Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

"Hope" (Jodie Dunne, 2014)
Endometriosis Awareness through Art

Immunobiology of endometriosis: unraveling the pathogenesis of the disease

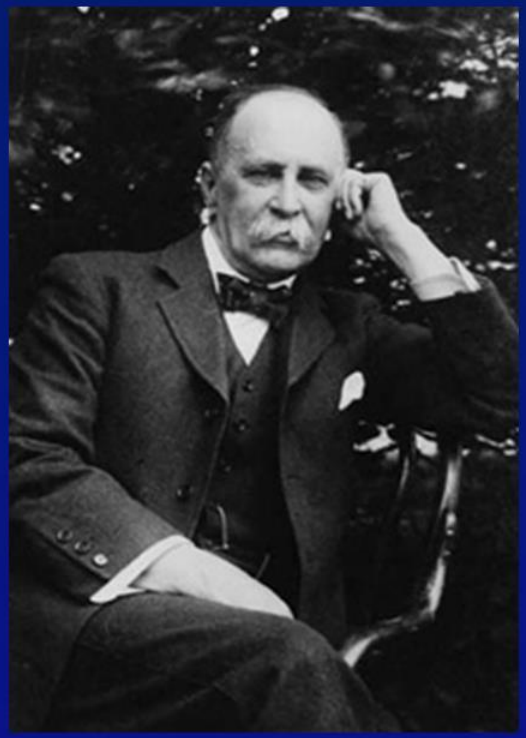
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

“If you listen carefully to the patients they will tell you the diagnosis”

(William Osler
Hopking Hospital - Baltimora)



Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation

European Society of Human Reproduction and Embryology

International Society Of Gynecological Endocrinology

Giorgio Pardi's Foundation

Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

… let's go back in time …

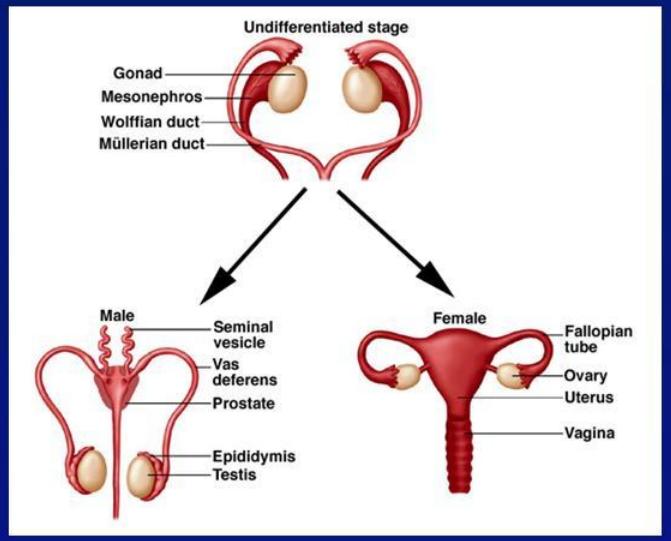
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

Around the 5th week of pregnancy, Mullerian ducts (or paramesonephric ducts) appear as developing structures. Their different parts have different outcomes:

- **the caudal extremity of the ducts is destined to merge and to constitute superior 2/3rd parts of the vagina and uterine cervix**
- **the intermediate part melts and creates the uterine body**
- **the upper portions maintain their own independence and, opening in the coelomic cavity (future peritoneal cavity), develop in the fallopian tubes.**



(Pizzo A et al, 2013)

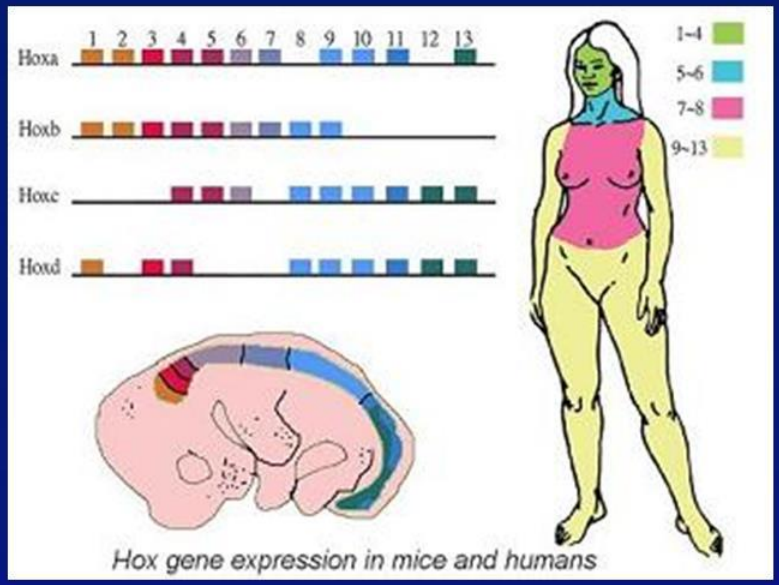
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

- In the early phases of the pelvic structure's organogenesis, Hoxa and Wnt gene clusters seem to play a key role, leading spatially and temporally correct tissue-specific gene expression of several developing organs.
- Mutations in these clusters may alter the correct process of organogenesis, so leading to the ectopy of the developing structures, also modifying biological function and cell-to-cell interaction.

