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Structural abnormalities of the uterine wall in women with endometriosis and infertility visualized by vaginal sonography and magnetic resonance imaging

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In women with endometriosis, the peristaltic activity of the uterus is significantly enhanced and may even become dysperistaltic at midcycle. Since uterine peristalsis is confined to the endometrium and the subendometrial myometrium with its predominantly circular arrangement of muscular fibres it was assumed that this dysfunction might be associated with structural abnormalities that could be visualized by high resolution ultrasonography and magnetic resonance imaging (MRI). Therefore, the uteri of women with and without endometriosis were subjected to endovaginal sonography (EVS) and to MRI. In EVS, women with laparoscopically proven endometriosis and infertility exhibited an infiltrative expansion of the archimetra in that the halo surrounding the uterine endometrium and representing the subendometrial myometrium was significantly enlarged compared with controls. The expansion was more pronounced in older than in younger women. There was, however, no relationship between the width of the expansion and the severity of the endometriotic disease. Similar data were obtained by MRI in that the 'junctional zone' in women with endometriosis and infertility was expanded in comparison with controls. The results of this study provide further support to the notion that endometriosis is primarily a uterine disease.

Key words: adenomyosis/archimetra/endometriosis/junctional zone/uterine sonography

Introduction

There is growing evidence that endometriosis constitutes primarily a dysfunction and disease of the uterus with the spread and implantation of altered eutopic endometrial tissue outside the uterine cavity representing a secondary phenomenon (Leiva *et al*., 1994; Wingfield *et al*., 1995; Noble *et al*., 1996; Jolicoeur *et al*., 1998; for review: Leyendecker *et al*., 1998). Recently, by means of vaginal sonography of uterine peristalsis (VSUP) (Kunz *et al*., 1996), it was demonstrated that in women with endometriosis the peristaltic activity of the uterus is significantly enhanced and may even become dysperistaltic at midcycle (Leyendecker *et al*., 1996). Since uterine peristalsis is confined to the endometrium and the subendometrial myometrium with its predominantly circular arrangement of muscular fibres (stratum subvasculare of the myometrium or archimyometrium), it was assumed that this dysfunction might be associated with structural abnormalities that could be visualized by high resolution ultrasonography and magnetic resonance imaging (MRI). In order to test this hypothesis the uteri of women with and without endometriosis were subjected to endovaginal sonography (EVS) and to MRI.

Materials and methods

Subjects

A total of 74 patients of our infertility clinic with regular menstrual cycles aged 19–44 years (mean 32) consecutively entered this study after giving informed consent.

Of these women 41 (aged 19–44 years; mean 32) had a history of infertility of 1–10 years (mean 4) duration and were suffering from endometriosis as demonstrated by laparoscopy. Almost half of these patients were suffering from minimal or mild endometriosis ($n = 20$) and the rest from moderate or severe endometriosis ($n = 21$), according to the revised classification of the American Society of Reproductive Medicine (ASRM) (American Fertility Society, 1985). No additional factors responsible for the infertility could be demonstrated in these patients.

The control group consisted of 33 healthy women (aged 20–43 years; mean 32) with their husbands suffering from andrological infertility. In all controls the absence of endometriosis was confirmed by laparoscopy. Patients with irregular menstrual cycles, bleeding disorders or abnormalities of the uterine structure such as fibromas or malformations were excluded from the study. None of the healthy women complained of dysmenorrhoea.

Endovaginal sonography

The sonographic measurements were performed during the follicular ($n = 47$) and luteal phases ($n = 27$) of the cycles in both groups. The women were examined before the laparoscopic fertility work-up, hence before the diagnosis of endometriosis was established or excluded.

The analysis of the subendometrial myometrium was performed with a 7.5 MHz vaginal probe (Logiq 500, Kranzbühler, Solingen, Germany). After placing the probe in the dorsal fornix of the vagina, the dominant follicle or corpus luteum was localized. Then a mid-sagittal section of the uterus was adjusted and the endometrium and the myometrial layers were visualized. The layer comprising the subendometrial myometrium could be documented either as a sonographically hypoechoic band ('halo'), which regularly encircled the endometrium as well as the isthmical and cervical parts of the cervical canal, or, on the level of the uterine cavity, as a band with varying echogenicity and width.

The EVS real-time measurements were performed on the height of the transition between the upper and the lower half of the dorsal wall of the uterine corpus. There the diameters of the subendometrial myometrium ('halo') and of the total myometrium were documented

Table I. The diameter of the dominant follicle and the oestradiol and progesterone serum concentrations during the follicular and luteal phases of cycles in women with endometriosis (indicated with +) and healthy women (indicated with –) (values are means with ± SD)

Phase of the cycle	*n*		Follicular diameter (mm)[a]		Serum oestradiol (pg/ml)[a]		Serum progesterone (ng/ml)[a]	
	(+)	(–)	(+)	(–)	(+)	(–)	(+)	(–)
Follicular	26	21	14.9 ± 3.2	14.5 ± 4.0	98 ± 67	50 ± 39	0.3 ± 0.2	0.5 ± 0.3
Luteal	15	12	–	–	72 ± 43	52 ± 29	6.5 ± 4.9	4.7 ± 3.8

[a]There were no significant differences between the patients and these controls.

by electronic calipers and expressed in millimetres. The sonographic measurements were performed by two investigators (G.K., G.L.). During most of the measurement both investigators were present and there was always consensus with respect to the placement of the calipers.

After each scan a venous blood sample was drawn in order to determine oestradiol and progesterone serum concentrations.

Magnetic resonance imaging

In 15 women with endometriosis aged 26–36 years (mean 32) and in five healthy women aged 25–36 years (mean 32) the uteri were examined by means of MRI.

