18. Irseer Fortbildungsveranstaltung

Einfluss ω3-haltiger Fettemulsionen auf die Lungenfunktion

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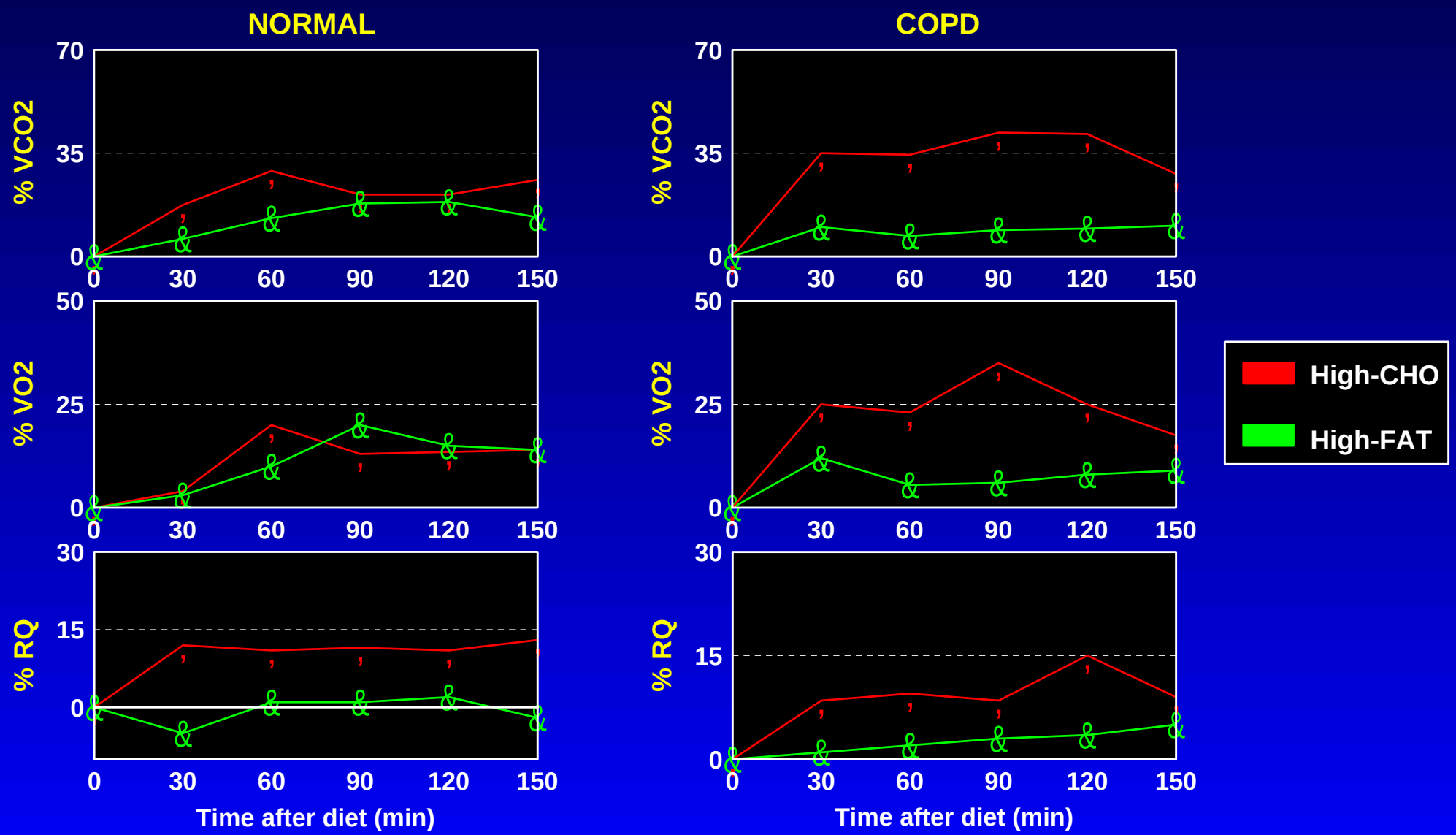
The Effects of High-fat and High-carbohydrate Diet Loads on Gas Exchange and Ventilation in COPD Patients and Normal Subjects



KUO et al; Chest 104: 189 - 196 (1993)

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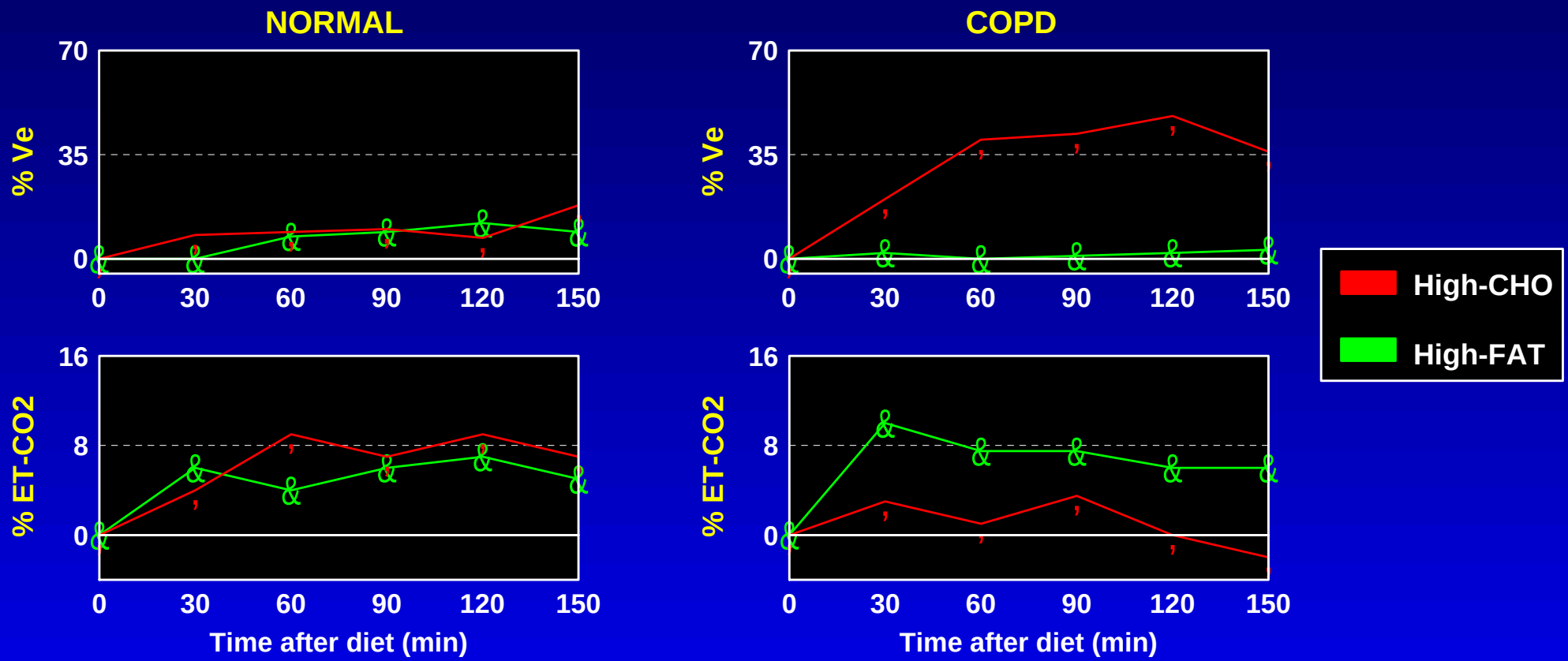
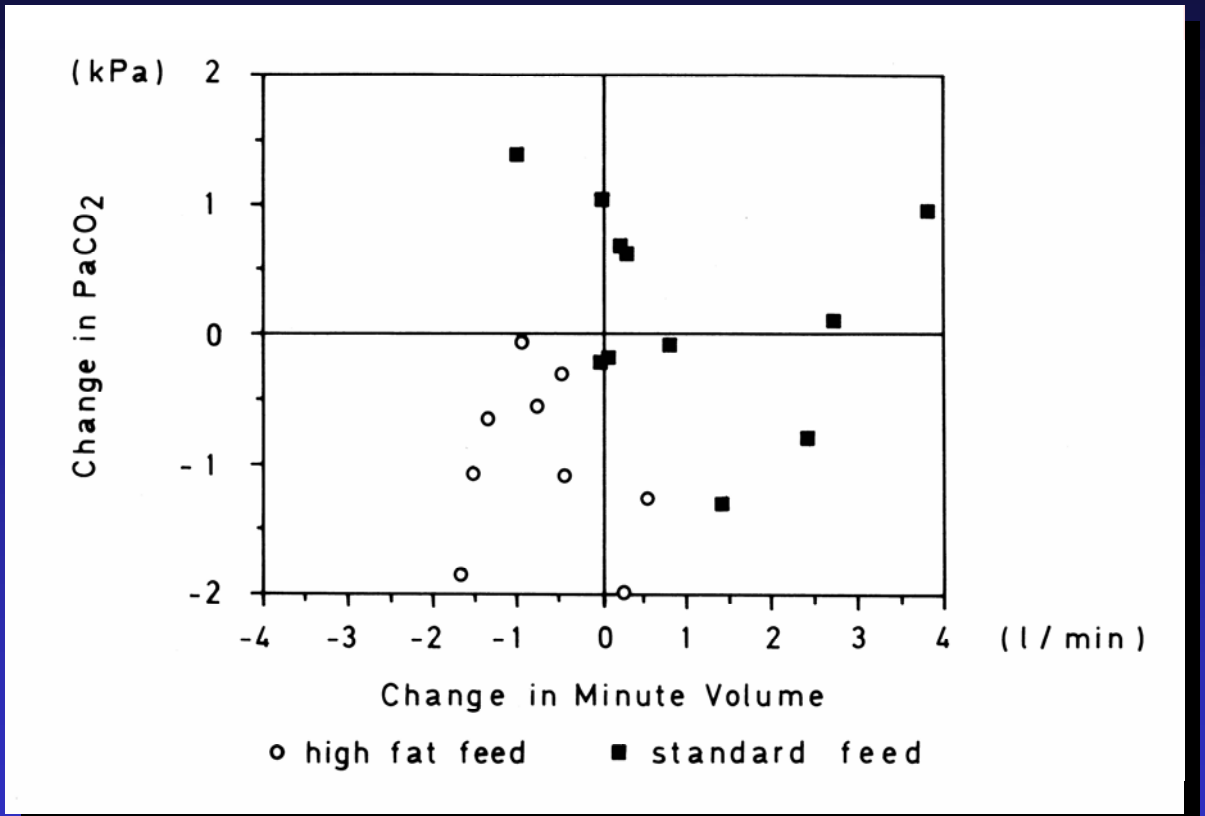


