

**Surgical treatment  
of endometriosis -  
associated pain in  
confirmed disease.**



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**Endometriosis and pelvic pain**

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- Relationship and difficulties
  - Results of surgery
  - Future
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## Chronic Pelvic Pain: Etiology

<b>Gynecological</b>	Endometriosis, Adenomyosis, PCO, Adhesions Pelvic venous congestion, Pelvic inflammatory disease
<b>Gastrointestinal</b>	Inflammatory bowel disease Irritable bowel syndrome, Diverticular disease
<b>Urological</b>	Interstitial cystitis, calculi, Urethral syndrome
<b>Musculoskeletal</b>	Fibromyalgia, Disc disease Hernia, Arthritis
<b>Psychosocial</b>	Depression    Physical or sexual abuse Hypochondriasis, Somatisation, Drug dependency

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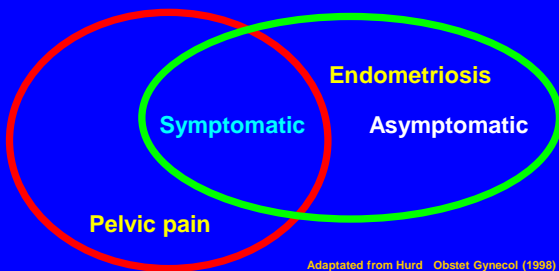
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## Relationship between endometriosis and chronic pelvic pain



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## Criteria that indicate that endometriosis is the cause of pelvic pain

- **Cyclic** pelvic pain
- **Prolonged pain relief** after appropriate treatment of endometriosis:
  - Histology: heterogeneous lesions, evolutivity
  - Association
- **Histological** diagnosis

Hurd    Obstet.Gynecol. (1998)

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## Deeply infiltrating endometriosis: Relationship between endometriotic foci and nerves

SYMPTOMS	% of NERVES located with	
	Intrafibrotic	Intraglandular
DM	-G1	40.5 +/- 6.5*
	-G2	23.4 +/- 4.3*
DP	-G1	39.4 +/- 8.0**
	-G2	22.8 +/- 4.0**
CPP	-G1	41.2 +/- 6.0*
	-G2	24.0 +/- 4.2*



\*: p < 0.001; \*\*: p < 0.01 Anaf et al. Hum. Reprod. (2000)

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## Deeply infiltrating endometriosis: Relationship between endometriotic foci and nerves

SYMPTOMS	Perineurial invasion (%)	Intraneurial invasion (%)
	• DM	
-G1	29.0 +/- 6.0*	35.0 +/- 8.5*
-G2	13.5 +/- 7.3*	11.5 +/- 6.0*
• DP		
-G1	27.4 +/- 7.5*	33.5 +/- 10.6*
-G2	13.1 +/- 7.0*	12.2 +/- 6.0*
• CPC		
-G1	29.0 +/- 5.7*	35.8 +/- 7.8*
-G2	13.8 +/- 7.0*	12.3 +/- 6.0*

\*: p < 0.001

Anaf et al. Hum. Reprod. (2000)

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## Deep endometriosis: Painful heterogeneity

### Is rectovaginal endometriosis a progressive disease?

Luigi Fedele, MD,<sup>a,\*</sup> Stefano Bianchi, MD,<sup>b</sup> Giovanni Zanconato, MD,<sup>c</sup>  
Ricciarda Raffaelli, MD,<sup>c</sup> Nicola Berlanda, MD<sup>d</sup>

Prospective observational study  
88 patients with untreated asymptomatic DIE  
Median follow-up time: 5.7 years (1 - 9)  
No DIE treatment during laparoscopy  
Peritoneal and ovarian lesions fully treated  
DIE lesions biopsied

Progression of disease and/or appearance of pain symptoms attributable to DIE:  
6 patients; **6.8%** 95% CI: 1.9% - 11.7%

Estimated cumulative proportion of patients with progression of disease and/or appearance of pain symptoms attributable to DIE after 6 years: **6.7%**

Fedele et al, AJOG (2004)

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## Deep endometriosis Painful heterogeneity



Bladder Osis	N	%	Reoperation for recurrence n
<i>N = 75 Follow-up: 59.9 ± 44.6 months (range 3 – 182)</i>			
Isolated	27	36.0	0
Associated posterior DIE	48	64.0	
Symptomatic (Surgical exeresis)	33	44.0	0
<b>No symptoms (NO Surgical exeresis)</b>	<b>15</b>	<b>20.0</b>	<b>1</b>

Chapron *et al.*, Hum Reprod (2010; in press)

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## Ureteral endometriosis Associated DIE lesions (n = 29 patients)



	Patients	
	N	%
No urologic symptoms	17	58.6
Severe posterior painful symptoms	26	89.6
Haematuria	2	6.9
Rectorrhagia	5	17.2

Chapron *et al.*, Fertil Steril (2010; in press)

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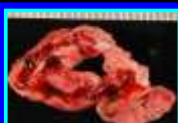
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## Ureteral endometriosis Associated DIE lesions (n = 29 patients)



	Patients		
	N	%	
Nephrectomy	7	24.1	!!!!!!

Chapron *et al.*, Fertil Steril (2010; in press)

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## Pelvic Pain and Endometriosis

Symptoms	Anatomical lesions	Mecanisms
DM DP CPP Intestinal FS Urinary FS Others	<p>Superficial: P and O OMA Adhesions DIE Associations</p>	<p>Inflammation Adhesions Location Depth Neurial pathol. - Fibrosis - Invasion</p>

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## Pelvic Pain and Endometriosis Clinical signs

Two types of pain	Genesis of pain
<p><u>Spontaneous</u> → Functional</p>	<p>Type: Inflammation Medical Approach</p>
<p><u>Mechanical stimuli</u> → Organic</p>	<p>Type: Fibrosis, Adhesions, DIE nodules Surgical Approach</p>

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## Endometriosis and pelvic pain Two main difficulties

- To be sure that Osis is the cause of pelvic pain.
- Which anatomic Osis lesions is responsible for pelvic pain.

