Diagnosis Criteria and Assessment of Endometriosis and Adenomyosis Chronic Pain Syndromes

Convergences PP, Nantes 2009


Endometriosis and Pain

http://www.cice.fr/
Is it Painfull?

Yes, more and more!!

*Prevalence of endometriosis in women with chronic pelvic pain*

Guo and Wang  Gynecol Obstet Invest  2006
Pain:

*main symptom in endometriosis!*

- Dysmenorrhea
- Dyspareunia
- Pain during defecation, micturation
- Chronic pelvic pain
- Neuropathic pain: sciatalgia, pudendalgia...

*Cyclic character, menstrual reinforcement,*

*Negatively affect quality of life*

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Not always!!

- Patients operated in the department

<table>
<thead>
<tr>
<th>Pain score</th>
<th>Endometriosis (n=110)</th>
<th>No endometriosis (n=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9 (8.1%)</td>
<td>19 (23.8%)</td>
</tr>
<tr>
<td>1</td>
<td>29 (26.4%)</td>
<td>28 (35%)</td>
</tr>
<tr>
<td>2</td>
<td>17 (15.5%)</td>
<td>18 (22.5%)</td>
</tr>
<tr>
<td>3</td>
<td>55 (50%)</td>
<td>15 (18.8%)</td>
</tr>
</tbody>
</table>

0; no pain, 1; Mild pain (some loss of work efficiency)
2; Moderate pain (occasional loss of work)
3; Severe pain (incapacitation)
Is pain related to the extent of the disease?

« Registre Auvergne Endometriose »

- Patients included if the disease is diagnosed for the first time
- Patients living in Auvergne
- A biopsy is required
- Aim to assess the long term effect of the usual management of endometriosis
Aim of the study: To compare clinical data of patients with minimal disease and patients with severe disease (i.e. patients with deep infiltrating and or ovarian endometrioma)

- Severe deep infiltrating nodule and or ovarian endometrioma ≥ 1 cm
- Minimal AFS Stage I
Among the first 202 patients included, we identified,

- 111 patients with « severe » endometriosis (disease)
- 47 patients with minimal endometriosis (ASRM classification stage I) (epiphenomena)

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>32.5 ± 6.2</td>
</tr>
<tr>
<td>Epiphenomena</td>
<td>32.4 ± 7.5</td>
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</table>
## Incidence of Dysmenorrhea and Severity

<table>
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<tr>
<th>Group</th>
<th>Dysm.</th>
<th>Pain score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>88.2 %&lt;sup&gt;*&lt;/sup&gt;</td>
<td>7.3 ± 2.4&lt;sup&gt;#&lt;/sup&gt;</td>
</tr>
<tr>
<td>Epiphenomena</td>
<td>74.5 %&lt;sup&gt;*&lt;/sup&gt;</td>
<td>7.4 ± 2.5&lt;sup&gt;#&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

* P<0.04 ; # N.S.

## Incidence of Dyspareunia and Severity

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<th>Group</th>
<th>Pain score</th>
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<tr>
<td>Disease</td>
<td>54.5 %&lt;sup&gt;*&lt;/sup&gt;</td>
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<tr>
<td>Epiphenomena</td>
<td>54.5 %&lt;sup&gt;*&lt;/sup&gt;</td>
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* NS ; # N.S.
Quality of life (SF 36)

<table>
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<tr>
<th></th>
<th>Disease</th>
<th>Epiphenomena</th>
<th>Control *</th>
</tr>
</thead>
<tbody>
<tr>
<td>General health</td>
<td>63.5 ± 19</td>
<td>62.1 ± 26</td>
<td>75.1</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>64.3 ± 27.8</td>
<td>66.7 ± 28.5</td>
<td>80.1</td>
</tr>
<tr>
<td>Health Transition</td>
<td>42.2 ± 20.5</td>
<td>44.1 ± 19.7</td>
<td></td>
</tr>
<tr>
<td>Social functioning</td>
<td>67.9 ± 25.5</td>
<td>68.5 ± 27.0</td>
<td>82.83</td>
</tr>
<tr>
<td>Mental health</td>
<td>53.4 ± 24.1</td>
<td>50.5 ± 19.4</td>
<td>68.18</td>
</tr>
<tr>
<td>Vitality</td>
<td>44.3 ± 22.8</td>
<td>48.7 ± 21.2</td>
<td>60.57</td>
</tr>
<tr>
<td>Role emotional</td>
<td>68.6 ± 38.3</td>
<td>60.3 ± 41.5</td>
<td>86.13</td>
</tr>
<tr>
<td>Role physical</td>
<td>68.9 ± 38.6</td>
<td>62.2 ± 43.6</td>
<td>85.98</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>90.0 ± 15.0</td>
<td>84.4 ± 18.4</td>
<td>92.42</td>
</tr>
</tbody>
</table>

