



Role of Nutrition in Prevention and Treatment of Male Infertility From cell to Society

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Importance of topic

❖ 50% of cases of infertility stem solely from the male unhealthy lifestyle:

✓ Quality of human semen has deteriorated by 50%–60% over the last 40 years.

Not only structure of spermatozoa, but also the development of offspring and their health in later stages of life.

Epigenetic involvement in transgenerational reproductive control

My previous Selected Topics:

- Strength of evidence link male infertility specifically semen parameters to:
 - Dietary habits
 - Nutrition
 - Supplementation with antioxidants or micro nutrients



Are we doing the right interventions at right time

- **Transgenerational** effect of dietary intake influence male fertility through epigenetic mechanisms



Review

Diet and sperm quality: Nutrients, foods and dietary patterns

- Studies investigating the relation between diet and semen quality can be classified into three groups:
 1. Nutrients, dietary supplements and antioxidants
 2. Food
 3. Dietary patterns
 - Adherence to the Mediterranean diet improves sperm concentration, motility and morphology in humans (Karayiannis et al., 2017)

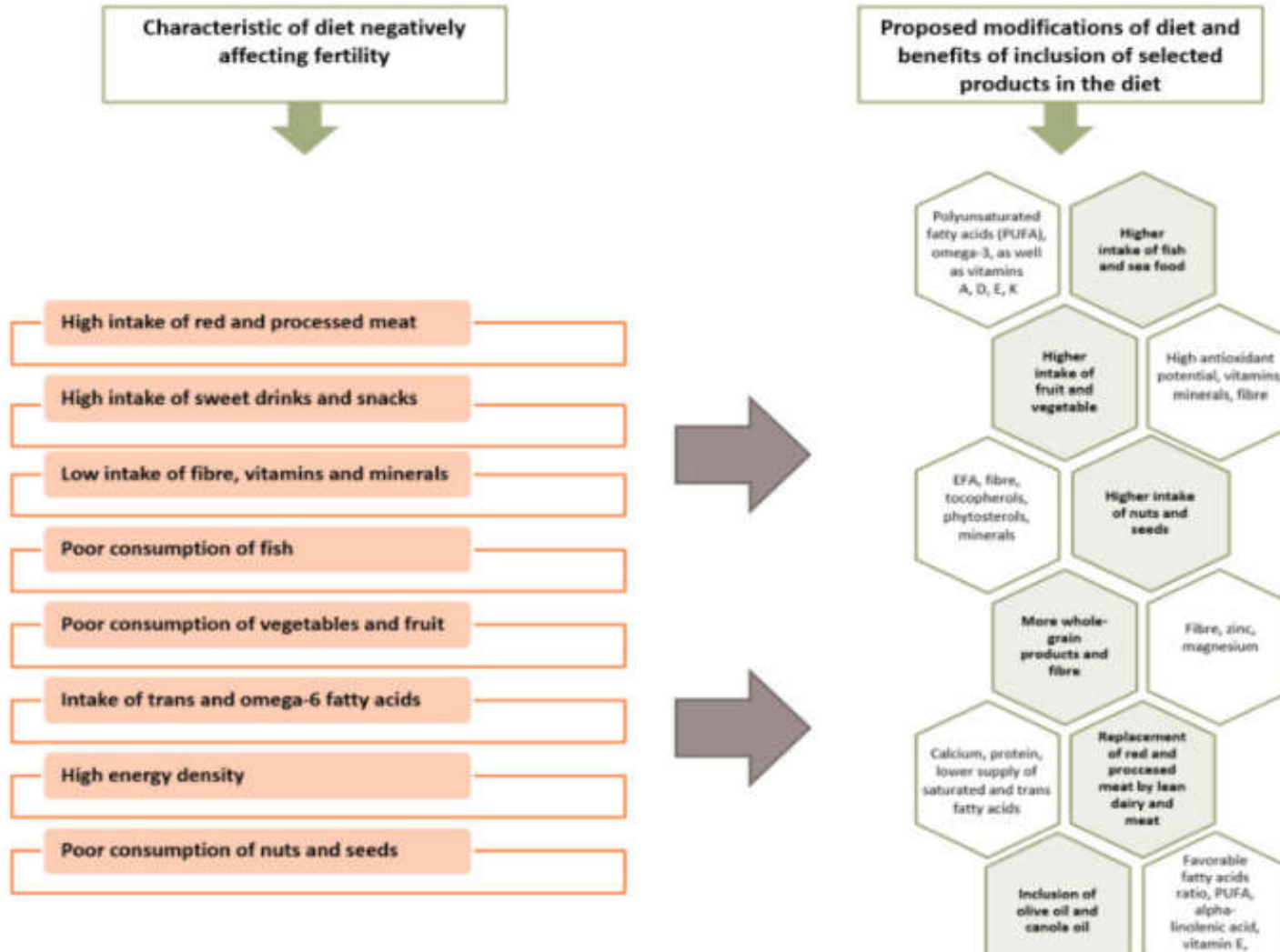
Healthy dietary models clearly correlate with

- Better Sperm count
- Better Sperm morphology
- Better Sperm motility
- Lower DNA fragmentation

- mineral components such as zinc and selenium
- omega-3 fatty acids
- Antioxidant vitamins