KUO et al; Chest 104: 189 - 196 (1993)

High fat, low carbohydrate, enteral feeding lowers $PaCO_2$ and reduces the period of ventilation in artificially ventilated patients

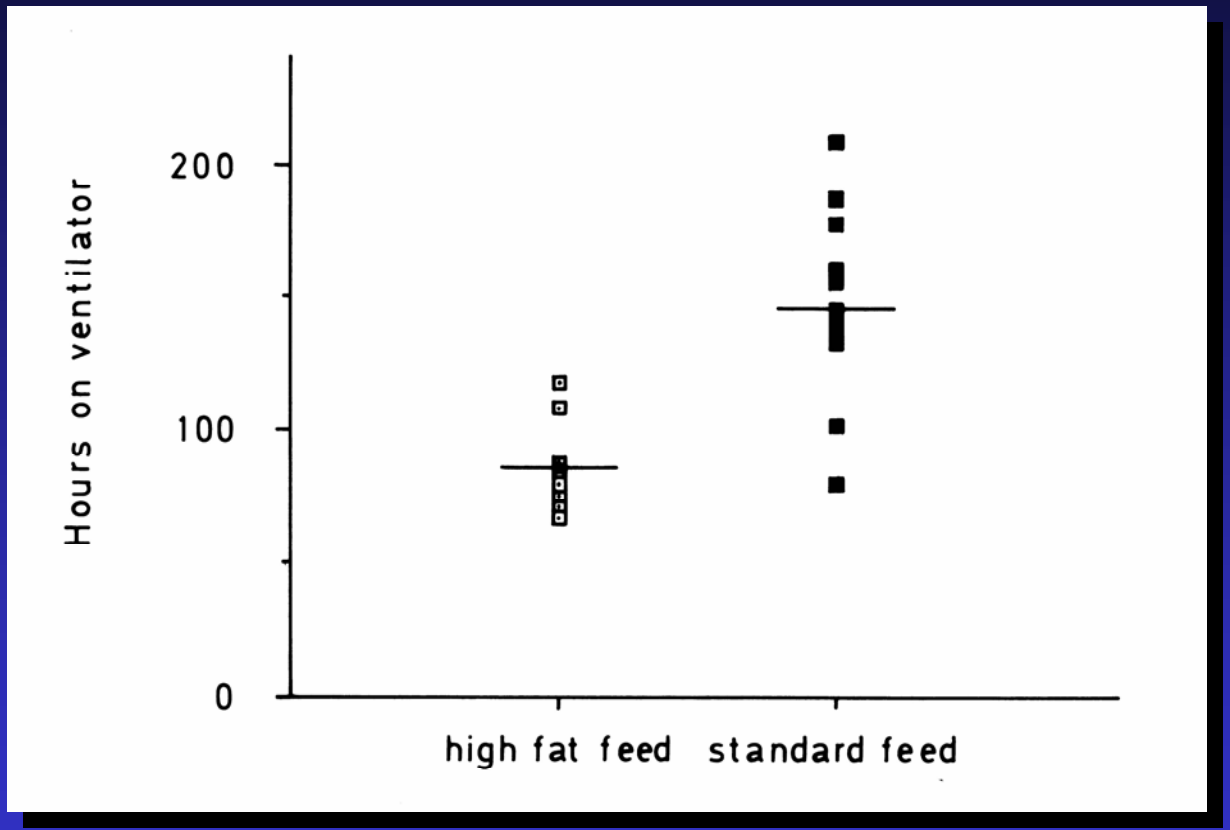


Changes in minute volume and $PaCO_2$ for both nutrition groups:

>> During the feeding period, $PaCO_2$ just prior to weaning fell by 16% in the high fat group but increased by 4% in the standard feed group (p=0.003).

Al-SAADY et al, Intensive Care Med (1989) 15: 290-295

High fat, low carbohydrate, enteral feeding lowers $PaCO_2$ and reduces the period of ventilation in artificially ventilated patients

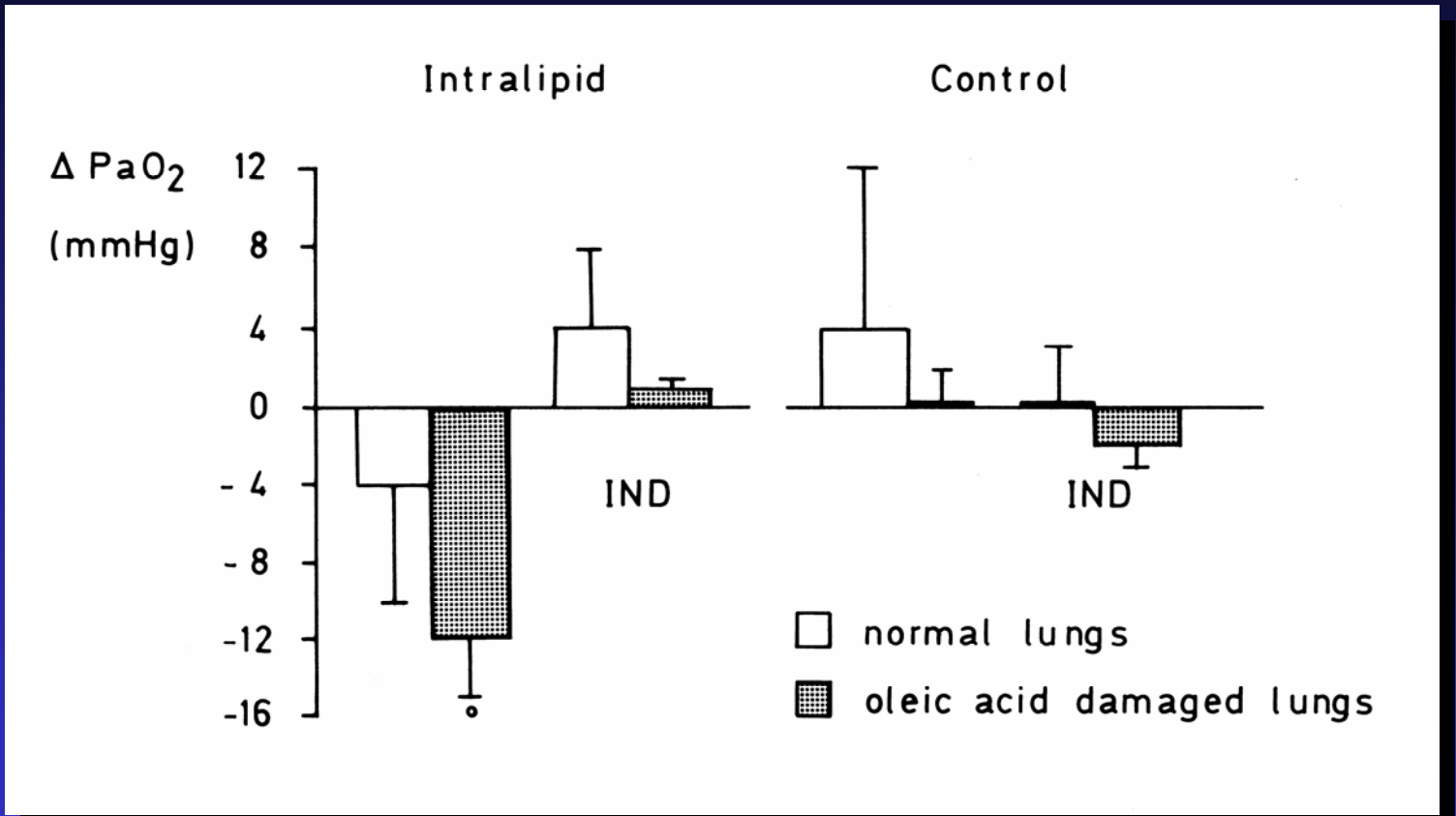


Hours spent on ventilator following commencement of feed:

>> The high fat group spent a mean of 62 hours less time on the ventilator (p=0.006).