(Taylor et al, 1997)



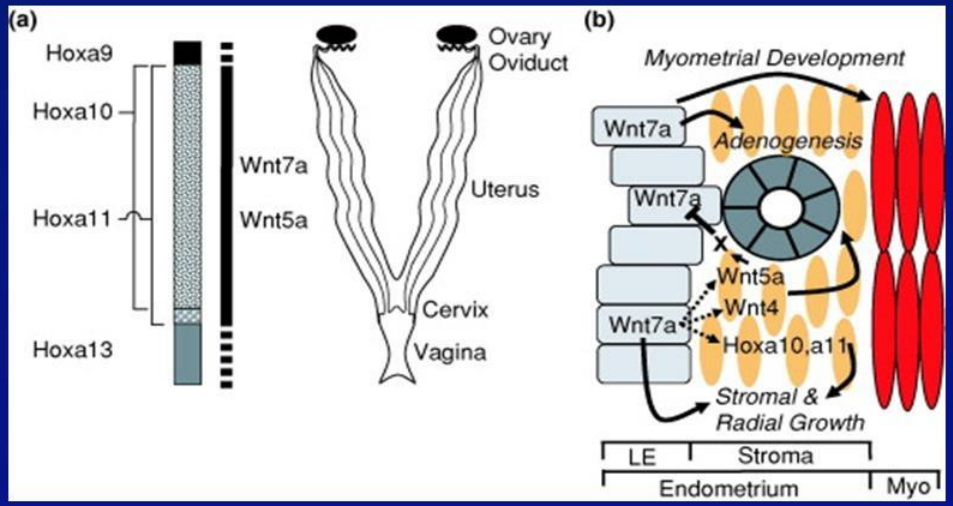
Hox gene expression in mice and humans

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

- **Hoxa and Wnt gene clusters are also fundamental to mantain the endometrial plasticity later in life and to preserve the endometrial stem cell pool, required to restore the endometrium from the basal layer after the menstruation.**



- **Moreover, they play a key role in the maintenance of «endometrial receptivity» during early embryo implantation: mutation in these gene clusters may cause unexplained infertility/sterility**

(Sonderegger et al, 2010)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

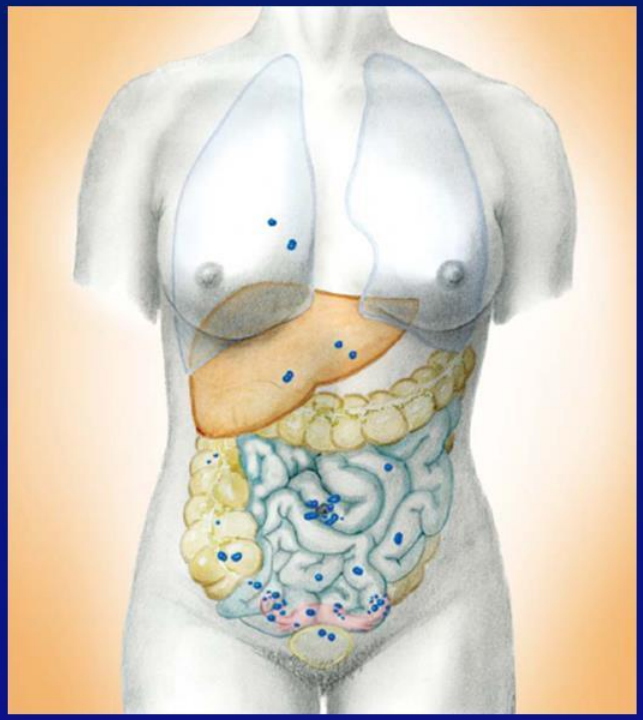
Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: DEFINITION

Presence and estrogen-dependent growth of functional endometrial tissue, glands and stroma outside the uterine cavity.

Distinguish between:

1. **Endometrial tissue within the myometrial layer (adenomyosis)**
2. **Endometrial tissue outside the uterine cavity (endometriosis).**



Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: EPIDEMIOLOGY

- 14 million of women affected in the EU.
- globally in the world it affects approximately 10% of women in reproductive age, and up to 50% of infertile women

(ESHRE Guideline, 2014)
(Census Bureau, 2004)

human reproduction ORIGINAL ARTICLE *ESHRE pages*

ESHRE guideline: management of women with endometriosis†

G.A.J. Dunselman[1,*], N. Vermeulen[2], C. Becker[3], C. Calhaz-Jorge[4], T. D'Hooghe[5], B. De Bie[6], O. Heikinheimo[7], A.W. Horne[8], L. Kiesel[9], A. Nap[10], A. Prentice[11], E. Saridogan[12], D. Soriano[13], and W. Nelen[14]

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: EPIDEMIOLOGY

It heavily and negatively affects woman's quality of life, causing not only pain, but also interfering with her social role (family, work, fertility).