Minimization of oxidative stress and the inflammation process

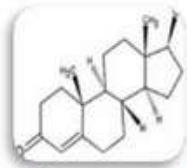
FOOD Studies



Foods containing vital nutrients for male fertility

Selenium	Vitamin E	Vitamin C	Zinc	Arginine	Carnitine	Vitamin B12	Folic Acid
Brazil nuts	Nut & seed oils	Citrus fruits	Meat	Nuts especially	Beef	Meat	Green leafy vegetables
Wheat germ	Nuts & seeds	Kiwi fruit	Fish	Walnuts	Pork	Fish esp. trout, salmon, sardines	Beans
Oats		Strawberries	Chicken	Almonds	Lamb		Lentils
Garlic & onions	Wheat germ & wheat germ oil	Blackcurrants	Eggs	Brazil nuts	Dairy products	Eggs	Asparagus
Barley	Whole grains	Red pepper	Pumpkin / Sunflower seeds	Beans		Cheese esp. Edam	Oatmeal
Butter		Brussels sprouts	Whole grains	Lentils			Dried figs
Smoked herring	Eggs	Melon	Beans & pulses				Avocado
Brown rice	Green leafy vegetables	Mango	Ginger root				
Whole grains		Watercress	Rye				
Red Swiss chard		Spinach	Oats				
		Papaya					
		Parsley					

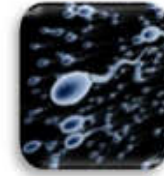
EFFECTS ON SPERMIOGENESIS



**Hormonal
Regulation**



**Morphology/
Density**

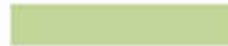


**Energy/
Motility**



**Enzym/
Capazitation**

L-Carnitin 440 mg



L-Arginine 250 mg



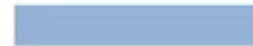
Vitamin E 120 mg



Folic-acid 800 ug



Zinc 40 mg



Selenium 60 ug



Glutathione 80 mg



Coenzyme Q 10 15 mg



Semen quality is positively associated with:

- Diet rich in fruits, vegetables, fish, whole grains, omega- 3 fatty acids (1.8 g/day DHA)
- Number of meals per day
- supplementation **with L-carnitine** (2-3 g/day for minimum 24 wks), **CoQ10** (200 mg/day at least 26 weeks) improves sperm quality and pregnancy outcome.
- Among antioxidants only **vitamin E** (400 mg/day) significantly improves main outcome measures.

Semen quality is negatively associated with:

- Lipophilic foods as well as soy isoflavones and sweets decline semen quality.
- Macronutrient balance
- Saturated fats


Typical Sources of free radicals in Iranian Men

- Processed foods
- Fast foods
- Animal fat
- **Poor quality fats and oils** (pastries, biscuits,...)
- Barbeques
- Burnt food

Why are sperms susceptible to ROS damage?

Plasma membrane rich in unsaturated fats
+
Sperm cytoplasm contains low levels of scavenging antioxidant enzymes

Oxidative stress likely



Oxidative stress-mediated damage to sperm membrane may account for defective sperm function observed in high proportion of infertility patients^{1,2}

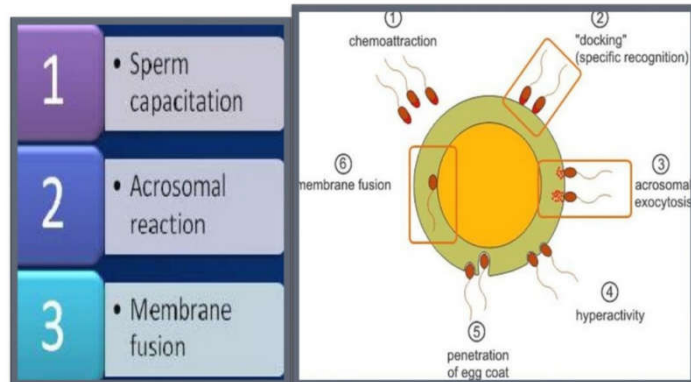
Oxidative stress affects fluidity of sperm plasma membrane and integrity of DNA³

May accelerate decline in sperm counts associated with male infertility

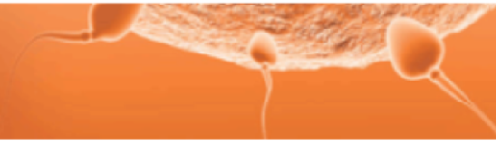
Nutritional Considerations

Various micronutrients are associated with male fertility, which their deficiency may result in infertility.

Some ROS activity in sperms is a necessity



Nutritional Factors	Free radical scavengers
L-Carnitine	Lycopene
Coenzyme Q10	Vitamin C
Zinc	Vitamin E
Arginine	Glutathione
Vitamin B12	Selenium



Fatty acid intake in relation to reproductive hormones and testicular volume among young healthy men

The intake of omega-3 polyunsaturated fatty acids was positively related to testicular volume while the intake of omega-6 polyunsaturated fatty acids and *trans* fatty acids was inversely related to testicular volume

High dietary intake of saturated fat is associated with reduced semen quality among 701 young Danish men from the general population FREE