The uteri were imaged during the proliferative phase of the cycle by means of a superconducting magnet at 1.0 T (Magnetom Impact, Siemens, Erlangen, Germany) with the use of the body coil. T2-weighted fat-saturated turbo–spin echo sequences were used (TR/TE 3500–3800/90–99 ms, four acquisitions, slice thickness 3–4 mm, slice gap 0.1 mm) to obtain sagittal, axial and coronal planes. The image matrix consisted of 256 elements in frequency-encoded direction and of 154–220 elements in phase-encoded direction. The field of view was 263×350 mm. All examinations were performed in supine position. In order to compensate for artefacts due to respiratory movements, the abdominal wall was compressed by a broad belt. All patients received an antispasmodic intravenously (hyoscine butylbromide; Buscopanâ; Boehringer, Ingelheim, Germany) to decrease bowel peristalsis. The measurements of total myometrium and the diameters of the subendometrial myometrium ('junctional zone') were performed, as in EVS, in a mid-sagittal plane on the height of the transition between the upper and the lower half of the dorsal wall of the uterine corpus. There the diameters of the subendometrial myometrium and of the total myometrium were documented by electronic calipers and expressed in millimetres.

Hormone measurements

For the measurement of the serum oestradiol and progesterone concentrations, a commercially available radioimmunoassay kit was used (Serono Diagnostics GmBH, Freiburg, Germany).

Statistical analysis

The diameters of the 'halo' and the 'junctional zone' as well as of the total myometrium, as measured by EVS and MRI respectively, of infertile women with endometriosis were compared with those of women without endometriosis. The statistical analysis was performed using Student's *t*-test and significance was assumed when $P < 0.05$.

Results

Endovaginal sonography

Endovaginal sonography was performed during the follicular as well as during the luteal phase of the cycle. Table I summarizes the results of the serum oestradiol, progesterone and follicular size measurements obtained during the study. There was no difference between the patients and their controls with regard to the endocrine parameters within the respective phases of the cycle.

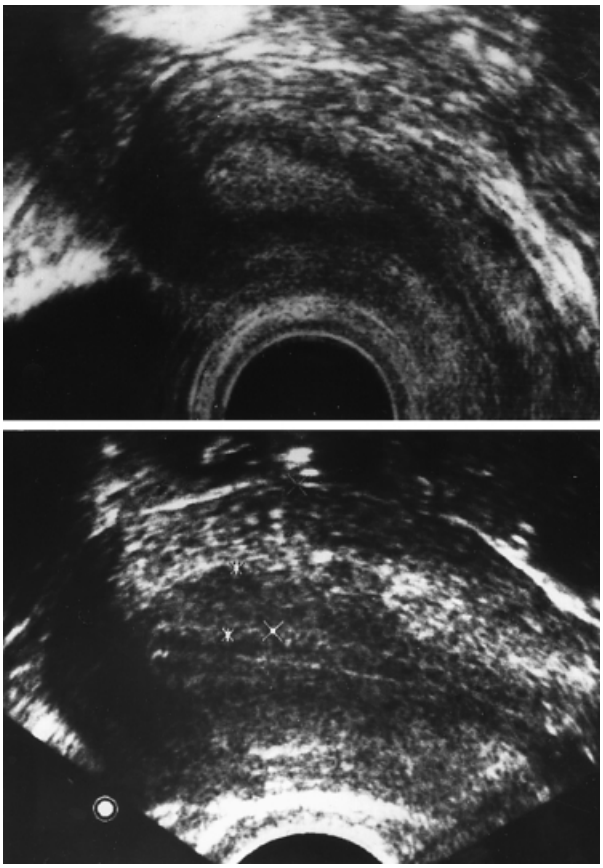

Figure 1. Vaginal sonography in a sagittal scan of the whole uterus of a women without endometriosis (top). The subendometrial myometrium is visible as a halo immediately adjacent to the endometrium. The thickness of the halo comprises about one-quarter of the total thickness of the myometrium on the mid-corporal section of the uterus. In a woman with endometriosis (bottom) the halo is irregularly expanded and comprises about the half of the thickness of the endometrium.

Typical examples of the sonographic findings in women with and without endometriosis are shown in Figure 1. Figure 2 summarizes the findings in 74 women. The mean (± SD) diameter of the total myometrium of 14.7 ± 2.96 mm in patients with endometriosis did not differ from the mean of 15.1 ± 2.4 mm in healthy women. The mean value of the

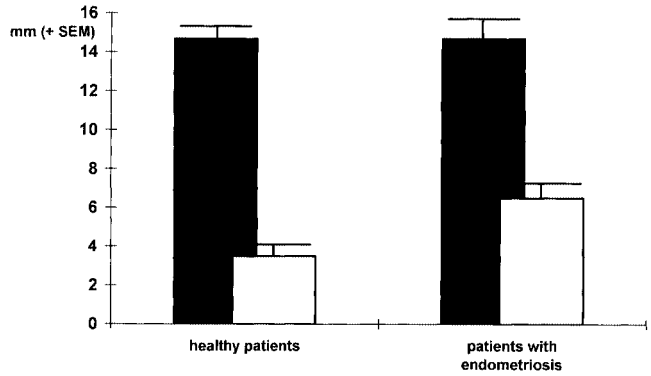

Figure 2. Summary of the findings of vaginal sonography in 41 women with endometriosis and infertility and 33 controls. In women with endometriosis the diameter of the halo (white bars) is significantly enlarged ($P < 0.0001$) in comparison to healthy women while the respective diameters of the thickness of the total myometrium (black bars) were the same.

diameter of the halo, however, was 6.5 ± 2.5 mm in women suffering from endometriosis and infertility and differed significantly ($P < 0.0001$) from the mean of 3.5 ± 1.1 mm in healthy subjects. The difference between the two groups of patients was seen in the follicular as well as in the luteal phase of the cycle.

