

An Investigation of the Influence of Fish Oil Supplementation on IL-8: A Possible Protection Against Preeclampsia

*Sara Edwards CNM, MN, MPH, PhD Student
Emory University
Atlanta, Georgia
USA*

Disclosures

Author: Sara Edwards CNM, MN, MPH, PhD Student

Learner Objectives:

- ▶ To understand the role of polyunsaturated fatty acids from fish oil supplementation in the diet
- ▶ To understand the unique properties of interleukin-8 that may affect the development of preeclampsia
- ▶ To understand the factors that predict the use of fish oil in pregnancy
- ▶ To understand the association between fish oil supplementation and serum levels of IL-8 in pregnancy

Disclosures

Conflict of Interest and Commercial Support: None

Employer: Emory University

Sponsorship: T32- "*Training in Interventions to Improve Outcomes in Chronic Conditions*"
(PO1 NR011587)

Disclosures

Funding Support:

This work was supported by the National Institutes of Nursing Research (NINR)

"Psychoneuroimmune Contributions to Postpartum Depression"

(R01 NR011278)

PI: Dr. Elizabeth Corwin



Preeclampsia



Preeclampsia

Strikes 10 Million Women Every Year



Preeclampsia

Strikes 10 Million Women Every Year

76 Thousand Women Die



Preeclampsia

Strikes 10 Million Women Every Year

76 Thousand Women Die

500 Thousand Infants Die



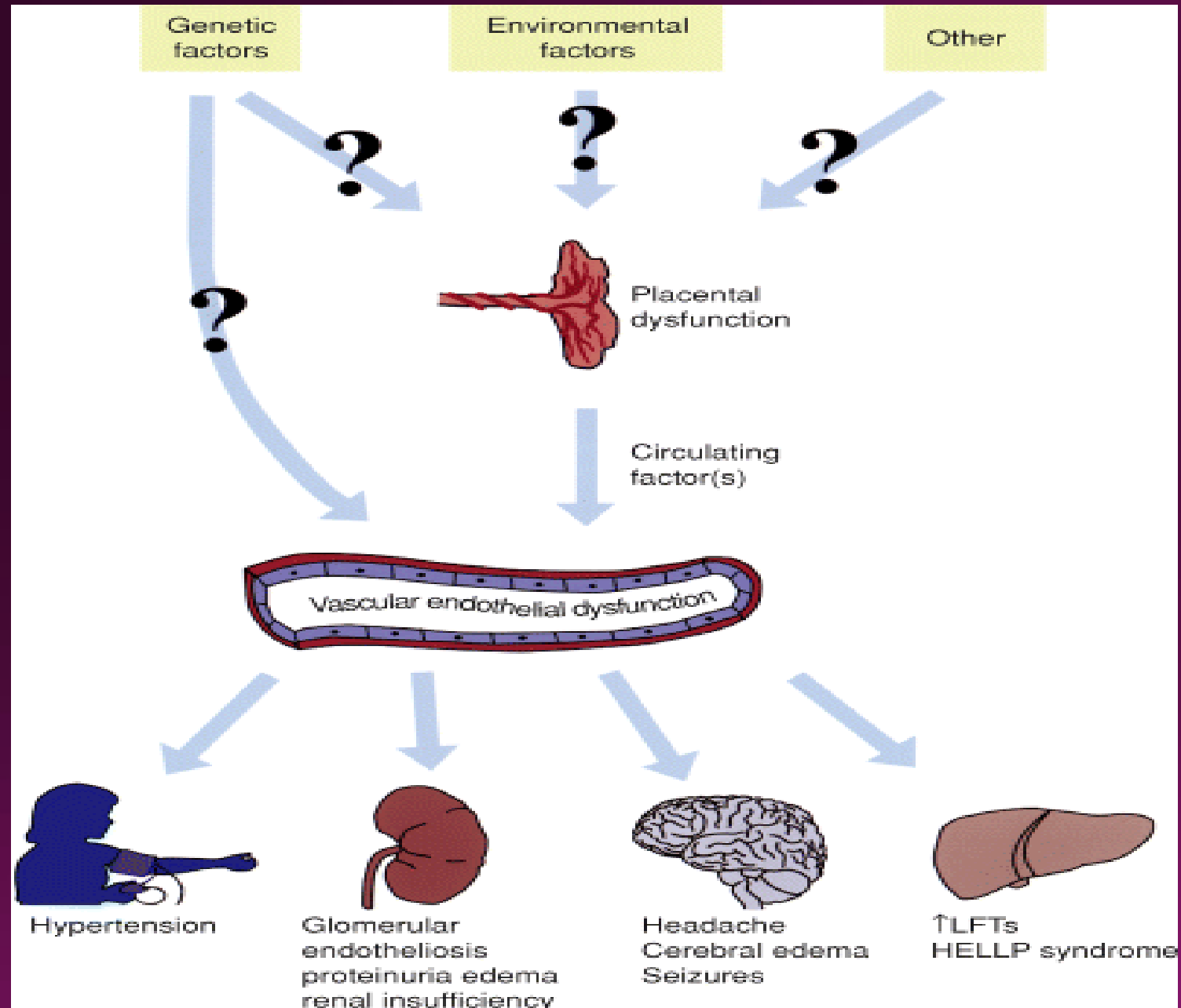
Preeclampsia

Strikes 10 Million Women Every Year

76 Thousand Women Die

500 Thousand Infants Die

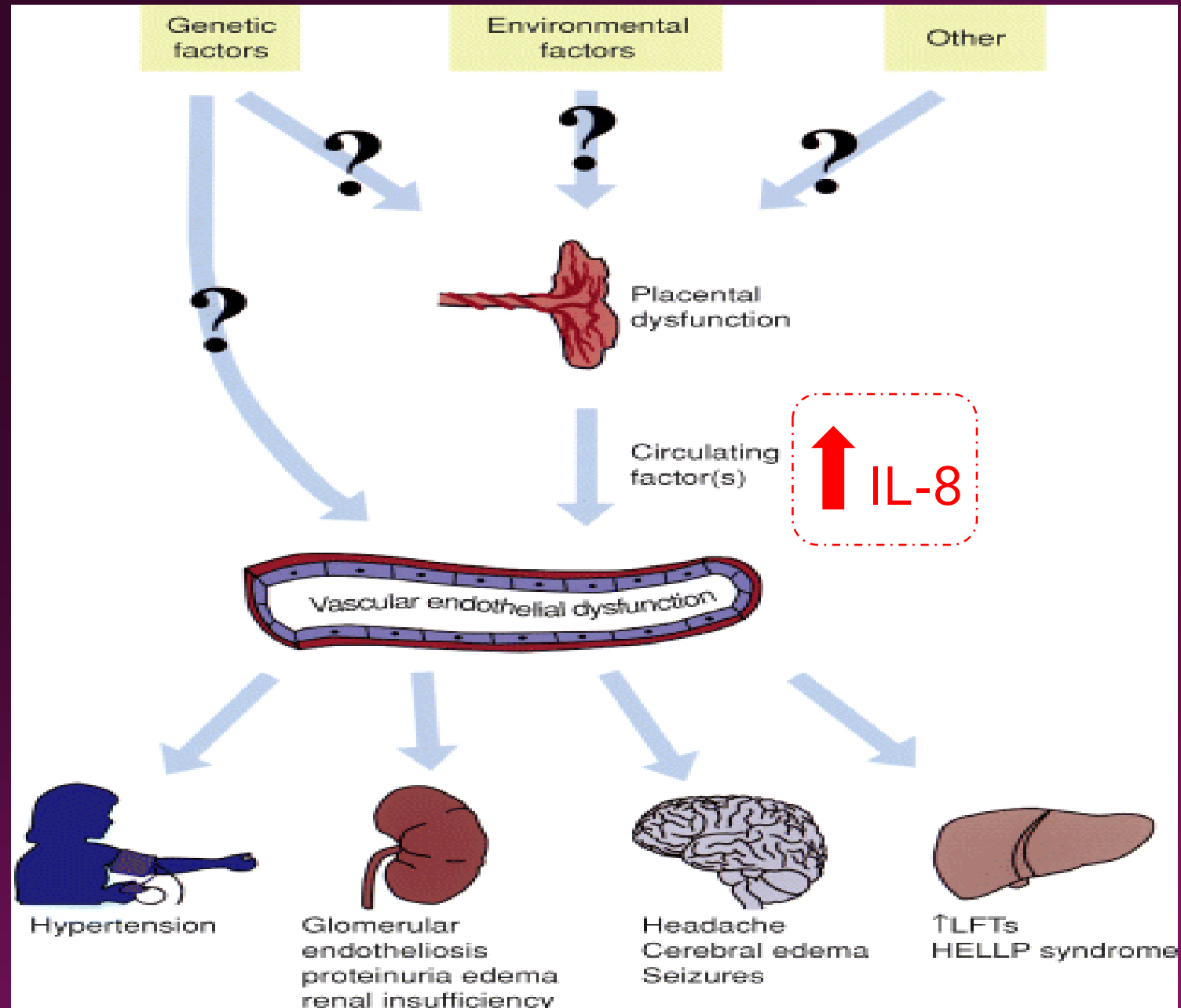
7 Times More Likely in a Developing Country