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## Endometriosis: Anatomical lesions

\* Superficial OSIS



\* Adhesions



\* Ovarian endometriomas

\* Deep endometriosis  
Heterogeneous  
disease ++++




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## Ovarian endometriomas

Right OMA with few adhesions



Right OMA



Bilateral OMAs: « Kissing ovaries »

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## Pelvic pain and endometriosis

Multivariate analysis and logistic regression

Significant contribution to CPP

Pelvic area of endometriosis	NO
Presence of OMA	NO
Volume of OMA	NO
Depth of infiltration	YES +++

Konincks et al. Fertil. Steril. (1991)

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## Endometriosis and Pelvic Pain

### Logistic regression

Symptoms	Prognosis factors	p
Deep dyspareunia	- Presence of DIE	0.01
	- OMA <b>with</b> adhesions	0.008
Chronic pelvic pain	- Presence of DIE	0.0001
	- OMA <b>with</b> adhesions	0.03
Total pain	- Presence of DIE	0.0001
	- OMA <b>with</b> adhesions	0.03
	- Adnexal adhesions without OMA	0.01

Porpora et al., J of AAGL (1998)

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## Posterior DIE and intensity of DM

### Ordinal multiple logistic regression analysis

Independant variable	Adjusted OR for severity of DM	95 % CI
Location sub-P infiltration		
* Sub-peritoneal only	1	Ref
* Rectal	2.5	1.1 - 5.9
* Vaginal	4.1	1.6 - 10.2
* Both	4.3	1.7 - 10.7
Extent of adnexal adhesions		
* 0 or < 12	1	Ref
* 12 and more	1.9	1.1 - 3.5

Chapron et al., Hum. Reprod. (2003)

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## Pelvic pain and endometriosis

### - Deeply infiltrating endometriosis +++

- Depth of infiltration
- Intrafibrotic and glandular nerves
- Perineurial and endoneurial invasion

### - Adhesions

### - Endometriomas ?????

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## Endometriomas and pelvic pain

**Objective:** Is there a relationship between intensity of DM and OMAs characteristics?

**Prospective** study, unicentric (Cochin hospital).

**Inclusion criteria:**

- 310 patients
- surgery for endometriosis
- complete surgical treatment
- one or more OMAs ( $\geq 2\text{cm}$ ) histologically confirmed.

Chopin – Chapron Acta Scand Obstet Gynecol (2007)

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## Ovarian endometriomas (n = 239): Associated pelvic pain

Dysmenorrhea	N	%
< 7/10	154	64.4
$\geq 7/10$	85	35.6

Chopin - Chapron Acta Obstet Gynecol Scand (2008)

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## Endometriomas and pelvic pain Determinants for severity of DM (multiple logistic regression analysis)

OMAs characteristics	DM < 7	DM $\geq 7$	
Nb OMA	1.4 $\pm$ 0.6	1.6 $\pm$ 0.8	0.36
Size 1 <sup>st</sup> OMA	43.8 $\pm$ 26.6	40.2 $\pm$ 17.8	0.68
Size 2 <sup>nd</sup> OMA	27.4 $\pm$ 13.5	29.5 $\pm$ 14.9	0.65
Laterality			0.17
Right	36%	22%	
Left	80%	34%	
Bilateral	38%	29%	
Ca 125 assay (U/ml)	61.7 $\pm$ 78.6	62.0 $\pm$ 54.8	0.39

Chopin – Chapron Acta Scand Obstet Gynecol (2007)

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## Endometriomas and pelvic pain

### Determinants for severity of DM

(multiple logistic regression analysis)

Independent variable	Odd ratios	95%CI
<b>Rectal infiltration</b>		
Yes	1	-
No	0.082	[0.01 - 0.69]
<b>rAFS implants score</b>		
≥ 24	1	-
< 24	0.52	[0.3 - 0.9]

Chopin – Chapron Acta Scand Obstet Gynecol (2007)

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## Endometriomas and deep endometriosis:

### Patient's characteristics (n = 500)

Pre op PP	OMA -	OMA +	p
DM	6.8 ± 2.9	7.3 ± 2.5	NS
DP	5.1 ± 3.5	4.3 ± 3.6	NS
NCCPP	3.3 ± 3.4	2.9 ± 3.0	NS
Intestinal FS	4.3 ± 3.8	5.5 ± 3.6	NS
Urinary FS	2.9 ± 3.6	2.6 ± 3.3	NS

Chapron et al., Fertil Steril (2009)

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## Deeply infiltrating endometriosis

(n = 500 patients).

### Results according to the presence of OMA

	OMA -	OMA +	P-value#
Mean number of DIE lesions	1.64 ± 1.0	2.51 ± 1.72	< 0.0001
rAFS score			
Implants	6.7 ± 4.9	28.1 ± 10.1	< 0.0001
Adhesions	16.5 ± 23.7	36.2 ± 28.7	< 0.0001
Total	23.6 ± 25.7	65.6 ± 33.1	< 0.0001

#Pearson's Chi-square test

Main DIE lesion	R	OR	95% CI	P-value
USL	0.118	-	-	NS
Vagina	5.98	1.70	1.1-2.6	0.014
Bladder	0.137	-	-	NS
Intestine	34.5	3.59	2.3-5.6	< 0.0001
Ureter	8.6	3.71	1.4-10.4	0.003

OR, odds-ratio; CI: confidence interval

Chapron et al., Fertil Steril (2009)

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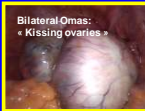
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**Deep endometriosis:**  
Frequency of associated ovarian endometriomas  
(n = 636 patients)