Age of the patient and diameter of the halo were related in women with endometriosis. The halo of women with endometriosis aged <31 years (mean 27; $n = 13$) was significantly ($P < 0.05$) smaller (5.2 ± 1.5 mm) than that of patients aged ⩾31 years (mean age: 34 years; $n = 28$) (6.8 ± 2.5 mm). No such age-related difference was observed in the control group. The halo in healthy women aged <31 years (mean 25; $n = 10$) had a mean diameter of 3.4 ± 1.2 mm and that of healthy women ⩾31 years (mean 36; $n = 23$) had a mean diameter of 3.6 ± 1.1 mm.

No relationship was observed between the stage of the endometriotic disease and the mean diameter of the expanded halo.

In individual sonographic scans in women with endometriosis, particularly during the luteal phase, the halo was focally disrupted by areas of higher echogenicity (Figures 3 and 4), while in women without endometriosis the halo was usually intact (Figure 1 top). The disruptions were mostly localised on or close to the sagittal line of the uterine wall.

MRI

Figure 5 shows a representative sagittal MRI scan of a healthy woman while Figure 6 depicts the expansion of the junctional zone in a woman with endometriosis in a coronal section.

The expanded junctional zone exhibits variable signal intensity among different patients. While there is homogeneously low signal intensity of the expanded band in some patients similar to the normal junctional zone, there may be interspersed spots of higher signal intensity resulting in a more patchy image of the expanded junctional zone in other patients (Figure 7).

Figure 8 summarizes the findings in 15 women. The mean (± SD) diameter of the total myometrium of 17.2 ± 3.5 mm in patients with endometriosis did not differ from that of 17.4

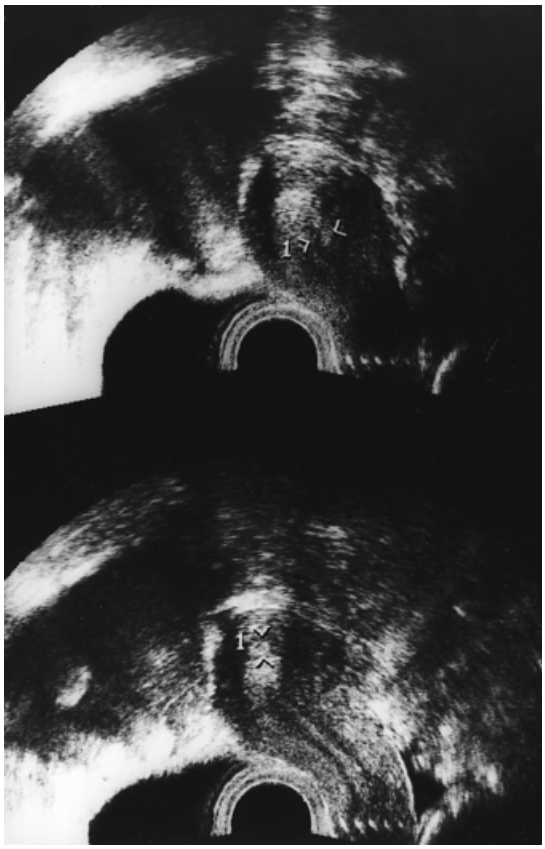

Figure 3. Vaginal sonography during the luteal phase of the cycle. The halo is disrupted with spots of high echogenicity in the posterior wall (top) and at the fundal part (bottom) of the uterus representing luteinized endometrial infiltrations.

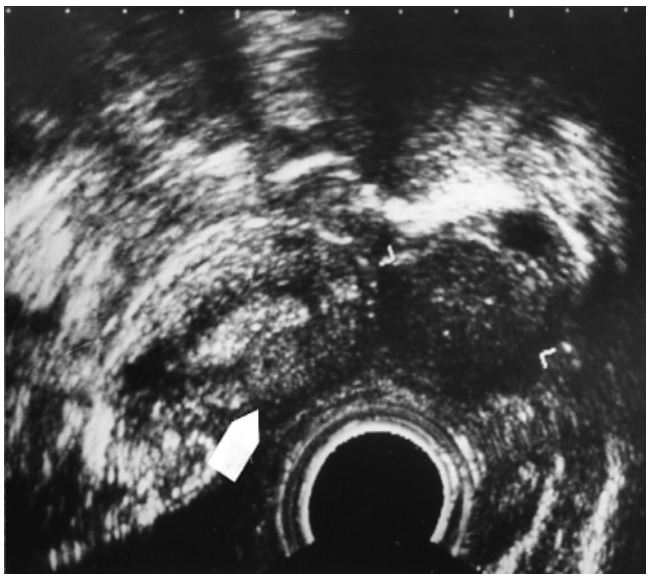

Figure 4. Vaginal sonography during the luteal phase showing a coronal section of the uterine corpus and the left ovary bearing an endometrioma (calipers). The anterior wall of the uterus shows near midline a focus of intermediate echogenicity extending from the endometrium through the stratum subvasculare into the stratum vasculare, resulting in a disruption of the continuity of the 'halo' (arrow).

