European Menopause and Andropause Society

EMAS

Endometriosis - another significant contributor

EMAS School, 14 May 2020

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EMAS board member

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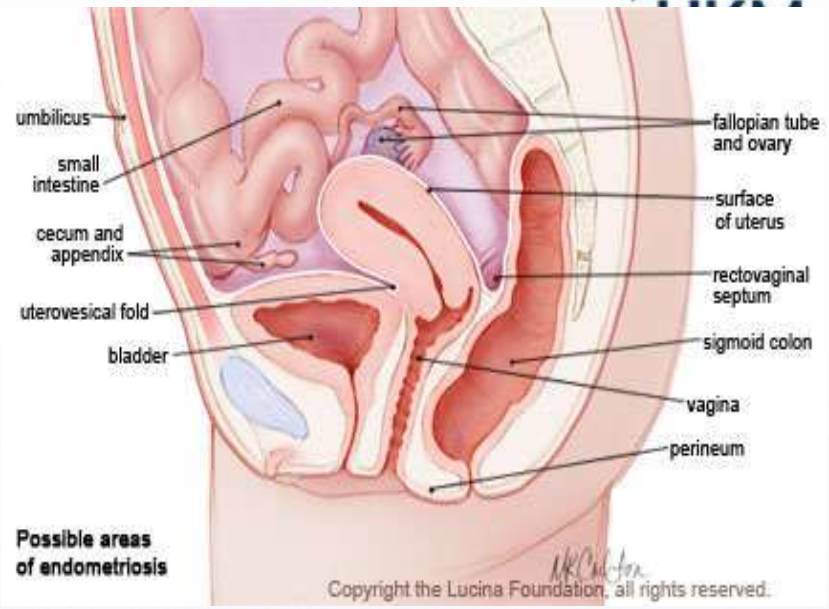
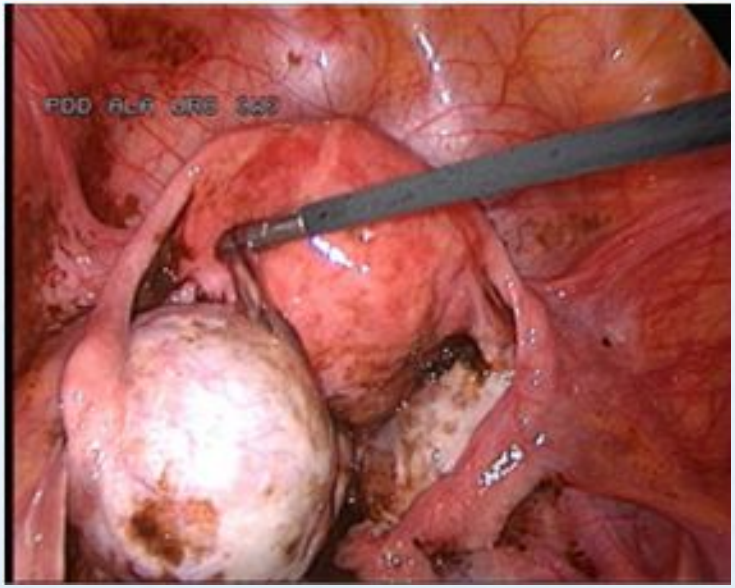
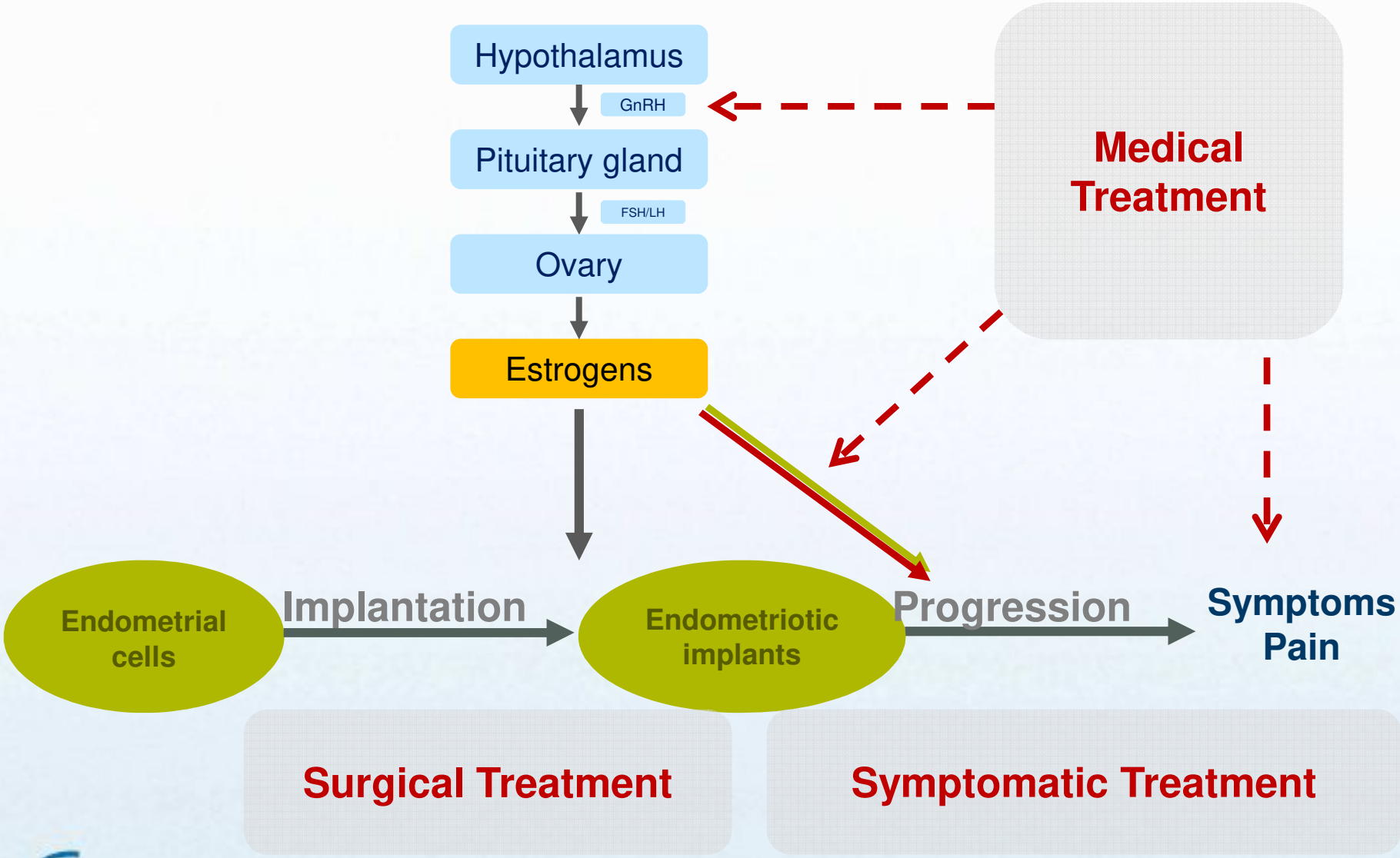
Endometriosis

