune function by the high provision of PUFAS[4,5]

- EPA and DHA: immunomodulatory and anti-inflammatory effects[3,5]

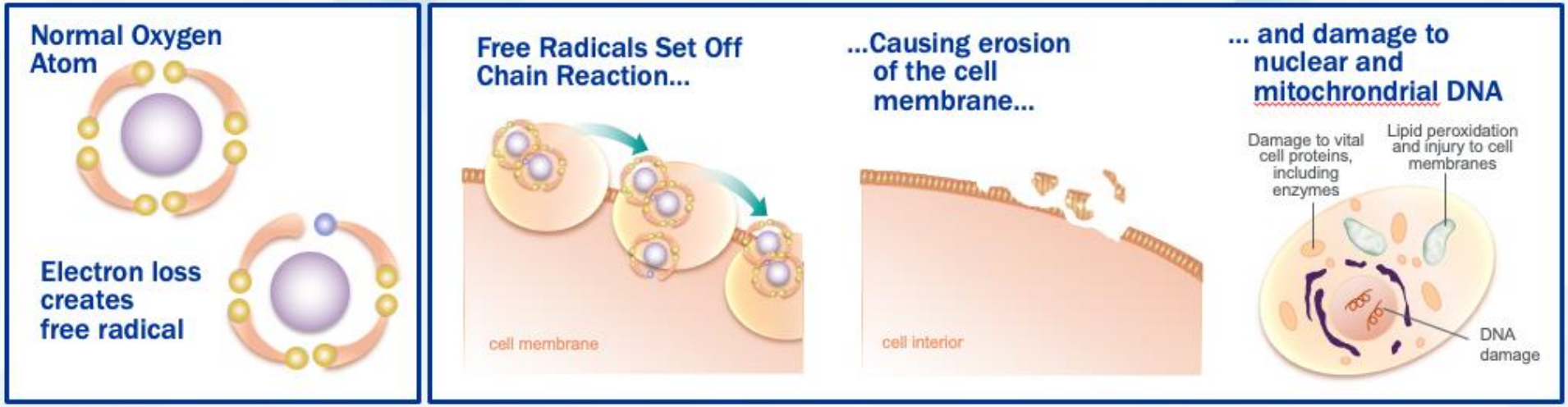
EPA and DHA from Fish Oil[3]

- Synthesis of eicosanoids
- Activity of the nuclear receptor
- Nuclear transcription factors
- Production of resolvins

1. Mayer K, Seeger W. *Curr Opin Clin Nutr Metab Care.* 2008, 2. Manzoni Jacintho T, et al. *Nutr Hosp.* 2009; 3. Waitzberg DL, et al. *Nutr Clin Pract.* 2009; 4. Reimund JM, et al. *Clin Nutr.* 2004; 5. Furst P, Kuhn KS. *Clin Nutr.* 2000;19:7-14.

Oxidative stress

- Oxidative stress: an imbalance between reactive oxygen species (ROS) production and antioxidant systems[1]
- Generation of free radicals results in a disruption of cellular processes[2]



1. Sies H. *Am J Med.* 1991;91:31S-38S; 2. Free radicals and reactive oxygen. www.vivo.colostate.edu/hbooks/pathphys/topics/radicals.html..

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Oxidative degradation leads to cell damage

- Increased numbers of double bonds (PUFAs) may increase risk of lipid peroxidation
- Most studies: no differences in oxidative stress markers between olive oil-based and soybean oil-based, MCT/LCT, or fish oil-based ILE

Roggero P Nutrition 2010,
Deshpande G J Ped Gastroent Nutr 2014

Metabolic side effects

Parenteral nutrition → Plasma cholesterol and triglyceride levels

‘Hypertriglyceridemia in ICU associated with sepsis, propofol, lipid solutions and overfeeding’

‘Concentrations of triglycerides exceeding 500 mg/l (5.6 mmol/L), levels that are considered very high in non-critically ill subjects, should trigger prompt investigation’

Berger M, Clin Nutr 2018

Metabolic side effects

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Parenteral nutrition → Plasma cholesterol and triglyceride levels

'The regular determination of blood cholesterol (total or HDL) has never been shown to be of relevance during critical illness'

Monitoring nutrition in the ICU

Mette M. Berger [a,*], Annika Reintam-Blaser [b,c], Philip C. Calder [d,e], Michael Casaer [f], Michael J. Hiesmayr [g], Konstantin Mayer [h], Juan Carlos Montejo [i,j], Claude Pichard [k], Jean-Charles Preiser [l], Arthur R.H. van Zanten [m], Stephan C. Bischoff [n], Pierre Singer [o]

Berger M, Clin Nutr 2018

Liver function

- 24 studies, 3 meta-analysis: no clear pattern
- Statistically significant differences different ILEs
- Majority of studies: hepatobiliary functional marker levels within normal ranges or within 1.5 × ULN
- Adults, preterm neonates, and children suggest that olive oil-based ILE is safe and not associated with adverse effects on hepatobiliary function.

Klek S, Nutrition 2017
Johnston D.E.. Am. Fam. Phys. 1999

Outcome

- Currently there is limited evidence that one (olive oil-based) ILE offers any significant benefit over other ILEs on morbidity or mortality outcomes.
- Newer ILEs such as those containing fish oil also have not been shown to consistently confer benefits on these important outcomes.

Manzanares W, Intensive Care Med 2013

Outcome

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Discussion and Conclusions

The findings from this qualitative narrative review do not demonstrate that FO or FOC-IVLE significantly improves any of the clinical outcomes assessed. There is very little high-quality published evidence that FOC-IVLE has a beneficial effect on clinical outcomes. Although there was some evidence of a positive effect for FO on inflammatory and immune markers, these findings did not translate to improved clinical outcomes.