Main lesion	Associated OMAs	
	N	n (%)
BLADDER	51	8 (15.7)
USL	279	49 (17.6)
VAGINA	93	19 (20.4)
URETER	29	13 (44.8)
INTESTINE	184	86 (46.7)
<b>Total</b>	<b>636</b>	<b>175 (27.5)</b>



Chapron et al., (2009)

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**Deeply infiltrating endometriosis and ovarian endometriomas**

**ENDOMETRIOSIS**

**Associated ovarian endometrioma is a marker for greater severity of deeply infiltrating endometriosis**

Cherise Chapron, M.D.,<sup>1,2,3,4</sup> Elodie Pichon-Hadji, M.D.,<sup>1,2</sup> Anne-Charlotte, M.D.,<sup>1,2,3</sup> Coline Deroo, M.D.,<sup>1,2</sup> Marie-Pierre, M.D.,<sup>1,2</sup> and Nicolas Juyon, M.D.<sup>1,2</sup>

<sup>1</sup>Univ. Paris Descartes, UFR de Médecine, Assistance Publique-Hopital de Paris (AP-HP), Hôpital Européen Marie-Louise (HLE), Centre d'Endocrinologie, Gynécologie, Obstétrique, et de Médecine de la Fertilité, Paris, France; <sup>2</sup>Univ. Paris Descartes, CHU de Saint-Denis, Paris, France; <sup>3</sup>Univ. Paris Descartes, CHU de Saint-Denis, Paris, France; <sup>4</sup>Univ. Paris Descartes, CHU de Saint-Denis, Paris, France

**Objective:** To investigate whether the presence of an ovarian endometrioma is a marker for severity of deeply infiltrating endometriosis (DIE).

**Design:** Observational study. January, June, 1992 and December, 2003.

**Setting:** University gynecology center.

**Patients:** First surgical patients with histologically confirmed DIE.

**Interventions:** Laparoscopic or total hysterectomy with bilateral salpingo-oophorectomy.

**Main Results:** Among 102 patients with DIE, 30 (29.4%) had associated ovarian endometriomas (OMA). The mean severity of DIE, based on the modified organopathy score (0-10), was 5.0. The mean severity of OMA, based on maximum depth of endometrial penetration (0-10), was 4.0. The mean severity of DIE was significantly higher in patients with associated OMA (mean 6.0, SD 1.1) vs. 4.5, SD 1.0, for patients with no associated OMA (mean 4.5, SD 1.0). Mean body mass index was not associated with DIE, endometriosis, and OMA.

**Conclusions:** Associated ovarian endometrioma is a marker for the severity of DIE. In a clinical context, presence of OMA, when there is no ovarian endometrioma, characterizes deeply infiltrating endometriosis. The absence of OMA is linked to the severe and multiple DIE lesions. (Fertil Steril 2009;92:1119-1123, DOI:10.1016/j.fertnstert.2009.06.014)

**Key Words:** Deeply infiltrating endometriosis, ovarian endometrioma, endometriosis, endometriosis, severity

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**Endometriomas and pelvic pain**

Physical abnormalities may not be the cause of the symptoms: **ovarian endometriomas +++**

Two different types of endometriomas:

- No painful OMA
- Painful OMA: associated DIE

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## Endometriosis and pelvic pain

- Relationship and difficulties
- Results of surgery
- Future

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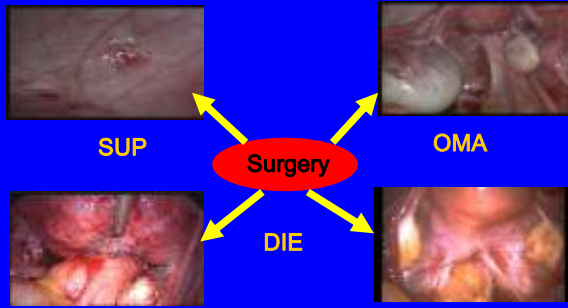
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## Endometriosis: Surgery for pelvic pain



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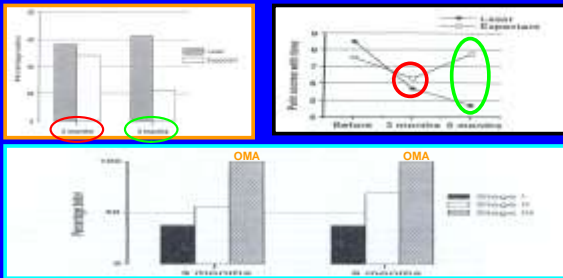
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## Endometriosis and pelvic pain:

### Laser laparoscopic treatment versus placebo surgery

Stages 1,2 and 3 (PRT)



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## Endometriosis and pelvic pain: Laparoscopic excision versus placebo surgery (PRT)

Pain	Surgery group	
	Placebo (n = 19)	Immediate (n = 20)
Improvement	6 <b>32%</b>	16 <b>80%</b>
Worse	13 <b>68%</b>	4 <b>20%</b>

**p = 0.002**

Abbott et al., Fertil Steril (2004)

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## Surgical treatment of endometriosis: Ablation versus excision for stage 1 and 2 (PRT)

	Dif.	95% CI	p	p
<b>Symptoms</b>				
Ablation	7.1	2.5 - 11.7	0.006	t-test: p = 0.84
Excision	7.8	1.1 - 14.6	0.026	MW U test: p = 0.95
<b>Signs</b>				
Ablation	1.6	-0.9 - 4.0	0.182	t-test: p = 0.18
Excision	3.3	2.2 - 4.5	< 0.001	MW U test: p = 0.20
<b>Total</b>				
Ablation	8.7	2.2 - 15.2	0.013	t-test: p = 0.57
Excision	11.2	4.3 - 18.0	0.004	MW U test: p = 0.75

Wright et al. Fertil Steril (2005)