Al-SAADY et al, Intensive Care Med (1989) 15: 290-295

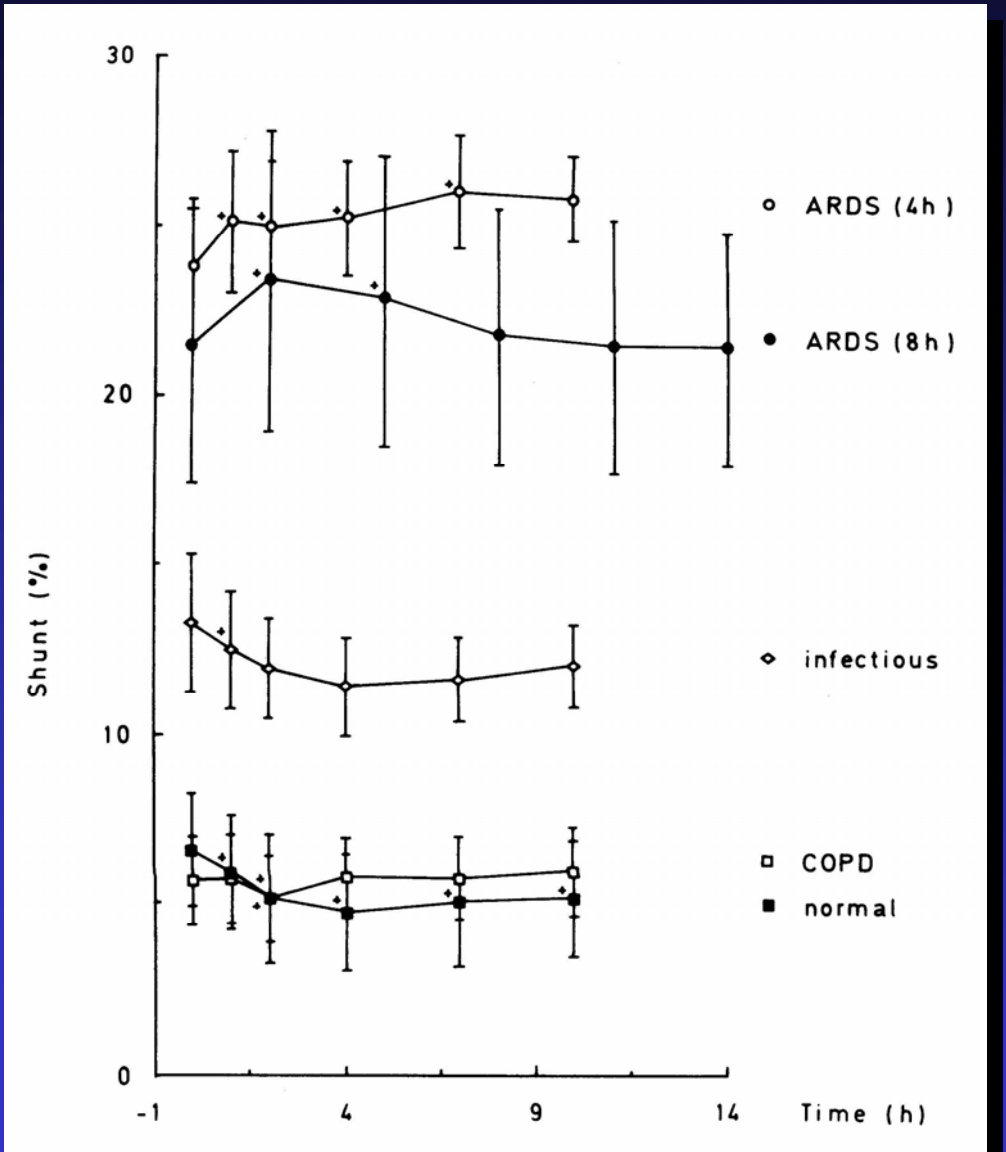
Intralipid alterations in pulmonary prostaglandin metabolism and gas exchange



Changes in PaO_2 occuring as a result of infusion over 1 hour of 4 ml/kg Intralipid. The only significant PaO_2 decrease according to an increased pulmonary production of vasodilatry PGs occurred in the lung injury group. Both the increased PG production and the decrease in PaO_2 were blocked by indomethacin (IND) (mean ± SEM; ° $p < 0.001$).

HAGEMAN et al, Clin Chest Med (1986) 7: 69

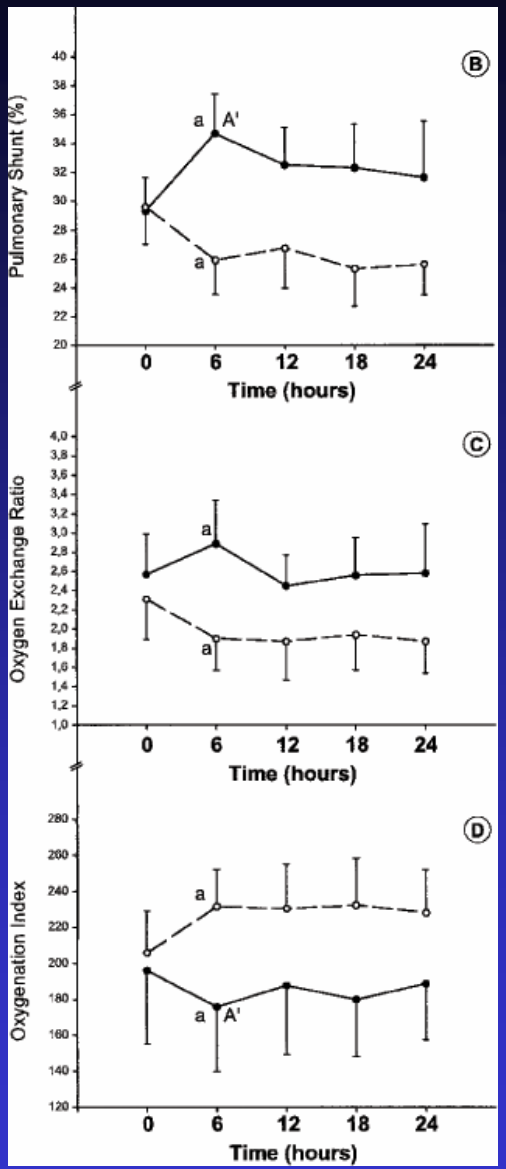
Effects of Intravenous Fat Emulsion on Respiratory Failure

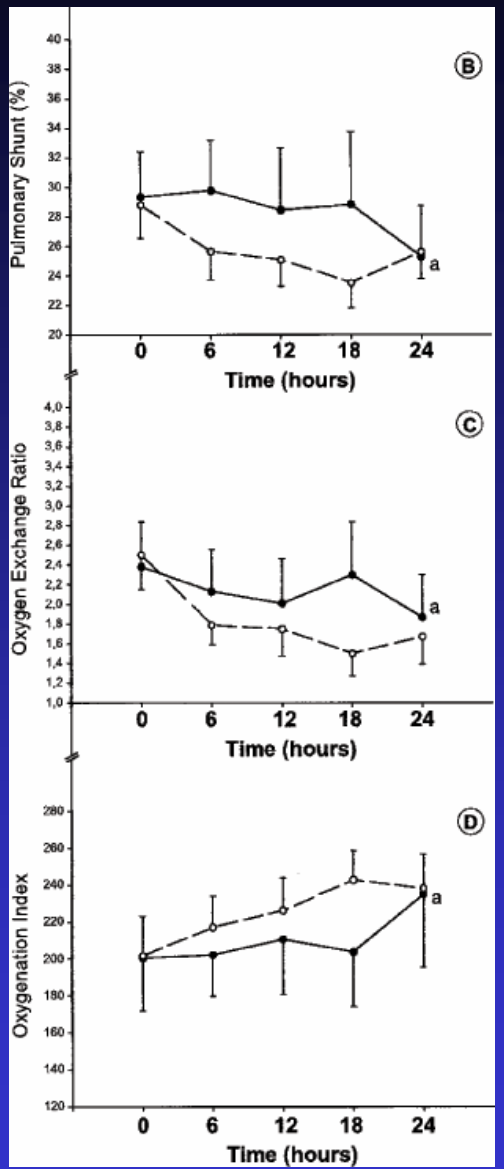


Effect of intravenous fat emulsion on respiratory failure: serial changes of intrapulmonary shunt in different patient groups (500 ml LCT 10% infused over 4 or 8 hours; * $p < 0.05$)

HWANG et al, Chest (1990) 97: 934-938

Effects of intravenous fat emulsions on lung function in patients with acute respiratory distress syndrome or sepsis





Pulmonary shunt, oxygen exchange ratio, and oxgenation index before, during, and after rapid or slow fat infusion.

dashed lines = severe sepsis,
solid lines = ARDS,
mean ± SEM;

SUCHNER et al, Crit Care Med 29: 1569-1574 (2001)

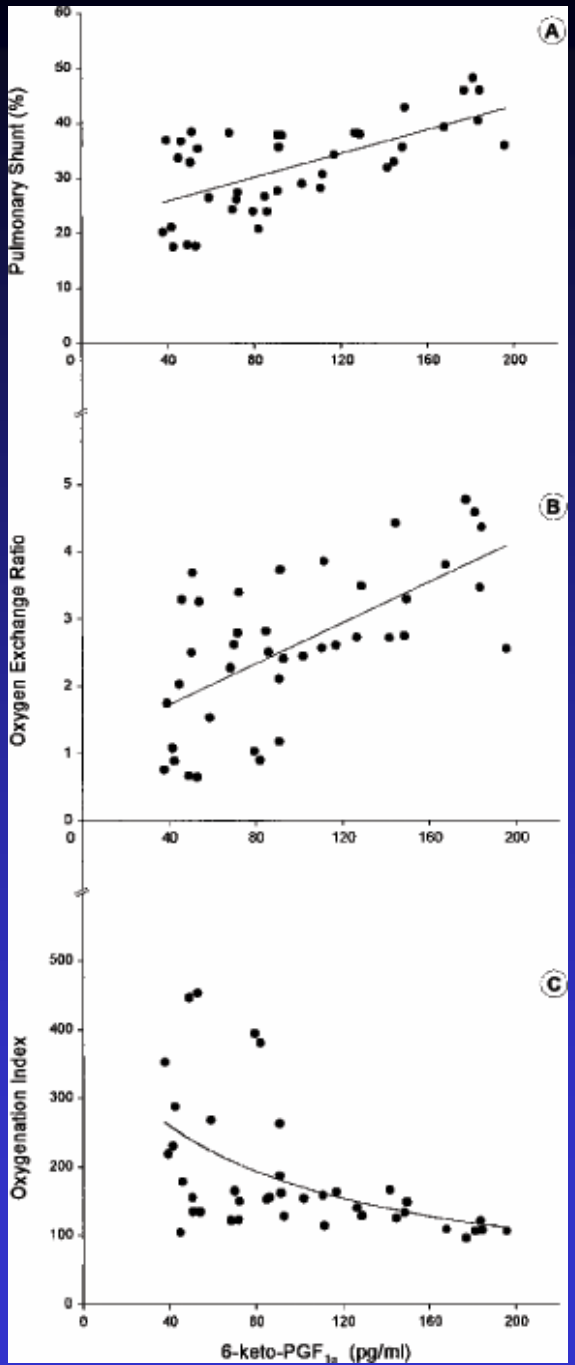
rapid

slow

Effects of intravenous fat emulsions on lung function in patients with acute respiratory distress syndrome or sepsis