FO: Fish Oil, IVLE: Intra Venous Lipid Emulsion.

Abbasoglu O, JPEN 2017

IVLE: Specific fatty acids

4. n-3/n-6/n-9/MCT

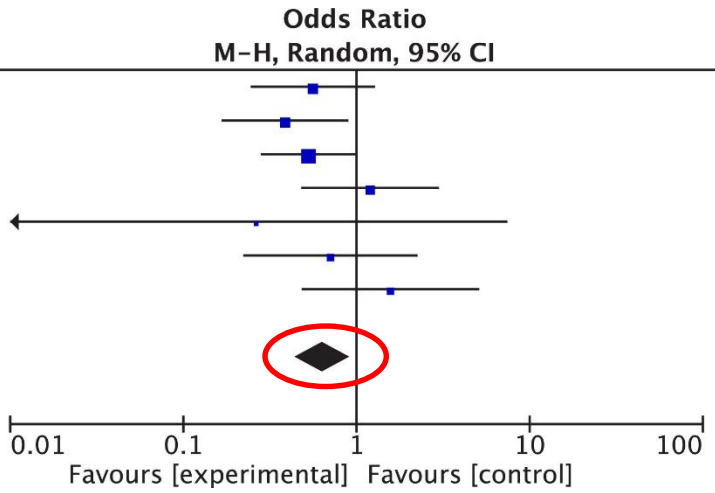
Enteral

Effect of enteral fish oil on mortality in acute respiratory distress syndrome

Study or Subgroup	n-3 PUFAs Events	n-3 PUFAs Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Gadek 1999	11	70	19	76	18.1%	0.56 [0.24, 1.28]	1999
Singer 2006	14	46	26	49	17.5%	0.39 [0.17, 0.90]	2006
Pontes-Arruda 2006	26	83	38	82	30.0%	0.53 [0.28, 1.00]	2006
Grau-Carmona 2011	11	61	11	71	14.8%	1.20 [0.48, 3.00]	2011
Elamin 2012	0	9	1	8	1.1%	0.26 [0.01, 7.43]	2012
Parisch 2014	7	29	9	29	9.4%	0.71 [0.22, 2.25]	2014
Kagan 2015	8	62	5	58	9.1%	1.57 [0.48, 5.11]	2015
Total (95% CI)		**360**		**373**	**100.0%**	**0.64 [0.45, 0.92]**	
Total events	77		109				

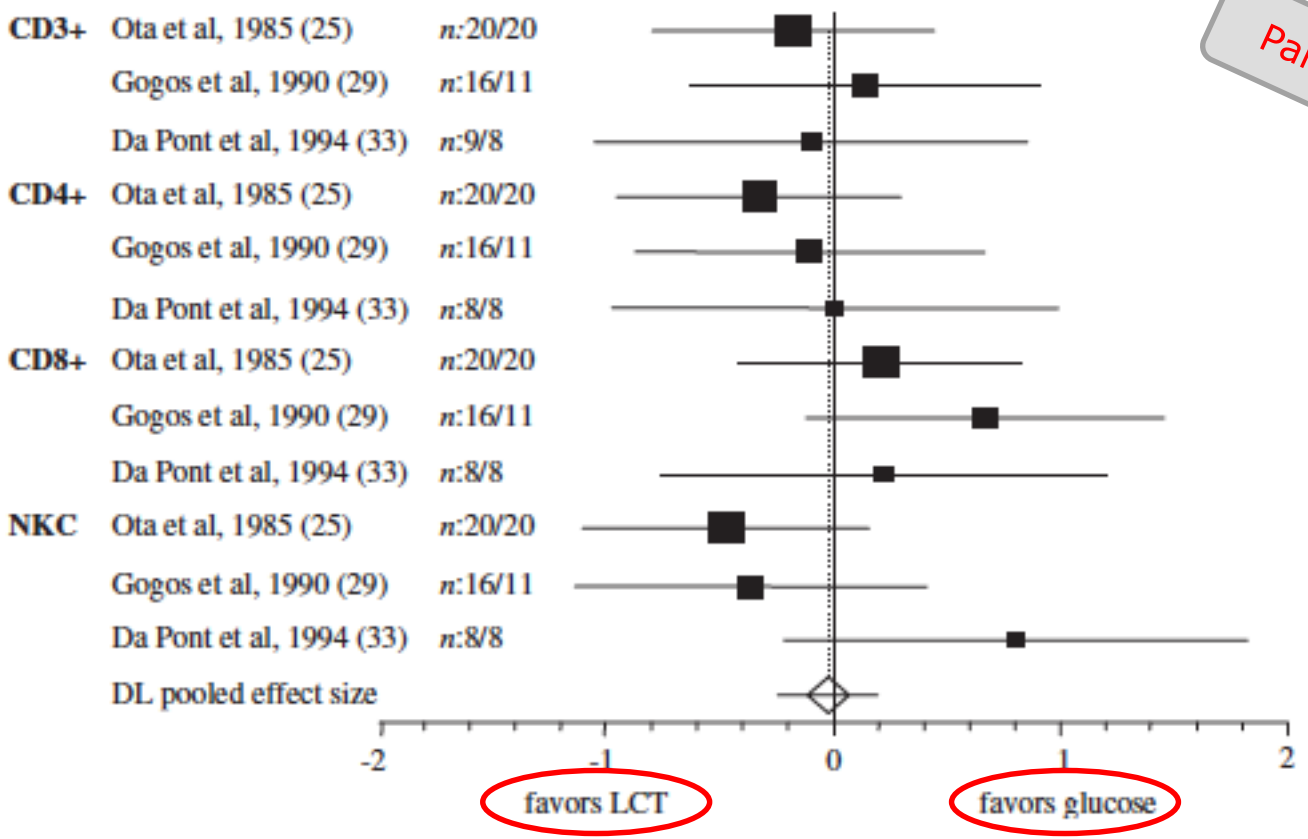
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.16$, df = 6 (P = 0.41); $I^2 = 3\%$