- Growth of endometrial tissue outside of the uterus (e.g. in the peritoneum, rectovaginal septum, ovary)
- Benign condition in upto 10% of women
- Frequent cause of unspecific, menstrual cycle-dependent pelvic pain
- It is estimated that 30-40% of women with endometriosis may not be able to have children





Treatment Options for Endometriosis



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Medical Therapeutic Options

- Analgesics
- GnRH-analogues (agonists, antagonists) ± add back-therapy
- Progestins /Dienogest
- Oral Contraceptives
- Danazol
- Levonorgestrel-IUD
- Aromatase inhibitors

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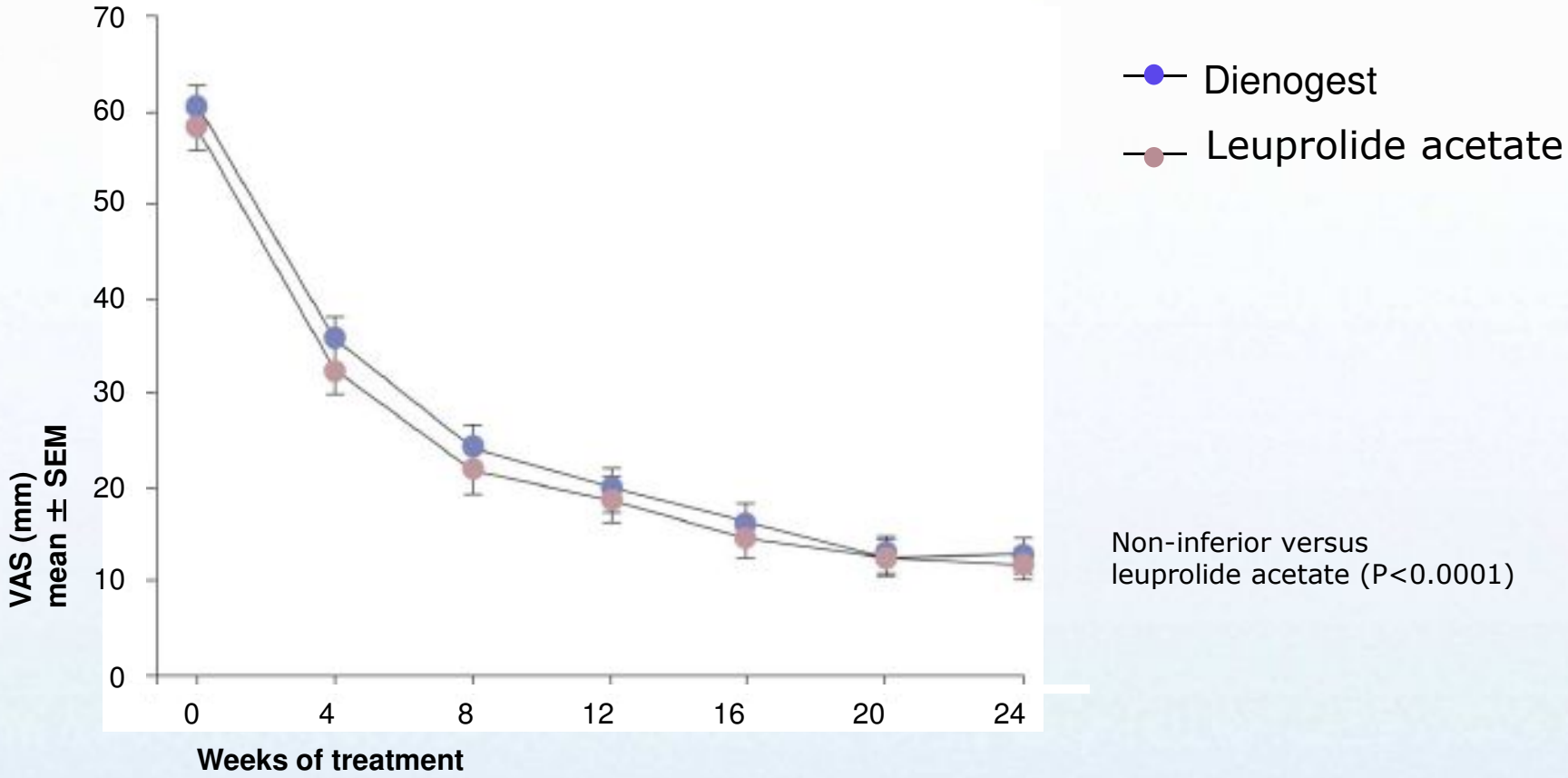
Efficacy: Reduction of Pain
Dienogest versus Leuprolide Acetate



Non-inferior versus leuprolide acetate (P<0.0001)

VAS, visual analog scale.

Strowitzki T, *et al.* Hum Reprod 2010.

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Medical Therapy of Endometriosis (VIPOS)

Country	DNG		GnRH-a		Danazol		CHC		Other progestins		Other NAED		Allocation unknown**		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Germany	512	27.1	81	4.3	0	0.0	941	49.9	348	18.4	4	0.2	1	0.1	1,887
Poland	621	52.7	11	0.9	110	9.3	383	32.5	44	3.7	7	0.6	3	0.3	1,179
Russia	1,053	8.0	1,786	13.6	241	1.8	7,838	59.6	2,155	16.4	86	0.7	0	0.0	13,159
Hungary	656	7.3	422	4.7	1	0.0	7,570	84.2	311	3.5	32	0.4	0	0.0	8,992
Switzerland*	63	82.9	0	0.0	0	0.0	9	11.8	4	5.3	0	0.0	0	0.0	76
Ukraine	346	13.6	278	10.9	537	21.1	775	30.4	575	22.6	18	0.7	18	0.7	2,547
Total	**3,251**	**11.7**	**2,578**	**9.3**	**889**	**3.2**	**17,516**	**62.9**	**3,437**	**12.3**	**147**	**0.5**	**22**	**0.1**	**27,840**

