

FONDAZIONE ITALIANA ENDOMETRIOSI

**ENDOCRINE DISRUPTORS:
Endometriosis and Infertility**

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Introduction

P.G.Signorile

ENDOCRINE DISRUPTORS: Endometriosis and Infertility

Endocrine Disruptors

Rachel Carson 1962 book, "Silent Spring"

1980s, was researching the health of vertebrates living in the Great Lakes . Healthy problems were observed **in the offspring** of exposed animals, and not the adult animals themselves.

1991 scientists presented the effects of endocrine disruptors on gene imprinting, sexual differentiation, and reproductive function in mammals and fish, neurobehavioral development, and autoimmune diseases.

Over 80,000 chemicals, and approximately 1000–2000 new chemicals are introduced each year,

Bisphenol A

BPA was first synthesized by A. P. Dianin in 1891 Is a combination of two equivalents of phenol with one equivalent of acetone.

Bisphenol-A (BPA) is over 3 billion Kg produced each year. 100 tons released into the atmosphere by yearly production.

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Evolution of sentiment on BPA

The chemical industry maintains that BPA is a component of consumer products that "**make our lives easier, healthier and safer**"

NTP's Center for the Evaluation of Risks to Human Reproduction (CERHR). Conclusion:

"BPA has no effect on "changes in prostate weight, age at puberty (rat), pathology or tumors in any tissue, or reproductive tract malformations." 2006

NTP (National Toxicology Program). Final conclusions about BPA risk assessment:

"there is some concern for neural and behavioral effects and the prostate gland in fetuses, infants, and children at current human exposures ,the levels of concern for effects on the mammary gland and an earlier age for puberty were downgraded to minimal." 2008

FDA. Conclusion:

"... FDA-regulated products containing BPA currently on the market are safe and that exposure levels to BPA from food contact materials, including for infants and children, are below those that may cause health effects" 2008

FDA subcommittee. Conclusion:

*"Coupling together the available qualitative and quantitative information (including application of uncertainty factors) provides a sufficient scientific basis to conclude that **the margins of safety defined by FDA as 'adequate' are, in fact, inadequate**" . 2008*

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Exposure to BPA during the Organogenesis

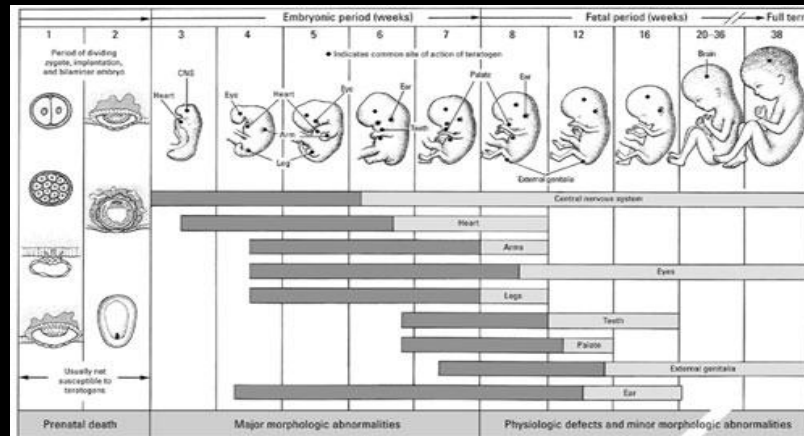
Current information on the exact timing and sensitivity during these windows is limited

Identification of times when the system is potentially most vulnerable to the action of toxic agents.

BPA can have very different effects on development based on the period in which they are administered.

The timing at the BPA exposures is critical

In utero exposure to low dose (nanograms) can induce alterations in estrogen-target organs of the fetuses



Environmental Health Perspectives Supplements Volume 108, Numbers S3, June 2000. Identifying Critical Windows of Exposure for Children's Health Sherry G. Selevan,¹ Carole A. Kimmel,¹ and Pauline Mendola²

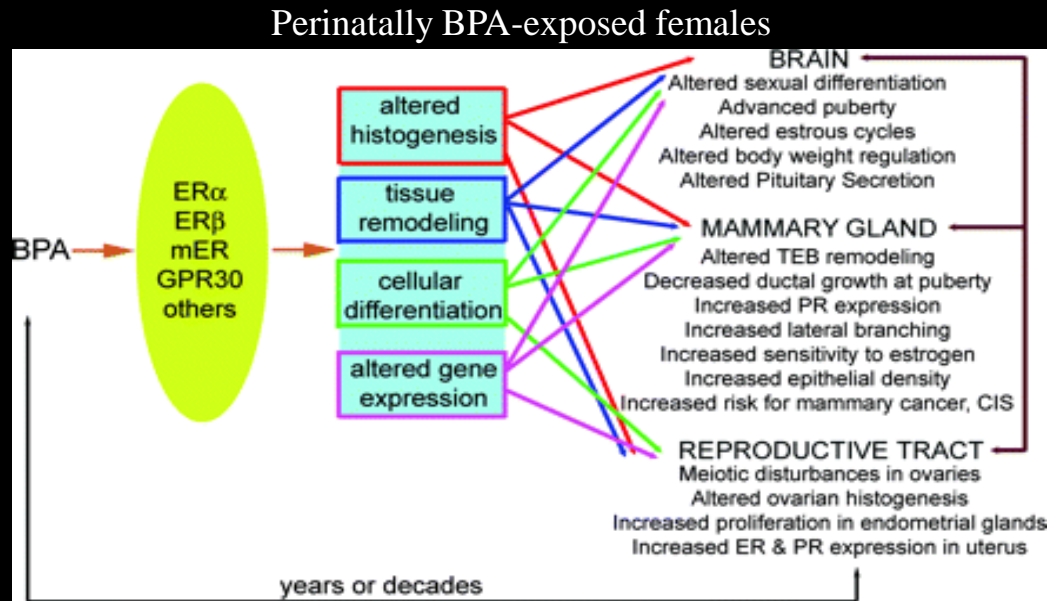
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The Embryo “Critical Windows”