Test for overall effect: Z = 2.42 (P = 0.02)



Langlois P, *Nutrition*, 2019

Immune function

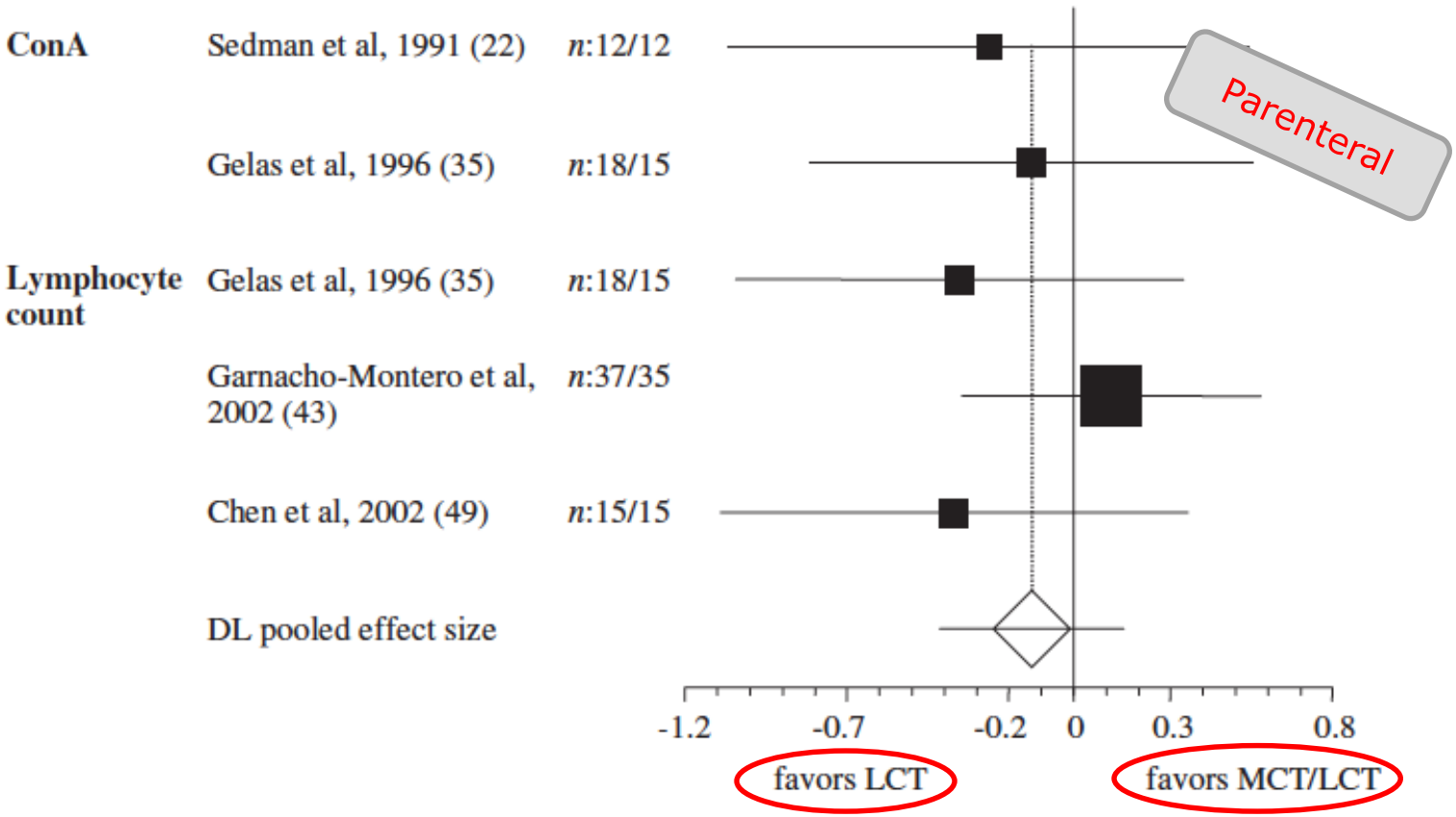


Parenteral

No significant favourable/harmful effect

Wirtitsch M, *Clin Nutr 2007*

Immune function



No significant favourable/harmful effect

Wirtitsch M, *Clin Nutr 2007*

Lipid component of PN: different fatty acids

Oil Source	100% Soybean	80% Olive 20% Soybean	50% MCT 50% Soybean	36% MCT 64% Soybean	100% Fish	50% MCT 40% Soybean 10% Fish	30% MCT 30% Soybean 25% Olive 15% Fish
Fatty acid composition, % of total							
Medium-chain FA							
Caprylic	ND	ND	27.0	14.47	ND	24.18–30.1	16.0–20.5
Capric	ND	ND	17.95	9.34	ND	16.13–19.4	9.85–13.0
Long-chain FA							
Oleic acid	20.92	59.69	11.68	16.55	10.15	7.9–13.44	25.2–30.77
α-linolenic	6.65	1.71	ND	5.72	1.23	2.42–3.41	2.0–2.75
Eicosapentaenoic	ND	ND	ND	NA	19.34	2.75–3.69	2.35–3.03
Docosahexaenoic	0.11	0.06	0.06	0.19	17.67	2.3–2.53	1.73–2.75
Arachidonic	0.18	0.16	0.19	0.24	1.47	0.52–0.66	0.27–0.5
Linoleic	54.68	18.56	28.89	39.18	2.98	20.88–25.72	17.8–21.42

Cai W, Calder P, De Waele E et al Nutrients, 2018

Lipid component of PN: different fatty acids

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Different characteristics, no survival difference

PUFA= polyunsaturated fatty acids; LCT=long-chain triglycerides; MUFA=monounsaturated fatty acids; EPA=eicosapentaenoic acid; DHA=docosahexaenoic acid; SFA-saturated fatty acid.