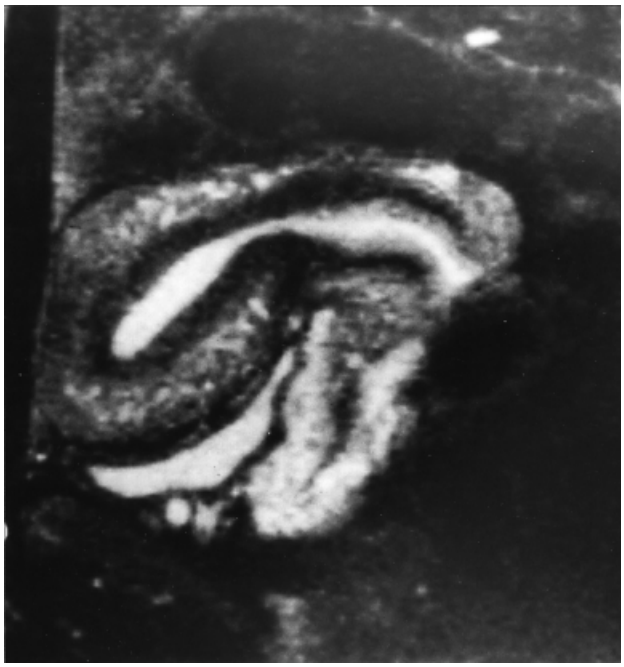

Figure 5. Magnetic resonance imaging of the sagittal section of the anteflected uterus of a fertile woman without endometriosis. The layers of the uterine wall can clearly be distinguished from each other. From inside to outside on the level of the uterine cavity: the endometrium with high signal intensity; the stratum subvasculare of the myometrium with low signal intensity ('junctional zone'), the stratum vasculare of the myometrium with high but more irregular signal intensity and the stratum supravasculare of the myometrium with intermediate signal intensity. The halo comprises about one-quarter of the thickness of the whole myometrium on the level of the uterine corpus.

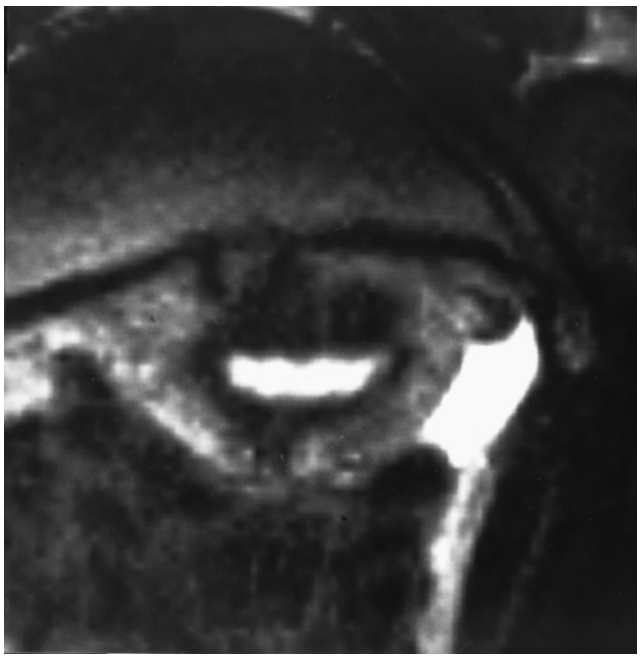

Figure 6. Magnetic resonance imaging of the uterus of a woman with endometriosis in a coronal section. The image shows a preponderance of the archimetrial infiltrations near the sagittal midline.

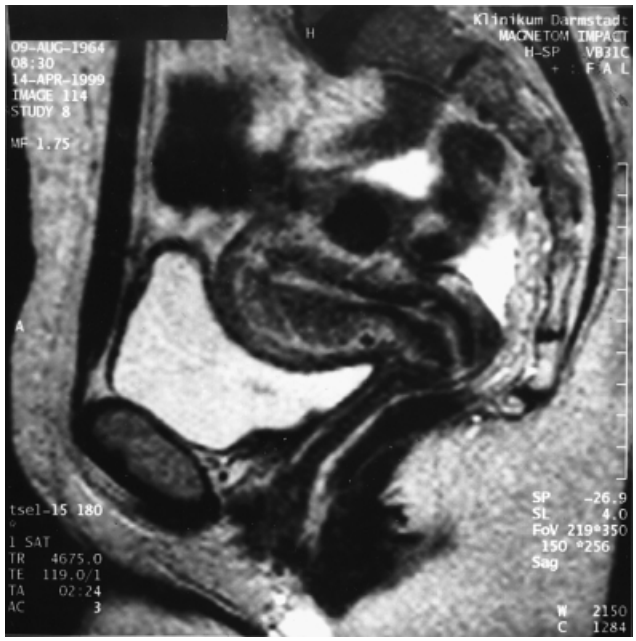

Figure 7. Magnetic resonance imaging of an anteflected uterus of a 34 year old woman suffering from infertility and endometriosis. The 'junctional zone' is broadened, especially in the anterior wall of the uterus, and has a patchy appearance in contrast to homogeneous low intensity appearance of the intact archimyometrium in the isthmical and cervical part of the uterus. There is a subserosal fibroma in the posterior wall of the uterus (dark spot of ~2 cm in diameter).

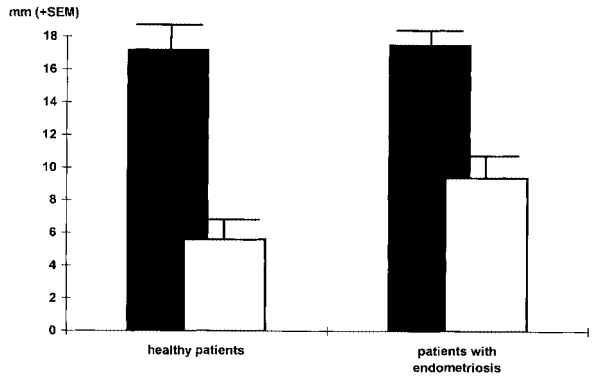

Figure 8. Summary of the findings of magnetic resonance imaging in 10 women with endometriosis and infertility and five controls. In women with endometriosis the diameter of the junctional zone (white bars) was significantly enlarged ($P < 0.04$) in comparison to healthy women while the respective diameters of the total myometrium (black bars) were the same.

