I NUTRACEUTICI AL FEMMINILE.
RAZIONALE PER UNA UTILE SUPPLEMENTAZIONE NELLA VITA DELLA DONNA

Ferrara, 20 marzo 2015

ALIMENTAZIONE, NUTRACEUTICA ED INFERTILITA' FEMMINILE

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INFERTILITA’

Problematica che interessa il 10-15% della popolazione nei Paesi industrializzati.

Il personale medico e sanitario frequentemente viene interpellato dalle coppie in cerca di una gravidanza, sui problemi relativi loro potenziale riproduttivo.

Sempre più spesso le coppie si rivolgono al medico per avere informazioni sui comportamenti più adeguati anche in epoca preconcezionale.

Queste coppie sono molto **motivate** a seguire i consigli relativi all’impatto che determinati fattori o stili di vita possono avere sulla fertilità, oltre che sulla salute in generale.

INFERTILITA’

È risaputo che alcuni fattori o stili di vita hanno effetti quantitativamente piccoli, ma cumulativi nel tempo, che possono portare ad un prolungamento del tempo di ricerca della gravidanza.

È altrettanto noto che le modificaizoni di questi fattori sembrano migliorare le capacità riproduttive della coppia.

STILE DI VITA ED INFERTILITA'

Aumento dell'età materna

Ritardo nell'inizio delle terapie

Fumo di sigaretta

Body Mass Index

Consumo di alcohol e caffeina

Interferenti Endocrini

Infezioni del tratto genitale

Stress

NON ci sono in letteratura **trials clinici randomizzati** su larga scala che esaminino in modo accurato l'effetto che questi fattori potrebbero avere sulla fertilità.

La maggior parte degli studi in merito sono ***osservazionali*** ed, in quanto tali, soggetti potenzialmente a molti *bias.*

Rooney KL Curr Opin Obstet Gynecol 2014

BMI

La maggior parte degli studi riporta che BMI maggiori di 27 kg/m^2 o BMI minori di 17 kg/m^2 sono associati ad infertilità per disordini ovulatori.

Elevato BMI: insulino resistenza, iperinsulinismo. Elevati valori di Leptina.

Basso BMI : anovulazione. Influenza della leptina?

PMA: > rischio di cancellazione dei cicli di stimolazione e dei transfer

↓

Peggiore outcome delle tecniche di PMA

Caillon H Obes Res Clin Pract. 2015

ALCOHOL

Low intake: <2 drinks/day (1 drink = 10 g of ethanol)
Moderate intake: 3 to 13 drinks per week
Heavy intake: ≥14 drinks per week

Low intake: no or minimal adverse effects on fertility

Moderate alcohol use may affect fertility and IVF success rates

Heavy female drinkers: - longer time to achieve a pregnancy
- higher risk of infertility evaluation

Rossi BV, Obstet Gynecol 2011
Chavarro, Epidemiology 2009

ALCOHOL

Le donne che sono alla ricerca di una gravidanza dovrebbero ***evitare il consumo di alcohol***, considerando che non ci sono evidenze su quali siano i livelli di consumo alcolico effettivamente sicuri in epoca prenatale e nella gravidanza iniziale.

Rossi BV, Obstet Gynecol 2011
Chavarro, Epidemiology 2009

CAFFEINE

INCONSISTENT EVIDENCE

-High caffeine use (>5–7 cups per day) has been associated with decreased natural fertility in some investigations (dose related)

- > 50 mg/day is linked to lower number of eggs, lower pregnancy rates in IVF patients.

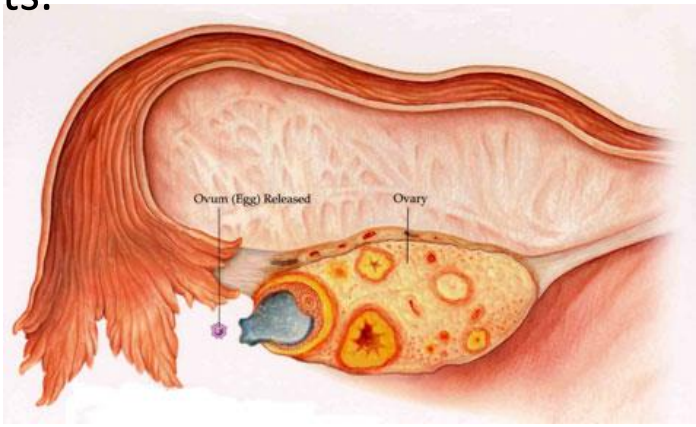
Rooney, c.o.obgyn 2014
Huang, Fertil Steril 2012

FERTILITY DIET?