(Fourquet et al, 2011)
(Jones et al, 2004)

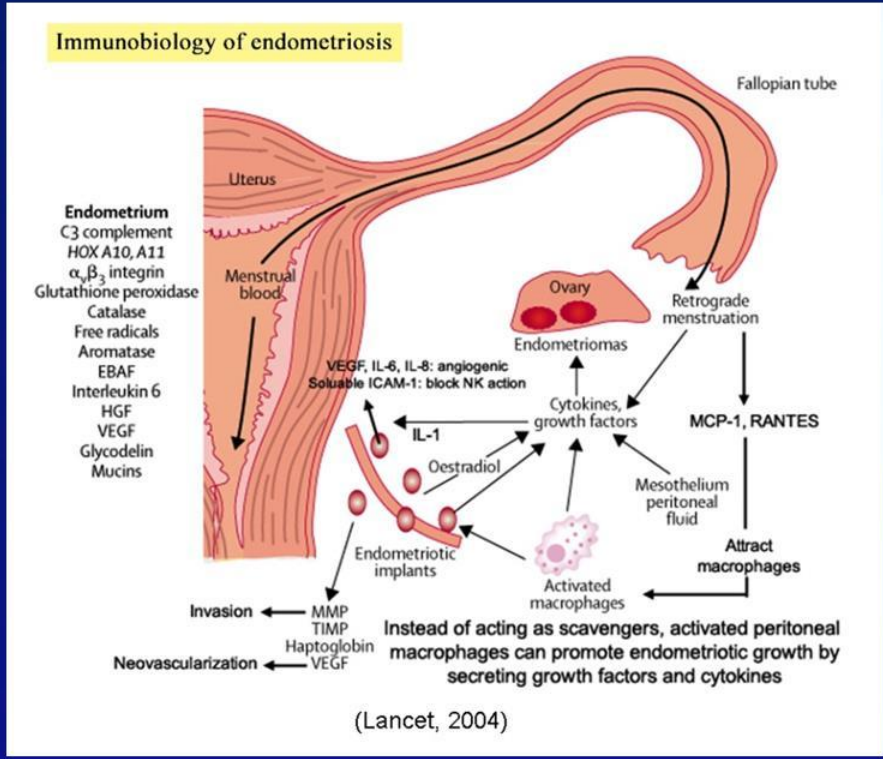
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

- ***How do endometrial cells arrive in ectopic sites?***
- ***What mechanism allows their implantation and proliferation?***



(Lancet, 2004)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation · *European Society of Human Reproduction and Embryology* · *International Society Of Gynecological Endocrinology* · *Giorgio Pardi's Foundation* · *Italian Association of Endometriosis*

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

1. **Retrograde menstruation (Sampson's theory, 1927):** endometrial cells flake from the endometrium during menstruation and arrive, through the tubes, into the peritoneal cavity.

Evidence for:

- The retrograde menstruation has been demonstrated.
- The most affected sites are fallopian tubes, ovaries and Douglas pouch.
- Nulliparous women with short and heavy menstrual flow are at a greater risk.
- The experimental implantation of endometrial cells in the peritoneal cavity caused the disease in the animal model.
- Association between obstructed menstrual flow and endometriosis.

Evidence against:

- The retrograde menstruation has been demonstrated in 90% of women with fallopian tube patency, bur without the disease!

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

2. Dissemination of endometrial cells through the uterine venous (blood-borne) or lymphatic drainage.

Evidence for:

- Implantation sites far from the pelvic cavity (CNS, spinal cord, lung, etc.)

Evidence against:

- The uterine venous drainage comes to an end in the lungs, before oxygenating and merging into the arterial circulation. For this reason, we would expect a high incidence of the disease in the "pulmonary filter" (not verified in clinical practice!)
- Few and inconsistent reports of isolated lymph node endometriosis not associated to endometriotic foci in the related drainage region.

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

3. Post-surgical (iatrogenic) implantation of endometrial cells

Evidence for:

- Endometriotic implants have been demonstrated in post-surgical scars and after the rupture of endometrial cysts for leaking of their content into the pelvic cavity.

Evidence against:

- Few and inconsistent reports in literature.

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

4. **Coelomic metaplasia:** transformation of peritoneal mesothelial cells (coelomic origin) in endometrial cells through a process of metaplasia.

Evidence for:
- High incidence of peritoneal endometriosis.
- Compatible with the formation of endometriosis in prostate and bladder in males who underwent anti-androgen therapy for cancer.

Evidence against:
- It does not explain the extraperitoneal implants.
- Substantial lack of studies in support of it.

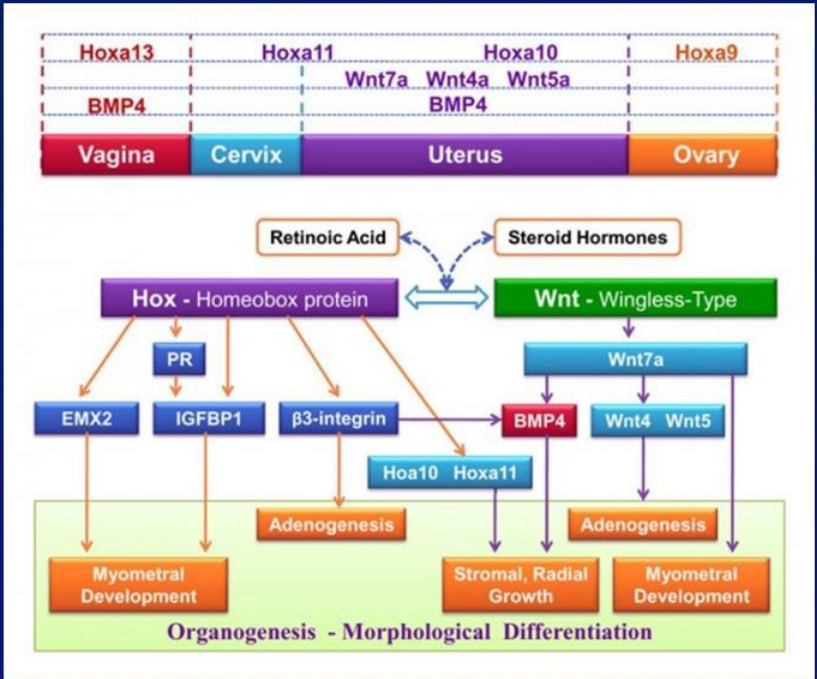
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