$\pm$ 4.5 mm in healthy women. The mean value of the diameter of the junctional zone, however, was 9.4 $\pm$ 3.1 mm in women suffering from endometriosis and infertility and differed significantly ($P < 0.04$) from that of 5.6 $\pm$ 2.0 mm in healthy subjects.

Discussion

In EVS the endometrium is surrounded by a contour of low echogenicity (E), a 'halo', that extends, in a sagittal image of the whole uterus, from the fundus down to the cervix. In normal patients this contour has, on the level of the uterine

cavity, a thickness of about 3.5 mm thus comprising about one-quarter of the thickness of the whole myometrium (Figures 1 and 2). There is compelling evidence that this halo represents the stratum subvasculare of the myometrium, also termed the archimyometrium (Werth and Grusdew, 1898; Noe *et al*., 1999), which exhibits, according to histological data obtained in adult females, similar thickness (Werth and Grusdew, 1898).

In MRI the endometrium is surrounded by a similar contour of similar width characterized by low signal intensity (Figures 5 and 8). It had been termed the 'junctional zone' (Hricak *et al*., 1983) because it was considered to represent a hypodense interface between endometrium and myometrium. The stratum subvasculare, however, is directly adjacent to the endometrium (Werth and Grusdew, 1898; Wetzstein, 1965; Fujii *et al*., 1989; Scoutt *et al*., 1991). Thus, the 'junctional zone' in MRI represents the archimyometrium (Werth and Grusdew, 1898; Noe *et al*., 1999) as does the halo in sonography (Mitchell *et al*., 1990; Reinhold *et al*., 1996). The archimyometrium as measured by MRI, however, appears to be broader as measured by EVS (Figures 2 and 8) (Mitchell *et al*., 1990).

The low signal intensity of the archimyometrium in MRI and the apparent difference to the outer myometrial layers, the stratum vasculare and the stratum supravasculare have been discussed by several authors (Lee *et al*., 1985; Brown *et al*., 1991; Scoutt *et al*., 1991; Reinhold *et al*., 1998; Brosens *et al*., 1998). The subendometrial myometrium differs in various respects from the outer two layers. These differences include embryology (Werth and Grusdew, 1898; Leyendecker *et al*., 1998; Noe *et al*., 1999), function and activity during the menstrual cycle (Kunz *et al*., 1996; Leyendecker *et al*., 1996) as well as cellular (Wetzstein, 1965; Schwalm and Dubrauszky, 1966; Fujii *et al*., 1989; Scoutt *et al*., 1991) and biochemical composition (Campbell *et al*., 1998; Noe *et al*., 1999). Of the myometrial wall only the stratum subvasculare is of paramesonephric origin (Werth *et al*., 1898; Noe *et al*., 1999) and it is the only myometrial layer that is, with its cyclically changing peristaltic contractions, active during the menstrual cycle (Lyons *et al*., 1991; Kunz *et al*., 1996; Lesny *et al*., 1998a,b). A decrease of the relative content of connective tissue within the myometrium from the two outer to the inner layer (Schwalm and Dubrauszky, 1966; Brown *et al*., 1991) in addition to the more densely packed myocytes of the subendometrial myometrium (Scoutt *et al*., 1991) might be related to the specific embryology and function of the stratum subvasculare and might result in the specific image in MRI as well as in the hypoechogenic halo in EVS.

In women with endometriosis this halo or band of low signal intensity is significantly expanded in EVS (Figures 1 and 2) and MRI respectively (Figures 6–8). While this could be easily documented in MRI, it was more difficult in EVS and required real-time measurement (Ascher *et al*., 1994; Reinhold *et al*., 1995, 1996). In EVS, the expanded halo was in some cases hypoechoic (Figure 1), in other cases of intermediate echogenicity (Figure 4) or isoechoic in comparison to the middle layer of the myometrium. With real-time measurements, however, it was always possible to determine the boundary between the expanded halo and the outer myometrium.

There was no relationship between the thickness of the halo in EVS and the stage of the disease. These alterations, however, appear to progress with age since the expanded halo was significantly broader in women older than 31 years as compared to younger women. The thickness of the whole myometrium did not differ between women with and without endometriosis, suggesting that the widening of the halo in women with endometriosis represents, as in adenomyosis, infiltrative growth of endometrium. In all 10 hysterectomy specimens examined from women with endometriosis, infiltrations of endometrial glands with endometrial stroma into the myometrium resulting in the morphological picture of adenomyosis could be observed (M.Herbert, M.Loe, G.Kunz, *et al*., unpublished observations). Moreover, our findings obtained with EVS and MRI in women with external endometriosis are similar to or do not differ from the respective findings obtained in adenomyosis (Fleischer *et al*., 1986; Brosens *et al*., 1995, 1998; Reinhold *et al*., 1995, 1996, 1998), supporting the view that our findings in endometriosis represent endometrial infiltrations into the underlying myometrium.

These data add further evidence to the notion that endometriosis is primarily a disease of the archimetra (Leyendecker *et al*., 1998) with external endometriosis being a secondary phenomenon, which had been suggested previously on the basis of functional (Leyendecker *et al*., 1996), biochemical (Noble, *et al*, 1996; Jolicoeur *et al*., 1998), immunocytochemical (Wingfield *et al*., 1995) and immunological (Leiva *et al*., 1994; Ota *et al*., 1996, 1997, 1998) alterations of the uterus and the eutopic endometrium, respectively, in women with endometriosis.