Plot of linear / nonlinear regression analysis between 6-keto-prostaglandin (PG)-$F_{1\alpha}$ and pulmonary shunt, oxygen exchange ratio, or oxygenation index. Data analysis relates to patients with ARDS during and after rapid fat infusion.

dashed lines = severe sepsis,
solid lines = ARDS,
mean ± SEM;

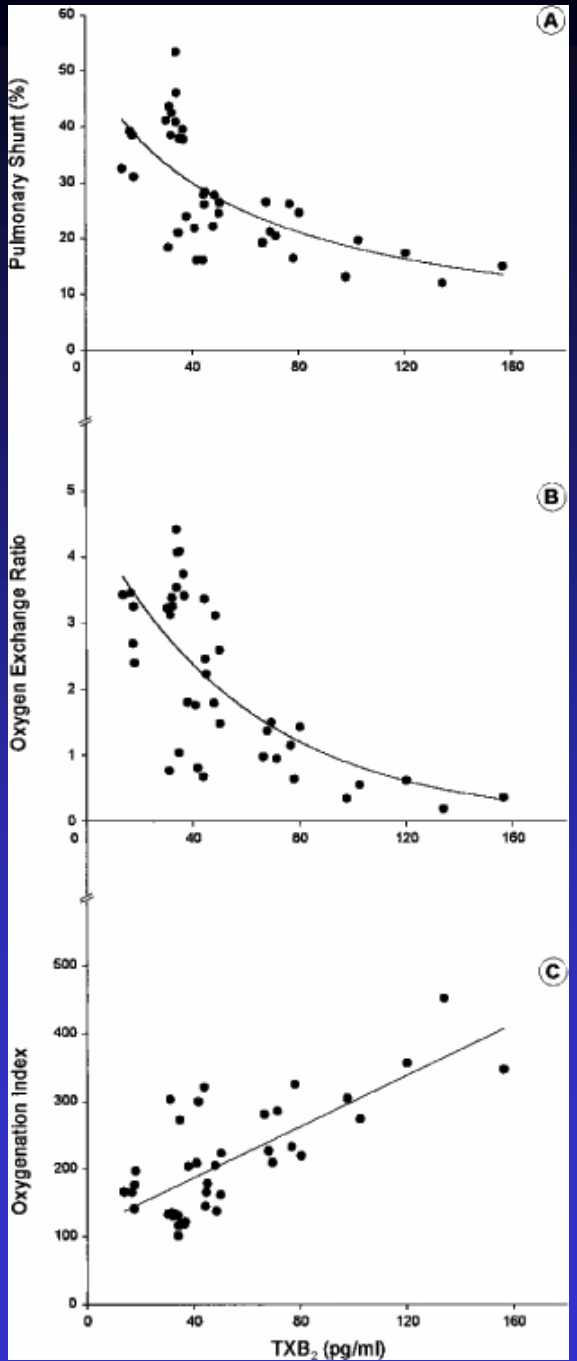


SUCHNER et al, Crit Care Med 29: 1569-1574 (2001)

Effects of intravenous fat emulsions on lung function in patients with acute respiratory distress syndrome or sepsis

Plot of linear / nonlinear regression analysis between thromboxane (Tx)-B_2 and pulmonary shunt, oxygen exchange ratio, or oxygenation index.
Data analysis relates to patients with ARDS during and after slow fat infusion.

dashed lines = severe sepsis,
solid lines = ARDS,
mean ± SEM;



SUCHNER et al, Crit Care Med 29: 1569-1574 (2001)

Developments in Lipid Emulsions

Conventional Lipid Emulsions	Lipid Emulsions with a Reduced Content of PUFA	Lipid Emulsions with a Specific Fatty Acid Pattern
LCT	MCT / LCT	MCT / LCT / Fish Oil [1]
LCT rich in α-tocopherol	MCT / LCT rich in α-tocopherol	SMOF [2]
	Structured Lipids	Fish Oil
	Olive Oil containing emulsion	

[1] MCT / LCT / Fish Oil = 50 / 40 / 10 %
[2] Soybean Oil / MCT / Olive Oil / Fish Oil = 30 / 30 / 25 / 15 %

Hemodynamic and respiratory effects of medium-chain and long-chain triglyceride fat emulsions

Objective

This study was aimed at comparing cardiopulmonary effects of intravenous fat emulsions with different composition (MCT/LCT vs. LCT).

Design

prospective, double-blind, randomized, parallel-group controlled trial

Patients

26 spontaneously breathing patients after open heart surgery

Interventions

Patients were randomized into two groups, to receive 1 ml/kg/hr (3.3 mg/kg/min) of MCT/LCT- versus LCT-based IVFE.

Parameters

Pulmonary gas exchange / Shunt, etc.:

- PaO_2
- SaO_2
- SvO_2
- $PaCO_2$
- Qs/Qt
- VO_2
- DO_2
- O_2 Extraction

Hemodynamic Parameters:

- CI
- MAP
- SVRI
- CVP
- PCWP
- MPAP
- PVRI

FIACCADORI et al, RINPE 15: 6-14 (1997)

Hemodynamic and respiratory effects of medium-chain and long-chain triglyceride fat emulsions

Parameter		*Lipid Emulsion*	*Baseline*	*After 30 Minutes*	
CI	mmHg	MCT/LCT	3.27 (0.17)	3.17 (0.20)	
		LCT	3.14 (0.15)	2.66 (0.16)	**
MPAP	mmHg	MCT/LCT	27 (2)	28 (2)	
		LCT	26 (2)	30 (2)	*
PVRI	dyne x sec x 10^{-5}	MCT/LCT	341 (50)	378 (52)	
		LCT	364 (52)	477 (80)	*
PaO_2	mmHg	MCT/LCT	74 (3)	77 (4)	
		LCT	71 (3)	67 (2)	*
DO_2	ml/min/m^2	MCT/LCT	441 (20)	419 (22)	
		LCT	412 (21)	347 (26)	**

* p < 0.05, ** p < =.01 versus base line values; mean ± SEM;

FIACCADORI et al, RINPE 15: 6-14 (1997)

Lung function: MCT/LCT vs. LCT

Gas exchange during lipid infusion (500 ml/8h)in septic patients with ARDS (n = 21).

	Group 1 > LCT			Group 2 > MCT/LCT		
	Before	During	After	Before	During	After
pH	7.36 ± 0.7	7.35 ± 0.9	7.36 ± 0.8	7.38 ± 0.2	7.35 ± 0.8	7.35 ± 0.9
Qva / Qt (%)	24 ± 5	**37 ± 6 * °**	25 ± 4	23 ± 5	25 ± 4	24 ± 4
PaO_2 / FiO_2	240 ± 30	**180 ± 35 * °**	235 ± 35	240 ± 30	235 ± 30	235 ± 25
VO_2 (ml/min)	333 ± 12	359 ± 11 °	338 ± 10	329 ± 14	396 ± 12 *	336 ± 13

Mean ± SD; * p<0.05 vs before and after infusion in the same cohort / ° p<0.05 vs the other cohort during infusion time

Conclusion:
LCT administration was associated with a more significant change in the gas exchange parameters.

SMIRNIOTIS et al, Int Care Med (1998) 24: 1029-1033

The Impact of intravenous Fat Emulsion Administration in Acute Lung Injury

Objective	**… to evaluate the effect of parenteral nutrition containing medium- and long-chain triglycerides on the function of the respiratory system …**
Patients	**13 patients with acute respiratory distress syndrome (ARDS), 8 receiving lipid and 5 placebo, and 6 without ARDS receiving lipid.**
Interventions	**Bronchoalveolar lavage was performed before and 1 hour after administration of lipid or placebo. Lipid emulsion: MCT/LCT 3.5 mg/kg/minute for 1 hour**
Parameters	**BAL Protein Content, Surfactant Phospholipids, PLA_2 and PAF-AcH Activities, PAF-Levels, BAL Cells**

LEKKA et al, Am J Resp Crit Care Med (2004) 169: 638-644

The Impact of intravenous Fat Emulsion Administration in Acute Lung Injury

ARDS group with lipids

Parameters	*before MCT/LCT*	*after MCT/LCT*	
PaO_2/FiO_2	129 ± 37	95 ± 42	
Compliance	39.2 ± 12	33.1 ± 9.2	ml/cm H_2O
Pulmonary Vascular resistance	258 ± 47	321 ± 58	dyne/s/cm H_2O

BAL Fluid >> increase in total protein and phospholipid concentrations, phospholipase activities, platelet activating factor and neutrophils; alterations in BAL lipid profile

Conclusions

…this study indicates that administration of MCT/LCT in patients with ARDS causes alterations in lung function and hemodynamics, inflammatory cells, possibly activated by lipids, release phospholipase A_2 and PAF, enhancing edema formation, inflammation, and surfactant alterations.