5. Embryological theory:

Accumulating evidence is suggesting that dysregulation of Wnt and/or Hox genes may affect cell migration during organogenesis and differentiation of Müllerian structures of the female reproductive tract, with possible dislocation and dissemination of primordial endometrial stem cells (which have a high possibility to differentiate into mature endometrial cells) in ectopic regions.



(Laganà et al, 2013)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

5. Embryological theory:

during postpubertal age, under the influence of different stimuli, these misplaced and quiescent ectopic endometrial cells could acquire new phenotype, biological functions, and immunogenicity. So, they may differentiate, specializing in epithelium, glands, and stroma to form a functional ectopic endometrial tissue.

(Laganà et al, 2013)

Hindawi Publishing Corporation
Obstetrics and Gynecology International
Volume 2013, Article ID 527041, 20 pages
http://dx.doi.org/10.1155/2013/527041

Hindawi

Review Article

Interplay between Misplaced Müllerian-Derived Stem Cells and Peritoneal Immune Dysregulation in the Pathogenesis of Endometriosis

Antonio Simone Laganà,[1] Emanuele Sturlese,[1] Giovanni Retto,[1] Vincenza Sofo,[2] and Onofrio Triolo[1]

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

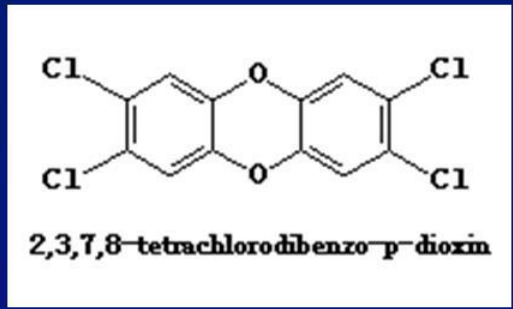
Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

6. Action of environmental pollutants:

- In the induction and progression of endometriosis, there would be the influence of environmental pollutants such as dioxin and dioxin-like compounds. These substances induce local estrogenic-like activity that promotes the growth of endometriotic foci.

(Anger and Foster, 2008)



2,3,7,8-tetrachlorodibenzo-p-dioxin

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

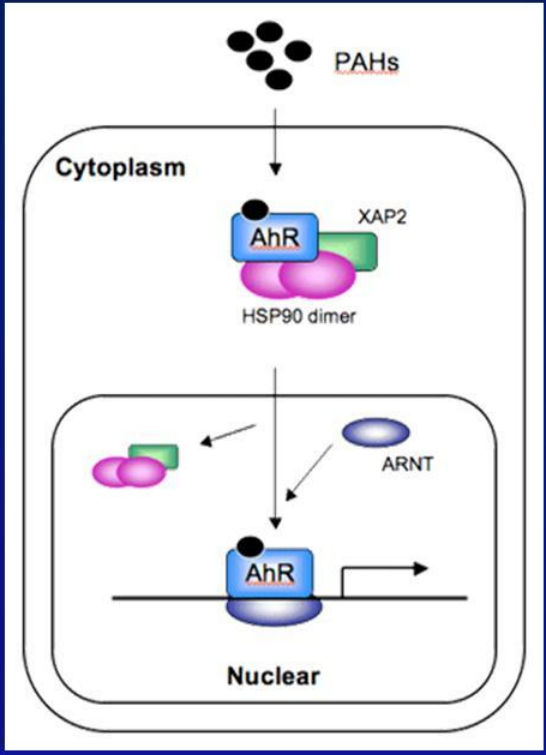
Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

6. Action of environmental pollutants:

Dioxins and dioxin-like compounds bind with high affinity to the aryl hydrocarbon receptor (AhR), which plays a key role in gene regulation for reproductive processes.

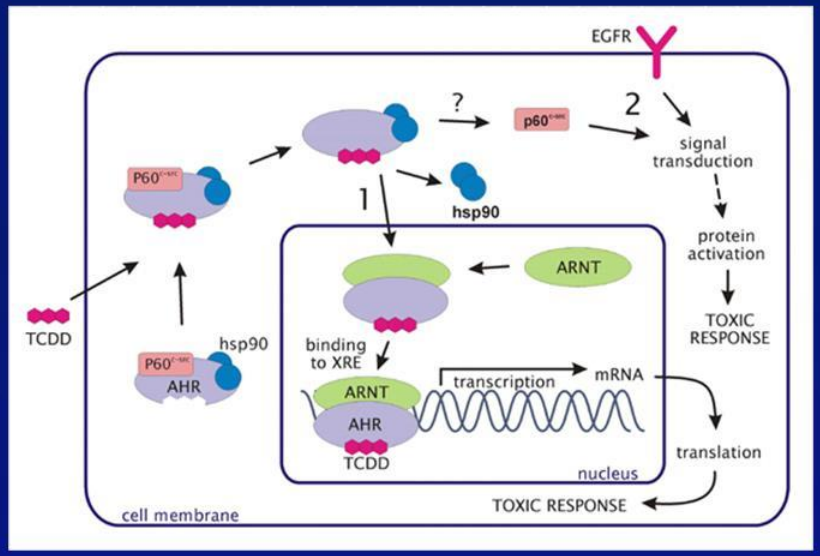
(Rier & Foster, 2002)



Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY



6. Action of environmental pollutants:

Within the nucleus, the AhR-ligand complex dimerizes with the "AhR nuclear translocator" (ARNT), to form a complex of activated transcription that binds to the "xenobiotic responsive element" (XRE).

(Carlson & Perdew, 2002)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: AETIOLOGY

What is the correlation between dioxin and endometriosis?

Already in utero, these toxic compounds may alter some of the cell-to-cell signaling needed for the organogenesis of the female reproductive tract.

These are epigenetic changes and persist for many generations in the offspring

- ***alteration of organogenesis of the female reproductive tract***
- ***alteration of the hormonal response and interference with the receptors' action***
- ***alteration of epithelial-stromal endometrial communications***
- ***up-regulation of NF-kB-related pathways (induction of chronic pelvic inflammation!)***

(Sofo et al, in press)

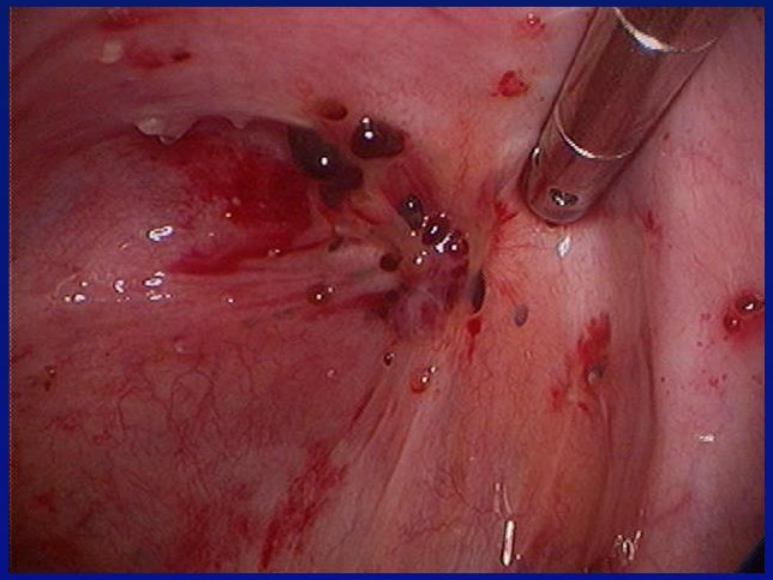
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

ENDOMETRIOSIS: PATHOGENESIS

- The endometrial cells within the pelvic cavity (ectopic) should be attacked and eliminated by the immune system (macrophages and peripheral blood lymphocytes).
- In endometriosis, endometriotic cells "escape" the immune system surveillance, implant into the pelvic cavity and proliferate.



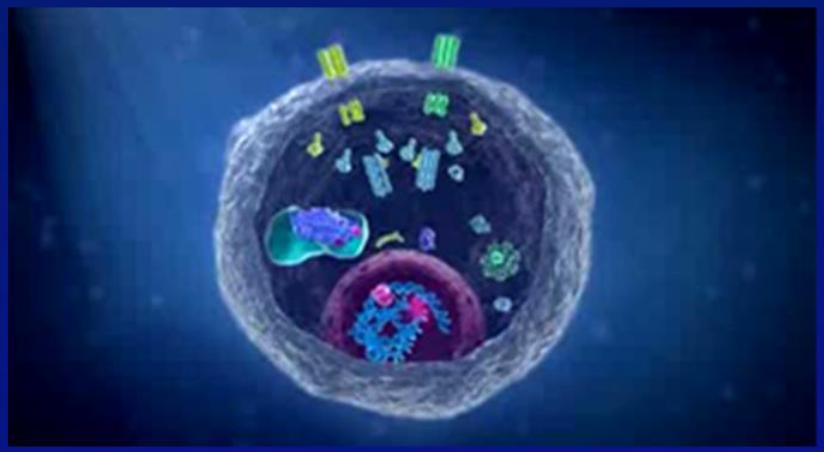
Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

APOPTOSIS

Apoptosis can be activated by two pathways:

- **Intrinsic:** activated by mythochondria.
- **Extrinsic:** activated by the bond between the membrane Death Receptors present on the target cells and their respective ligands.