The "critical window" of exposure differs depending upon the time at which specific tissues or organs develop.

Exposures to chemicals can have multiple periods of sensitivity, after days, years, or decades

Beta-glucuronidase and arylsulfatase C consent embryo-fetal contaminations of free BPA



Endocrine Reviews, doi:10.1210/er.2008-0021, Endocrine Reviews 30 (1): 75-95

Bisphenol-A and the Great Divide: A Review of Controversies in the Field of Endocrine Disruption. Laura N. Vandenberg, Maricel V. Maffini, Carlos Sonnenschein, Beverly S. Rubin and Ana M. Soto

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Low dose of BPA induce in mice:

earlier vaginal opening and earlier first estrus

adult estrous cycles after perinatal exposure

significant increase in antral follicles was observed at 3 months of age

increase in the number of blood-filled ovarian bursae at 6 months of age; advanced reproductive aging.

increase in the number of oocytes with gross aberrations,aneuploid eggs .

> weight of the vagina

> volume of the uterine lamina propria

> receptor expression and cell proliferation in multiple compartments of the uterus .

endometriosis

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Endocrine Disruptors and Endometriosis

1998 WHO

2000 Scientific Committee on Food (EU)

2003 WHO/UNEP/ILO International Programme on Chemical Safety

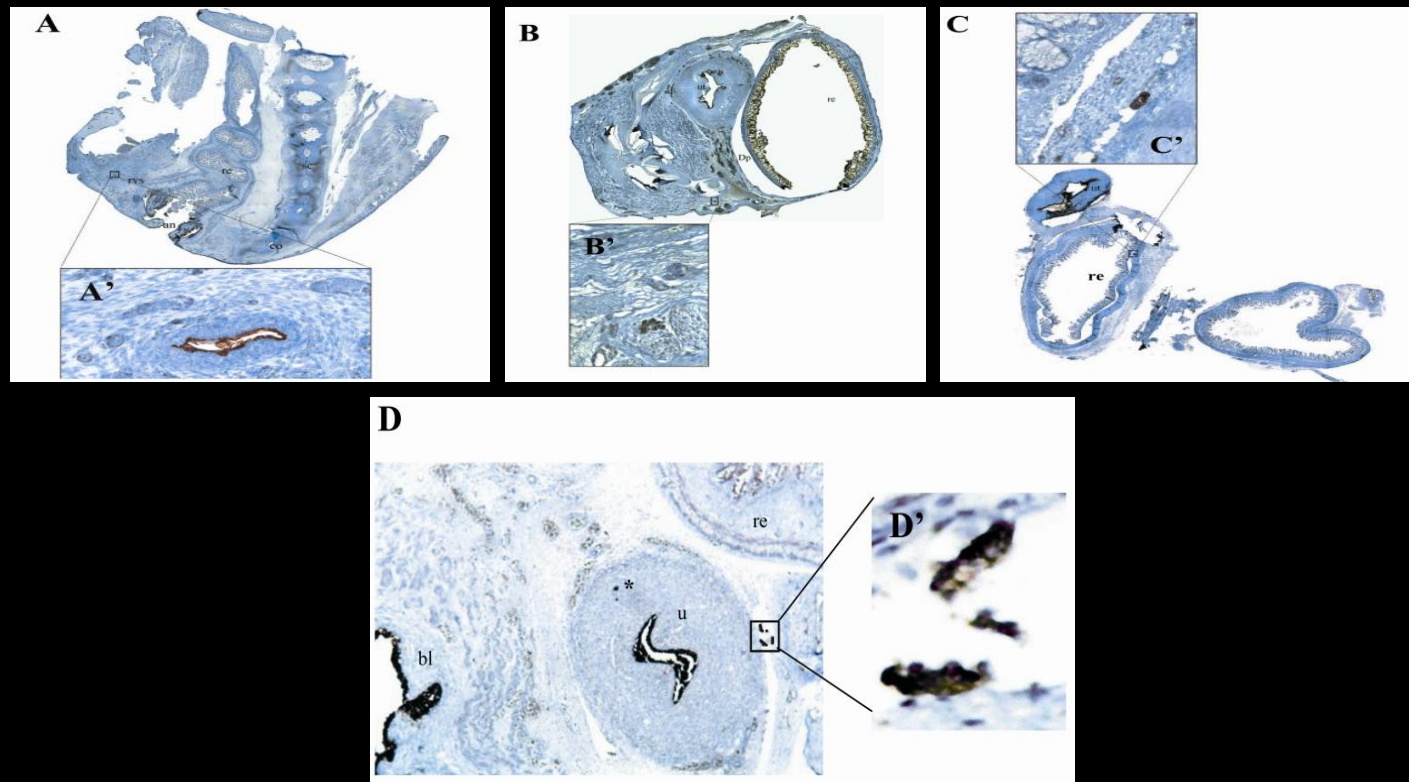
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Ectopic endometrium in human foetuses is a common event and sustains theory of müllerianosis in the pathogenesis of endometriosis, a disease that predispose to cancer.