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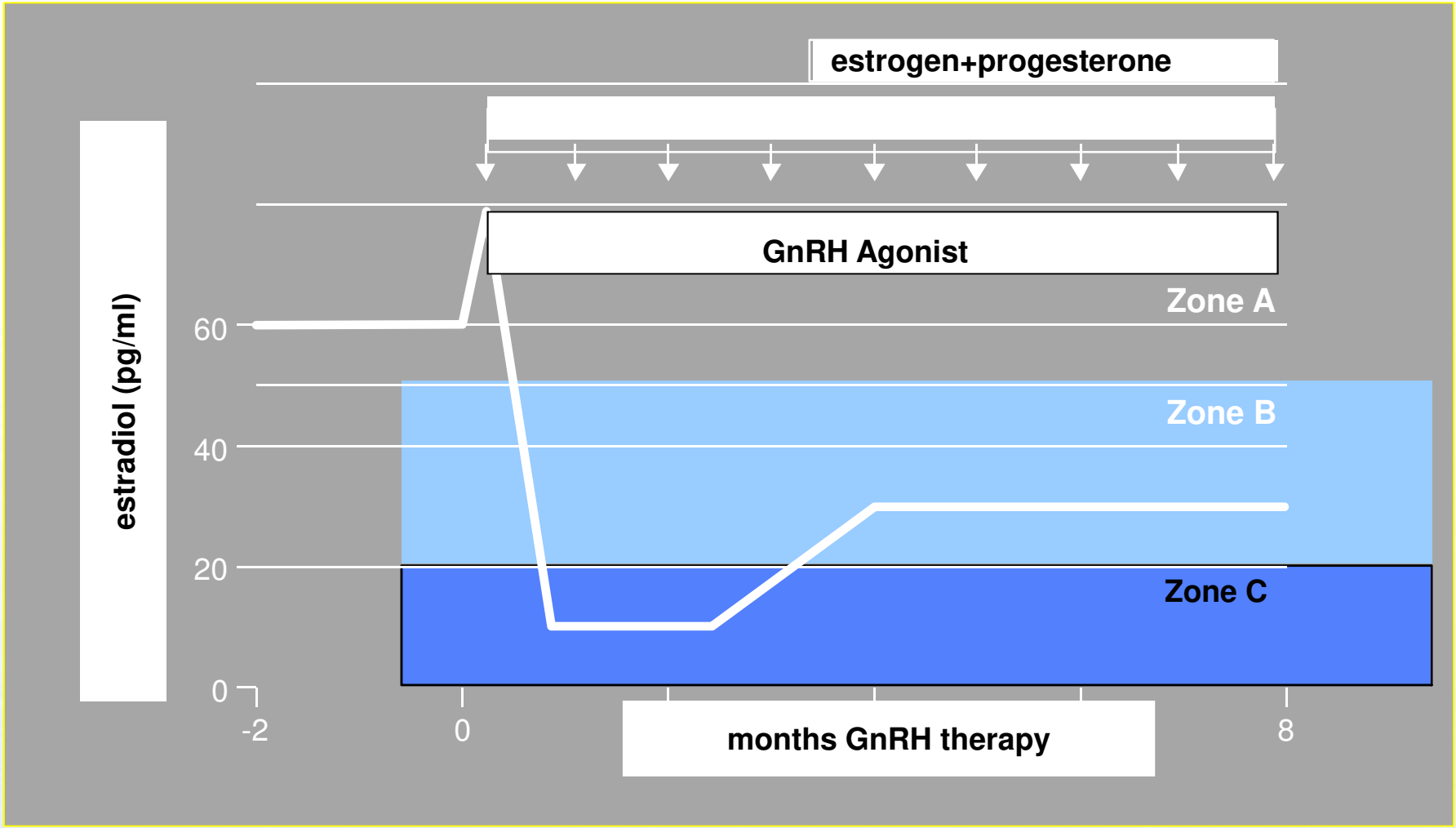
Treatment of Endometriosis: Estrogen-threshold hypothesis