Kidney International (2005)
67, 2101–2113;
doi:10.1111/j.1523-
1755.2005.00316.x

Preeclampsia: A renal
perspective

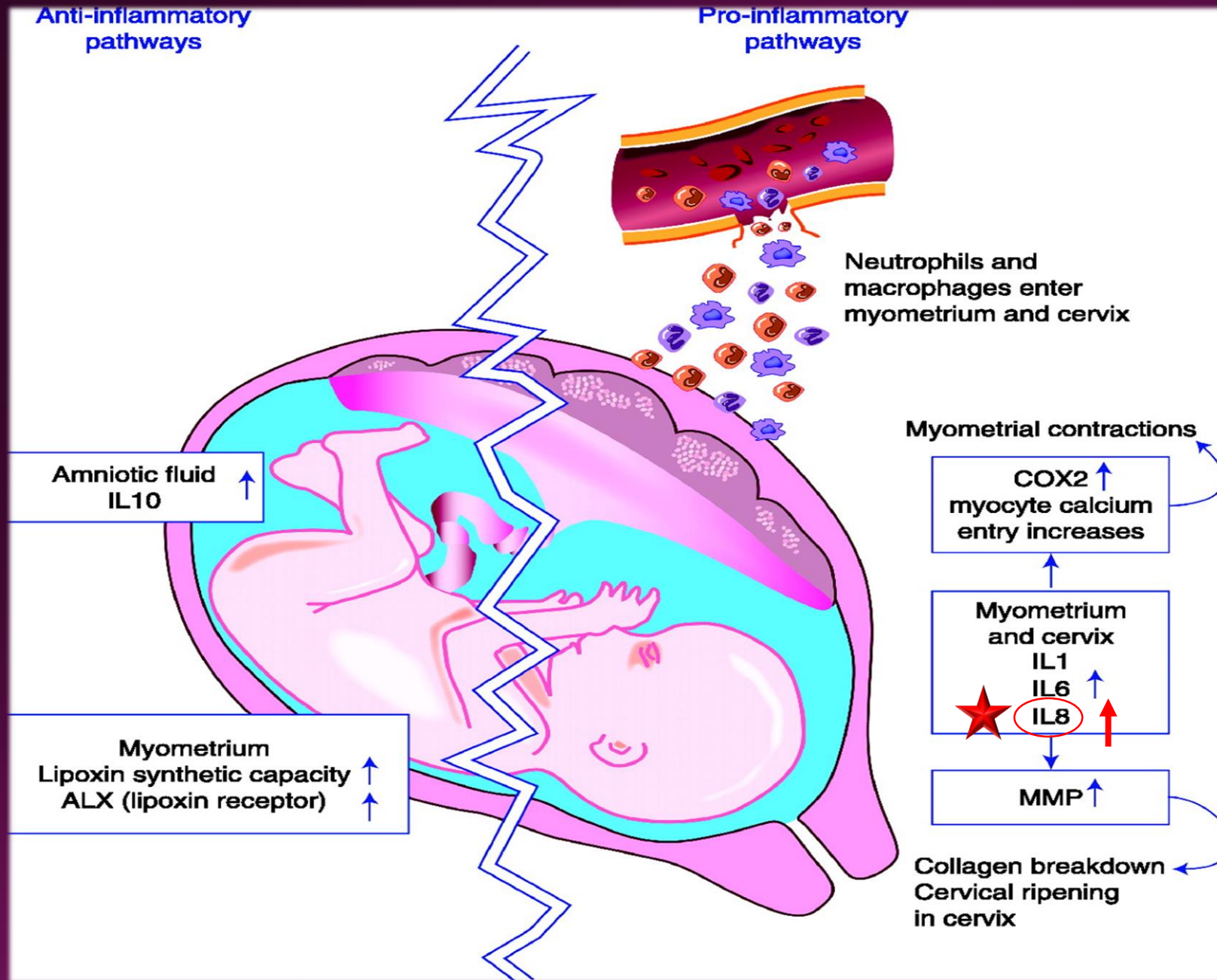
S ANANTH KARUMANCHI,
SHARON E MAYNARD,
ISAAC E STILLMAN,
FRANKLIN H EPSTEIN and
VIKAS P SUKHATME



