



REVIEW

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# Epigenetics and male reproduction: the consequences of paternal lifestyle on fertility, embryo development, and children lifetime health

Liborio Stuppia<sup>1,2\*</sup>, Marica Franzago<sup>1</sup>, Patrizia Ballerini<sup>2</sup>, Valentina Gatta<sup>1,3</sup> and Ivana Antonucci<sup>1,3</sup>

## Abstract

The correlation between epigenetics and human reproduction represents a very interesting field of study, mainly due to the possible transgenerational effects related to epigenetic modifications of male and female gametes. In the present review, we focused our attention to the role played by epigenetics on male reproduction, evidencing at least four different levels at which sperm epigenetic modifications could affect reproduction: (1) spermatogenesis failure; (2) embryo development; (3) outcome of assisted reproduction technique (ART) protocols, mainly as concerning genomic imprinting; and (4) long-term effects during the offspring lifetime. The environmental agents responsible for epigenetic modifications are also examined, suggesting that the control of paternal lifestyle prior to conception could represent in the next future a novel hot topic in the management of human reproduction.

**Keywords:** Male infertility, Gametogenesis, Epigenetics, DNA methylation, Transgenerational effect

## Background

*You shall not bow down to them or worship them; for I, the Lord your God, am a jealous God, punishing the children for the sin of the parents to the third and fourth generation of those who hate me (Exodus, 20.5)*

Infertility represents a growing emergency in western countries, affecting about one out of seven couples who attempt to generate a child. In 2010, an estimated 48.5 million couples worldwide were infertile, against 42 million in 1990 [1]. In about 50 % of the cases, this condition is ascribable to the male partner, mainly due to a failure in the spermatogenesis process causing azoospermia or oligozoospermia at the sperm count [2]. Despite

the large number of tools available for the identification of the pathogenesis of male infertility, in many cases, no specific cause is detected and no personalized therapeutic protocol can be established. A large number of studies have investigated in the last decades the presence of genetic alterations responsible for the failure of spermatogenesis, which are nevertheless identified only in 15–30 % of infertile males, even when stringent selection criteria are used [3, 4]. Despite the identification of several rare genetic variants associated to disruption of spermatogenesis, so far, the only two categories of genetic alterations responsible for a significant portion of cases of male infertility, and thus commonly tested in the clinical practice, are represented by chromosomal alterations and Yq microdeletions [5–10]. The presence of other genetic mechanisms, such as partial Yq microdeletions [11–14], specific Y-chromosome haplogroups [15–18], and polymorphism in genes related to mitochondrial function [19–21] as risk factors for infertility have been suggested, but with inconclusive results. More recently, the presence of X-linked copy number variants (CNVs) in infertile males has been reported by several studies [22, 23], but the overall

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# Concept Review Lifetime Health Reproduction

**Sandra Alters, Wendy Schiff**



## **Concept Review Lifetime Health Reproduction:**

**Textbook of Contraception, Sexual and Reproductive Health** Johannes Bitzer, Tahir A. Mahmood, 2024-01-25 This practical evidence based handbook will meet the needs of those working in the field of SRH care and will also help those preparing for the joint EBCOG and ESCRH Certificate and Diploma examination in Sexual and Reproductive Health and is designed to closely follow the examination s curriculum

**Obstetrics: Normal and Problem Pregnancies E-Book** Mark B. Landon, Henry L. Galan, Eric R.M. Jauniaux, Deborah A. Driscoll, Vincenzo Berghella, William A. Grobman, Sarah J. Kilpatrick, Alison G. Cahill, 2024-08-31 Selected for 2025 Doody s Core Titles in Obstetrics Maternal Mortality A Global Perspective Multiple Gestations and Substance Use Disorder in Pregnancy Features detailed illustrations from cover to cover including more than 100 ultrasound images that provide an important resource for normal and abnormal fetal anatomy Provides access to videos that enhance learning in areas such as Cesarean delivery and operative vaginal delivery

**Early life epigenetic programming of health and disease through DOHaD perspective** Luis Antonio Justulin, Elena Zambrano, Susan Ozanne, Thomas Prates Ong, 2023-03-15

**Lifetime Health** Holt Rinehart and Winston, 2005

Childhood Adversity and Life-course Consequences Cheryl Zlotnick, Naixue Cui, Nadya Golfenshtein, Yang Li, 2022-08-05

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**Family**

**Medicine** John L. Buckingham, E.P. Donatelle, Thomas A. Jr. Johnson, Joseph E. Scherger, Robert B. Taylor, 2013-11-21 New material in a new format is contained in this third edition of Family Medicine The comprehensive text nevertheless remains true to the goal of previous editions in offering a scientific approach to health and illness within the context of the family Using up to date clinical material the book demonstrates how the family physician may provide comprehensive health care to persons of all ages The first part of Family Medicine discusses such topics as the conceptual basis of family as discipline and specialty problem differentiation family centered health care longitudinal care clinical reasoning and resource management The second part explores both problems related to organs and systems and problems related to the person family and community including pregnancy care of infants children adolescents and the elderly behavioral and psychiatric problems emergency and critical care sports medicine alcoholism and substance misuse environmental health and neoplastic and infectious diseases Family Medicine with its greatly expanded in depth coverage of the most commonly encountered clinical core problems and procedures in family medicine continues to be a textbook written and edited by family physicians for family physicians     *Nutrition Abstracts and Reviews* ,2003     **The Birth Control Review** Margaret Sanger,1917

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