Note: this is a relative (not absolute) figurative scale to demonstrate relative inflammatory activity.

Adapted from Vanek VW, et al. *Nutr Clin Pract.* 2012;27:150-192.

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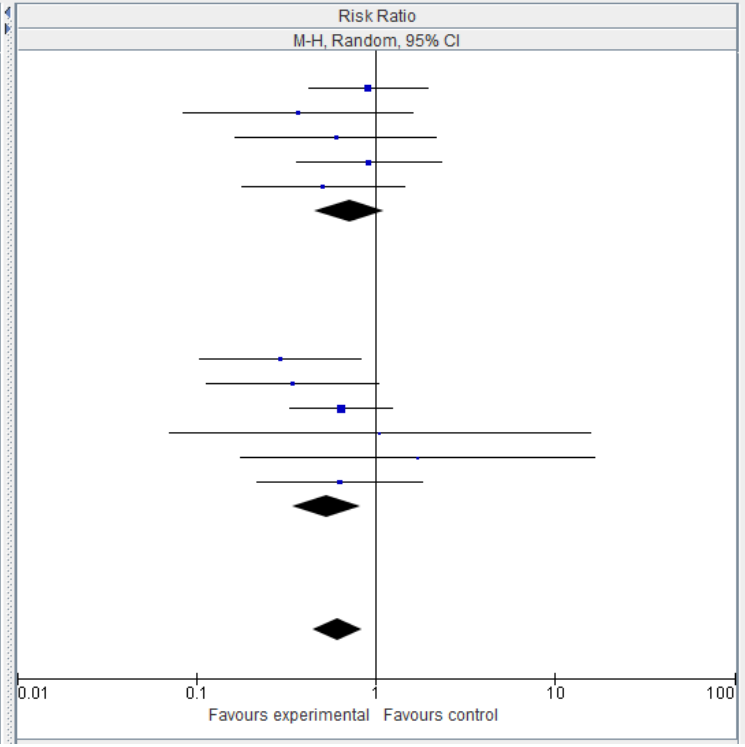
Fish-oil Metaanalysis: ICU & surgery Infections

Study or Subgroup	Omega-3 Events	Omega-3 Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 ICU patients						
Friesecke 2008	11	83	12	82	17.1%	0.91 [0.42, 1.93]
Wachtler 1997	2	19	6	21	4.5%	0.37 [0.08, 1.61]
Wang 2008	3	20	5	20	5.9%	0.60 [0.17, 2.18]
Weiss 2002	5	12	5	11	11.4%	0.92 [0.36, 2.33]
Wichmann 2007	5	127	10	129	9.0%	0.51 [0.18, 1.44]
Subtotal (95% CI)		261		263	47.9%	0.71 [0.45, 1.12]
Total events	26		38			
Heterogeneity: Tau² = 0.00; Chi² = 1.94, df = 4 (P = 0.75); I² = 0%						
Test for overall effect: Z = 1.47 (P = 0.14)						
1.2.2 Not ICU patients						
Badia-Tahull 2010	3	13	11	14	9.3%	0.29 [0.10, 0.82]
Jiang 2010	4	100	12	103	8.2%	0.34 [0.11, 1.03]
Klek 2005	9	29	14	29	22.6%	0.64 [0.33, 1.24]
Liang 2008	1	20	1	21	1.3%	1.05 [0.07, 15.68]
Makay 2011	2	14	1	12	1.9%	1.71 [0.18, 16.65]
Senkal 2007	4	19	7	21	8.8%	0.63 [0.22, 1.82]
Subtotal (95% CI)		195		200	52.1%	0.53 [0.34, 0.82]
Total events	23		46			
Heterogeneity: Tau² = 0.00; Chi² = 3.58, df = 5 (P = 0.61); I² = 0%						
Test for overall effect: Z = 2.86 (P = 0.004)						
Total (95% CI)		456		463	100.0%	0.61 [0.45, 0.84]
Total events	49		84			
Heterogeneity: Tau² = 0.00; Chi² = 6.35, df = 10 (P = 0.79); I² = 0%						
Test for overall effect: Z = 3.08 (P = 0.002)						
Test for subgroup differences: Chi² = 0.84, df = 1 (P = 0.36), I² = 0%						