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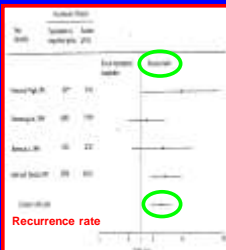
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## Surgical management of endometriomas Intraperitoneal cystectomy



Common OR 3.09 (95% CI 1.76 - 5.36)

### Reduce rate of:

- Recurrence OMA OR : 0.41 ; CI 0.18 - 0.93
- Further surgery OR : 0.21 ; CI 0.05 - 0.79
- Recurrence DIM OR : 0.15 ; CI 0.06 - 0.06
- Recurrence DP OR : 0.08 ; CI 0.01 - 0.51
- Recurrence NCPP OR : 0.10 ; CI 0.02 - 0.56

### Increase of:

- Spontaneous pregnancy OR : 5.21 ; I2.04 - 13.29

Hart et al., Cochrane Reviews (2005)

Vercollini & Chapron et al., AJGO (2003)

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## Surgery for DIE: Radical excision

Symptoms	Pre-op	Post-op	Delta
DM*	8.1 ± 1.8	2.8 ± 3.1	5.2 ± 3.5
DP*	6.5 ± 2.2	1.9 ± 2.6	4.6 ± 3.0
Painful defecation*	6.6 ± 2.4	2.1 ± 2.8	4.5 ± 3.5
Urinary tract S.*	6.1 ± 2.1	1.2 ± 2.6	4.9 ± 3.2
Gastrointestinal S.*	6.8 ± 2.2	2.7 ± 3.1	4.1 ± 3.5
CPP*	7.5 ± 1.6	2.8 ± 3.6	4.8 ± 3.4

\*: p < 0.001

Chopin – Chapron J Minim Invasive Gynecol (2005)

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## Surgery for deep endometriosis

Objective evaluation:  
Pre versus postoperative pain score



	N	DM	DP	NCCPP	
Anaf	2001	26	< 0.0001	< 0.001	< 0.001
Wright	2001	28	< 0.0001	< 0.0001	< 0.0001
Redwine	2001	67	< 0.0005	< 0.0005	< 0.0005
Abbott – Garry	2003	135	< 0.0001	< 0.0001	< 0.0001
Thomassin – Daraï	2004	27	< 0.0001	0.0002	0.001
Chopin – Chapron	2005	152	< 0.001	< 0.001	< 0.001

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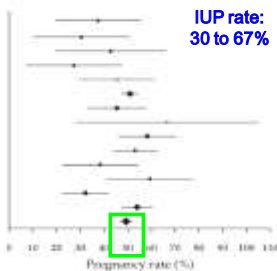
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## Laparoscopic excision of OMAs:

Pregnancy rates

Source, year	Pregnancies/Total
Danielli et al., 1991	12/32
Mares et al., 1991	7/23
Batemann et al., 1994	9/21
Cosignani et al., 1996	6/22
Mombrano et al., 1996	5/11
Dommez et al., 1996	415/814
Sutton et al., 1997	30/66
Beretta et al., 1998	6/9
Busacca et al., 1999	39/62
Milingos et al., 1999	17/32
James & Sutton, 2002	15/39
Alborzi et al., 2004	19/32
Fedele et al., 2006	29/90
Vercellini et al., 2006a	128/237
Overall weighted mean	



Vercellini et al., Hum Reprod (2009)

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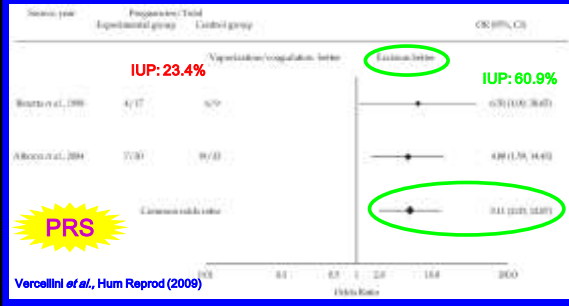
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## Laparoscopic surgery for OMAs: Pregnancy rates




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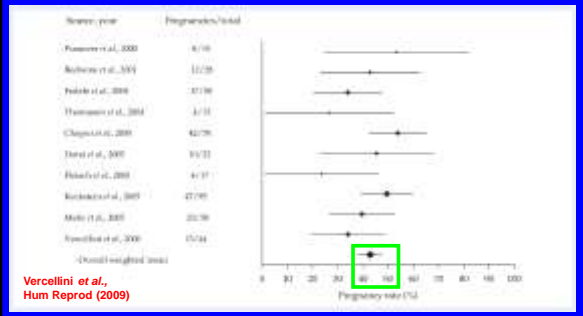
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## Deep endometriosis: Excisional surgery Pregnancy rates




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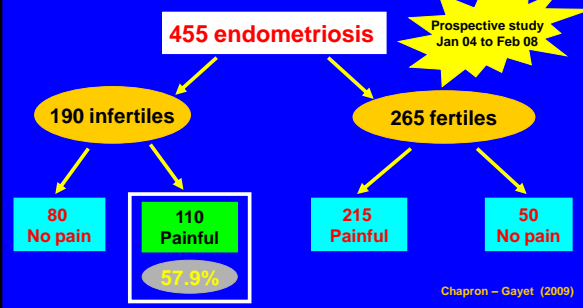
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## Endometriosis - related infertility (n = 110 infertile painful patients)




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## Endometriosis and pelvic pain

- Relationship and difficulties
- Results of surgery: Principles
- Future

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## Deep endometriosis:

Frequency of associated other OSIS forms

Forms of the disease	n	%	95%CI
Superficial peritoneal	57	61.3	51.4-71.2
Ovarian endometriomas	47	50.5	40.3-60.7
Pelvic adhesions	69	74.2	65.3-83.1
Overall	87	93.5	87.7-97.2

Somigliani et al., Hum Reprod (2004)