Moreover, the data provide evidence that endometriosis and adenomyosis are merely clinical variants of the same disease process (Leyendecker *et al*., 1998), which have been separated from each other in the past due to various reasons such as the prevailing theories of the pathogenesis of endometriosis as well as clinical bias. The theory of transtubal shedding of normal endometrial cells and tissue elements by retrograde menstruations as well as the theory of coelomic metaplasia, (Sampson, 1927) directed research efforts to the peritoneum as the primary site of disease development. In addition, histological examination of the uterus is usually impossible when endometriosis is diagnosed in a sterile patient and it is unlikely that in the past, when hysterectomies were performed due to symptoms related to adenomyosis, the peritoneum was looked at for endometriotic foci or scars with the same scrutiny as it is done today by laparoscopy during a sterility work-up. That is probably why the reported association between adenomyosis and endometriosis and *vice versa* varies considerably over a large range (Emge, 1962; Bird *et al*., 1972; Pratt, 1972). Moreover, strict morphological criteria are required for the diagnosis of adenomyosis that exclude minor infiltrations of endometrium and stroma into the myometrium as insignificant (Emge, 1962; Bird *et al*., 1972; Ferenszy, 1998). Since the adenomyotic nodules, however, communicate with the uterine cavity (Otto, 1957), pathophysiologically, a continuous process from beginning to deep infiltration must exist. Our data suggest that the process of myometrial infiltration in endometriosis progresses with age.

Whether or not adenomyosis is accompanied by endometriosis may also largely depend on the localization of the active core of the adenomyotic nodule with respect to the proliferative and infiltrative potential of the cells. If this is, as in the beginning of the disease (adenomyosis sub-basalis; Bird *et al*., 1972), localized in or near the uterine cavity, there may be a great likelihood of transtubal seeding of altered endometrial tissue, which may even be enhanced by hyperperistalsis (Leyendecker *et al*., 1996) and increased intrauterine pressure (Mäkäräinen, 1988; Buletti *et al*., 1997). The transtubal seeding of altered tissue might be impeded when the active core of adenomyosis has grown into the depth of the myometrial wall or may even be terminated when the process of adenomyotic proliferation has 'burnt out'. This might be the pathophysiological basis of the notion (Evers, 1994) that all women might have endometriosis once in their lives. Eventually, an adenomyotic nodule might penetrate the uterine serosa with ensuing massive pelvic endometriosis (Jones and Jones, 1981).

In view of the fact that normal endometrium exhibits high signal intensity in MRI, which is even higher than that of the middle layer of the myometrium, the question has to be addressed more closely as to why the myometrial area of endometrial infiltration displays low signal intensity similar to the subendometrial myometrium, resulting in the impression of an expanded junctional zone.

Adenomyotic nodules are composed of endometrial glands, stroma and surrounding hyperplastic myometrium (Emge, 1962; Bird *et al*., 1972; Ferenszy, 1998; Reinhold *et al*., 1998). According to a prior report (Schwalm and Dubrauszky, 1966), the relative content of muscular versus connective tissue within the myometrium is increasing during pregnancy probably as a consequence of increasing steroid action. In adenomyosis as well as in endometriotic lesions and in the eutopic endometrium of women with endometriosis, a pathological expression of *P*450-aromatose resulting in elevated tissue concentrations of oestrogen has been demonstrated (Yamamoto *et al*., 1993; Noble *et al*., 1996, 1997; Kitawaki *et al*., 1997). Thus the lower signal intensity of the myometrium around adenomyotic nodules could result from increased local oestrogenic stimulation and hyperplasia. During pregnancy, however, there is no decrease in the signal intensity of the stratum vasculare. In contrast, the signal intensity of the subendometrial myometrium increases and the zonal differences become indistinct (Willms *et al*., 1995).

Alternatively, the hyperplastic myometrium around the adenomyotic nodules may be of paramesonephric origin, as previously suggested (Brosens *et al*., 1998), thus displaying the same structural characteristics as the stratum subvasculare of the myometrium with its low intensity appearance in MRI. This latter assumption may be derived from the observation that the archimyometrium is a differentiation of the endometrial stroma during embryology (Werth and Grusdew, 1898) and that during the menstrual cycle constant metaplastic changes between muscular and stromal cells are taking place at the myometrial–stromal interface (Fujii *et al*., 1989) that could also occur on the level of the infiltrating endometrial glands. Thus, adenomyotic/endometriotic infiltrations into the outer myometrium would consist according to this assumption of all archimetrial components, glandular and stromal endometrium as well as archimyometrium (Leyendecker *et al*., 1998; Noe *et al*., 1999). This conjecture has been recently supported by our observation that the muscular tissue of the adenomyotic nodules expanding and penetrating into the outer myometrium displays the same cyclic changes of steroid hormone receptor expression as the normal subendometrial myometrium, while the respective receptor expression of the surrounding outer myometrium remains on a constantly high level (Noe *et al*., 1999; M.Herbertz, M.Noe, G.Kunz, G.Mall, G.Leyendecker, unpublished observations). This characterizes adenomyosis as a disease of the archimetra (Leyendecker *et al*., 1998; Noe *et al*., 1999). In recto-vaginal endometriosis, with endometrial glands stroma and smooth muscle cells, all three components of the archimetra can be demonstrated. Recto-vaginal endometriosis, however, is believed to result from Müllerian remnants rather than from transplanted endometrium (Nisolle and Donnez, 1997).

It is well known that the composition of the adenomyotic nodules with respect to the relative distribution of endometrial and myometrial components varies to a large degree (Emge, 1962; Bird *et al*., 1972; Ferenszy, 1998; Brosens *et al*., 1998; Reinhold *et al*., 1998) as does the amount of remaining neometrial myometrium (Noe *et al*., 1999) in between the penetrating archimetrial myometrium (M.Herbertz, M.Noe, G.Kunz, G.Mall, G.Leyendecker, unpublished observations). This appears to have a differential impact on the images obtained with MRI and EVS respectively. While in MRI the expanded archimetra usually displays low signal intensity or may appear somewhat patchy (Reinhold *et al*., 1998; Figure 7) in comparison to the more homogeneous appearance of the normal subendometrial myometrium, in EVS, the echogenicity of the adenomyotic structures may vary considerably between patients and may even become similar to the surrounding myometrium allowing the determination of the boundary between adenomyotic and normal tissue only by real-time measurements.