Pradelli et al. Crit Care 2012: 16: R184

Fish-oil Systematic review Mortality Metaanalysis

Study or Subgroup	Fish Oils Events	Total	Non-Fish Oil lipids Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
5.11.1 PN based trials							
Grecu	2	28	3	26	2.7%	0.62 [0.11, 3.41]	2003
Friesecke	18	83	22	82	19.8%	0.81 [0.47, 1.39]	2008
Wang 2009	0	28	2	28	0.9%	0.20 [0.01, 3.99]	2009
Barbosa	4	13	4	10	6.0%	0.77 [0.25, 2.34]	2010
Gultekin	8	16	7	16	12.3%	1.14 [0.54, 2.40]	2014
Grau-Carmona	26	81	16	78	19.9%	1.56 [0.91, 2.68]	2014
Subtotal (95% CI)		**249**		**240**	**61.6%**	**1.05 [0.77, 1.45]**	
Total events	58		54				
Heterogeneity: Tau² = 0.00; Chi² = 4.90, df = 5 (P = 0.43); I² = 0%							
Test for overall effect: Z = 0.31 (P = 0.75)							
5.11.2 EN based trials							
Gupta	7	31	13	30	11.5%	0.52 [0.24, 1.13]	2011
Burkhart	13	25	13	25	20.3%	1.00 [0.59, 1.70]	2014
Hall	4	30	9	30	6.6%	0.44 [0.15, 1.29]	2014
Subtotal (95% CI)		**86**		**85**	**38.4%**	**0.69 [0.40, 1.18]**	
Total events	24		35				
Heterogeneity: Tau² = 0.08; Chi² = 3.10, df = 2 (P = 0.21); I² = 35%							
Test for overall effect: Z = 1.35 (P = 0.18)							
Total (95% CI)		**335**		**325**	**100.0%**	**0.90 [0.67, 1.20]**	
Total events	82		89				
Heterogeneity: Tau² = 0.03; Chi² = 9.62, df = 8 (P = 0.29); I² = 17%							
Test for overall effect: Z = 0.74 (P = 0.46)							
Test for subgroup differences: Chi² = 1.74, df = 1 (P = 0.19), I² = 42.5%							

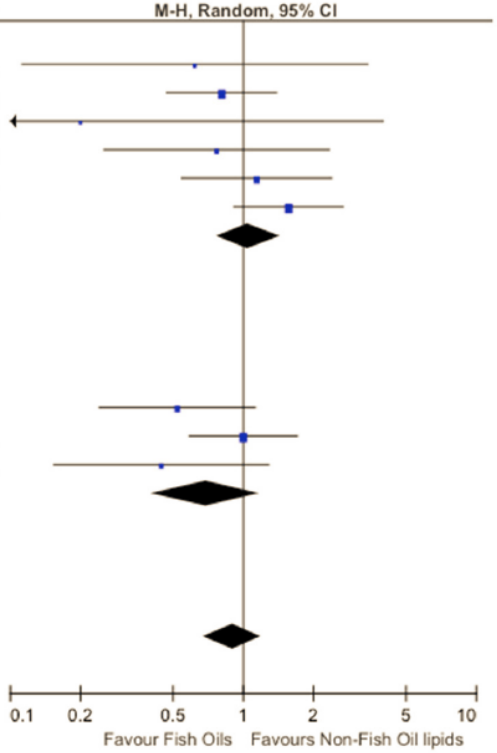


Figure 2 Effects on mortality of fish oil lipid emulsion strategies (n =9). CI, Confidence interval; EN, Enteral nutrition; LCT, Long-chain triglycerides; MCT, Medium-chain triglycerides; M-H, Mantel-Haenszel test; PN, Parenteral nutrition.

Manzanares et al. Crit care 2015; 19:167

Fish-oil Systematic review Infections Metaanalysis

Study or Subgroup	Fish Oils Events	Total	LCT or LCT+MCT Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
5.15.1 PN based trials							
Grecu	0	8	1	7	1.5%	0.30 [0.01, 6.29]	2003
Friesecke	10	83	11	82	21.4%	0.90 [0.40, 2.00]	2008
Wang 2009	6	28	9	28	17.3%	0.67 [0.27, 1.62]	2009
Grau-Carmona	17	81	29	78	52.3%	0.56 [0.34, 0.94]	2014
Subtotal (95% CI)		**200**		**195**	**92.4%**	**0.64 [0.44, 0.94]**	
Total events	33		50				
Heterogeneity: Tau² = 0.00; Chi² = 1.17, df = 3 (P = 0.76); I² = 0%							
Test for overall effect: Z = 2.26 (P = 0.02)							
5.15.2 EN based trials							
Hall	3	30	5	30	7.6%	0.60 [0.16, 2.29]	2014
Subtotal (95% CI)		**30**		**30**	**7.6%**	**0.60 [0.16, 2.29]**	
Total events	3		5				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.75 (P = 0.45)							
Total (95% CI)		**230**		**225**	**100.0%**	**0.64 [0.44, 0.92]**	
Total events	36		55				
Heterogeneity: Tau² = 0.00; Chi² = 1.18, df = 4 (P = 0.88); I² = 0%							
Test for overall effect: Z = 2.38 (P = 0.02)							
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%							

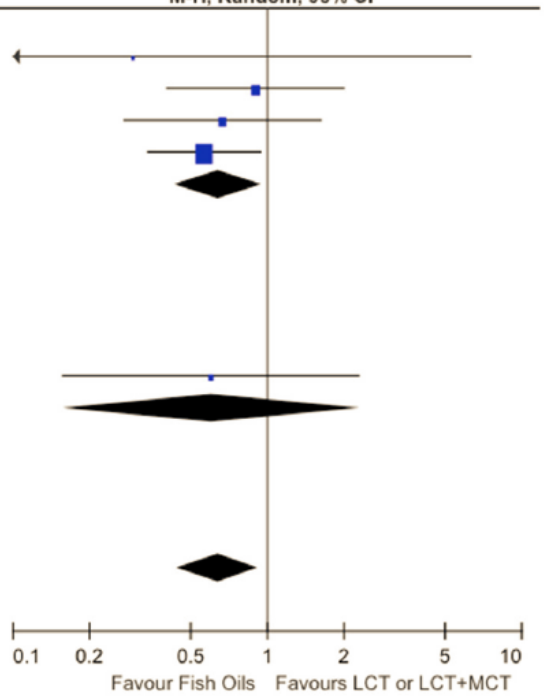


Figure 3 Effects on infections of parenteral fish oil containing emulsions (n =5). CI, Confidence interval; EN, Enteral nutrition; LCT, Long-chain triglycerides; MCT, Medium-chain triglycerides; M-H, Mantel-Haenszel test; PN, Parenteral nutrition.