LEKKA et al, Am J Resp Crit Care Med (2004) 169: 638-644

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Interventions	**Bronchoalveolar lavage was performed before and 1 hour after administration of lipid or placebo.**
	Lipid emulsion: MCT/LCT 3.5 mg/kg/minute for 1 hour
	3.5 mg x 70 kg bw x 60 min = 14.7 g per hr
	1.2 g x 70 kg bw = 84 g : 24 hrs = 3.5 g per hr
Parameters	**BAL Protein Content, Surfactant Phospholipids, PLA_2 and PAF-AcH Activities, PAF-Levels, BAL Cells**

LEKKA et al, Am J Resp Crit Care Med (2004) 169: 638-644

Peroxidation

) *Enhanced lipid oxidation*

- 6 increased haemolysis
- 6 pulmonary complications
- 6 impairment of the immune response
- 6 tissue damage
  (e.g. retinopathy in premature infants)

) *Potential factors for lipid peroxidation*

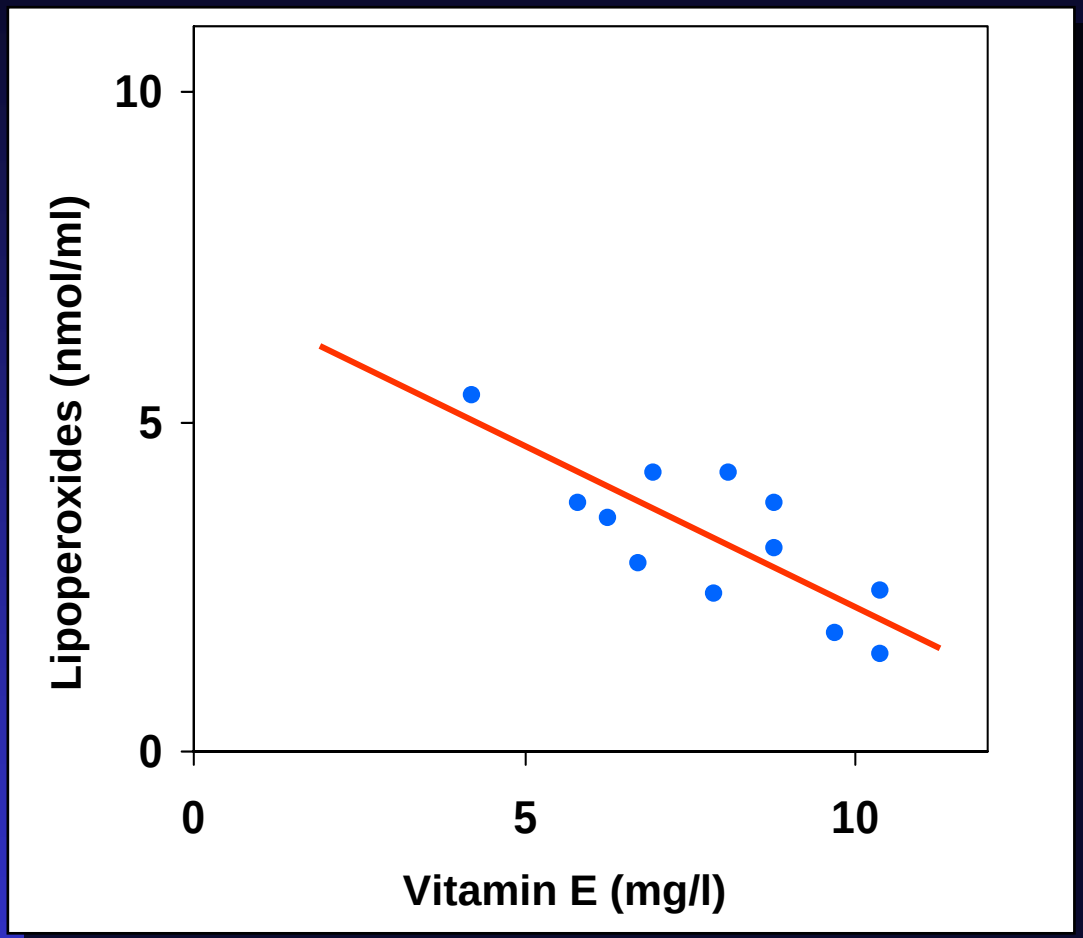
- 6 fat emulsions with a high amount of unsaturated fatty acids
- 6 light exposure (photo therapy)
- 6 deficiencies in the antioxidant protection

Vitamin E Deficiency and Lipoperoxidation during ARDS

	Plasma Vitamin E (mg/l)	Plasma Lipoperoxides (mmol/l)
ARDS	7.73 ± 0.54*	4.12 ± 0.35
Control	11.46 ± 0.55	2.94 ± 0.30

* P < 0.001

Inverse correlation between plasma Vitamin E and lipoperoxide levels:
Y = 0.51x + 8.03; r = 0.78; p < 0.01;

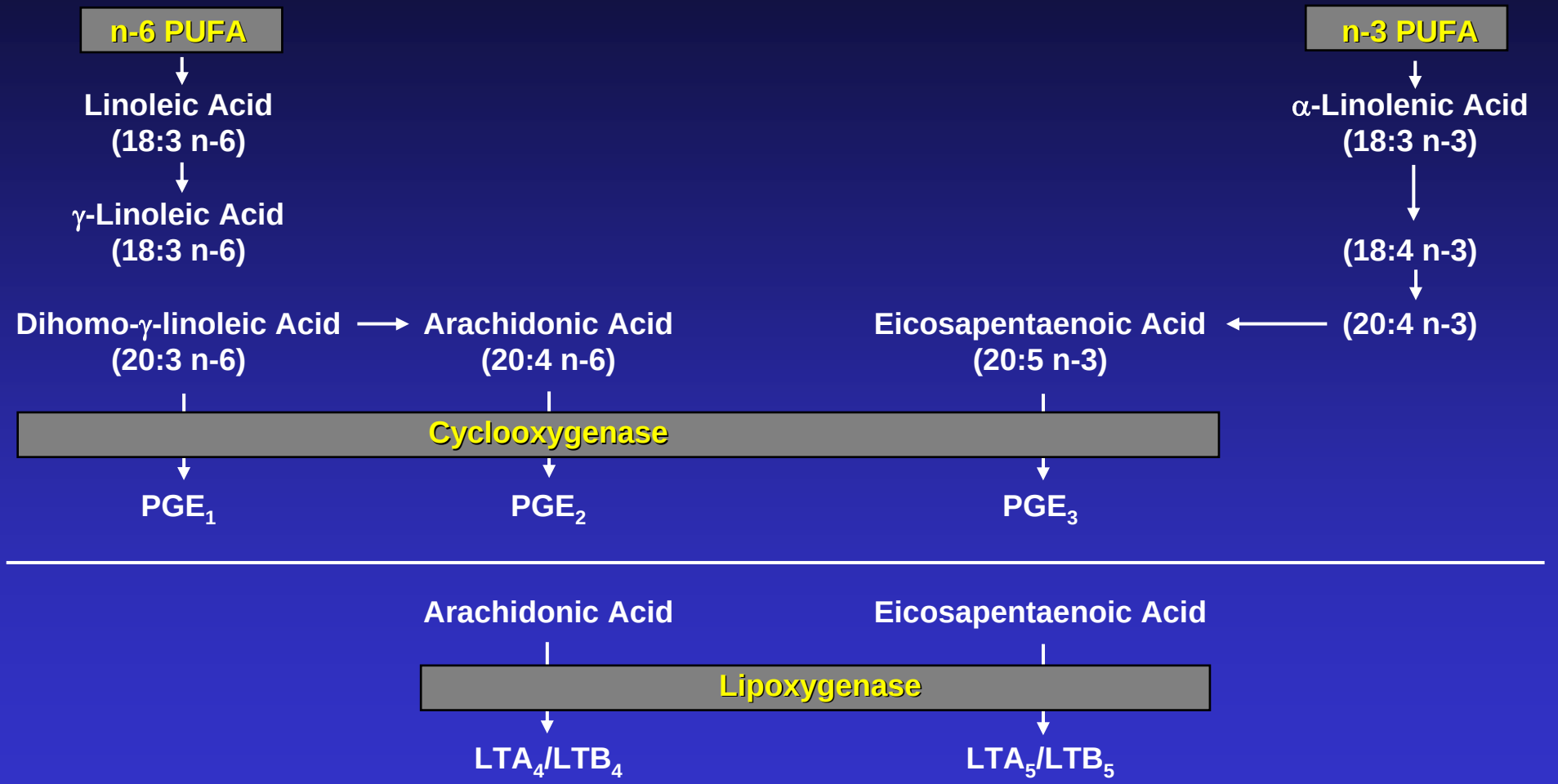


Conclusion

The ability of Vitamin E to prevent oxidant mediated cytotoxicity suggests the need for its parenteral administration in critically ill patients. This might delay the onset of acute respiratory failure !