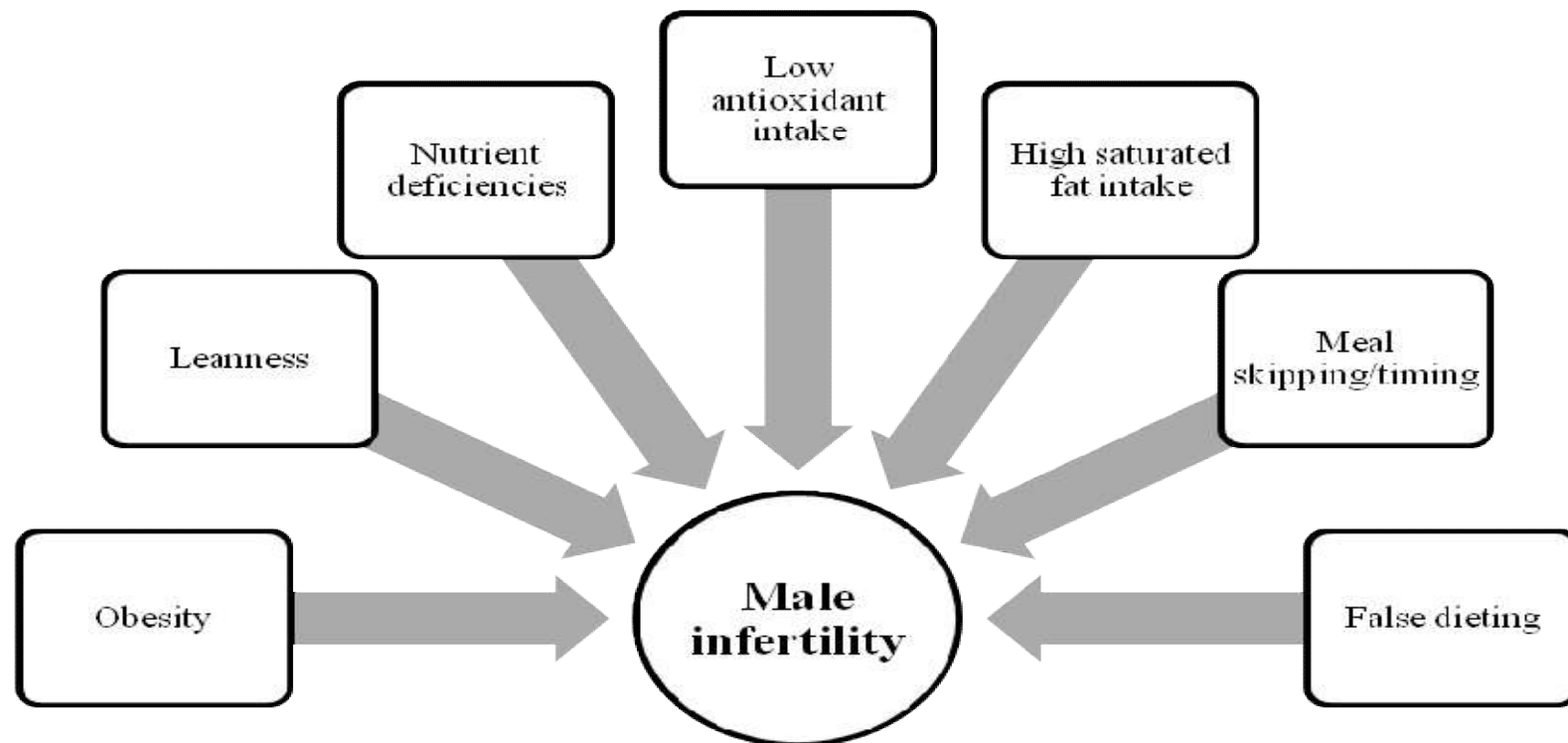
[Tina K Jensen](#) ✉, [Berit L Heitmann](#), [Martin Blomberg Jensen](#), [Thorhallur I Halldorsson](#), [Anna-Maria Andersson](#), [Niels E Skakkebaek](#), [Ulla N Joensen](#), [Mette P Lauritsen](#), [Peter Christiansen](#), [Christine Dalgård](#) ... [Show more](#)

The American Journal of Clinical Nutrition, Volume 97, Issue 2, February 2013, Pages 411–

Lead Article

Nutritional modifications in male infertility: a systematic review covering 2 decades

Ladan Giahi, Shayan Mohammadmoradi, Aida Javidan, Mohammad Reza Sadeghi



Pitfall in Comparison among Results of Empirical Medical Therapy

- No placebo controlled double blind trials
- Heterogenous patients population
- Variable dosages, treatment period and follow-up
- Tremendous fluctuation in an individual semen parameter
- Different criteria for success



ORAL ANTIOXIDANT THERAPY

Controversies

Methodological weakness of antioxidants trials make it difficult to determine “who”, “how” and “for how long??”

- Patient selection and controls
- Associated pathology
- Single or combination antioxidants
- Dosage & formulation
- Outcome measures
- Varying duration of treatment
- Lack of diagnostic markers for oxidative stress
- Presence of molecular and genetic differences




My New selected hot topics

- Nutritional Geometry and responses at cellular level
- Epigenetic signature of food through generations
 - human epidemiological data point toward a transgenerational effect of parental nutrition on offspring fertility
- Organismal metabolic fitness Interaction between nuclear genomics and mitochondrial genomics

Published: 31 August 2016

Epigenetics in male reproduction: effect of paternal diet on sperm quality and offspring health