Manzanares et al. Crit care 2015; 19:167

Fish-oil Systematic review, Meta-analysis and Trial sequential analysis

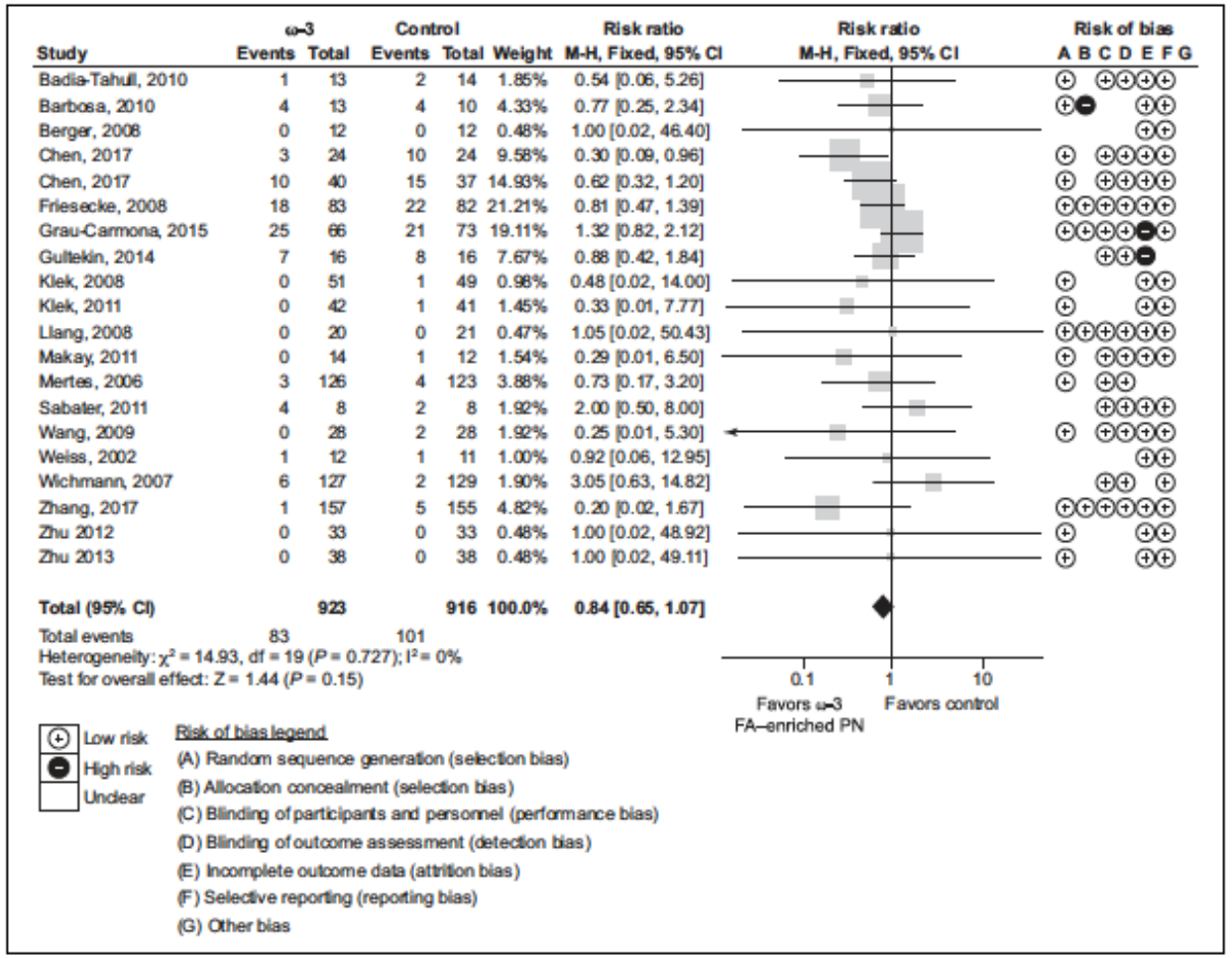


Figure 3. Thirty-day mortality rates. Forest plot of fixed effects meta-analysis showing individual study means, pooled estimates, and risk of bias for individual studies (C… to correct for the 0 event studies as per the protocol (to add 0.5 events in both arms), this meta-analysis …STATA software, as it is difficult to use RevMan for this correction. CI, confidence interval; FA, fatty acid; PN, parent… al nutrition.

Screenshot

Pradelli et al. JPEN 2019

ESPEN

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Clinical Nutrition (2007) 26, 302–313

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ORIGINAL ARTICLE

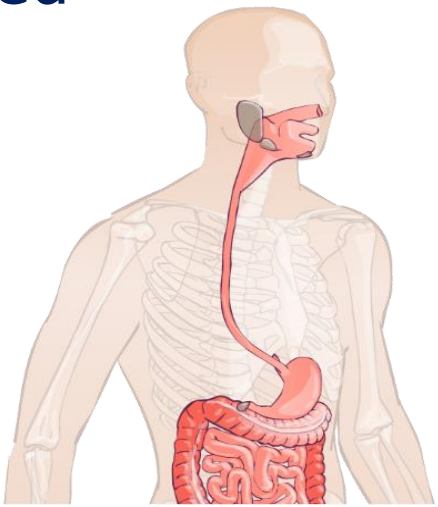
Effect of different lipid emulsions on the immunological function in humans: A systematic review with meta-analysis