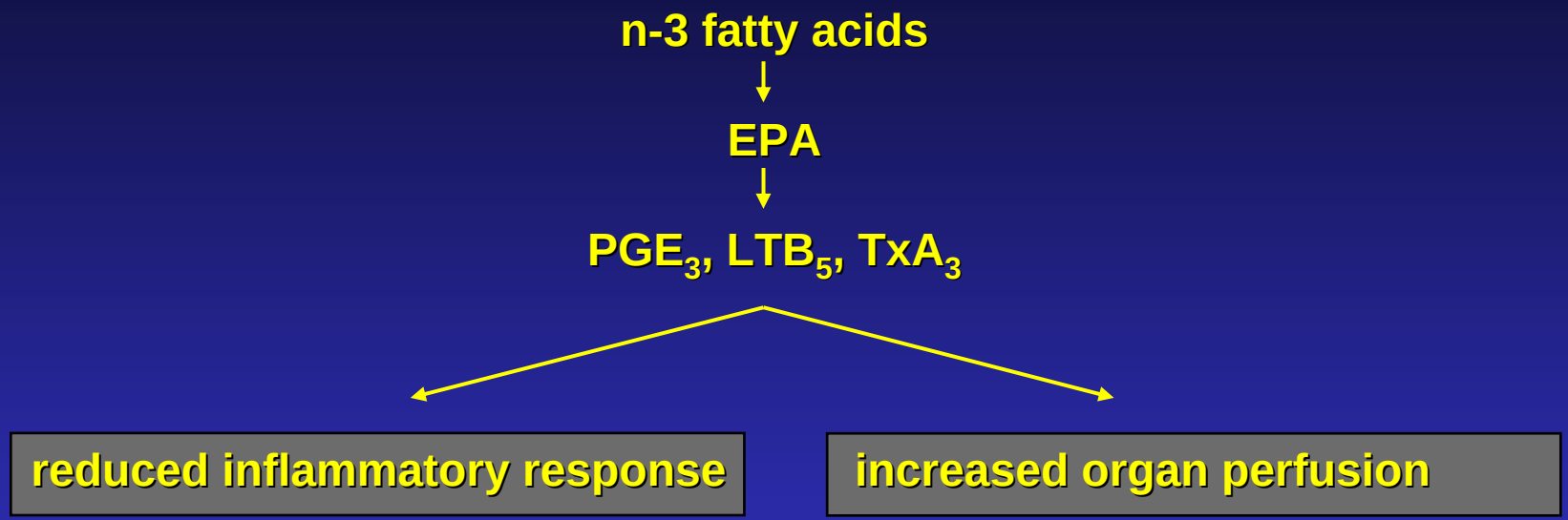
RICHARD et al, Crit Care Med (1990) 18: 4-9

Metabolic pathways for n-6 versus n-3 polyunsaturated fatty acids (PUFA)



AYALA et al, Clin Nutr 11: 1-11 (1997)

Pharmacological Effects of n-3 Fatty Acids



n-3 fatty acids yield in a:

- production of biologically less efficient lipid mediators of inflammation
- reduced production of interleukins
- improved organ perfusion

Modulation of Immune Function by Polyunsaturated Fatty Acids

- **Eicosanoid dependent modulation**
  - Prostaglandines
  - Leukotrienes
  - Cytokines
  - NO
- **Non eicosanoid dependent modulation**
  - Membrane fluidity
  - Signal transduction
  - Transcription (Gene-expression)

Yaqoob, Curr Opin Clin Nutr Metab Care 1998, 1: 153-161

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N-6 / N-3 – Ratio : *What is the optimum ?*

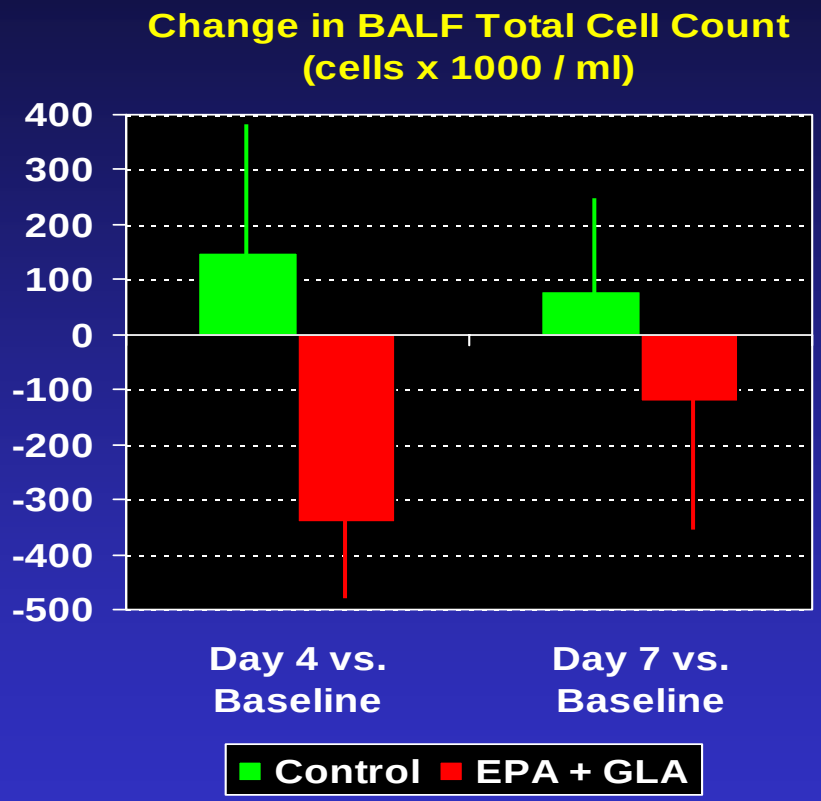
Pure LCT- or MCT/LCT- emulsions:	7 : 1
Olive-oil based emulsuions:	9 : 1
Morlion	2 : 1
Fürst et al	2,5 : 1
Pscheidl et al	2 : 1
Future perspectives	**2,5 – 3 : 1**

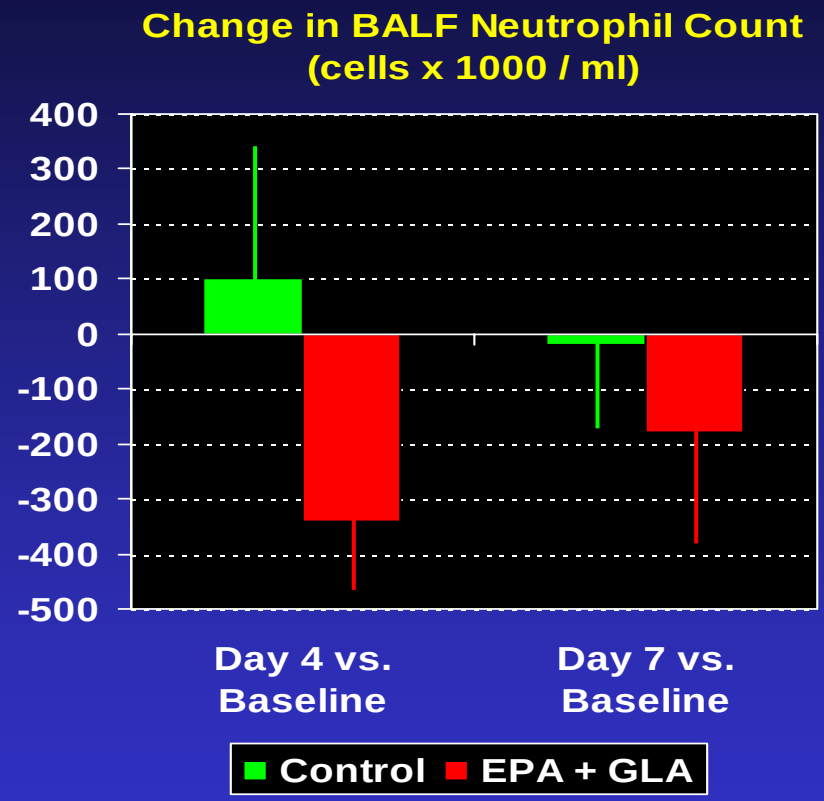
Effect of enteral feeding with eicosapentaenoic acid, γ - linolenic acid, and antioxidants in patients with acute respiratory distress syndrome

Objectives	**Recent studies in animal models of sepsis-induced acute respiratory distress syndrome (ARDS) suggest that enteral nutrition with EPA + GLA and antioxidants may reduce pulmonary inflammation and may improve oxygenation and clinical outcomes.**
Design	**prospective, multicentered, double-blind, randomized controlled trial**
Setting	**Intensive care units of five academic and teaching hospitals**
Interventions	**Patients were randomized and continuously tube-fed either EPA + GLA or an isonitrogenous, isocaloric standard diet at a minimum caloric delivery of 75% of basal energy expenditure x 1.3 for at least 4 - 7 days.**
Measurements	**arterial blood gases, ventilator settings, PaO_2/FiO_2, pulmonary neutrophil recruitment (by measuring the number of neutrophils and the total cell count in bronchoalveolar lavage fluid), clinical outcomes**

GADEK et al, Crit Care Med 27: 1409-1420 (1999)

Effect of enteral feeding with eicosapentaenoic acid, γ - linolenic acid, and antioxidants in patients with acute respiratory distress syndrome





Mean ± SE changes on study days 4 and 7 from baseline in bronchoalveolar fluid total cell and neutrophil count. Patients fed EPA + GLA had a significant lower number of total cells and neutrophils per ml of recovered fluid compared with patients fed the control diet.