Undraga Schagdarsurengin & Klaus Steger 

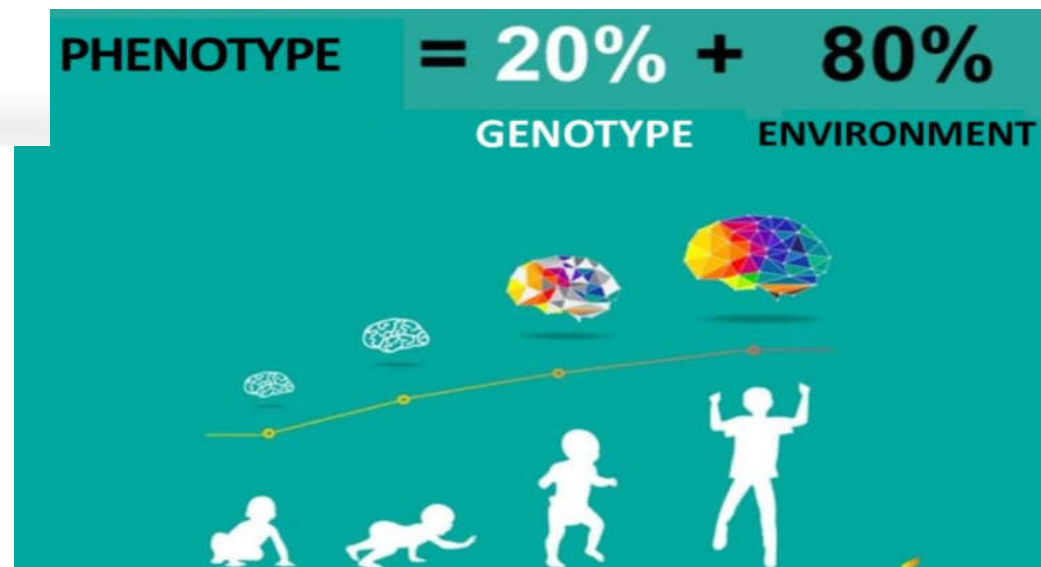
Nature Reviews Urology **13**, 584–595 (2016) | [Cite this article](#)

Fertilizing male and female germ cells deliver not only their haploid genomes but also their epigenomes which contain the code for:

- preimplantation
- postimplantation reprogramming
- Embryonal development.

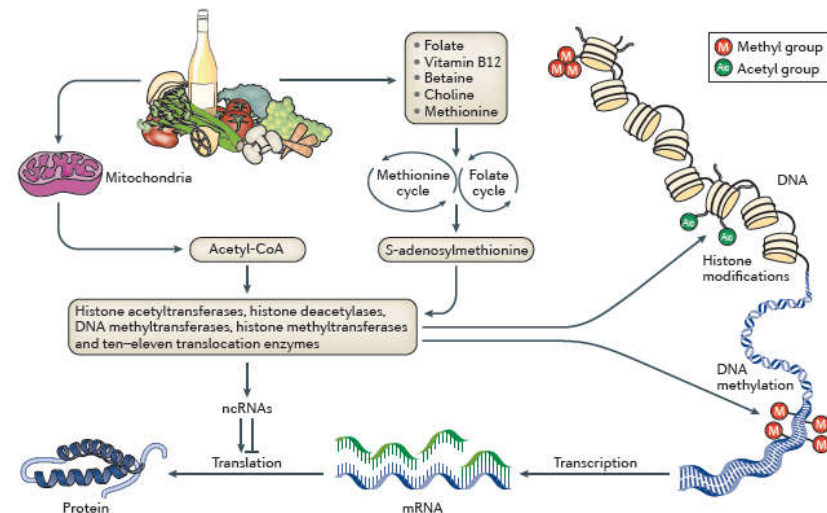
ART outcomes of couples with an obese male partner demonstrate decreased impregnation rate, live birth rates and compromised infant health.

Cellular responses are dependent on environmental exposures



Modifications of the epigenetic landscape by dietary compounds can affect overall health but also the reproductive health of both sexes

Dietary compounds, especially phytochemicals, minerals and vitamins, can effect changes in epigenetic signatures of somatic as well as germ cells



MiND
BODY
Silly
F O O D

Obesity, male infertility, and the sperm epigenome

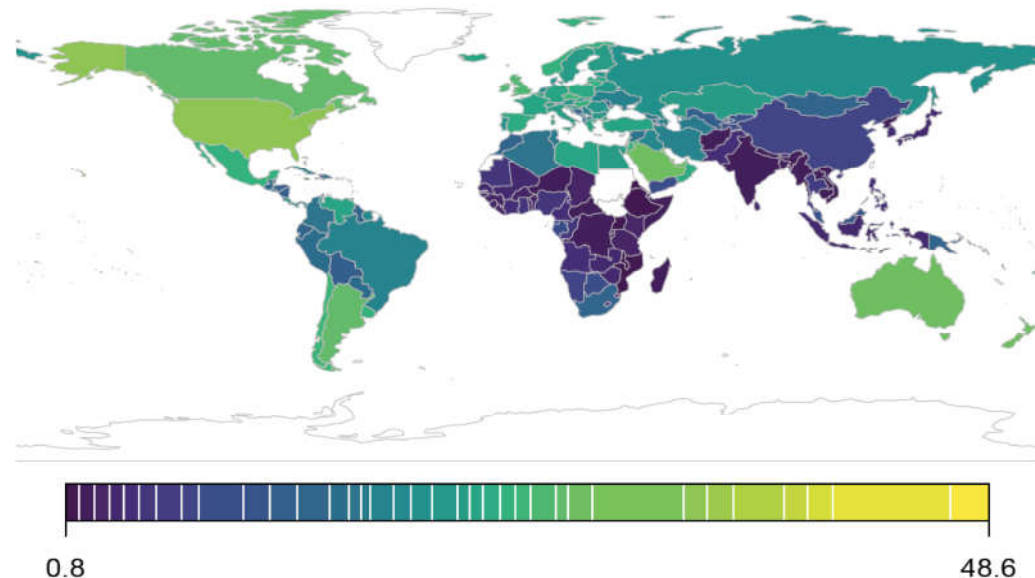
James R. Craig, M.D.,^{a,b} Timothy G. Jenkins, Ph.D.,^a Douglas T. Carrell, Ph.D., H.C.L.D.,^{a,c,d} and James M. Hotaling, M.D., M.S., F.E.C.S.M.^{a,b,c}