There is **no strong evidence that dietary variations** such as vegetarian diets, lowfat diets, and vitamin or antioxidant **enriched diets improve fertility**.

"FERTILITY DIET": - higher monounsaturated to trans fat ratio
- high % of protein from vegetable rather than animal sources
- low glycemic index carbohydrates
- high fat dairy foods
- iron and multivitamin supplements.

↓ risk of ovulatory disorder infertility.



Chavarro, Am J Obstet Gyencol 2006-2009

OXIDATIVE STRESS

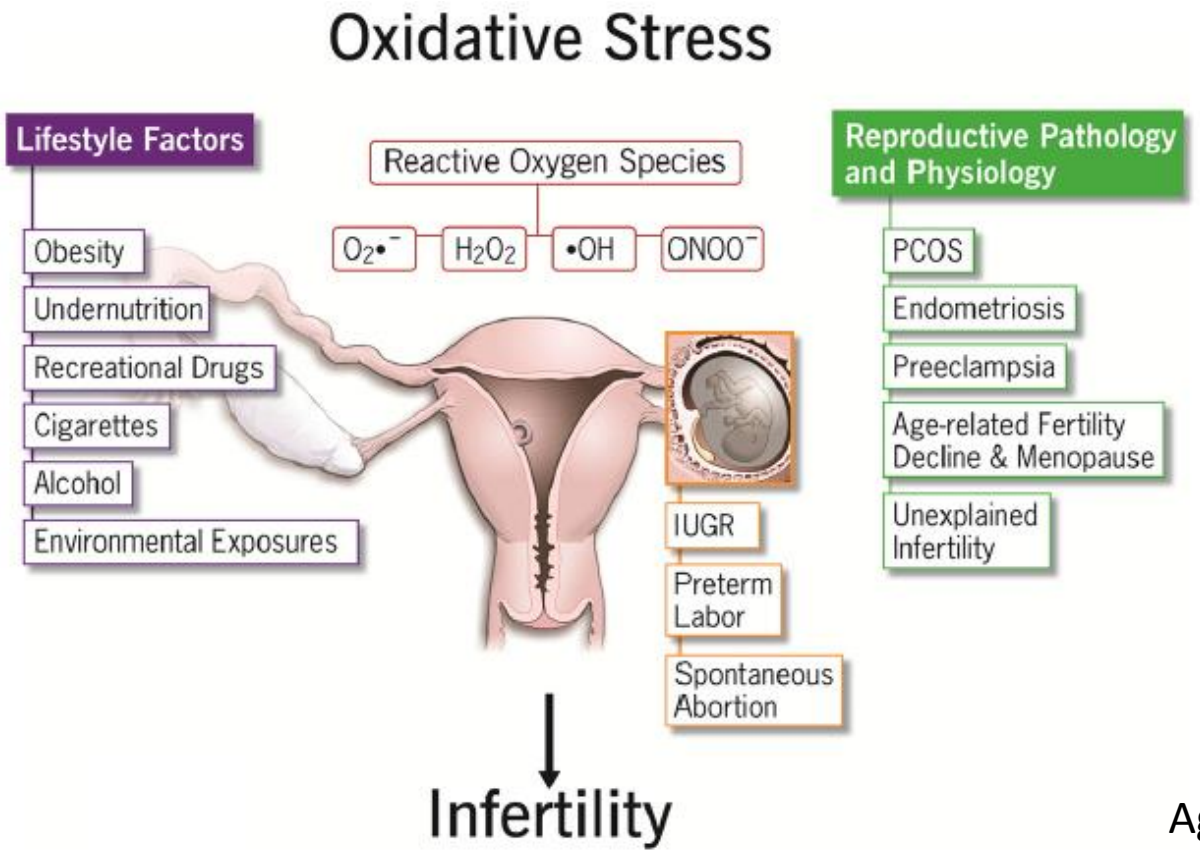
Agarwal et al. Reproductive Biology and Endocrinology 2012, 10:49
http://www.rbej.com/content/10/1/49

REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY

REVIEW Open Access

The effects of oxidative stress on female reproduction: a review

Ashok Agarwal*, Anamar Aponte-Mellado, Beena J Premkumar, Amani Shaman and Sajal Gupta



Agarwal 2012

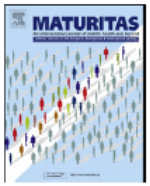
DIETARY VARIATIONS AND MITOCHONDRIAL FUNCTION

Maturitas 74 (2013) 309–312

Contents lists available at SciVerse ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas



Review

Nutrition and reproduction: Is there evidence to support a "Fertility Diet" to improve mitochondrial function?