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## DEEPLY INFILTRATING ENDOMETRIOSIS: LOCATION (n = 426 patients)

Main lesion	N	Associated lesions					Total	
		USL			Va	BI		Ur
		R	L	B				
BLADDER	37	2	1	3	3	37		49
USL	222	57	109	56				278
VAGINA	61	5	6	11	61			94
URETER	15	2	4	3	9	3	16	57
INTESTINE	91	12	12	22	50	8		155
	426	78	132	95	123	48	16	172

Multifocality +++

Chapron et al., Hum Reprod (2006)

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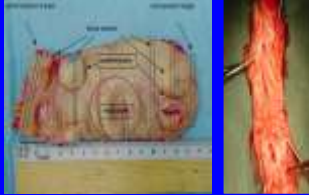
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## Bowel Deep Endometriosis: Location of microscopic infiltration

(n = 50 patients)

Endometriotic lesions		
	N	%
Multifocal (< 2 cm)	31	62
Multicentric (≥ 2 cm)	19	38
Unicentric and unilocular	0	0



Kavallaris *et al.*, Hum Reprod (2003)

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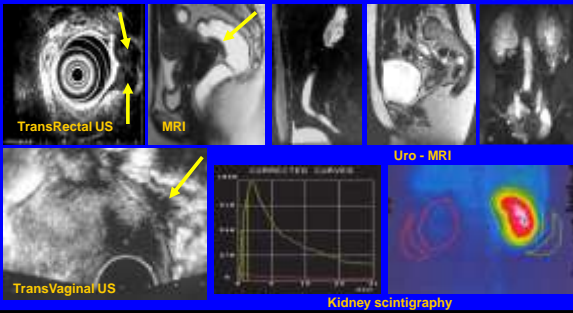
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## Deep endometriosis:

Preoperative work-up importance of imaging




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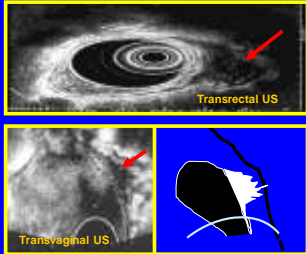
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## Deeply infiltrating endometriosis: Diagnosis of the rectum wall infiltration: Comparison between TRUS et TVUS

	TRUS	TVUS
Se	96	90
Sp	100	96
VPP	100	97
VPN	95	99



Piketty - Chapron *et al.*, Hum Reprod (2009)

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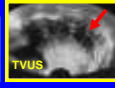
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## Deep endometriosis: Rectal wall infiltration

	N	Se	Sp	PPV	NPV	
<b>TRUS</b>						
Chapron <i>et al.</i> , (2004)	81	97	89	87	98	
Bazot <i>et al.</i> , (2007)	81	89	93	96	81	
Chapron <i>et al.</i> , (2009)	134	96	100	100	95	
<b>MRI</b>						
Chapron <i>et al.</i> , (2004)	81	76	98	96	85	
Abrao <i>et al.</i> , (2007)	104	83	98	97	84	
Bazot <i>et al.</i> , (2007)	88	83	93	96	79	
<b>TVUS</b>						
Abrao <i>et al.</i> , (2007)	104	98	100	100	98	
Bazot <i>et al.</i> , (2007)	81	93	100	100	87	
Chapron <i>et al.</i> , (2009)	134	90	96	97	89	

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## DIE: Principles for surgical treatment

### Principles

Surgery only when lesions give rise to symptoms

Patient's informed consent

Multidisciplinary approach: **Diagnosis:** *imaging work-up*  
**Treatment**

Radical surgery: complete exeresis of DIE lesions

Referral center for diagnosis and management

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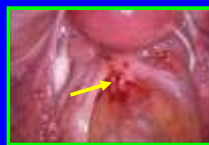
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## Deep endometriosis: Global approach



Chapron *et al.*,  
Hum Reprod (2006)

**DIE is NOT**  
« an organ pathology »




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## Endometriosis and pelvic pain

- Relationship and difficulties

- Results of surgery: Problems

- Future

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### Deep endometrisoïs: Complications

CHU Cochin – Paris' experience; n = 229 intestinal DIE

Major complications	N	Reoperation
Leakage of anastomosis	4	2 drainage
Recto - vaginal fistula	5	Ileostomy and vaginal drainage
Ureteral fistula	6	2 ureteroneocystotomy
<b>Total</b>	<b>9</b>	<b>3.4%</b>

Chapron – Leconte – Dousset (2008)

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### Deep endometrisoïs: Complications

Complication	Observed incidence (%)
Neurogenic bladder dysfunction	4-10
Neurological Bowls formation	3-10
Blood transfusion	2-6
Indivertent rectal perforation	1-3
Anastomotic leakage	1-3
Pelvic abscess	1-2
Temporary diverting loop ileostomy/colostomy	0.5-1.5
Intraoperative ureteral lesion	0.5-1
Post-operative ureteral fistula formation	0.5-1
Post-anastomotic rectal stenosis	0.5-1
Post-anastomotic ureteral stenosis	0.5-1

Vercellini et al., Hum Reprod (2009)

Poore-Vercellini et al. (2009, in press), Litnarova et al. (2000-2008), Possowar et al. (2008), Anaf et al. (2001), Chapron et al. (2003), Redwine and Wright (2001), Wright and Stalle (2001), Chapron et al. (2002), Fenech et al. (2004a), Reid et al. (2004), Thomassin et al. (2004), Vajpi et al. (2004), Campagnoni et al. (2005), Chapron et al. (2005), Dora et al. (2005), Hirsch et al. (2005), Kocak and Waininger (2005), Plohr et al. (2005), Sigal et al. (2005), Angioni et al. (2006), Duberand et al. (2006), Lendi et al. (2006), Lagaobakke et al. (2006), Lyons et al. (2006), Rizzo et al. (2006), Verstraete et al. (2006b), Brouwer and Woods (2007), Kristianson and Kjer (2007), Pines et al. (2007), Bechtel et al. (2007) and Garcia-Esteban et al. (2008).