^a Division of Urology, Department of Surgery, ^b Center for Men's Health and Reconstructive Surgery, and ^c Department of Obstetrics and Gynecology, University of Utah; and ^d Department of Human Genetics, University of Utah School of Medicine, Salt Lake City, Utah

Obesity is a growing epidemic and a common problem among reproductive-age men that can both cause and exacerbate male-factor infertility by means of endocrine abnormalities, associated comorbidities, and direct effects on the fidelity and throughput of spermatogenesis. Robust epidemiologic, clinical, genetic, epigenetic, and nonhuman animal data support these findings. Recent works in the burgeoning field of epigenetics has demonstrated that paternal obesity can affect offspring metabolic and reproductive phenotypes by means of epigenetic reprogramming of spermatogonial stem cells. Understanding the impact of this reprogramming is critical to a comprehensive view of the impact of obesity on subsequent generations. Furthermore, and perhaps more importantly, conveying the impact of these lifestyle changes on future progeny can serve as a powerful tool for obese men to modify their behavior. Reproductive urologists and endocrinologists must learn to assimilate these new findings to better counsel men about the importance of paternal preconception health, a topic recently being championed by the Centers for Disease Control and Prevention. (*Fertil Steril*® 2017;107:848-59. ©2017 by American Society for Reproductive Medicine.)

Frequency of Adult Male Obesity by Country

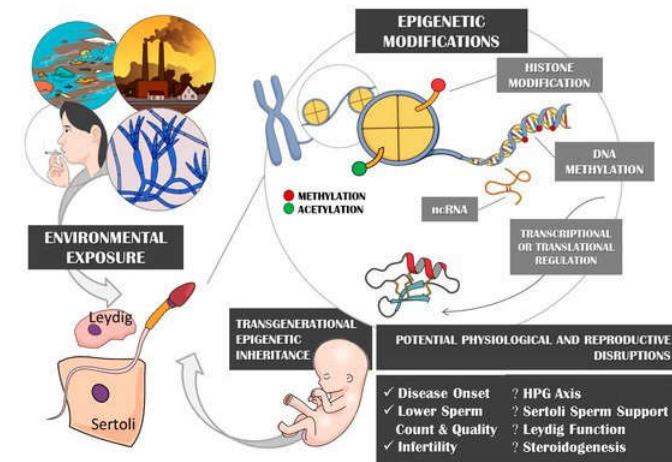
BMI of $>30 \text{ kg/m}^2$
more than 1.9 billion adults
over the age of 18 years
worldwide



Fertility and Sterility 2017 107:848-859 DOI:
(10.1016/j.fertnstert.2017.02.115)

Exposure with Obseogenic environment since embryogenesis

- smoking cigarettes and cannabis
- anabolic steroid use
- excessive alcohol consumption
- emotional stress
- environmental pollution
- sedentary lifestyle
- exposure to pesticides and toxins
- radiofrequency electromagnetic radiation
- cytotoxic drugs, cadmium, and lead
- hypercaloric diet that is pro-inflammatory, with low nutritional density
- **COVID 19**