Katherine M. Shaum[a], Alex J. Polotsky[b,*]

The wide array of dietary influences on ovulatory dysfunction suggests a complex balance of nutrition for optimal fertility and confirms the dictum that there is **no "one size fits all" dietary intervention** to boost fertility.

Shaum 2013

DIETARY VARIATIONS AND MITOCHONDRIAL FUNCTION

Normal function of mitochondria plays an essential role in enabling reproductive capacity.

Shaum 2013

Table 1
Dietary interventions potentially relevant for targeting mitochondrial function for fertility enhancement.

Nutrient	Experimental setting	Specific aspect of mitochondria biology impacted
Carnitine	Boar sperm	Improved sperm quality, morphology.
	Human sperm and serum	Improved sperm motility, decreased oxidative stress.
	Blood and sperm of patients with epididymitis	Reduced reactive oxygen species, increased sperm viability, increased spontaneous pregnancy.
Coenzyme Q10	Oocytes of mice receiving ovarian stimulation.	Improved oocyte mitochondrial activity.
N-acetylcysteine	Human luteal cells	Impaired mitochondrial metabolism and cell survival.
Proanthocyanidins	Human endothelial cells	Protection from apoptosis after exposure to advanced glycation end products, a diabetic model.
	Mouse fibroblasts	Decreased oxidative stress after toxic exposure.
	Adipose tissue of rats with diet-induced obesity	Protection from weight gain, enhancement of brown adipose tissue mitochondrial function, decreased triglycerides and increased oxidative capacity.
	Skeletal muscle of a rat model of genetic obesity	Improved muscle mitochondrial function, decreased reactive oxygen species production.
	Myocardium and blood of diabetic mice	Fewer advanced glycation end products, inflammatory cytokines, decreased mitochondria degeneration.
	Metabolic markers of rats with fructose-induced metabolic syndrome	Lowered serum glucose, total cholesterol, blood pressure and triglycerides, decreased inflammatory markers.
Vitamin E	Human placental mitochondria	Decreased lipid peroxidation.
	Adipose and connective tissue of vitamin E deficient rats	Decreased mitochondrial activity in brown adipose tissue, decreased endurance capacity.
Omega-3 Fatty Acids	Mouse oocytes	Decreased mitochondrial aggregation in oocytes and improved oocyte quality with advanced maternal age.

DIETARY ANTIOXIDANT INTAKE

Published in final edited form as:
Fertil Steril. 2014 March ; 101(3): 759–766. doi:10.1016/j.fertnstert.2013.11.008.

Female dietary antioxidant intake and time to pregnancy among couples treated for unexplained infertility

Elizabeth H. Ruder, Ph.D., M.P.H.[1], **Terryl J. Hartman, Ph.D., M.P.H.**[2], **Richard H. Reindollar, M.D.**[3], and **Marlene B. Goldman, Sc.D.**[3,4]

increased intake of certain antioxidants is associated with shorter time to pregnancy (TTP), but the relationship varied among patients

Ruder, Fertil Steril 2014

DIETARY ANTIOXIDANT INTAKE

VITAMIN C

shorter time to pregnancy among women with

BMI <25 kg/m2

< 35 y of age.

B-CAROTENE

shorter TTP among women with

BMI < 25 kg/m2

BMI ≥ 25 kg/m2

age < 35 y

VITAMIN E

Shorter TTP in women ≥ 35y

Ruder, Fertil Steril 2014

FOLATES

Original Research

Dietary Folate and Reproductive Success Among Women Undergoing Assisted Reproduction