* French population / women 25-34 years old

Evaluation de la qualité de vie (SF 36).
It is painful!

Pain of patients with minimal disease should also be taken in consideration!!

Patients personal history is essential

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### Pain and deep disease

**Pain and depth, volume of Deep endometriosis**

<table>
<thead>
<tr>
<th></th>
<th>Pain</th>
<th>No pain</th>
</tr>
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<tbody>
<tr>
<td><strong>Depth (mm)</strong></td>
<td>$5.3 \pm 4.7$ *</td>
<td>$3.3 \pm 2.7$ *</td>
</tr>
<tr>
<td><strong>Volume (mm$^3$)</strong></td>
<td>$1213 \pm 1975$ @/$ \hat{P}=0.049$</td>
<td>$194 \pm 355$ @/$ \hat{P}&lt;0.01$</td>
</tr>
</tbody>
</table>

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*Ripps and Martin J Reprod Med 37:620;1992*
Good correlation between type of pain and localization of deep infiltrating endometriosis (DIE)

<table>
<thead>
<tr>
<th>Type of Pain</th>
<th>Localization</th>
</tr>
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<tbody>
<tr>
<td>Deep dyspareunia</td>
<td>Utero sacral ligaments DIE</td>
</tr>
<tr>
<td>Periodic defecation pain</td>
<td>Rectovaginal septum DIE</td>
</tr>
<tr>
<td>Functional urinary symptoms</td>
<td>Urinary tract DIE</td>
</tr>
<tr>
<td>Chronic abdominal pain</td>
<td>Digestive DIE</td>
</tr>
</tbody>
</table>


We may propose

<table>
<thead>
<tr>
<th>Pain Description</th>
<th>Type of Endometriosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal cramps with thigh irradiation</td>
<td>Adenomyosis</td>
</tr>
<tr>
<td>Intermenstrual pain</td>
<td>Ovarian endometriosis</td>
</tr>
<tr>
<td>Right shoulder pain</td>
<td>Diaphragmatic endo</td>
</tr>
<tr>
<td>Cyclic pain of a scar</td>
<td>Scar endometriosis</td>
</tr>
</tbody>
</table>
Why is it painful??

A disease because it bleeds!!

- I Brosens Yokoama 1996
- Bleeding is common and often painful
- Pain during bleeding is often misunderstood as a recurrence or an active disease whereas it is often only an unadapted medical treatment
- Endometrial atrophy induces spotting and pain it does not imply that the disease is getting worse!!
Amenorrhea is an effective treatment of pain in most cases

✓ If pain is not influenced by the menstrual cycle and not improved by an induced amenorrhea endometriosis may not be the cause of the pain

✓ i.e. Recurrent pain is often associated with scars and sequelae not by an active form of the disease

Hyperalgesia: intense pain when pressure was applied in the posterior cul de sac

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<td>23</td>
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<td>II (peritoneal or ovarian)</td>
<td>28</td>
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Anaf et al Hum Reprod 2002
**Relationship / pain and nerves in endometriotic lesions**

<table>
<thead>
<tr>
<th>Pelvic pain</th>
<th>Group I n = 18 (pain score &gt;7)</th>
<th>Group II n = 10 (pain score ≤ 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter of lesions</td>
<td>23.0 ± 2.0</td>
<td>22.8 ± 1.9</td>
</tr>
<tr>
<td>N nerves</td>
<td>18.1 ± 2.0</td>
<td>17.6 ± 1.0</td>
</tr>
<tr>
<td>Intrafibrotic nerves</td>
<td>41.2 ± 6.0</td>
<td>24.0 ± 4.2 *</td>
</tr>
<tr>
<td>Intraglandular nerves</td>
<td>39.2 ± 7.0</td>
<td>24.3 ± 5.0 *</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>29.0 ± 5.7</td>
<td>13.8 ± 7.0 *</td>
</tr>
<tr>
<td>Endoneurial invasion</td>
<td>35.8 ± 7.8</td>
<td>12.3 ± 6.0 *</td>
</tr>
</tbody>
</table>