Melanie Wirtitsch[a], Barbara Wessner[a], Andreas Spittler[a], Erich Roth[a], Thomas Volk[b], Lucas Bachmann[c], Michael Hiesmayr[d,*]

”None of the lipid regimens showed any clear effect on the evolution of the immunological status or mortality in humans”

Enteral fish oil in ICU

- In continuous infusion as part of complete nutrition might improve outcome in acute lung injury/ARDS
- Bolus administration can not be recommended

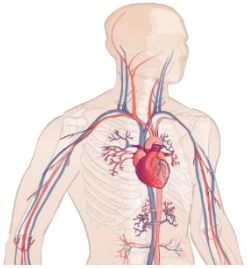


Glenn JO, *Curr Opin Clin Nutr Metab Care 2014*

Recommendations

Lipids in the intensive care unit: Recommendations from the ESPEN Expert Group ☆

- Supports the use of olive oil and fish oil in nutrition support in surgical and non-surgical ICU patients
- Possible potential for fish oil in surgical ICU
- Further research is required



Calder, Clin Nutr 2018

Recommendations

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Subject	ASPEN recommendation	ESPEN recommendation	Conclusion of the review
Lipid intake	Doses not defined Avoid soy-based lipids in the first week of hospitalization (2)	0.7–1.5 g · kg^{-1} · d^{-1} (17)	>1–1.2 g · kg^{-1} · d^{-1} (maximum; 2 g · kg^{-1} · d^{-1}) (97, 98) Avoid phytosterols and ω-6 FAs (51, 103–105)
Carbohydrate intake	Not defined Maintenance of blood glucose concentrations of 140–180 mg/dL (2)	≥2 g · kg^{-1} · d^{-1} (17) Maintenance of blood glucose concentrations <180 mg/dL (17)	1–2 g · kg^{-1} · d^{-1} (78) Maintenance of blood glucose concentrations of 120–150 mg/dL

Patkova A, Adv Nutr 2017

Recommendations

Clinical Nutrition xxx (2018) 1–32

Contents lists available at ScienceDirect

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ESPEN Guideline

ESPEN guideline on clinical nutrition in the intensive care unit

Regarding the FA composition of the lipid emulsions, the recent expert recommendations indicated that a blend of FAs should be considered, including medium chain triglycerides (MCTs), n-9 monounsaturated FAs, and n-3 polyunsaturated FAs. At this stage, the evidence for n-3 FA-enriched emulsions in non-surgical ICU patients is not sufficient to recommend it as a standalone [200].

Singer, Clin Nutr 2019

B. Carbohydrates

- Carbon, hydrogen and oxygen atom combination
- Glucose (dextrose): $C_6H_{12}O_6$
- Synonym = Saccharide

The major dietary carbohydrates

Class (DP*)	Subgroup	Components
Sugars (1–2)	Monosaccharides	Glucose, galactose, fructose, xylose
	Disaccharides	Sucrose, lactose, maltose, trehalose
	Polyols	Sorbitol, mannitol
Oligosaccharides (3–9)	Malto-oligosaccharides	Maltodextrins
	Other oligosaccharides	Raffinose, stachyose, fructo-oligosaccharides
Polysaccharides (>9)	Starch	Amylose, amylopectin, modified starches
	Non-starch polysaccharides	Glycogen, Cellulose, Hemicellulose, Pectins, Hydrocolloids

DP * = Degree of polymerization

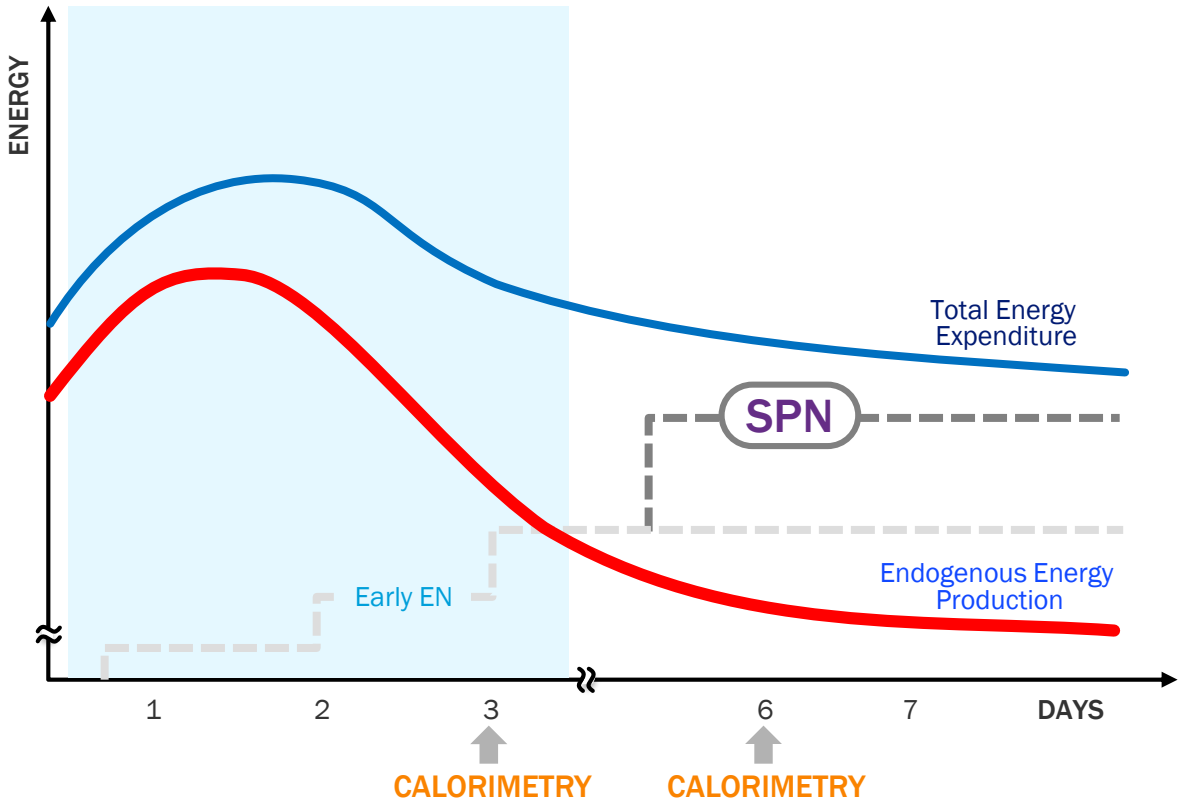
Carbohydrates in human nutrition. FAO Food and Nutrition Paper – 66. Food and Agriculture Organization of the United Nations.