Kidney International (2005)
67, 2101–2113;
doi:10.1111/j.1523-
1755.2005.00316.x

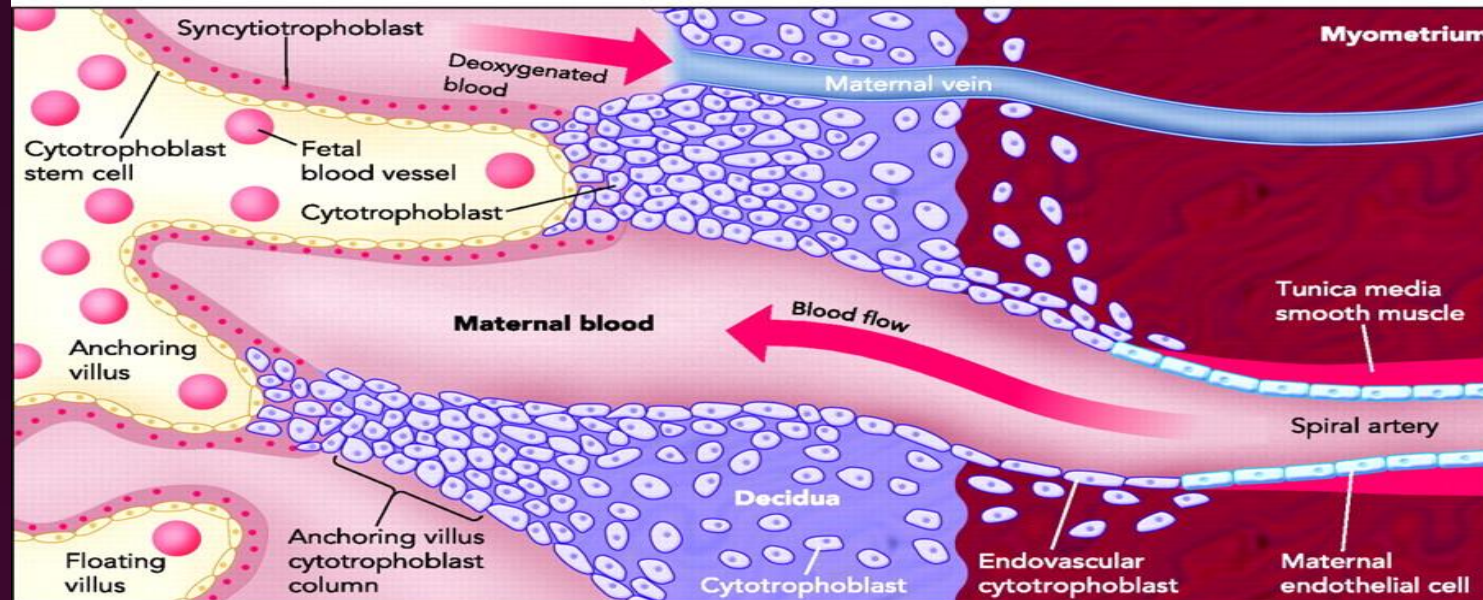
Preeclampsia: A renal
perspective

S ANANTH KARUMANCHI,
