

Historic Endometriosis References

Halme, J., et al. (1984). "Retrograde menstruation in healthy women and in patients with endometriosis." *Obstet Gynecol* 64(2): 151-154.

Blood was found in the peritoneal fluid in 90% of women with patent tubes at laparoscopy during perimenstrual time. If the fallopian tubes were occluded, then only 15% of patients had evidence of blood in the pelvis. Also, 90% of patients with endometriosis and eight of nine women on oral contraceptives had bloody fluid during the menstrual period. The present observations indicate that retrograde menstruation through the fallopian tubes into the peritoneal cavity is a very common physiologic event in all menstruating women with patent tubes.

Heaps, J. M., et al. (1990). "Malignant neoplasms arising in endometriosis." *Obstet Gynecol* 75(6): 1023-1028.

Ten cases of malignant tumors arising in foci of gonadal and extragonadal endometriosis are reported and added to 195 previously reported cases from the English literature. The ovary was the primary site in 165 (78.7%) of the cases, whereas extragonadal sites represented 44 (21.3%). Endometrioid adenocarcinomas accounted for 69% of the lesions, clear-cell carcinomas 13.5%, sarcomas 11.6%, and rare cell types 6%. Extragonadal lesions were mostly endometrioid tumors (66%) and sarcomas (25%). Tumors arising in endometriosis were predominantly low grade and confined to the site of origin. Radiation therapy was often able to control completely tumors limited to the pelvis, but was not beneficial in metastatic disease. Only one patient had a response to chemotherapy. Fourteen patients received postoperative progestin therapy, with a 77% 5-year survival. Follow-up has been reported in 86 patients. The tumor was either confined to the ovary (57), confined to the extragonadal site of origin (11), or spread throughout the peritoneal cavity (18). With each of these situations, the 5-year survival was 65, 100, and 10%, respectively. Fourteen patients had malignant transformation in endometriosis associated with presumed estrogenic stimulation; most lesions (69%) were well differentiated and the 5-year survival was 82%. After surgical resection, we recommend that progestin therapy be included in the treatment of cancer arising in endometriosis. The actual frequency of malignancy arising in endometriosis may be higher than reported.

Jenkins, S., et al. (1986). "Endometriosis: pathogenetic implications of the anatomic distribution." *Obstet Gynecol* 67(3): 335-338.

The authors have reassessed the anatomic distribution of ectopic endometrium by the laparoscopic study of the location of implants, adhesions, and uterine position in 182 consecutive patients with infertility and endometriosis. The ovary was the most common site of implants with 54.9% having either unilateral or bilateral involvement. This was followed, in order of frequency, by the posterior broad ligament (35.2%), the anterior cul-de-sac (34.6%), the posterior cul-de-sac (34.0%), and the uterosacral ligament (28.0%). Adhesion formation followed the same anatomic distribution. No patients were noted to have endometriosis of the cervix and vagina. Endometriosis of the anterior

compartment (anterior cul-de-sac, anterior broad ligament, and anterior uterine serosa) was significantly more common in patients with anterior uteri (40.7%) versus patients with posterior uteri (11.8%, P less than .0005). Exclusive anterior compartment disease was found only in patients with anterior uteri, and significantly more commonly in patients with severely anteflexed uteri (P less than .005). These data suggest that factors influencing implantation of retrograde menstrual debris include: the dependent pooling of peritoneal fluid as affected by uterine position; epithelial cell type at the site of implantation; unique ovarian susceptibility; route of entry; and mobility of the pelvic structures. The data support the Sampson hypothesis of retrograde menstruation as the primary model of development of endometriosis.

Kennedy, S., et al. (2005). "ESHRE guideline for the diagnosis and treatment of endometriosis." *Hum Reprod* 20(10): 2698-2704.

The objective was to develop recommendations for the diagnosis and treatment of endometriosis and its associated symptoms. A working group was convened comprised of practising gynaecologists and experts in evidence-based medicine from Europe, as well as an endometriosis self-help group representative. After reviewing existing evidence-based guidelines and systematic reviews, the expert panel met on three occasions for a day during which the guideline was developed and refined. Recommendations based solely on the clinical experience of the panel were avoided as much as possible. The entire ESHRE Special Interest Group for Endometriosis and Endometrium was given the opportunity to comment on the draft guideline, after which it was available for comment on the ESHRE website for 3 months. The working group then ratified the guideline by unanimous or near-unanimous voting; finally, it was approved by the ESHRE Executive Committee. The guideline will be updated regularly, and will be made available at <http://www.endometriosis.org/guidelines.html> with hyperlinks to the supporting evidence, and the relevant references and abstracts. For women presenting with symptoms suggestive of endometriosis, a definitive diagnosis of most forms of endometriosis requires visual inspection of the pelvis at laparoscopy as the 'gold standard' investigation. However, pain symptoms suggestive of the disease can be treated without a definitive diagnosis using a therapeutic trial of a hormonal drug to reduce menstrual flow. In women with laparoscopically confirmed disease, suppression of ovarian function for 6 months reduces endometriosis-associated pain; all hormonal drugs studied are equally effective although their side-effects and cost profiles differ. Ablation of endometriotic lesions reduces endometriosis-associated pain and the smallest effect is seen in patients with minimal disease; there is no evidence that also performing laparoscopic uterine nerve ablation (LUNA) is necessary. In minimal-mild endometriosis, suppression of ovarian function to improve fertility is not effective, but ablation of endometriotic lesions plus adhesiolysis is effective compared to diagnostic laparoscopy alone. There is insufficient evidence available to determine whether surgical excision of moderate-severe endometriosis enhances pregnancy rates. IVF is appropriate treatment especially if there are coexisting causes of infertility and/or other treatments have failed, but IVF pregnancy rates are lower in women with endometriosis than in those with tubal infertility. The management of severe/deeply infiltrating endometriosis is complex and referral to a centre with the necessary expertise is strongly recommended. Patient self-help groups can provide invaluable counselling, support and advice.