GADEK et al, Crit Care Med 27: 1409-1420 (1999)

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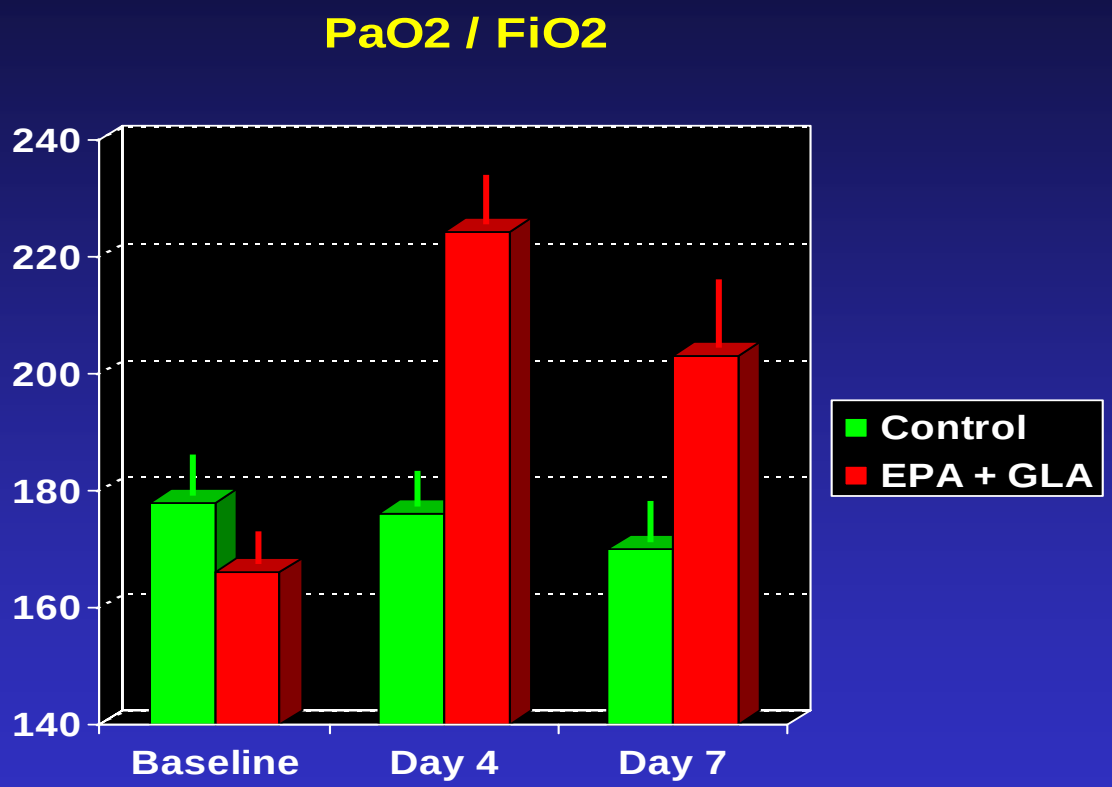
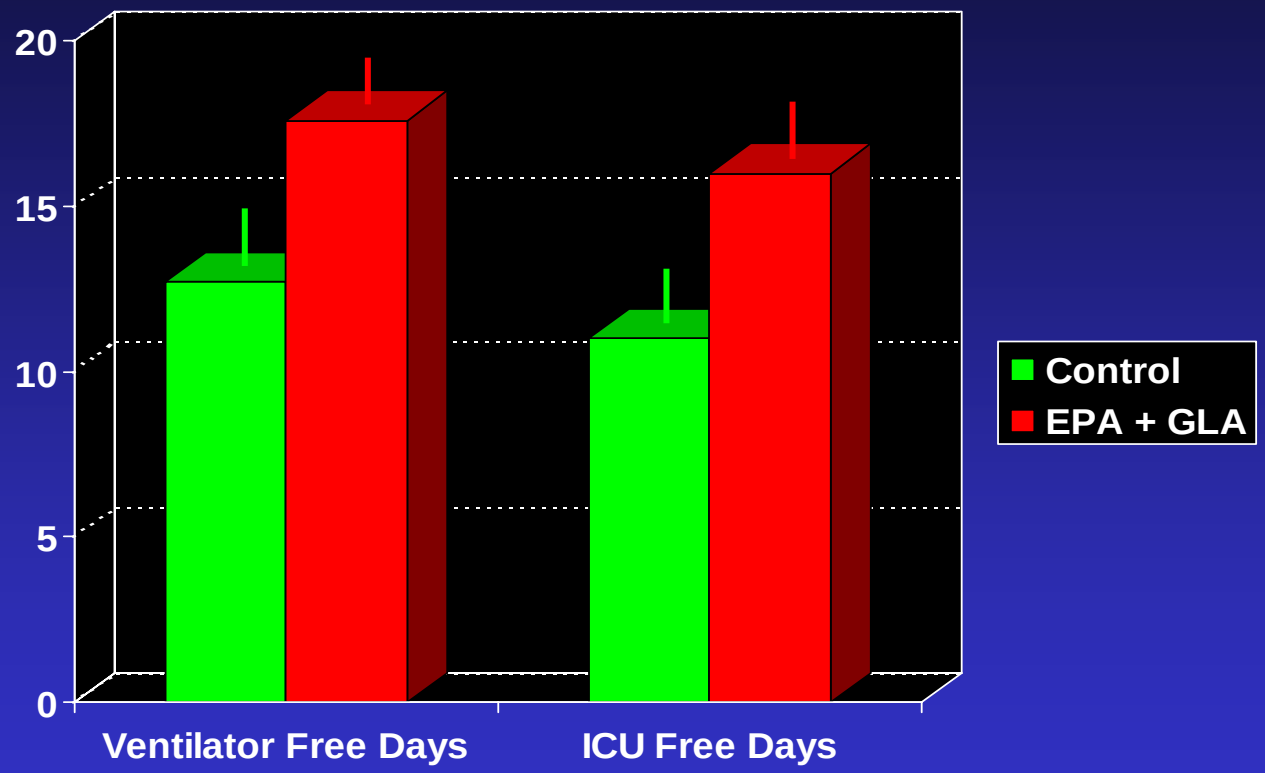


Mean ± SE ratio of PaO_2 to FiO_2 in patients fed control or eicosapentaenoic acid plus γ - linolenic acid (EPA + GLA) diet. Patients fed EPA + GLA had significant improvements in gas exchange on study days 4 and 7 compared with control ($p<.0499$).

GADEK et al, Crit Care Med 27: 1409-1420 (1999)

Effect of enteral feeding with eicosapentaenoic acid, γ - linolenic acid, and antioxidants in patients with acute respiratory distress syndrome



Mean ± SE number of 30-day ventilator free days and intensive care unit (ICU)-free days. Patients fed the eicosapentaenoic acid plus γ - linolenic acid (EPA + GLA) diet had 4.9 more ventilator-free days (p=.02) and 4.0 more ICU-free days (p=.01) compared with patients fed the control diet.

GADEK et al, Crit Care Med 27: 1409-1420 (1999)

Enteral nutrition with eicosapentaenoic acid, γ-linolenic acid, and antioxidants reduces alveolar inflammatory mediators and protein influx in patients with ARDS

Objective:

… In a subset of ARDS patients from this trial, we performed a preliminary examination of the potential mechanisms underlying these clinical improvements by retrospectively testing the hypothesis that enteral feeding with EPA + GLA could reduce alveolar-capillary membrane protein permeability and the production of interleukin (IL)-8, IL-6, tumor necrosis factor α, and leukotriene B_4 that are responsible, in part, for pulmonary inflammation.

PACHT et al, Crit Care Med 31: 491-499 (2003)

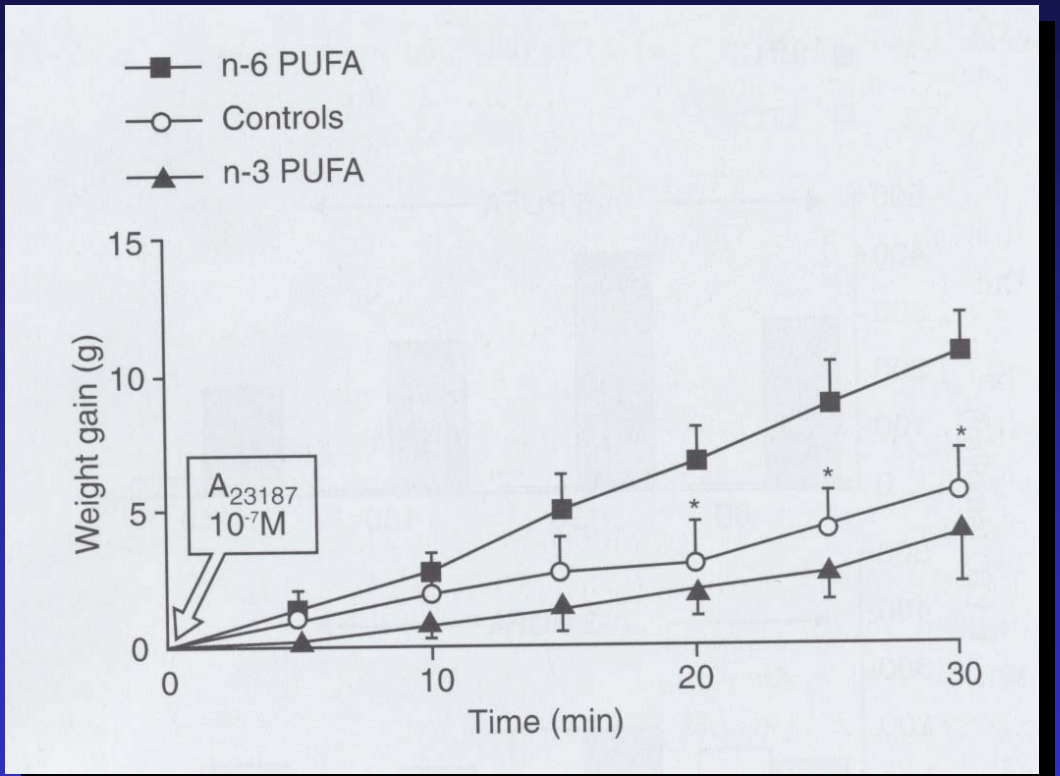
Enteral nutrition with eicosapentaenoic acid, γ-linolenic acid, and antioxidants reduces alveolar inflammatory mediators and protein influx in patients with ARDS

Conclusions:

. . . This preliminary investigation showing a decrease in BALF levels of IL-8 and leukotriene B_4 and the associated reduction of BALF neutrophils and alveolar membrane protein permeability in ARDS patients fed EPA + GLA support, in part, the potential mechanisms underlying the previously described clinical improvements with this diet . . .