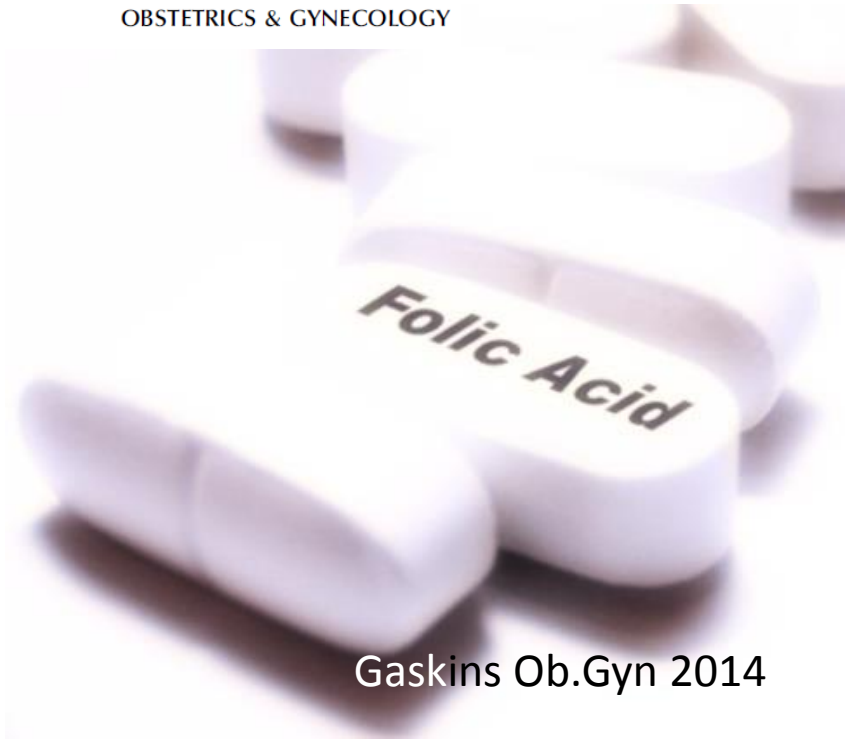
Audrey J. Gaskins, ScD, Myriam C. Afeiche, PhD, Diane L. Wright, PhD, Thomas L. Toth, MD, Paige L. Williams, PhD, Matthew W. Gillman, MD, ScM, Russ Hauser, MD, ScD, and Jorge E. Chavarro, MD, ScD

VOL. 124, NO. 4, OCTOBER 2014 OBSTETRICS & GYNECOLOGY

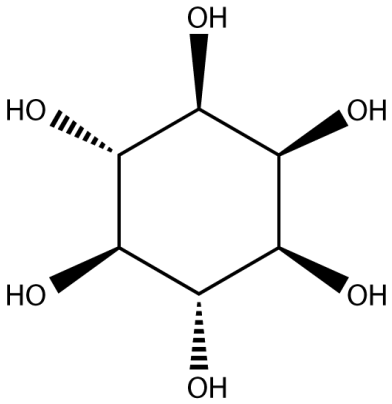
- Better-quality oocytes

- Higher degree of mature oocytes.

Supplemental folate (800-1000 mcg/d) is preferable to food folate for reproductive benefits.



Gaskins Ob.Gyn 2014



MYO-INOSITOL

Lisi *et al. Reproductive Biology and Endocrinology* 2012, **10**:52
http://www.rbej.com/content/10/1/52

RB&E REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY

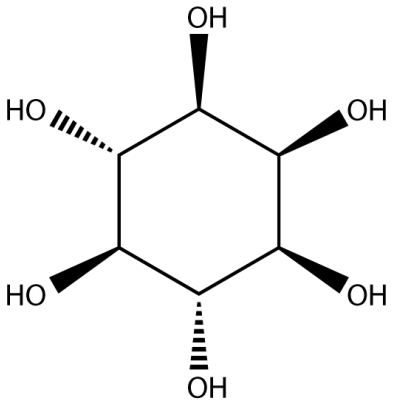
RESEARCH Open Access

Pretreatment with myo-inositol in non polycystic ovary syndrome patients undergoing multiple follicular stimulation for IVF: a pilot study

Franco Lisi[1*], Piero Carfagna[1], Mario Montanino Oliva[1], Rocco Rago[1], Rosella Lisi[1], Roberta Poverini[1], Claudio Manna[2], Elena Vaquero[3], Donatella Caserta[4], Valeria Raparelli[5], Roberto Marci[6] and Massimo Moscarini[4]

Physiological and therapeutic role of myo-inositol in human reproduction and in particularly in oogenesis, playing an important role in cell morphogenesis and cytogenesis, lipid synthesis, structure of cell membranes and cell growth

Lisi et al. Reproductive Biology and Endocrinology 2012



MYO-INOSITOL

NON-PCOS patients, daily dose of:

4,000 mg of myo-inositol 2 admin + 400 µg of folic acid

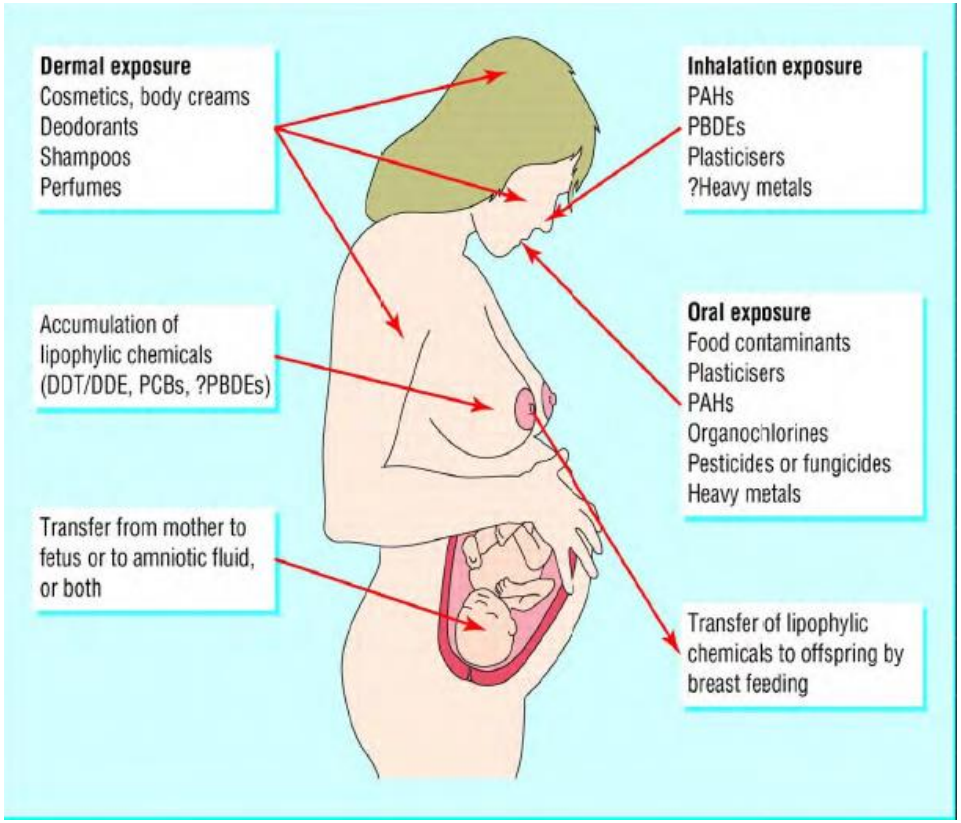
for the 3 months before and during rFSH administration, following the long protocol.

The addition of myo-inositol :

- reduces gonadotropin dosage
- reduces the number of MII oocytes retrieved
- same clinical pregnancy rate
- appearently increased implantation rate

Lisi et al. Reproductive Biology and Endocrinology 2012

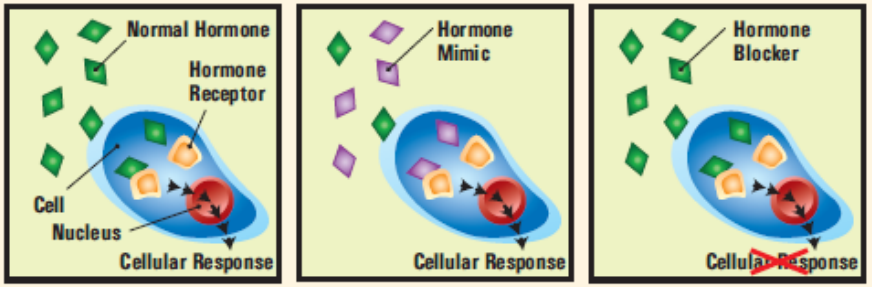
INTERFERENTI ENDOCRINI



Una vasta categoria di sostanze o miscele di sostanze, che alterano la funzionalità del sistema endocrino, causando effetti avversi sulla salute di un organismo, oppure della sua progenie o di una (sotto)popolazione. Queste interferenze possono provocare tumori, difetti alla nascita, e altri disturbi dello sviluppo.

ENDOCRINE DISRUPTORS

- **Effetto dato da piccole dosi**
- **Effetti ad ampio spettro**
- **Persistenza nel tempo dell'effetto biologico**
- **Ubiquitari**



When absorbed in the body, an endocrine disruptor can decrease or increase normal hormone levels (left), mimic the body's natural hormones (middle), or alter the natural production of hormones (right).

Caserta et al, Gynecol Endocrinol. 2013

KEY POINTS

- Stili di vita ed abitudini alimentari possono avere un impatto significativo sulla capacità di ottenere una gravidanza nelle donne infertili
- Nonostante gli sforzi nell'educazione delle pazienti, spesso le stesse non seguono le raccomandazioni ed i consigli
- Ruolo attivo del personale sanitario nell'educazione ed informazione delle pazienti