Carbohydrates

- Preferential substrate for production of energy
- Critical illness: often insulin resistance and hyperglycemia
- Brain, red blood cells, immune cells, renal medulla and transparent tissues of the eyes prefer glucose
- Endogenous energy production (by liver) is increased in critical illness and does not decrease when nutrients and insulin are administered

Singer P, Clin Nutr 2019

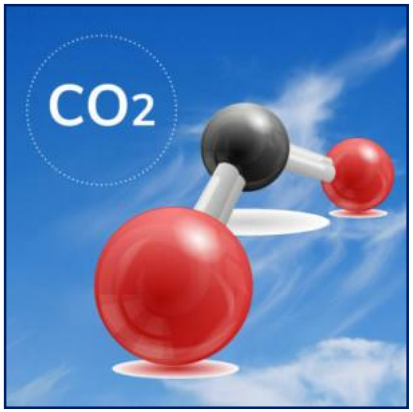
Endogenous energy production



Oshima T, et al. *Clin Nutr.* 2017;36(3):651-662

Carbohydrates

- Excessive glucose based energy provision associated with:
  - Hyperglycemia
  - Enhanced CO2 production
  - Enhanced lipogenesis
  - Increased insulin requirement
  - No advantage in protein sparing



- Enteral Nutrition specific Diabetes Type II might improve glucose profile

Singer P, Clin Nutr 2019

Carbohydrates

- Weak recommendation on requirement ICU:

  min. 150g/day

Recommendation 25

Intravenous lipid (including non-nutritional lipid sources) should not exceed 1.5 g lipids/kg/day and should be adapted to individual tolerance.

Grade of recommendation: GPP – strong consensus (100% agreement)

Singer P, Clin Nutr 2019

Carbohydrates

- Weak recommendation on requirement ICU:

  max. 5mg/kg/dayday

Recommendation 23

The amount of glucose (PN) or carbohydrates (EN) administered to ICU patients should not exceed 5 mg/kg/min.

Grade of recommendation: GPP – strong consensus (100% agreement)

Singer P, Clin Nutr 2019

C. Glucose control

- Hyperglycemia is associated with adverse outcome
- Ideal blood glucose target remains unclear
- Tight glucose control is well tolerated and effective in patients receiving early parenteral nutrition when provided with a protocol
- Patients with poorly controlled diabetes may need less aggressive glucose control

Gunst J, Van den Berghe G, Curr Opin Anaesthesiol. 2019

Glucose control

Situation	Check
Day 1 ICU	Every 4h
Unstable patients	More frequent than every 4h
Stable patients (>48h)	Less frequent

Target	Target
<10 mmol/L	6–8 mmol/l (110–145 mg/dL)

Check insulin need		
Increasing cumulative 24h dose	⇨	Accidental overfeeding

Berger MM, Clin Nutr. 2019

D. Clinical Guidance

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Nutritional prescription:

1. Calories: Resting Energy Expenditure by indirect calorimetry → 70% to 100% of REE

2. Protein: 1.3 g/kg/day

→ Choose route/combination routes and formula type

3. Check lipid volume and compare to min and max value

4. Check carbohydrate content and compare to min and max value

D. Clinical Guidance

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Nutritional prescription:

When to start lipids and carbohydrates:

- → At indication of nutrition therapy
- → As part of optimal nutrition
- → Well balanced and between stated requirements and upper limits

Benefits:

- → Global benefits of nutritional therapy
- → Possible benefits of specific Fatty Acids

Singer P, Clin Nutr 2019

Clinical Guidance: ESPEN Guideline

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Recommendation 23

The amount of glucose (PN) or carbohydrates (EN) administered to ICU patients should not exceed 5 mg/kg/min.

Grade of recommendation: GPP – strong consensus (100% agreement)

Recommendation 24

The administration of intravenous lipid emulsions should be generally a part of PN.

Grade of recommendation: GPP- strong consensus (100% agreement)

Recommendation 25

Intravenous lipid (including non-nutritional lipid sources) should not exceed 1.5 g lipids/kg/day and should be adapted to individual tolerance.

Grade of recommendation: GPP – strong consensus (100% agreement)

Singer P, Clin Nutr 2019

Conclusion

- Lipids/Fatty acids have different characteristics
- Lipids Are part of optimal nutrition
- Carbohydrates are necessary, within minimum and maximum quantities and with correct monitoring and anticipation in place
- Nutritional prescription and daily evaluation should result in balance between nutrients
- Recommendations are available