PACHT et al, Crit Care Med 31: 491-499 (2003)

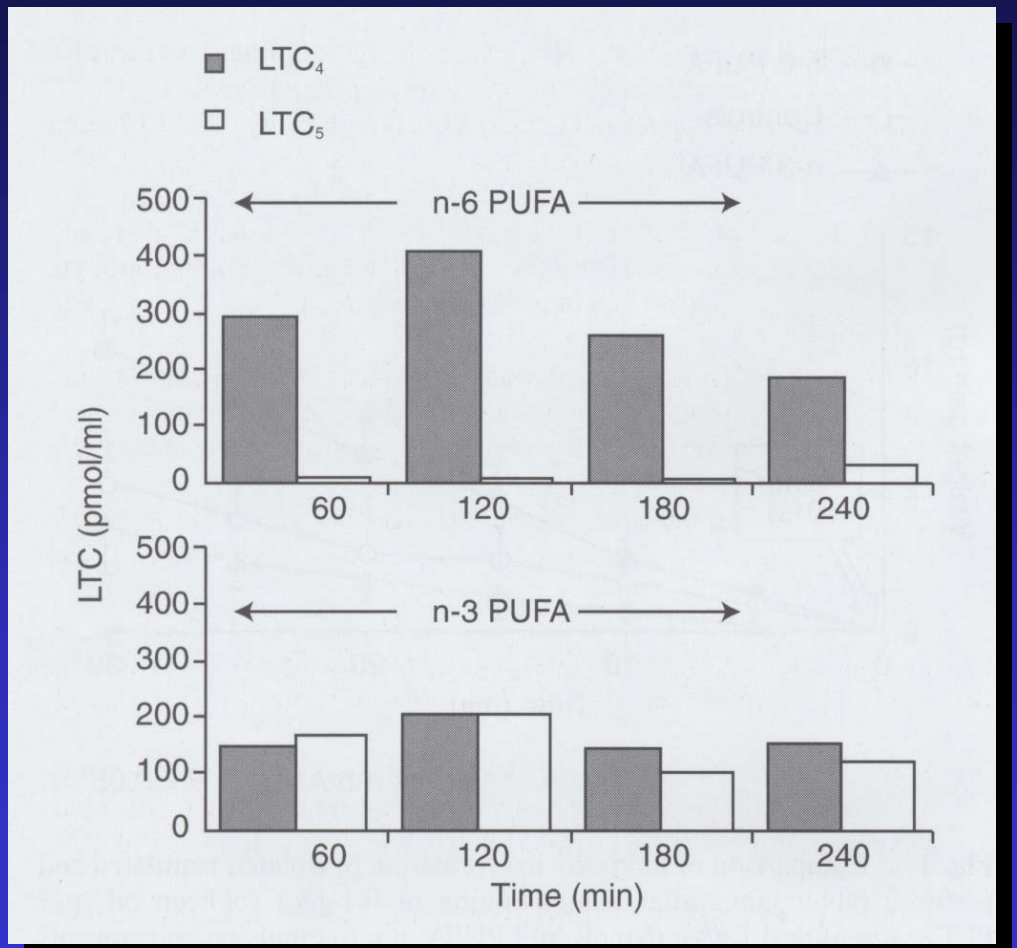
Modulation of pulmonary vascular resistance and edema formation by short term infusion of a 10% fish oil emulsion



Comparison of lung edema in isolated ventilated and perfused rabbit lungs after administration of 0.1 g/kg soybean oil (n-6 PUFA; n=6) or 0.1 g/kg fish oil (n-3 PUFA; n=6) emulsion and controls (n=6).

KOCH et al, Infusions Ther Transfus Med (1993) 20: 291-300

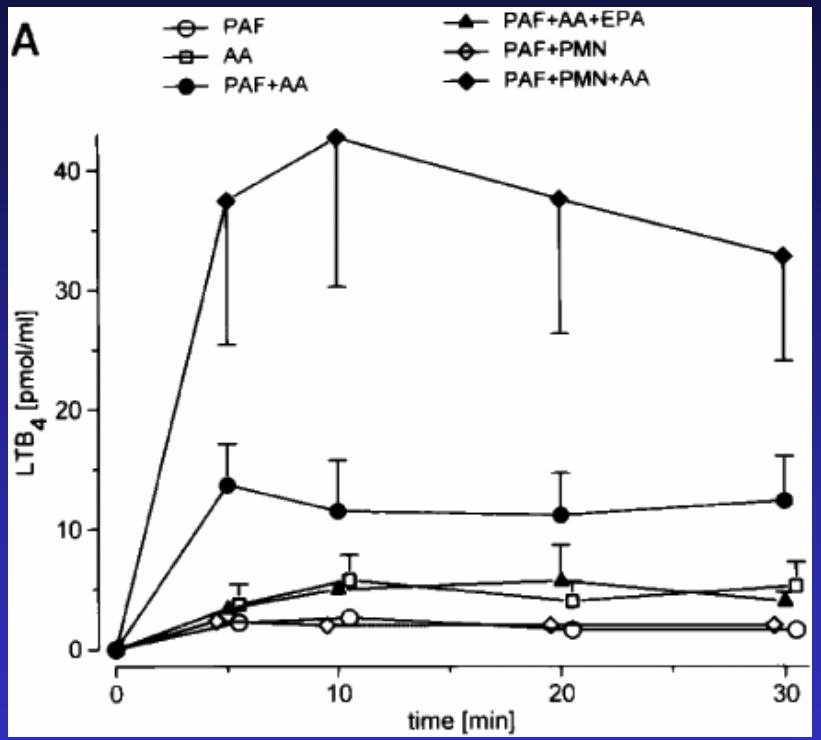
Alteration of n-3 fatty acid composition in lung tissue after short-term infusion of fish oil emulsion attenuates inflammatory vascular reaction

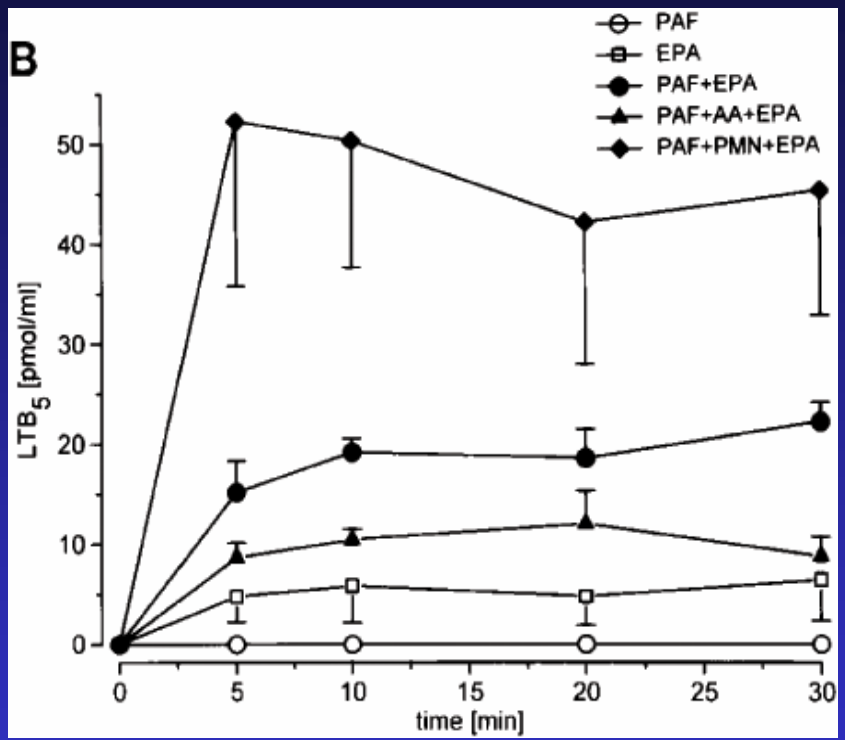


Time course of leukotriene C_4 and C_5 concentrations in the perfusate of isolated ventilated and perfused rabbit lungs after administration of 0.1 g/kg soybean (n-6 PUFA, n=6) or 0.1 g/kg fish oil (n-3 PUFA, n=6) emulsion.

BREIL et al, Crit Care Med (1996) 24: 1893-1902

PAF induced synthesis of tetraenoic and pentaenoic leukotrienes in the isolated rabbit lung





Time course of leukotriene (LT) B_4 and LTB_5 release in response to platelet activating Factor (PAF) and precursor fatty acid application. Lungs with and without infusion of neutrophils (PMNs) were stimulated with arachidonic acid (AA), eicosapentaenoic acid (EPA), PAF, or a combination of stimuli.

GRIMMINGER et al, Am J Physiol Lung Cell Mol Physiol 278: L268-L275 (2000)

PAF induced synthesis of tetraenoic and pentaenoicc leukotrienes in the isolated rabbit lung

Conclusions

. . . Notably, intravascular disposal of free EPA effected a complete shift of the metabolite profile to pentaenoic LTs with concomitant suppression of 4-series product formation . . .

Considering the strong inflammatory potencies of the AA-derived lipoxygenase metabolites and the markedly reduced or even antagonistic biological properties of the corresponding n-3 derivatives, these findings may be of interest for the development of antiinflammatory therapies.

The use of n-3 fatty acid-enriched (fish oil derived) lipid emulsions rather than the conventional n-6 fatty acid-rich preparations may be a plausible strategy to combine parenteral nutrition and suppression of PMN-related inflammatory events.

GRIMMINGER et al, Am J Physiol Lung Cell Mol Physiol 278: L268-L275 (2000)