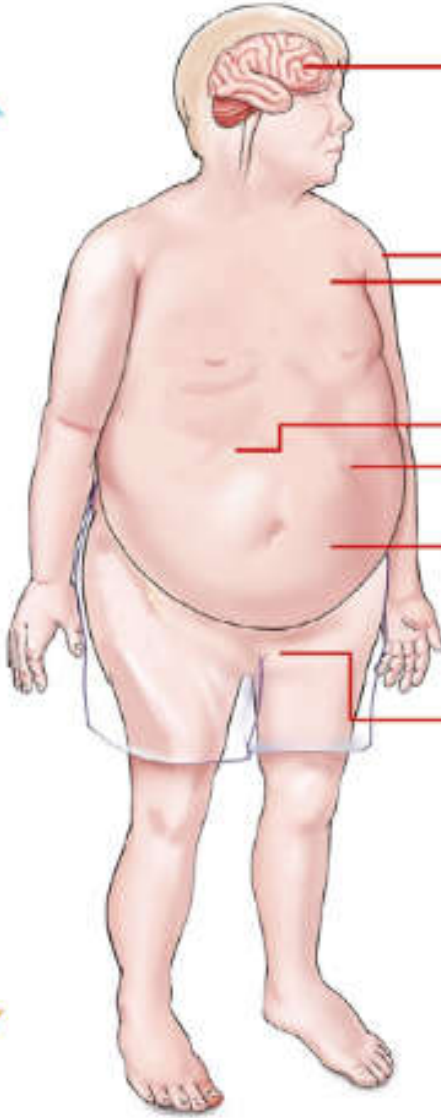


Obesogenic Environment

- M1
 - TNF α
 - IL1 β
 - IL6
- T_H1
 - IL8
 - TGF
 - INF γ

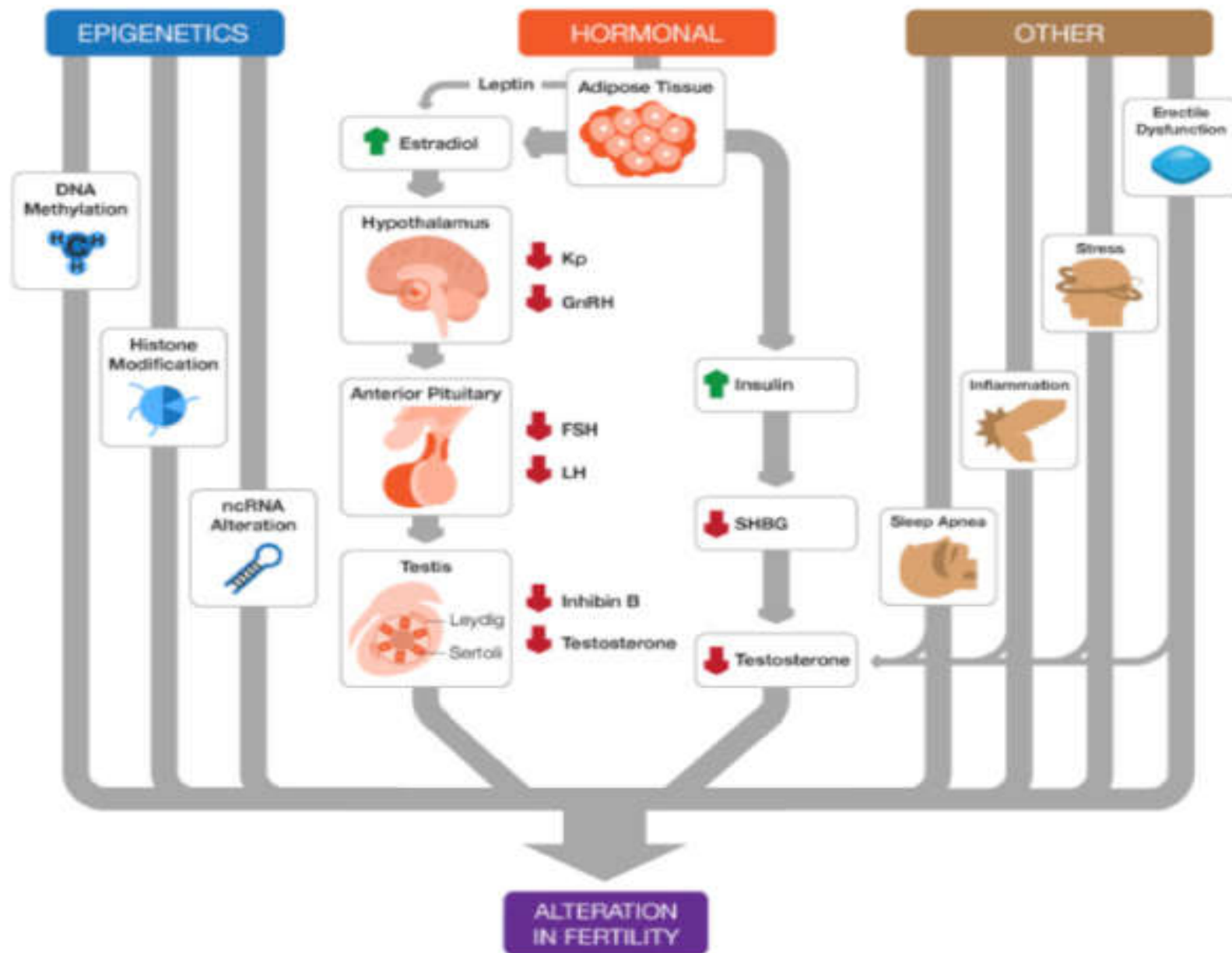
- Adipocytes
 - Leptin
 - Resistin

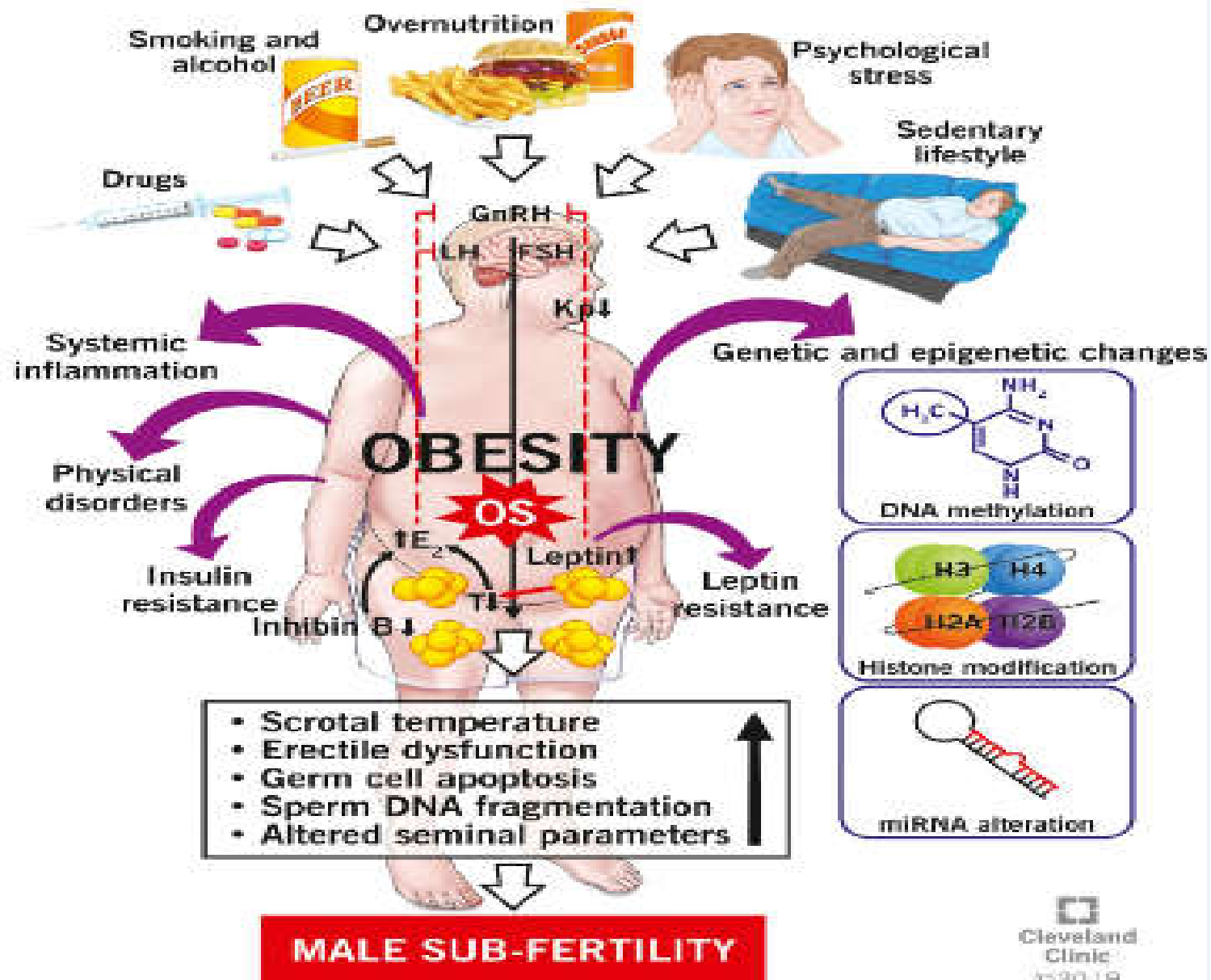
- T_H2
 - IL2
- T_{Reg}
 - IL4
 - IL10
- M2
 - TGF α