SHARON E MAYNARD,
ISAAC E STILLMAN,
FRANKLIN H EPSTEIN and
VIKAS P SUKHATME

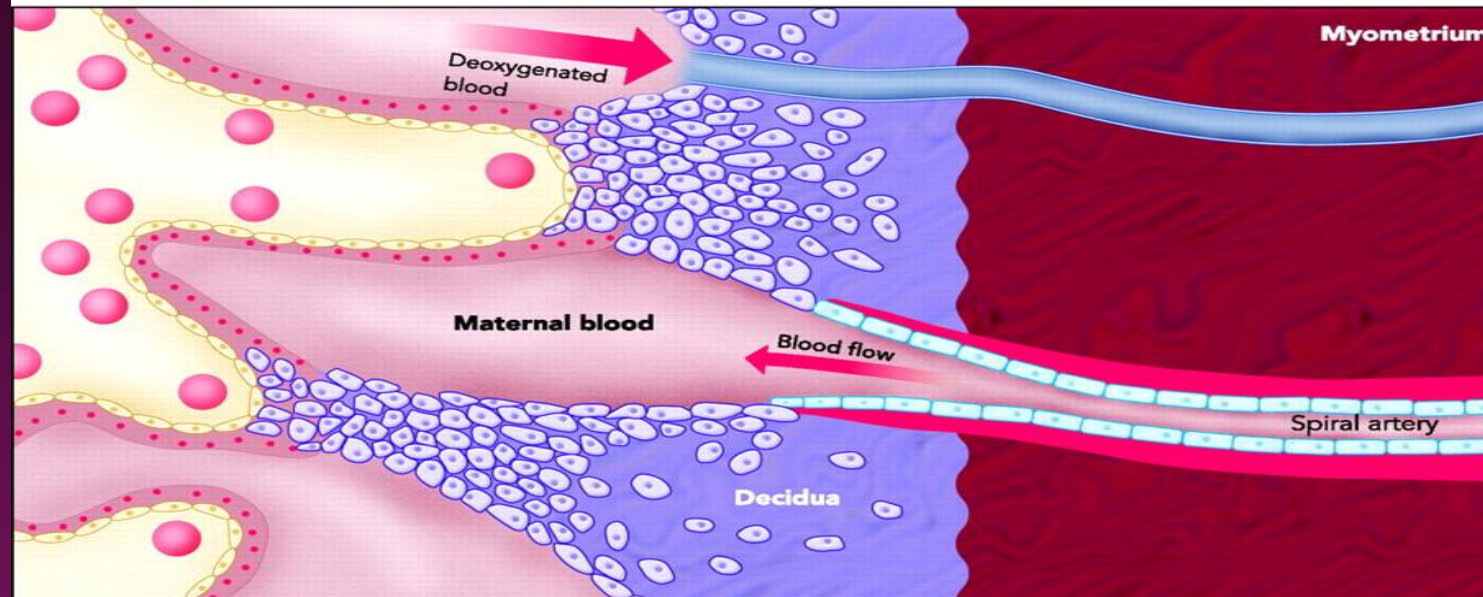


Jabbour, H.N. et al,,
Reproduction 2009;
138: 903-919.