Koninckx, P. R., et al. (1991). "Suggestive evidence that pelvic endometriosis is a progressive disease, whereas deeply infiltrating endometriosis is associated with pelvic pain." *Fertil Steril* 55(4): 759-765.

In a 3-year prospective study of 643 consecutive laparoscopies for infertility, pelvic pain, or infertility and pain, the pelvic area, the depth of infiltration, and the volume of endometriotic lesions were evaluated. The incidence, area, and volume of subtle lesions decreased with age, whereas for typical lesions these parameters and the depth of infiltration increased with age. Deeply infiltrating endometriosis was strongly associated with pelvic pain, women with pain having larger and deeper lesions. Because deep endometriosis has little emphasis in the revised American Fertility Society classification and after analyzing the diagnoses made in each class, considerations for a simplifying revision with inclusion of deep lesions are suggested. In conclusion, suggestive evidence is presented to support the concept that endometriosis is a progressive disorder, and it is demonstrated that deep endometriosis is strongly associated with pelvic pain.

Marcoux, S., et al. (1997). "Laparoscopic surgery in infertile women with minimal or mild endometriosis. Canadian Collaborative Group on Endometriosis." *N Engl J Med* 337(4): 217-222.

BACKGROUND: Minimal or mild endometriosis is frequently diagnosed in infertile women. It is often treated by resection or ablation of the lesions, but whether this improves fertility has not been established. We carried out a randomized, controlled trial to determine whether laparoscopic surgery enhanced fecundity in infertile women with minimal or mild endometriosis. **METHODS:** We studied 341 infertile women 20 to 39 years of age with minimal or mild endometriosis. During diagnostic laparoscopy the women were randomly assigned to undergo resection or ablation of visible endometriosis or diagnostic laparoscopy only. They were followed for 36 weeks after the laparoscopy or, for those who became pregnant during that interval, for up to 20 weeks of pregnancy. **RESULTS:** Among the 172 women who had resection or ablation of endometriosis, 50 became pregnant and had pregnancies that continued for 20 weeks or longer, as compared with 29 of the 169 women in the diagnostic-laparoscopy group (cumulative probabilities, 30.7 percent and 17.7 percent, respectively; $P=0.006$ by the log-rank test). The corresponding rates of fecundity were 4.7 and 2.4 per 100 person-months (rate ratio, 1.9; 95 percent confidence interval, 1.2 to 3.1). Fetal losses occurred in 20.6 percent of all the recognized pregnancies in the laparoscopic-surgery group and in 21.6 percent of all those in the diagnostic-laparoscopy group ($P=0.91$). Four minor operative complications (intestinal contusion, slight tear of the tubal serosa, difficult pneumoperitoneum, and vascular trauma) were reported (three in the surgery group and one in the control group). **CONCLUSIONS:** Laparoscopic resection or ablation of minimal and mild endometriosis enhances fecundity in infertile women.

Olive, D. L. and D. Y. Henderson (1987). "Endometriosis and mullerian anomalies." *Obstet Gynecol* 69(3 Pt 1): 412-415.

Although numerous etiologies for endometriosis have been proposed, it is clear that retrograde menstruation and cell-mediated lymphocytotoxicity each play a significant role in the disease's development. A comprehensive theory of pathogenesis of endometriosis holds that development of the disorder depends upon amount of retrograde menstruation and the ability of the immune response to

remove the debris. To test this theory, 64 women with mullerian anomalies and intra-abdominal surgery were evaluated for the presence or absence of endometriosis, patency of tubes, hematocolpos or hematometra, and outflow obstruction. Results demonstrated that endometriosis was present in ten of 13 women with functioning endometrium, patent tubes, and outflow obstruction, whereas it could be identified in only 16 of 43 women with no obstruction (77 versus 37%, P less than .01). Similarly, eight of nine women with hematocolpos or hematometra had endometriosis, while only 18 of 47 with functioning endometrium but no hematometra/hematocolpos had it (89 versus 38%, P less than .01). None of the eight women without endometrium had endometriosis. These data support the concept that an increase in retrograde menstruation will increase the likelihood of endometriosis.

Wheeler, J. M. (1989). "Epidemiology of endometriosis-associated infertility." J Reprod Med 34(1): 41-46.

To explain the great discrepancy between the prevalence estimates for endometriosis in the literature, a series of operations was studied from a combined patient population derived from a 21-physician collaborative. The reported discrepancy appears to have to do more with operative indications and technique than with an actual increase in the prevalence of endometriosis over time. The least-biased estimate for the overall prevalence of endometriosis in reproductive-age women is about 10% on the basis of a study of women operated on for symptoms other than those associated with endometriosis. Accepted criteria for causality applied to the endometriosis literature failed to demonstrate an association between endometriosis and infertility.

Wheeler, J. M. and L. R. Malinak (1987). "Recurrent endometriosis." Contrib Gynecol Obstet 16: 13-21.