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## Deep endometriosis: Complications

Urological complications

Deep endometriosis

Colo - rectal complications

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## Deep endometriosis: Complications

Urological complications

Deep endometriosis

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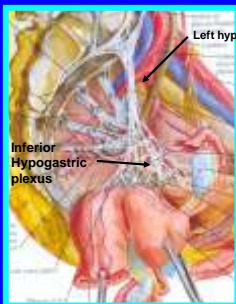
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## Laparoscopic Nerve sparing complete excision of DIE



	Laparoscopic Nerve Sparing		
	No (n = 20)	Yes (n = 25)	
Mean time to resume the voiding function	42.5	3.0	0.01
Very satisfied	25.0%	87.7%	0.013

Landi et al., Hum Reprod (2006)

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## Urinary complications after surgery for posterior DIE (n = 80 patients)

Symptoms	Preop %	Postop %	p
Hesitancy	5	32.5	0.02
Strain to start	6.2	32.5	0.04
Stopping flow	6.2	37.5	0.01
Acute retention	0	18.7	0.008
Incomplete emptying	12.5	47.5	0.02

Dubernard et al., JMIG (2008)

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## Urinary complications after surgery for posterior DIE (n = 80 patients)

Symptoms	RVS and USL %	Colorectal %	p
Hesitancy	10.7	36.5	0.01
Strain to start	14.3	32.7	0.07
Stopping flow	14.3	40.4	0.02
Acute retention	17.9	19.2	0.32
Incomplete emptying	17.9	42.3	0.004

Dubernard et al., JMIG (2008)

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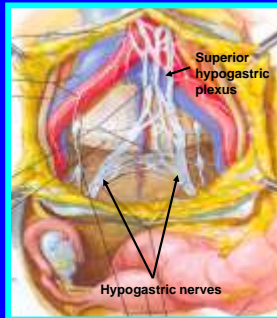
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## Laparoscopic Neuro-Navigation technique (LANN) (n = 91 with deep colorectal anastomosis for DIE)

The suprapubic catheter could be removed, on average, after 2 days of bladder training.

It was intraoperatively possible to preserve the parasympathetic nerves at least on one side.

All the patients were able spontaneously and continuously void their bladder.



Possover et al., J. Am. Coll. Surg. (2005)

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## Deep endometriosis: *Complications*

CHU Cochin - Paris experience: n = 229 intestinal DIE

Major complications	Before 2005 (n = 100)		After 2005 (n = 129)	
	n	%	n	%

Urinary retention	16	16	12	9.3
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Chapron - Leconte - Douset (2008)

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## Surgery for intestinal DIE

n = 100 patients; Minimum of follow-up: 5 years

Predictive factors for transient neurogenic bladder

Parameters	Transient neurogenic bladder				p
	Yes (n = 10)		No (n = 89)		
	n	%	n	%	
Age ≥ 35	6	37	28	33	NS
BMI > 25	4	25	16	19	NS
Multiple previous surgery	10	62	38	45	NS
Additional intestinal resection	2	12	7	8	NS
Coloanal anastomosis	9	56	7	8	< 0.001
Associated hysterectomy	4	25	4	5	< 0.01
N DIE lesions ≥ 4	11	69	44	52	< 0.05

Douset and Chapron. Ann Surg 2010 (in press)

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## Deep endometriosis: *Complications*

Deep endometriosis

Colo - rectal complications

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## Deep endometriosis: *Complications*

CHU Cochin – Paris' experience: n = 229 intestinal DIE

Major complications	Before 2005 (n = 100)		After 2005 (n = 129)	
	n	%	n	%
Linkage of anastomosis	2	2	2	1.5
Recto - vaginal fistula	4	4	1	0.8
<b>Total</b>	<b>6</b>	<b>6</b>	<b>3</b>	<b>2.3</b>

Chapron – Leconte – Douset (2008)

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## Endometriosis and pelvic pain

- Relationship and difficulties
- Results of surgery
- Future

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## Endometriosis: *Diagnosis process*

	N	Country	Delay in diagnosis
Hadfield <i>et al.</i> , (1996)	134	UK	7.9
Hadfield <i>et al.</i> , (1996)	84	USA	11.7
Sinaii <i>et al.</i> , (2002)	3 680	UK	10.0
Husby <i>et al.</i> , (2003)	-	Norway	6.7
Ballard <i>et al.</i> , (2006)	32	UK	8.5
Arruda <i>et al.</i> , (2003)	200	Brazil	7.0
Ballweg (2004)	4 000	USA	9.3
Matzusaki <i>et al.</i> , (2006)	95	France	6.6
Sinaii <i>et al.</i> , (2008)	940	UK	7.8
Greene <i>et al.</i> , (2009)	4 334	USA	9.3

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## CHU Cochin'experience

January 2004 – December 2008

Prospective study



### Previous medical treatment

Endometriosis	N	n	%
SUP	47	11	23.4
OMAs	120	66	55.0
DIE	245	174	71.0
<b>Total</b>	<b>412</b>	<b>251</b>	<b>60.9</b>

Chapron - Souza (2009)

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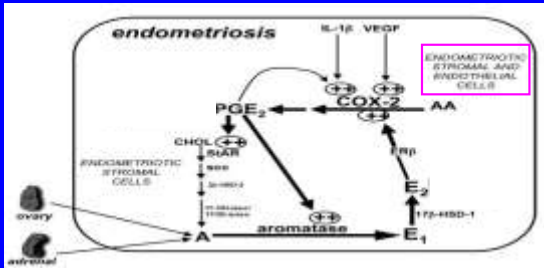
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## Endometriosis: Mechanisms of growth and inflammation