Normal



Preeclampsia



Kidney International (2005) 67, 2101–2113; doi:10.1111/j.1523-1755.2005.00316.x

Preeclampsia: A renal perspective

S ANANTH KARUMANCHI,
SHARON E MAYNARD, ISAAC
E STILLMAN, FRANKLIN H
EPSTEIN and VIKAS P
SUKHATME

A close-up photograph of a person's open palm, showing the texture of the skin. Three yellow, oval-shaped capsules are resting on the palm. The capsules are translucent and contain a yellowish liquid. The background is a soft, out-of-focus light color.

Polyunsaturated Fatty Acids (PUFAs)

A close-up photograph of a human palm with three yellow, oval-shaped capsules resting on it. The capsules are arranged in a diagonal line from the top left towards the bottom right. The skin of the palm is clearly visible, showing the texture and lines. The background is a soft, out-of-focus light color.

Polyunsaturated Fatty Acids (PUFAs)

- **Omega 6**

A close-up photograph of a human palm with three yellow, oval-shaped capsules resting on it. The capsules are arranged in a diagonal line from the top right towards the bottom left. The skin of the palm is clearly visible, showing the texture and lines. The background is a soft, out-of-focus light color.

Polyunsaturated Fatty Acids (PUFAs)

- Omega 6
- Omega 3

A close-up photograph of a human palm with three yellow, oval-shaped capsules resting on it. The skin's texture is clearly visible. The capsules are arranged in a slight arc across the palm.

Essential Fatty Acids

Polyunsaturated Fatty Acids (PUFAs)

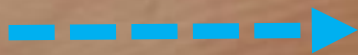
- Omega 6
- Omega 3



Essential Fatty Acids

Polyunsaturated Fatty Acids (PUFAs)

- Omega 6
- Omega 3





Essential Fatty Acids

Polyunsaturated Fatty Acids (PUFAs)

- Omega 6
- Omega 3

Decreased IL-8?

Methods:

- 203 Women in Colorado and Ohio Enrolled
- Longitudinal Study from 3rd Trimester to 6 months Postpartum:
- This analysis is of the one prenatal time point in the 3rd Trimester
 - Fish Oil Supplementation? Yes/No

“Psychoneuroimmune Contributions to Postpartum Depression”
(R01 NR011278)
PI: Dr. Elizabeth Corwin

Methods:

- 203 Women in Colorado and Ohio Enrolled
- Longitudinal Study from 3rd Trimester to 6 months Postpartum:
- This analysis is of the one prenatal time point in the 3rd Trimester
 - Fish Oil Supplementation? Yes/No
 - Demographic Surveys

"Psychoneuroimmune Contributions to Postpartum Depression"
(R01 NR011278)
PI: Dr. Elizabeth Corwin

Methods:

- 203 Women in Colorado and Ohio Enrolled
- Longitudinal Study from 3rd Trimester to 6 months Postpartum
- This analysis is of the one prenatal time point in the 3rd Trimester
 - Fish Oil Supplementation? Yes/No
 - Demographic Surveys
 - Plasma Cytokine levels

"Psychoneuroimmune Contributions to Postpartum Depression"

(R01 NR011278)

PI: Dr. Elizabeth Corwin

Table 1. Demographic and clinical characteristics of women who did or did not report taking prenatal fish oil supplements (mean $\pm$ SD)

	<u>FISH OIL USAGE</u>		
	<u>No (N=116)</u>	<u>Yes (N=40)</u>	<u>p value</u>
Age	28.1 (5.3)	31.1 (4.2)	p= 0.002**
BMI	25.1 (5.2)	22.8 (3.4)	p=0.01*
Married	73%	90%	p=0. 05
Caucasian	67%	93%	p=.002**
High Income	66%	93%	p=.001**

Table 2. Interleukin-8 plasma levels (pg/ml) in women who did or did not report taking prenatal fish oil supplements (mean $\pm$ SE)

FISH OIL USAGE

	<u>No (N=108)</u>	<u>Yes (N=40)</u>	<u>p value</u>
IFN-γ	0.82 (.05)	1.0 (.09)	NS
IL-1	0.38 (.03)	0.38 (.08)	NS
IL-6	1.00 (.04)	0.88 (.08)	NS
TNFα	1.81 (.05)	1.76 (.07)	NS
IL-8	1.60 (.04)	1.33 (.06)	p=.002**
IL-10	1.48 (.08)	1.53 (.15)	NS

Logistic Regression Results:

Performed to assess the impact of 4 factors (age, BMI, Caucasian race or other, Income (food voucher program) on the likelihood a woman would supplement with fish oil in pregnancy.