* P < 0.001

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**Implication of nervous infiltration**

Pain rises with:

- % of nervous and perinervous infiltration by DIE

- Perinervous secretion of inflammatory factors by endometriotic cells (EC) or macrophages

*Anaf V et al, Hum Reprod 2000*  
*Berkley KJ et al, Science 2005*
Nerve growth factor

NGF plays an important role in mediating neuropathological and non neuropathological pain. Trk-A is the high affinity receptor for NGF and is an essential component in the mediation of the NGF response.

NGF expression was significantly stronger in deep endometriosis than ovarian and peritoneal endometriosis. This was observed in the glands and in the stroma during the proliferative and the secretory phase.

Anaf et al Hum Reprod 2002

Why is it painful?

Because it is often undiagnosed and overlooked by clinicians!!
Pain is a learning experience

✓ Therefore

✓ A delayed diagnosis
  ✓ increases the severity of pain
  ✓ worsens the prognosis

Endométriose
Maladie souvent négligée

✓ Délai entre le début de la maladie a été évalué entre 6 et 9 ans dans des population de patientes anglo saxonnnes

✓ Hadfield et al (1996) délai avant le diagnostic de
  ✓ 11.7± 9.05 années aux USA
  ✓ 7.96 ± 7.92 années en Angleterre
Relationships between delay before surgical diagnosis and severity of disease in patients with symptomatic deep infiltrating endometriosis: A prospective study

Matsuzaki S., Canis M., Pouly J.L., Botchorishvili B., Houle C., Jardon K., Rabischong B., Mage G.

Polyclinique de l’Hotel Dieu, CHU Clermont-Ferrand, France

Objective

Is delay between onset of pain symptoms and surgical diagnosis associated with severity of disease in patients with endometriosis?
Patients with deep infiltrating endometriosis (DIE)

- Definition
  - deeper than 5 mm under the peritoneal surface.

- Inclusion criteria
  - first laparoscopy for pain symptoms
  - surgically and histologically confirmed DIE

- Exclusion criteria
  - history of previous pelvic surgery

Methods

- Face-to-face interviews:
  - Data on pain symptoms and other clinical information
  - between hospital admission and surgery

- Score of the revised American Society for Reproductive Medicine classification (rAFS)
Study population (n=95)

Age: median 31 y.o. (range 22-44)

Oct. 2001-Apr. 2005

Stage V: score >70


Delay and rAFS stage

Median delay: 5.0 years

*P<0.003
Delay and adnexal adhesion score

- Delay (median) vs. rAFS score
  - 0 delay
  - 1 to 31 delay
  - 32+ delay
  - *P<0.001

Delay and the size of DIE

- Delay (median) vs. rAFS score
  - (1 cm<)
  - (1 to 3 cm)
  - (3 cm>)
  - *P<0.001
Patients (n=20): Onset of pain at age < 20

In our study population, 60% (n=9) of patients with stage V (n=15) disease had pain symptoms as adolescents.

Adolescent Endometriosis: Diagnosis and Treatment Approaches

Marc R. Laufer, MD, Joseph Sanfilippo, MD, MBA, and Gillian Rose, MD, MBBS, MRCOG

*Department of Surgery, Children’s Hospital-Boston; Division of Reproductive Endocrinology, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women’s Hospital; and Harvard Medical School, Boston, Massachusetts, USA. 
7University of Pittsburgh School of Medicine and Magee-Women’s Hospital, Pittsburgh, Pennsylvania, USA. 
*Directorate of Women’s and Children’s Services, Queen Charlotte’s and Chelsea Hospital, London, England

- Adolescents frequently complain of dysmenorrhea and pelvic pain.
- Studies have shown that 25% to 38.3% of adolescents with chronic pelvic pain have endometriosis.
- Numerous series have shown rates of endometriosis at 50% to 70% of adolescents undergoing laparoscopy for pelvic pain who did not have control of pelvic pain with OCPs and NSAIDs.
Discussion

Patients with stage V: extremely long delay (median 14.0 years)

Delay, in particular, an extremely long delay, negatively affect quality of life in patients with DIE by

1. Creating a long duration of painful symptoms without an accurate diagnosis

2. worsening the prognosis for fertility: stage V (score >70)  
   (Canis et al., Fertil Steril. 1992, 57:691-2)

2. increasing the risk for repeated operative procedures: stage V (score >70) (Abotte et al., Hum Reprod. 2003, 18:1922-7)

Conclusions

✓ An earlier laparoscopic diagnosis might detect symptomatic DIE at a time when adhesions are less severe and lesions are of a smaller size.