Signorile PG, Baldi F, Bussani R, D'Armiento M, De Falco M, Baldi A.

J Exp Clin Cancer Res. 2009 Apr 9;28:49

Foetal Endometriosis



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Int J Biochem Cell Biol. 2010 Mar 15. [Epub ahead of print] Endometriosis: New concepts in the pathogenesis. Signorile P.G., Baldi A. Fondazione Italiana Endometriosi, Via E. Longoni 81, 00155 Rome, Italy.

Distribution of Endometriosis in the Foetuses

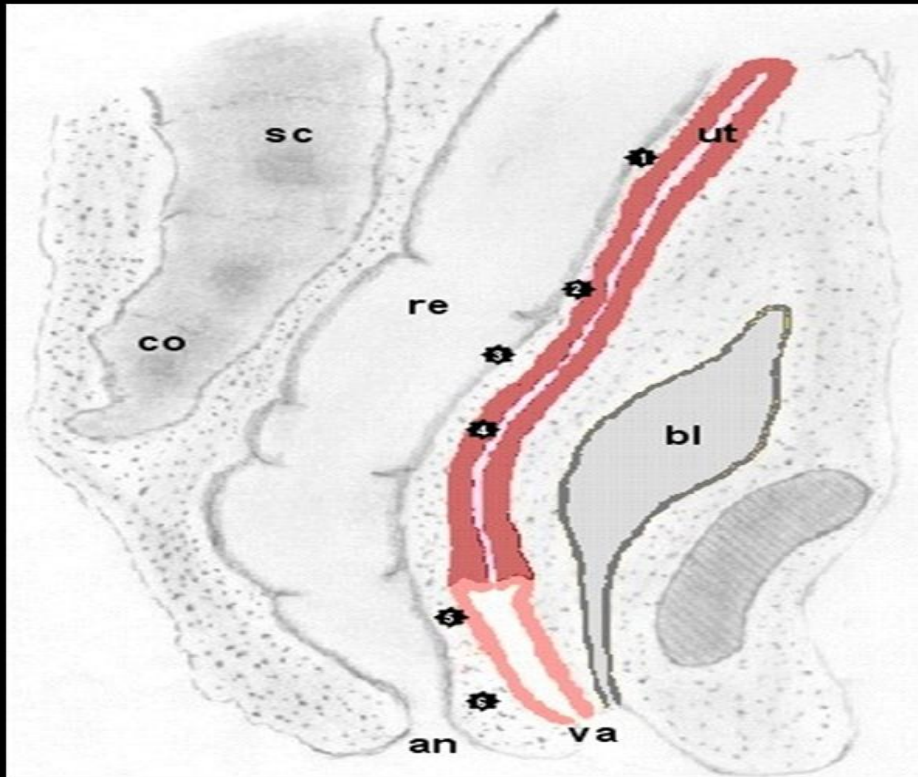


Fig 1. Anatomical distribution of the ectopic endometrium found in the female human foetuses. Schematic representation of the pelvic organs of a female foetus at around 25 weeks of gestation, that displays the anatomical relations between the organs and the endometriotic structures described. The different locations are indicated

by numbers (1 in the proximity of the Douglas pouch; 2, in the mesenchymal tissue close to the posterior wall of the uterus; 3, in the rectal tube at the level of muscularis propria; 4, in the wall of the uterus; 5 and 6, in the recto-vaginal septum) Abbreviations used: an, anus; co, coccyx; va, vagina; re, rectum; sc, spinal column; ut, uterus; bl, bladder.

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Prenatal exposure of mice to bisphenol a elicits an endometriosis – like phenotype in female offspring.

Signorile PG, Spugnini EP, Mita L, Mellone P, D'Avino A, Bianco M, Diano N, Caputo L, Rea F, Viceconte R, Portaccio M, Viggiano E, Citro G, Pierantoni R, Sica V, Vincenzi B, Mita DG, Baldi F, Baldi A.

Gen Comp Endocrinol. 2010 Mar 26. [Epub ahead of print

Endometriosis in offspring of Mices