This may also explain the finding that the normal archimyometrium appears to be thicker by MRI than by EVS measurement (Figures 2 and 8). In a transitional zone, muscular fibres of the archimyometrium blend with those of the stratum vasculare (Werth and Grusdew, 1898; Noe *et al*., 1999). The changing composition of the tissue within this transitional zone might differentially influence the images produced by MRI and EVS respectively. This might be the morphological basis of the finding that the boundary between the archimyometrium and the outer myometrium is different with MR imaging versus ultrasound (Mitchell *et al*., 1990).

We assume that, in the process of developing adenomyosis, archimyometrial expansion is secondary to endometrial infiltration. In MRI, early endometrial infiltration into the archimyometrium should result in focally increased signal intensity. Only following extensive metaplastic change of the endometrial stroma into archimetrial myometrium does either a patchy (Figure 7) image or an image with low signal intensity (Figure 6) result. In EVS, particularly during the luteal phase, when endometrium exhibits high echogenicity, early infiltration of the endometrium into the underlying myometrium results

in the disruption of the normal archimyometrial halo (Figures 3 and 4). According to our studies, a halo of normal thickness with no signs of focal infiltration is predictive of the absence of endometriosis (Figure 1 top).

In conclusion, infertile women with endometriosis show alterations of the myometrial wall in that, in both EVS and MRI, the archimetra is significantly expanded. These alterations are similar to or identical with those obtained in women with adenomyosis. These data further support the notion that endometriosis is primarily a uterine disease (Leyendecker *et al*., 1998).

References

American Fertility Society (1985) Revised American Fertility Society classification of endometriosis. *Fertil. Steril*., **43**, 351–352.

Ascher, S.M., Arnold, L.L., Patt, R.H. *et al*. (1994) Adenomyosis: prospective comparison of MR imaging and transvaginal sonography. *Radiology*, **190**, 803–806.

Bird, C.C., McElin, T.W. and Manalo-Estrella, P. (1972) The elusive adenomyosis of the uterus-revisited. *Am. J. Obstet. Gynecol*., **112**, 583–593.

Brosens, J.J., de Souza, N.M. and Barker, F.G. (1995) Uterine junctional zone: function and disease. *Lancet*, **346**, 558–560.

Brosens, J.J., Barker, F.G. and de Souza, N.M. (1998) Myometrial zonal differentiation and uterine junctional zone hyperplasia in the non pregnant uterus. *Hum. Reprod. Update*, **4**, 496–502.

Brown, H.K., Stoll, B.S., Nicosia, S.V. *et al*. (1991) Uterine junctional zone: Correlation between histological findings and MR imaging. *Radiology*, **178**, 409–413.

Bulletti, C., Rossi, S., de Ziegler, D. *et al*. (1997) The uterine contractility in endometriosis. International Meeting on Infertility and Assisted Reproductive Technology, Porto Cervo, Italy, June 11–14, 1997. Abstract Book, p. 129.

Campbell, S., Young, A., Stewart, C.J.R. *et al*. (1998) Laminin b2 distinguishes inner and outer layers of the human myometrium. *J. Reprod. Fertil*., Abstr. Series Number 22, 12.

Emge, L.A. (1962) The elusive adenomyosis of the uterus. *Am. J. Obstet. Gynecol*., **83**, 1541–1563.

Evers, J.L.H. (1994) Endometriosis does not exist; all women have endometriosis. *Hum. Reprod*., **9**, 2206–2209.

Ferenczy, A. (1998) Pathophysiology of adenomyosis. *Hum. Reprod. Update*, **4**, 312–322.

Fleischer, A.C., Kalemeris, G.C., Macin, J.E. *et al*. (1986) Sonographic depiction of normal and abnormal endometrium with histopathologic correlation. *J. Ultrasound Med*., **5**, 445–452.

Fujii, S., Konishi, I. and Mori, T. (1989) Smooth muscle differentiation at endometrio-myometrial junction. An ultrastructural study. *Virch. Archiv. A Pathol. Anat*., **414**, 105–112.

Hricak, H., Alpers, C., Crooks, L.E. and Sheldon, P.E. (1983) Magnetic resonance imaging of the female pelvis: initial experience. *Am. J. Radiol*., **141**, 119–1128.

Jolicoeur, C., Boutouil, M., Drouin, R. *et al*. (1998) Increased expression of monocyte chemotactic protein-1 in the endometrium of women with endometriosis. *Am. J. Pathol*., **152**, 125–133.

Jones, H.W. and Seegar Jones, G. (1981) *Novak's Textbook of Gynecology*, 10th edn. Williams and Wilkins, Baltimore/London, p. 443.

Kitawaki, J., Noguchi, T., Amatsu, T. *et al*. (1997) Expression of aromatase cytochrome P450 protein and messenger ribonucleic acid in human endometriotic and adenomyotic tissues but not in normal endometrium. *Biol. Reprod*., **57**, 514–519.

Kunz, G., Beil, D., Deininger, H. *et al*. (1996) The dynamics of rapid sperm transport through the female genital tract. Evidence from vaginal sonography of uterine peristalsis (VSUP) and hysterosalpingoscintigraphy (HSSG). *Hum. Reprod*., **11**, 627–632.

Lee, J.K.T., Gersell, D.J., Balfe, D.M. *et al*. (1985) The uterus: *in vitro* MR — anatomic correlation of normal and abnormal specimens. *Radiology*, **156**, 175–179.