✓ One of the strategies to prevent disease progression and ameliorate quality of life in endometriosis patients might be to solve the problem of diagnostic delay.
Conclusions

✓ Delay in patients whose pain symptoms began during adolescence was particularly long.

✓ One of the targets to solve the problem of diagnostic delay in endometriosis might be to focus on adolescent patients.

Adolescent Endometriosis

Table 1. Symptoms of Adolescents with Endometriosis

<table>
<thead>
<tr>
<th>Presenting Symptoms</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclic and cyclic pain</td>
<td>62.5</td>
</tr>
<tr>
<td>Acyclic pain</td>
<td>28.1</td>
</tr>
<tr>
<td>Cyclic pain</td>
<td>9.4</td>
</tr>
<tr>
<td>Gastrointestinal pain</td>
<td>34.3</td>
</tr>
<tr>
<td>Urinary symptoms</td>
<td>12.5</td>
</tr>
<tr>
<td>Irregular menses</td>
<td>9.4</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>6.3</td>
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☐ An ultrasound should be utilized to exclude the possible existence of a pelvic mass or structural anomaly.
An example

- Severe and old primary dysmenorrhea treated by oral contraception
- After stopping oral contraception, pain recurrence with digestive symptoms and increasing dyspareunia
- Vain and useless consultations for 5 years

- Laparoscopy shows:

Rectovaginal Nodule $\geq 3$ cm
Nodule > 3 cm

- Uterus
- Nodule

Rectal exeresis

- Muscular injury
- Nodule
- Rectum
Final View

End of the history

✓ Rectovaginal fistula
✓ 6 months colostomy
✓ Fistula cicatrization
✓ Laparoscopic adhesiolysis
✓ 3 spontaneous pregnancies et 3 C-sections related to previous rectovaginal fistula
That should be avoided !!!

To avoid similar situations.

- You need two very sophisticated instruments available everywhere:

- Two ears and one or two fingers !!!
Listen, listen, listen

✓ Be aware of the existence of dysmenorrhoea

✓ by patients
✓ by GP doctor
✓ by gynecologists

Listen, listen, listen

✓ Objective assessment of pain, VLS

✓ Social dysfunction:
  ✓ Loss of work efficiency…according to poor pain management

✓ Kind of pain killer, treatment duration

✓ Personal and familial history ++
Examine, examine, examine

- Be patient
- Gently
- Slowly
- Do it again +++++
- During menstruation (better sensitivity)

Speculum examination

- Research of characteristic blue lesion
  (5 to 17%)

  - Vaginal wall
  - Retrocervical area
Digital examination of vagina

Allows:

- Uterus examination
- Adnexal masses palpation sometimes
- Seldom normal ovaries examination
- Always vaginal wall examination and specially rectovaginal cul de sac
- Nodular lesion research, sensitive stiffness +/- der

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Anaf et al Hum Reprod 2002
Imaging

- Ultrasound is essential
  - Adnexal masses research
  - Adenomyosis
  - Rectovaginal nodule

- MRI

- Endorectal ultrasound
- IVU

Conclusions

- Endometriosis is painful

- The patient history is essential!

- The management should be based on the clinical symptoms of the patient

- The delay should be improved

- Multidisciplinary approach

- Adequate surgical treatment should be performed in expert centers
M Canis
JL Pouly
G Mage
B Rabischong
S Matsuzaki
R Botschorschvili
S Tamburro
Dept Gyn Obst

C Darcha
P Dechelotte
Dept Pathology

E Albuisson
P Jaffeux
A Aublet Cuvelier
C Lasnier
Dept of Biostatistics

F Bolandard
Ph Duband
M Bonnin
JM Constantin
JE Bazin

Dept Anesth.