Barbieri, RL. Infertil Reprod Med Clin N Amer 1992; 3: 187–200

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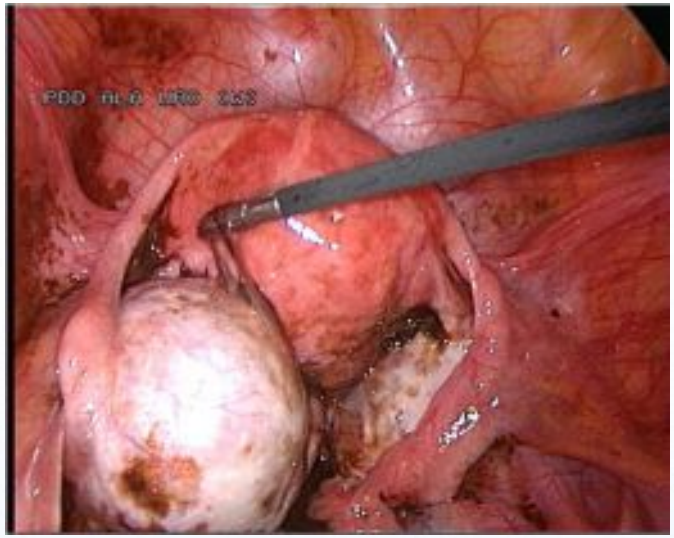
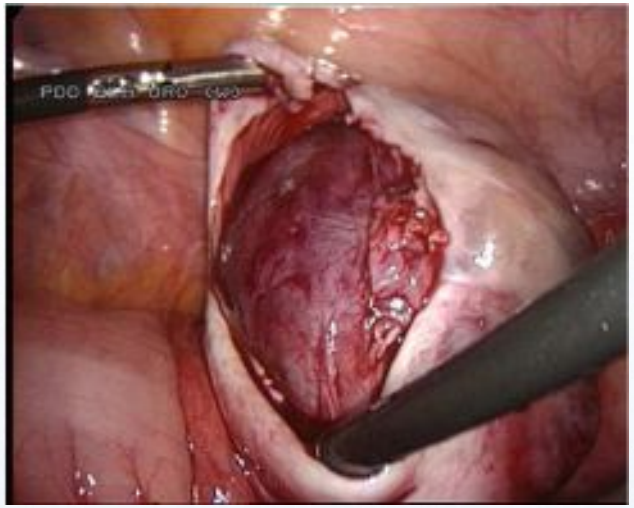
Effects of Surgery on Ovarian Reserve





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AMH: preop and postop at laparoscopy

	Endometrioma group (n=40)	Tubal factor infertility group (n=36)	Other benign ovarian cyst group (n=22)	P
Preoperative	1.53 ± 1.37[a]	2.82 ± 1.74[c]	2.20 ± 1.23[b]	0.001
Postoperative	0.69 ± 0.89[a]	2.80 ± 1.57[c]	1.48 ± 0.86[b]	
Rate of decline	0.62 ± 0.35	0.02 ± 0.15	0.32 ± 0.30	<0.001

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Chen et al 2014

Treatment of Endometriosis
Ovarian function and age at menopause

- Ovarian endometrioma
  - No endometrioma (peritoneal only): 45.1 ± 3.0 years
  - Monolateral endometrioma + surgery: 47.1 ± 3.5 years
  - Bilateral endometrioma + surgery: 42.1 ± 5.1 years

- Mild peritoneal endometriosis: 47.1 ± 3.5 years

- Effect depends highly on the surgery technique used
  - Ablative surgery: lower pregnancy rate, higher recurrence rate
  - Excisional surgery: injuries of ovarian vascular bed, ovarian trauma, follicles removal
  - Combined technique: no reduction of ovarian volume or number of antral follicles, but less follicles in removed tissue