Leiva, M.C., Hasty, L.A. and Lyttle, C.R. (1994) Inflammatory changes of the endometrium in patients with minimal-to-moderate endometriosis. *Fertil. Steril*., **62**, 967–972.

Lesny, P., Killick, S.R., Tetlow, R.L. *et al*. (1998a) Embryo transfer — can we learn anything new from the observation of junctional zone contractions? *Hum. Reprod*., **13**, 1540–1546.

Lesny, P., Killick, S.R., Tetlow, R.L. *et al*. (1998b) Uterine junctional zone contractions during assisted reproduction cycles. *Hum. Reprod. Update*, **4**, 440–445.

Leyendecker, G., Kunz, G., Wildt, L. *et al*. (1996) Uterine hyperperistalsis and dysperistalsis as dysfunctions of the mechanism of rapid sperm transport in patients with endometriosis and infertility. *Hum. Reprod*., **11**, 1542–1551.

Leyendecker, G., Kunz, G., Noe, M. *et al*. (1998) Endometriosis: A dysfunction and disease of the archimetra. *Hum. Reprod. Update*, **4**, 752–762.

Lyons, E.A., Taylor, P.J., Zheng, X.H. *et al*. (1991) Characterisation of subendometrial myometrial contractions throughout the menstrual cycle in normal fertile women. *Fertil. Steril*., **55**, 771–775.

Mäkäräinen, L. (1988) Uterine contractions in endometriosis: effects of operative and danazol treatment. *J. Obstet. Gynecol*., **9**, 134–138.

Mitchell, D.G., Schonholz, L., Hilpert, P.L. *et al*. (1990) Zones of the uterus: discrepancy between US and MR images. *Radiology*, **174**, 827–831.

Nisolle, M. and Donnez, M. (1997) Peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. *Fertil. Steril*., **68**, 585–596.

Noble, L.S., Simpson, E.R., Johns, A. and Bulun, S.E. (1996) Aromatase expression in endometriosis. *J. Clin. Endocrinol. Metab*., **81**, 174–179.

Noble, L.S., Takayama, K., Zeitoun, K.M. *et al*. (1997) Prostaglandin E2 stimulates aromatase expression in endometriosis-derived stromal cells. *J. Clin. Endocrinol. Metab*., **82**, 600–606.

Noe, M., Kunz, G., Herbertz, M. *et al*. (1999) The cyclic pattern of the immunocytochemical expression of oestrogen and progesterone receptors in human myometrial and endometrial layers: Characterisation of the endometrial-subendometrial unit. *Hum. Reprod*., **14**, 101–110.

Ota, H., Igarashi, S., Hayakawa, M. *et al*. (1996) Effect of danazol on the immunocompetent cells in the eutopic endometrium in patients with endometriosis: a multicenter cooperative study. *Fertil. Steril*., **65**, 545–551.

Ota, H., Igarashi, S., Hatazawa, J. and Tanaka, T. (1997) Distribution of heat shock proteins in eutopic and ectopic endometrium in endometriosis and adenomyosis. *Fertil. Steril*., **68**, 23–28.

Ota, H., Igarashi, S., Hatazawa, J. and Tanaka, T. (1998) Is adenomyosis an immune disease? *Hum. Reprod. Update*, **4**, 360–367.

Otto, K. (1957) Über Vorkommen und Ätiologie der Adenomyosis uteri mit Berichten über zwei atypische Fälle. *Zentralbl. Gynäk*., **79**, 471–480.

Pratt, J.H. (1972) The elusive adenomyosis of the uterus — revisited. Discussion. *Am. J. Obstet. Gynecol*., **112**, 591–592.

Reinhold, C., Atri, M., Mehio, A. *et al*. (1995) Diffuse adenomyosis: morphologic criteria and diagnostic accuracy of endovaginal sonography. *Radiology*, **197**, 609–614.

Reinhold, C., McCarthy, S., Bret, P.M. *et al*. (1996) Diffuse adenomyosis: Comparison of endovaginal US and MR imaging with histopathologic correlation. *Radiology*, **199**, 151–158.

Reinhold, C., Tafazoli, F. and Wang, L. (1998) Imaging features of adenomyosis. *Hum. Reprod. Update*, **4**, 337–349.

Sampson, J.A. (1927) Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am. J. Obstet. Gynaecol*., **14**, 422–429.

Schwalm, H. and Dubrauszky, V. (1966) The structure of the musculature of the human uterus — muscles and connective tissue. *Am. J. Obstet. Gynecol*., **94**, 391–404.

Scoutt, L.M., Flynn, S.D., Luthringer, D.J. *et al*. (1991) Junctional zone of the uterus: Correlation of MR imaging and histologic examination of hysterectomy specimens. *Radiology*, **179**, 403–407.

Werth, R. and Grusdew, W. (1898) Untersuchungen über die Entwicklung und Morphologie der menschlichen Uterusmuskulatur. *Arch. Gynäkol*., **55**, 325–409.

Wetzstein, R (1965) Der Uterusmuskel: Morphologie. *Arch. Gynecol*., **202**, 1–13.

Willms, A.B., Brow, E.D., Kettritz, U.I. *et al*. (1995) Anatomic changes in the pelvis after uncomplicated vaginal delivery: evaluation with serial MR imaging. *Radiology*, **195**, 91–94.

Wingfield, M., Macpherson, A., Healy, D.L. and Rogers, P.A.W. (1995) Cell proliferation is increased in the endometrium of women with endometriosis. *Fertil. Steril*., **64**, 340–346.

Yamamoto, T., Noguchi, T., Tamura, T. *et al*. (1993) Evidence for oestrogen synthesis in adenomyotic tissues. *Am. J. Obstet. Gynecol*., **169**, 734–738.

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