A full model using these 4 predictors (age, BMI, Caucasian race or other, Income (food voucher program) was statistically significant.

- Chi-square (6, N=188) = 23.43, $p < .000$

Logistic Regression Results:

Fish oil users were more likely to be older ($p < .002^*$), thinner ($p = .01^*$), Caucasian ($p = .002^{**}$) and not receiving food vouchers ($.001^{**}$).

The whole model explained 11.7-17.8% of the variance in fish oil intake and correctly classified 76.6% of cases.

Linear Regression Results:

After controlling for age, BMI, marital status, Caucasian race, and income:

- IL-8 levels were significantly lower among women taking fish oil supplements ($p=0.026^*$, $t=3.157$, $df = 145$) compared to those not taking it.
- Fish oil usage **explains 5.8% of the variance in prenatal IL-8 plasma levels**



*Why are women
using Fish Oil and
how much are
they ingesting?*

*Could Fish Oil Use
Reduce
Preeclampsia
Risk?*





*Could IL-8 levels
serve as an early
marker of
preeclampsia?*

References

- Assies, J., Mocking, R. J., Pouwer, F. C. O. N. J. O., & Pmid. (2011). Maternal depression and child development after prenatal DHA supplementation. *JAMA : the journal of the American Medical Association*, 305(4), 360; author reply 360-361.
- Bastek, J. A., & Elovitz, M. A. (2013). The role and challenges of biomarkers in spontaneous preterm birth and preeclampsia. *Fertility and Sterility*, 99(4), 1117-1123. doi: 10.1016/j.fertnstert.2013.01.104
- Bowen, R. S., Gu, Y., Zhang, Y., Lewis, D. F., & Wang, Y. (2005). Hypoxia promotes interleukin-6 and -8 but reduces interleukin-10 production by placental trophoblast cells from preeclamptic pregnancies. *Journal of the Society for Gynecologic Investigation*, 12(6), 428-432. doi: 10.1016/j.jsgi.2005.04.001
- Calder, P. C. (2010). Omega-3 fatty acids and inflammatory processes. *Nutrients*, 2(3), 355-374.
- Carlson, S. E., Colombo, J., Gajewski, B. J., Gustafson, K. M., Mundy, D., Yeast, J., . . . Shaddy, D. J. (2013). DHA supplementation and pregnancy outcomes. *The American journal of clinical nutrition*, 97(4), 808-815.
- Cousens S, Blencowe H, Stanton C, Chou D, Ahmed S, Steinhardt L, Creanga AA, Tunçalp O, Balsara ZP, Gupta S, Say L, Lawn JE. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. *Lancet*, 2011, Apr 16;377(9774):1319-30.
- Conde-Agudelo A, Belizan JM, Lammers C. Maternal-perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: Cross-sectional study. *American Journal of Obstetrics and Gynecology*, 2004. 192:342–349.