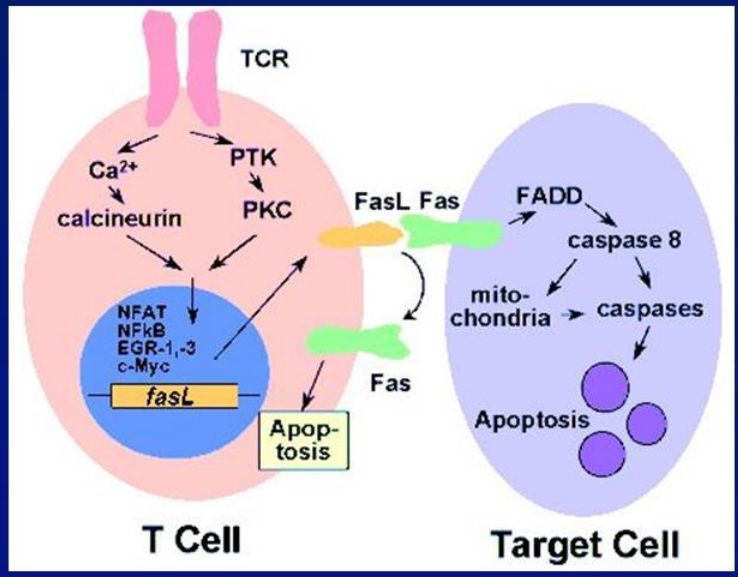


Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

In the extrinsic pathway of apoptosis Fas / FasL system seems to play a key role:

- **Fas** is a type I membrane protein (mFas), which has an extracellular domain that binds to FasL and a cytoplasmic domain that transduces the death signal.
- **FasL** is a type II membrane protein (mFasL) that is expressed on effector lymphocytes.



Soluble forms of the receptor (sFas) and of the respective ligand (sFasL) can act as antagonists of membrane FasL.

(Lettau et al, 2009)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

Journal of Reproductive Immunology 92 (2011) 74–81
Contents lists available at SciVerse ScienceDirect
Journal of Reproductive Immunology
journal homepage: www.elsevier.com/locate/jreprimm
ELSEVIER

Dysregulation of the Fas/FasL system in mononuclear cells recovered from peritoneal fluid of women with endometriosis

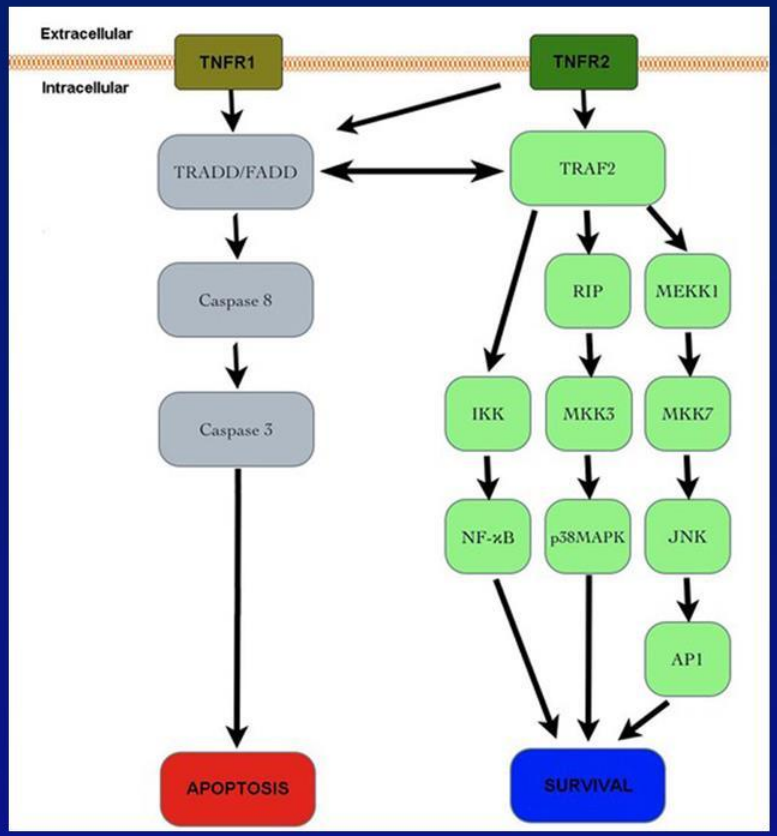
Emanuele Sturlese[a], Francesca Maria Salmeri[b], Giovanni Retto[a], Alfonsa Pizzo[a], Rosanna De Dominici[a], Francesca Venera Ardita[a], Irene Borrielli[a], Norma Licata[b], Antonio Simone Laganà[a], Vincenza Sofo[b,*]

- Our results lead us to hypothesize that the Fas / FasL system is progressively unbalanced during the course of the disease, and for this reason endometriotic cells do not receive the "death signal" by PFMCs and therefore do not undergo Fas/ FasL-mediated apoptosis.
- In this way **endometriotic cells escape the immune system surveillance** and can implant and proliferate in the pelvic cavity.

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932



TNFα, another member of the family of "death ligands", can bind to two different receptors, with different biological activities:

- **type I receptor (TNFR1)**: induces apoptosis of the target cell.
- **type II receptor (TNFR2)**: induces proliferation of the target cell and neo-angiogenesis.