- Hypothalamic Inflammation → ↓ GnRH
- Muscle Inflammation → ↑ Myokines and insulin resistance
- Cardiac and Vascular Inflammation → Atherogenesis and Erectile Dysfunction
- Liver Inflammation → Hepatic and glucose dysregulation
- Pancreatic Inflammation → Pancreatic steatosis
- Adipose Tissue Inflammation → Hyperleptinaemia and insulin resistance
- Prostate Inflammation → BPH and Ca
- Testicular Inflammation → Impaired spermatogenesis and steroidogenesis
- Seminal Fluid → Inflammatory cytokines

Obesity and Male Infertility: Potential Mechanisms





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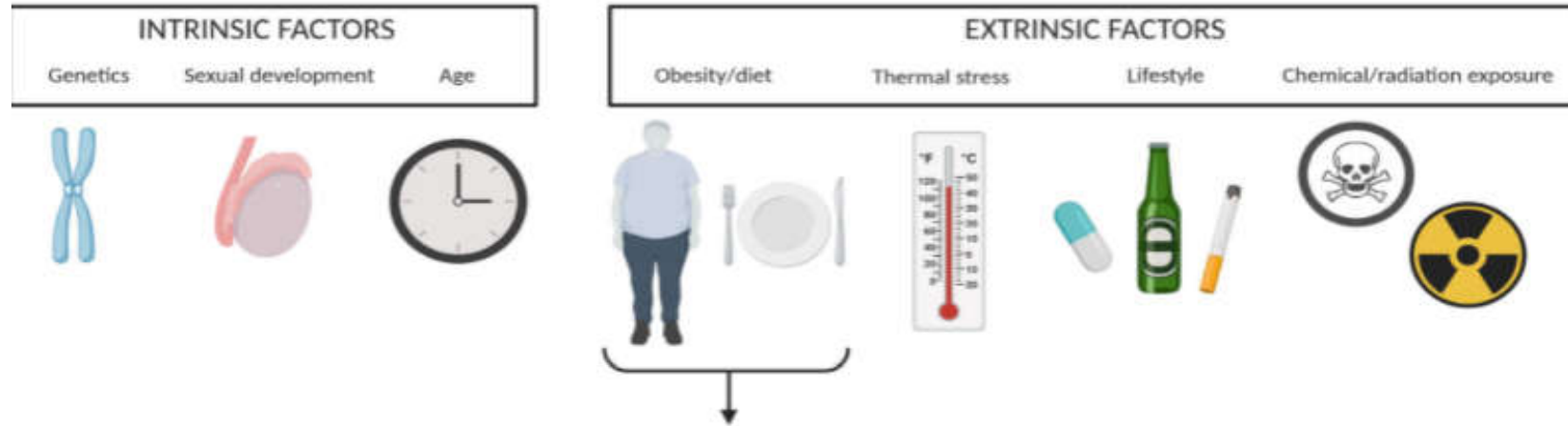
INVITED REVIEW