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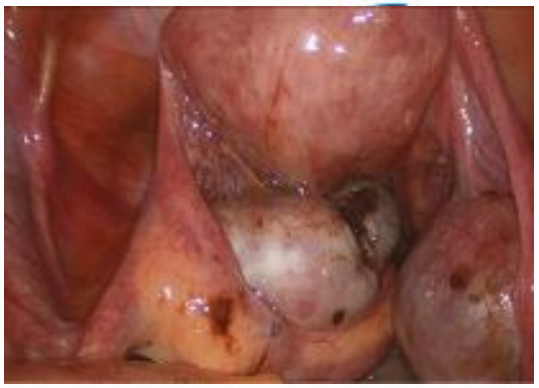
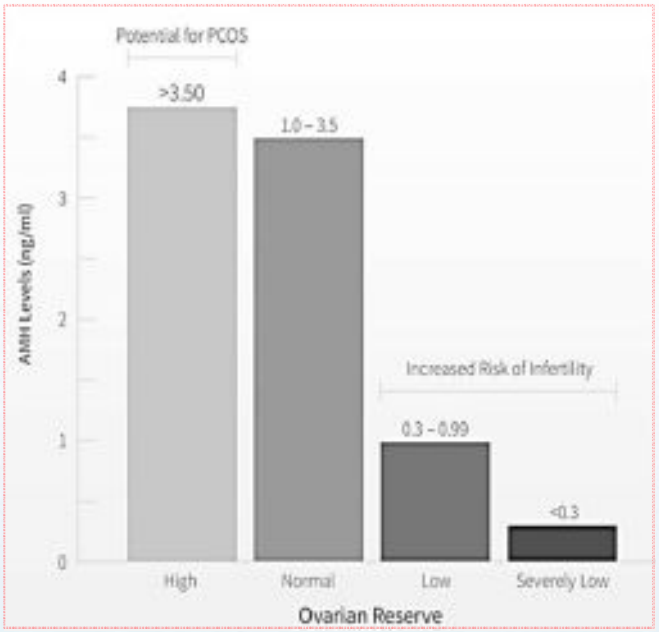
Coccia et al. 2011
Hart RJ et al., 2008

Benefits of Fertility Preservation in Endometriosis





Patients with:

1. Endometrioma (especially bilateral)
2. history of ovarian surgery
3. isolated deep endometriosis

Effects on retrieved oocyte quantity to be considered

- Age (p = 0.001)
- AMH levels (p = 0.001)

D'Argent et al. 2020

Surgical menopause:
Indications

- Pelvic pain or endometriosis (31.7%);
- Gynecologic malignancy (20.6%),
- BRCA carrier (17.4%);
- Breast cancer (9.5%);
- Lynch syndrome (4.8%);
- Other (abnormal uterine bleeding, pelvic mass, pelvic organ prolapse, vulvar intraepithelial neoplasia grade 3) (15.8%).

Garg et al. 2020

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HRT in women with history of endometriosis

- Issue:
  - Hormone replacement therapy (HRT) in climacteric women is debated
    - Possible reactivation of residual endometriosis
    - Possible production of new implants
    - Potential risk of malignant transformation
  - **But** women with a history of endometriosis are at particular risk of the long term consequences of estrogen deficiency
    - Premature or early menopause is a risk for
      - Overall mortality
      - Cardiovascular disease
      - Dementia
      - Osteoporosis
      - Parkinsonism
  - **Need of thoughtful HRT management**

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Shuster et al. 2010

Treatment of menopausal women with a history of endometriosis (EMAS, 2010)

Recommendations for HRT treatment

- Estrogen-based hormone therapy is required in women with premature or early menopause until the average age of the natural menopause and should be considered in older women with severe climacteric symptoms
- The data regarding hormone therapy regimens are limited
  - It may be safer to give either continuous combined estrogen–progestogen therapies or tibolone in both hysterectomised and nonhysterectomised women as the risk of recurrence and malignant transformation of residual endometriosis may be reduced
- Alternative pharmacological treatment for climacteric symptoms or skeletal protection if indicated should be considered in women not taking hormone therapy
- Herbal preparations are not recommended as their efficacy is uncertain and some may contain estrogenic compounds

**Moen, M. H., M. Rees, et al. (2010).
"EMAS position statement: Managing the menopause in women with a past history of endometriosis." Maturitas 67(1): 94-97.**

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