Adapted from Bulun SE Pharm Reviews (2005)

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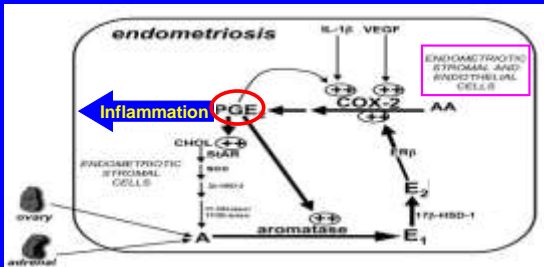
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## Endometriosis: Mechanisms of growth and inflammation



Adapted from Bulun SE Pharm Reviews (2005)

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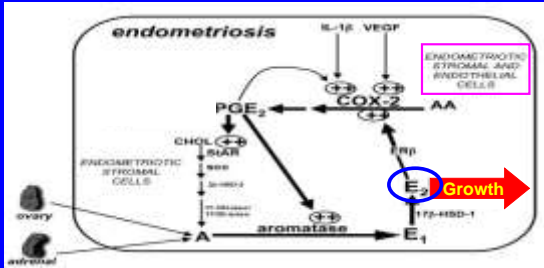
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## Endometriosis: Mechanisms of growth and inflammation



Adapted from Bulun SE Pharm Reviews (2005)

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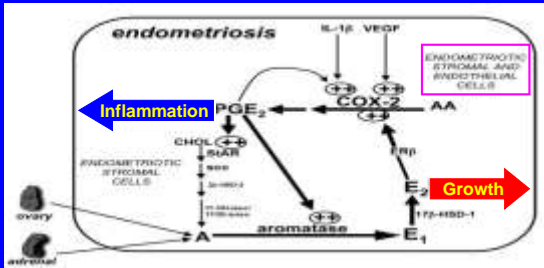
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## Endometriosis: Mechanisms of growth and inflammation



Adapted from Bulun SE Pharm Reviews (2005)

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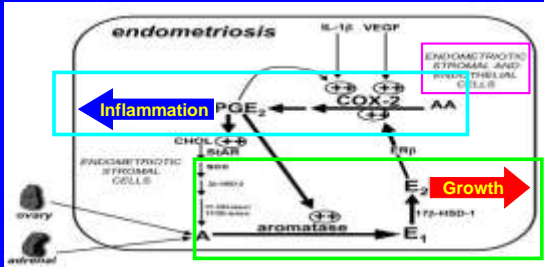
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## Endometriosis: Mechanisms of growth and inflammation



Adapted from Bulun SE Pharm Reviews (2005)

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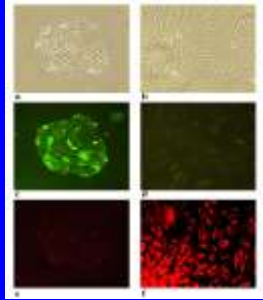
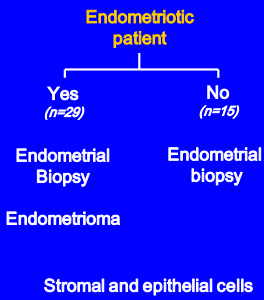
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## Endometriosis: Oxidative stress



Ngô, Chapron, Batteux Am J Pathol (2009)

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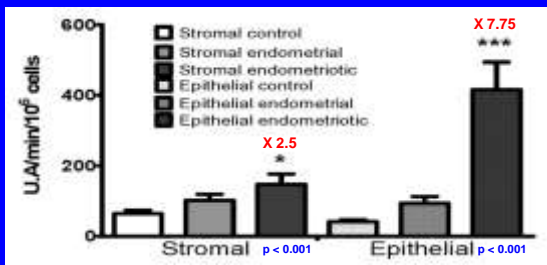
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## Endometriosis: Oxidative stress

Hydrogen peroxide ( $H_2O_2$ ) production



Ngô, Chapron, Batteux Am J Pathol (2009)

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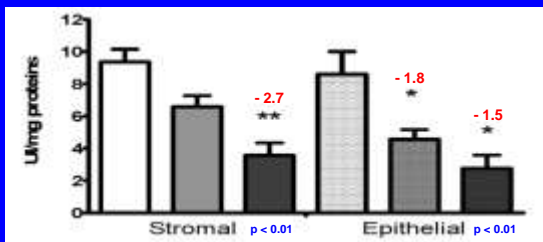
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## Endometriosis: Oxidative stress

Hydrogen peroxide ( $H_2O_2$ ) detoxification: Catalase activity



Ngô, Chapron, Batteux Am J Pathol (2009)

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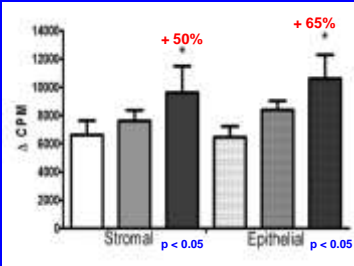
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# Endometriosis: Oxidative stress

## Cellular proliferation

- Stromal control
- ▒ Stromal endometrial
- Stromal endometriotic
- Epithelial control
- ▒ Epithelial endometrial
- Epithelial endometriotic

Production of endogenous ROS correlate with cellular proliferation



Ngô, Chapron, Batteux Am J Pathol (2009)

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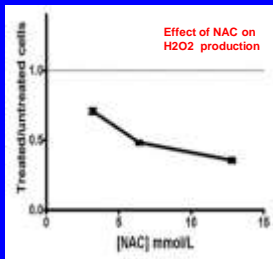
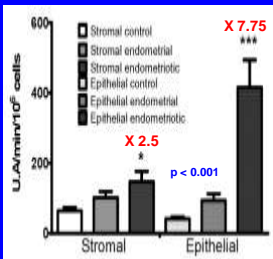
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# Endometriosis: Oxidative stress