First International Journal of Andrology
andrologia WILEY

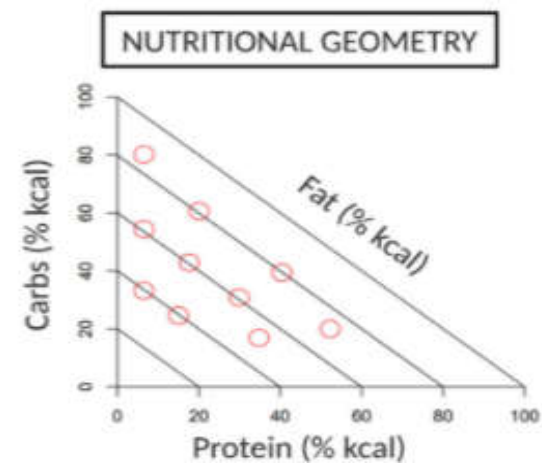
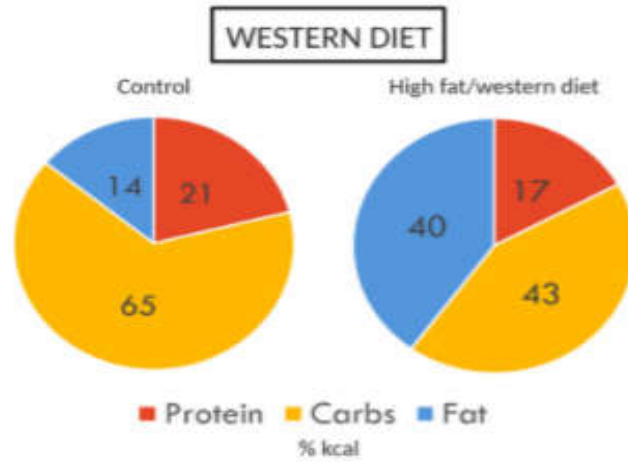
Obesity and male infertility: Mechanisms and management

BMI is considered to have a **low sensitivity** to appropriately determining adiposity and may **under-estimate** or **overestimate** the risk of obesity in a significant proportion of the population

Risk factors for male infertility



Models for studying the effect of diet



Research



Cite this article: Camus MF, Moore J, Reuter M. 2020 Nutritional geometry of mitochondrial genetic effects on male fertility. *Biol. Lett.* **16**: 20190891.

<http://dx.doi.org/10.1098/rsbl.2019.0891>

Evolutionary biology

Nutritional geometry of mitochondrial genetic effects on male fertility

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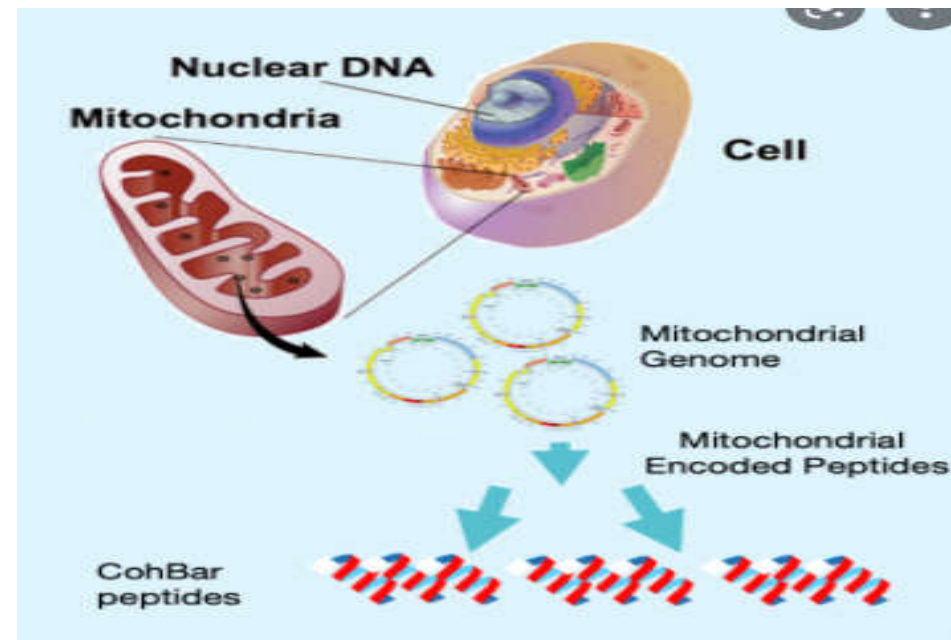
Organismal fitness is partly determined by how well the nutritional intake matches sex-specific metabolic requirements. Metabolism itself is underpinned by complex genomic interactions involving products from both nuclear and mitochondrial genomes. Products from these two genomes

Nutritional geometry can study :

Nuclear genes (nuDNA) are not the only genetic determinant of metabolic function.

Genes encoded within the mitochondria (mtDNA) also play a major role in metabolism, signalling and its regulation .

We would therefore expect fitness to depend on the interaction between both genomes



Organismal fitness

- Organismal fitness is partly determined by how well the nutritional intake matches sex-specific metabolic requirements.
- Metabolism itself is underpinned by complex genomic interactions involving products from **both nuclear** and **mitochondrial** genomes.
- Products from these two genomes must coordinate how nutrients are extracted, used and recycled, processes vital for fuelling reproduction

The factors driving **food selection**, **feeding** and **nutrition-** related performance are multiple and complex.

Many nutrients obtained from foods usually cannot be considered in isolation, but interact in complex ways in their effects on animals.

Most models of nutrition have ignored this complexity, rather opting for the simplifying assumption that the effects of nutrients can be understood in isolation.

Conclusion:

- Reproductive urologists and endocrinologists must learn to assimilate these new findings to better counsel men about the importance of paternal preconception health, a topic recently being championed by the Centers for Disease Control and Prevention.
- Couples seeking assisted reproduction treatments must be advised about the drastic effect of both the male and female lifestyle on treatment success
- Shall we think for new protocols in Andrology clinic?
- Do we need to have collaboration with Nutrition clinic?
- If yes, What is your suggested roadmap?



Thanks For Your Attention

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