(Cabal-Hierro & Lazo, 2012)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

Original Article

Behavior of Tumor Necrosis Factor-α and Tumor Necrosis Factor Receptor 1/Tumor Necrosis Factor Receptor 2 System in Mononuclear Cells Recovered From Peritoneal Fluid of Women With Endometriosis at Different Stages

Reproductive Sciences
1-8

DOI: 10.1177/1933719114536472
rs.sagepub.com
SAGE

Francesca M. Salmeri, MD[1], Antonio S. Laganà, MD[2], Vincenza Sofo, PhD[1], Onofrio Triolo, MD, PhD[2], Emanuele Sturlese, MD[2], Giovanni Retto, MD[2], Alfonsa Pizzo, MD[2], Angela D'Ascola, PhD[3], and Salvatore Campo, PhD[3]

In early stages, high percentages of TNFR1-bearing PFMCs and high levels of sTNF-α could address signals towards complex I pathway, favouring the inflammatory response. As the disease gets worse, the low percentages of TNFR1-bearing PFMCs are probably due to decreased TNFR1 mRNA transcription and protein translation rate.

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

Original Article

Behavior of Tumor Necrosis Factor-α and Tumor Necrosis Factor Receptor 1/Tumor Necrosis Factor Receptor 2 System in Mononuclear Cells Recovered From Peritoneal Fluid of Women With Endometriosis at Different Stages

Reproductive Sciences
1-8

DOI: 10.1177/1933719114536472
rs.sagepub.com
SAGE

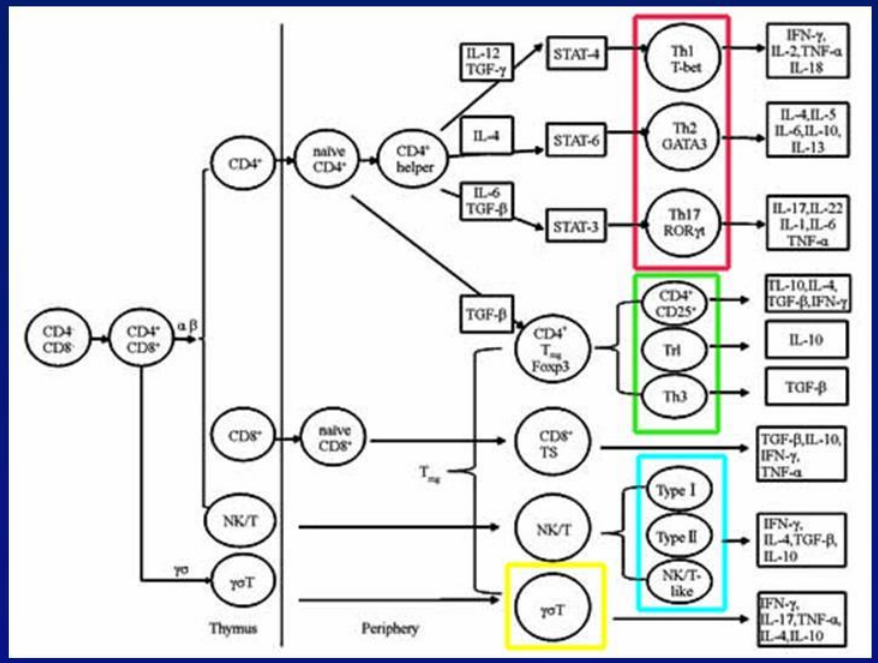
Francesca M. Salmeri, MD[1], Antonio S. Laganà, MD[2], Vincenza Sofo, PhD[1], Onofrio Triolo, MD, PhD[2], Emanuele Sturlese, MD[2], Giovanni Retto, MD[2], Alfonsa Pizzo, MD[2], Angela D'Ascola, PhD[3], and Salvatore Campo, PhD[3]

In early stages (minimal and mild), the percentages of both TNFR2- and mTNF-α-bearing PFMCs are so low, due to decreased mRNA transcription and protein translation rate, that subsequent cellular events may minimally depend on this interaction. The high levels of sTNF-α may be rerouted to bind TNFR1. In contrast, in the moderate and severe stages, the high percentages of TNFR2-bearing PFMCs may be saturated by high percentages of mTNF-α-bearing PFMCs, triggering death process.

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932



- The peritoneal fluid mononuclear cells (PFMCs) secrete different patterns of cytokines, which can polarize the immune response towards a Th1 or Th2 profile and regulate several cellular processes.
  (Pizzo et al, 2002)
- The cytokines induce the differentiation programme of T CD4 $^{+}$ lymphocytes towards Th1 (pro-inflammatory), Th2 (pro-fibrotic and pro-angiogenic), Th17 (pro-inflammatory and pro-autoimmunity) and Treg (immunosuppressive).
  (Zhou et al, 2009)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

JE Journal of Endometriosis
Volume 4 No. 4 - October-December 2012

mRNA EXPRESSION OF Foxp3 AND RORc TRANSCRIPTION FACTORS AND OF IL-10 AND IL-17A CYTOKINES IN OVARIAN ENDOMETRIOMA OF WOMEN WITH ENDOMETRIOSIS

Laganà AS[1], D'Ascola A[2], Salmeri FM[3], Sofo V[3], Pizzo A[1], Retto G[1], Sturlese E[1], De Dominici R[1] and Campo S[2]

Reproductive SCIENCES
The Official Journal of the Society for Gynecologic Investigation
Volume 20 Number 3 (Supplement) March 2013

mRNA Expression of Transcription Factors and Cytokines in Immune Cells of Ovarian Endometrioma.

Antonio S Lagana,[1] Pizzo Alfonsa,[1] Angela D'Ascola,[2] Francesca M Salmeri,[3] Vincenza Sofo,[3] Giovanni Retto,[1] Emanuele Sturlese,[1] Rosanna De Dominici,[1] Irene Borrielli,[1] Salvatore Campo.[2]
[1]Gynecological Sciences, University of Messina, Italy; [2]Biomedical Sciences, University of Messina, Italy; [3]SASTAS, University of Messina, Italy.