## Effect of N-acetylcysteine on Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) production



Ngô, Chapron, Batteux Am J Pathol (2009)

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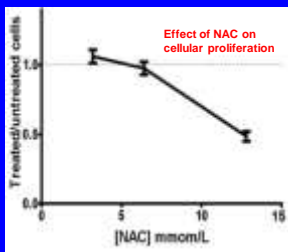
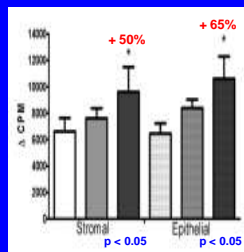
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# Endometriosis: Oxidative stress

## Effect of N-acetylcysteine on cellular proliferation



Ngô, Chapron, Batteux Am J Pathol (2009)

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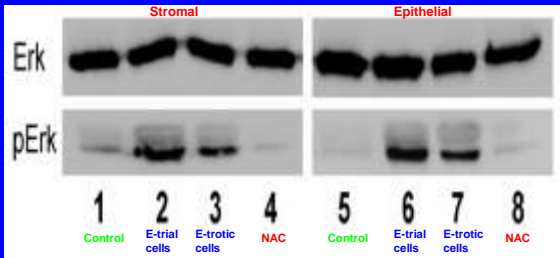
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## Endometriosis: Oxidative stress



Ngô, Chapron, Batteux Am J Pathol (2009)

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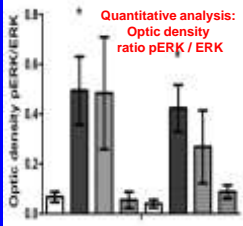
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## Endometriosis: Oxidative stress



The rate of proliferation of endometriotic cells is increased through the activation of the ERK pathway as a consequence of high constitutive endogenous oxidative stress



Ngô, Chapron, Batteux Am J Pathol (2009)

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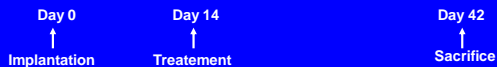
## Endometriosis: Oxidative stress :

### Mouse model

Implants from ovarian endometriomas in 28 nude mice



N-acetylcystéine  
PBS



Ngô, Chapron, Batteux Am J Pathol (2009)

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## Endometriosis: Oxidative stress




Control




Control



In vivo



NAC



N-acetylcysteine

Histological score:  
2.0 ± 0.25

Histological score:  
1.19 ± 0.13

p < 0.05

Ngô, Chapron, Batteux  
Am J Pathol (2009)

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## Endometriosis: Oxidative stress

### Future

ROS

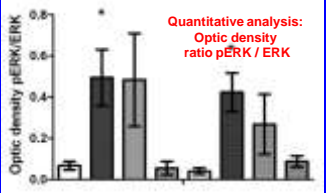
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★

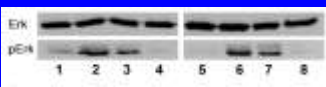
Activation de pERK

pERK inhibitor

Prolifération



Quantitative analysis:  
Optic density ratio pERK / ERK



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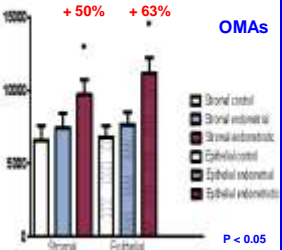
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## Endometriosis: Effects of antiproliferative drugs

### Basal proliferation: proliferative rate

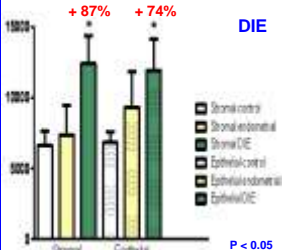
OMAs



+ 50%   + 63%

P < 0.05

DIE



+ 87%   + 74%

P < 0.05

Ngô, Batteux, Chapron Fertil Steril (2010, in press)

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# Take home messages



- Global approach
- Referral center

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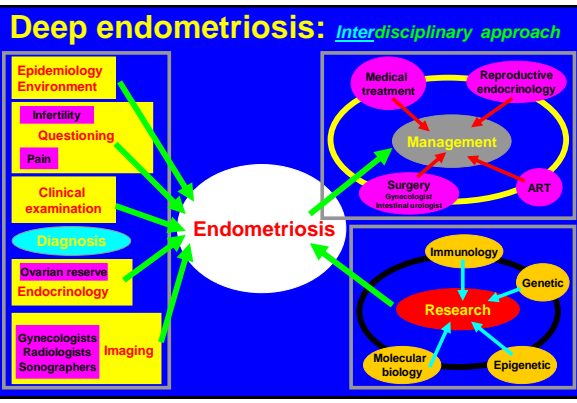
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# Take home messages



**Surgery for endometriosis +++**

Surgery is efficient but is not the only option  
 Global management of the patient: *pain, infertility, both*  
 Satisfactory preoperative work-up  
 Effective surgery: *the first operation must be the good one*  
 Earlier and better diagnosis: *minimize aggressivity of surgery ???*  
 New strategies: *Adjuvant therapy ???*  
*Preoperative treatment ???*

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Thanks



**Gynecology**

**Surgical unit:**

B Borghese, H Foulot, C Ngo,  
MC Lafay-Pillet, G Pierre,  
P Santulli, C Souza

**Reproductive endocrinology unit:**

V Gayet, A Marszalek,  
I Streuli, FX Aubriot

**Intestinal surgery**

B Dousseat, M Leconte.

**Laboratory: Genetic**

D Valman, F Mondon,  
S Barbaux

**Laboratory: Immunology**

B Weill, F Batteux,  
C Nicco, C Chéreau

**Statistical unit**

F Goffinet

D de Ziegler, Professor and Head, Reproductive Endocrinology and Infertility unit,  
C Chapron, Professor and Chair, Dpt Gynecology Obstetrics II and Reproductive Medicine

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