References

- Donahue, S. M., Rifas-Shiman, S. L., Olsen, S. F., Gold, D. R., Gillman, M. W., & Oken, E. (2009). Associations of maternal prenatal dietary intake of n-3 and n-6 fatty acids with maternal and umbilical cord blood levels. Prostaglandins, leukotrienes, and essential fatty acids, 80(5-6), 289-296.
- Elovitz, M. A. (2006). Anti-inflammatory interventions in pregnancy: now and the future. Seminars in fetal & neonatal medicine, 11(5), 327-332. doi: 10.1016/j.siny.2006.03.005
- Emmett, R., Akkersdyk, S., Yeatman, H., & Meyer, B. J. (2013). Expanding awareness of docosahexaenoic acid during pregnancy. Nutrients, 5(4), 1098-1109.
- Genuis, S. J. C. I. N. R. T. J., & Pmid. (2008). To sea or not to sea: benefits and risks of gestational fish consumption. Reproductive toxicology (Elmsford, N.Y.), 26(2), 81-85.
- Jabbour, H. N., Sales, K. J., Catalano, R. D., & Norman, J. E. (2009). Inflammatory pathways in female reproductive health and disease. Reproduction (Cambridge, England), 138(6), 903-919.
- Karumanchi, S. A., Maynard, S. E., Stillman, I. E., Epstein, F. H., & Sukhatme, V. P. (2005). Preeclampsia: a renal perspective. Kidney International, 67(6), 2101-2113. doi: 10.1111/j.1523-1755.2005.00316.x
- Kuklina EV, et al. Hypertensive Disorders and Severe Obstetric Morbidity in the United States. Obstet Gynecol 2009; 113:1299-306.
- Mocking, R. J., Ruhe, H. G., Assies, J., Lok, A., Koeter, M. W., Visser, I., . . . Schene, A. H. (2013). Relationship between the hypothalamic-pituitary-adrenal-axis and fatty acid metabolism in recurrent depression. [Journal Article]. Psychoneuroendocrinology, 38(9), 1607-1617.

References

Mozurkewich, E., Chilimigras, J., Klemens, C., Keeton, K., Allbaugh, L., Hamilton, S., . . . Vahratian, A. (2011). The mothers, Omega-3 and mental health study. *BMC pregnancy and childbirth*, 11, 46. doi: 10.1186/1471-2393-11-46

Mozurkewich, E. L., Clinton, C. M., Chilimigras, J. L., Hamilton, S. E., Allbaugh, L. J., Berman, D. R., . . . Djuric, Z. (2013). The Mothers, Omega-3, and Mental Health Study: a double-blind, randomized controlled trial. *American Journal of Obstetrics and Gynecology*, 208(4), 313.e311-319. doi: 10.1016/j.ajog.2013.01.038

Olafsdottir, A. S., Skuladottir, G. V., Thorsdottir, I., Hauksson, A., Thorgeirsdottir, H., & Steingrimsdottir, L. (2006). Relationship between high consumption of marine fatty acids in early pregnancy and hypertensive disorders in pregnancy. *BJOG : an international journal of obstetrics and gynaecology*, 113(3), 301-309. doi: 10.1111/j.1471-0528.2006.00826.x

Olsen, S. F., Osterdal, M. L., Salvig, J. D., Weber, T., Tabor, A., & Secher, N. J. (2007). Duration of pregnancy in relation to fish oil supplementation and habitual fish intake: a randomised clinical trial with fish oil. *European Journal of Clinical Nutrition*, 61(8), 976-985. doi: 10.1038/sj.ejcn.1602609

Olsen, S. F., Secher, N. J., Tabor, A., Weber, T., Walker, J. J., & Gluud, C. (2000). Randomised clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials In Pregnancy (FOTIP) Team. *BJOG : an international journal of obstetrics and gynaecology*, 107(3), 382-395.

Patton GC, Coffey C, Sawyer SM, Viner RM, Haller DM, Bose K, Vos T, Ferguson J, Mathers CD. Global patterns of mortality in young people: a systematic analysis of population health data. *Lancet*, 2009, 374:881–892.

References

Villar J, Say L, Gulmezoglu AM, Meraldi M, Lindheimer MD, Betran AP, Piaggio G; Eclampsia and pre-eclampsia: a health problem for 2000 years. In Pre-eclampsia, Critchly H, MacLean A, Poston L, Walker J, eds. London, RCOG Press, 2003, pp 189-207.

World Health Organization Fact Sheet, May 2012.

Zhou, S. J., Yelland, L., McPhee, A. J., Quinlivan, J., Gibson, R. A., & Makrides, M. (2012). Fish-oil supplementation in pregnancy does not reduce the risk of gestational diabetes or preeclampsia. *The American journal of clinical nutrition*, 95(6), 1378-1384. doi: 10.3945/ajcn.111.033217