- In positive samples, the presence of T-bet, RORC, IFNγ and IL-17A mRNAs represents an index of inflammation.
- Since only half of the samples includes Foxp3^{+} cells, upregulation of GATA-3 mRNA could be responsible of IL-10 mRNA overexpression.

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics
ISSN: 2161-0932
Open Access

JE Journal of Endometriosis
Volume 4 No. 4 - October-December 2012

mRNA EXPRESSION OF Foxp3 AND RORc TRANSCRIPTION FACTORS AND OF IL-10 AND IL-17A CYTOKINES IN OVARIAN ENDOMETRIOMA OF WOMEN WITH ENDOMETRIOSIS

Laganà AS[1], D'Ascola A[2], Salmeri FM[3], Sofo V[3], Pizzo A[1], Retto G[1], Sturlese E[1], De Dominici R[1] and Campo S[2]

Reproductive SCIENCES
The Official Journal of the Society for Gynecologic Investigation
Volume 20 Number 3 (Supplement) March 2013

mRNA Expression of Transcription Factors and Cytokines in Immune Cells of Ovarian Endometrioma.

Antonio S Lagana,[1] Pizzo Alfonsa,[1] Angela D'Ascola,[2] Francesca M Salmeri,[3] Vincenza Sofo,[3] Giovanni Retto,[1] Emanuele Sturlese,[1] Rosanna De Dominici,[1] Irene Borrielli,[1] Salvatore Campo.[2]
[1]Gynecological Sciences, University of Messina, Italy; [2]Biomedical Sciences, University of Messina, Italy; [3]SASTAS, University of Messina, Italy.

- **This, together with IL-4 mRNA overexpression could represent a sign of the polarization of immune cells towards the Th2 profile.**
- **These results arise from the coexistence of inflammatory and reparative phenomena in endometriosis.**

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics
ISSN: 2161-0932
Open Access

Elmer Press
Review
J Clin Med Res • 2013;5(3):153-163

Chronic Pelvic Pain in Endometriosis: An Overview

Onofrio Triolo[a], Antonio Simone Laganà[a, b], Emanuele Sturlese[a]

Endometriosis can cause pain during menstruation (dysmenorrhea), sexual intercourse (dyspareunia) or not linked to the menstrual cycle (chronic pelvic pain).

(Triolo et al, 2013)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation
European Society of Human Reproduction and Embryology
International Society Of Gynecological Endocrinology
Giorgio Pardi's Foundation
Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

Pain & Relief

Laganà et al., J Pain Relief 2013, 2:3
http://dx.doi.org/10.4172/2167-0846.1000123

Review Article Open Access

Obstacles and Pitfalls of Endometriosis-Related Chronic Pelvic Pain Management: Trying to Alleviate the Burden

Laganà AS[1]*, Salmeri FM[2], Sofo V[2], Pizzo A[1], Retto G[1], Sturlese E[1], Granese R[1] and Triolo O[1]

[1]Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences, University of Messina, Via C. Valeria 1, 98125 - Messina, Italy
[2]Department of Environmental Sciences, Safety, Territory, Food and Health, University of Messina, Via C. Valeria 1, 98125 - Messina, Italy

- **Among women who undergo laparoscopy for CPP, endometriosis appears to be present in approximately one third of cases.**
- **Among women who do not have CPP, endometriosis is present in about 5% of cases.**
- **Endometriosis appears to be responsible for the CPP in more than half of histologically confirmed cases.**

(Laganà et al, 2013)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics

Open Access

ISSN: 2161-0932

Department of Gynecology & Obstetrics, University of Messina (Italy)

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation

European Society of Human Reproduction and Embryology

International Society Of Gynecological Endocrinology

Giorgio Pardi's Foundation

Italian Association of Endometriosis

Gynecology & Obstetrics
Open Access
ISSN: 2161-0932

… acknowledgments!

GIMBE EVIDENCE FOR HEALTH

Gruppo Italiano per la Medicina Basata sulle Evidenze

ISGE INTERNATIONAL SOCIETY OF GYNECOLOGICAL ENDOCRINOLOGY

International Society of Gynecological Endocrinology

Associazione Italiana Endometriosi — Educazione Sostegno Ricerca

Italian Association of Endometriosis

FGP FONDAZIONE GIORGIO PARDI

Giorgio Pardi's Foundation

SRI

Society for Reproductive Investigation

eshre Science Moving People

European Society of Human Reproduction and Embryology

Dr. Antonio Simone Laganà
Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences - University of Messina (Italy)

Society for Reproductive Investigation | *European Society of Human Reproduction and Embryology* | *International Society Of Gynecological Endocrinology* | *Giorgio Pardi's Foundation* | *Italian Association of Endometriosis*

Gynecology & Obstetrics Related Journals

- Journal of Women's Health Care
- Journal of Pregnancy and Child Health
- Reproductive System & Sexual Disorders

Gynecology & Obstetrics
Related Conferences

- International Conference on Women's Health, Gynecology & Obstetrics
- 2nd International conference on HIV/AIDS, STDs & STIs-2014