

## ENDOMETRITIS

# What is endometritis and does it require treatment?

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## The answer is not straightforward

The concept of lower genital tract infection with chlamydia or gonorrhoea causing cervicitis and vaginal discharge is familiar to most sexual health physicians. Likewise, upper genital tract infection with inflammation of the fallopian tubes and adnexae in the form of pelvic inflammatory disease (PID) is also a common clinical syndrome with well recognised implications for future fertility. It is assumed that most PID develops secondary to the spread of infection from the lower genital tract, through the uterine cavity into the upper genital tract. What is less certain, and where no clear guidance is currently available, is whether this intermediate step of endometritis is a distinct clinical condition in its own right and, if so, how it should be diagnosed and treated.

Endometritis is a pathological diagnosis with infiltration of the normal vascular architecture by inflammatory cells. Agreeing a precise histological definition of endometritis is difficult since a variety of different features are seen—the inflammatory infiltrate may be confined to the surface epithelium or spread more deeply into the stroma; inflammatory cells may comprise neutrophils and/or plasma cells; and lymphoid aggregates or subepithelial haemorrhages have also been reported. The features which correlate most closely to “true” PID are the presence of both neutrophils and plasma cells, leading to the most commonly accepted definition of endometritis which is five or more neutrophils per 400 power field in the superficial endometrium, in addition to one or more plasma cells per 120 power field in the endometrial stroma.<sup>1</sup>

Sampling of the endometrium is usually performed using an endometrial suction biopsy device, which is inserted through the cervix to obtain a small piece of endometrial tissue. This is generally a simple, well tolerated procedure performed in an outpatient setting. Unfortunately the fixing, staining, and reporting of the endometrial sample takes several days and even small delays in confirming the diagnosis and starting therapy for pelvic infection can have

serious effects on future fertility. This limits the clinical applicability of this approach for making a diagnosis, as does the theoretical risk of introducing infection into the upper genital tract when taking the endometrial biopsy.<sup>2</sup>

A more rapid assessment of endometrial inflammation can be obtained by looking at a Gram stained smear or wet mount of vaginal discharge. Increasing numbers of polymorphs in the discharge are associated with endometritis, although the correlation is not particularly strong.<sup>3</sup> The main purpose of looking for pus cells in vaginal secretions lies more in excluding PID than diagnosing it—the negative predictive value of such an approach is around 95%, compared to positive predictive value of only around 20%. In other words the absence of pus cells makes endometritis (and PID) very unlikely, but their presence lacks specificity. Other features on the vaginal smear such as reduced numbers of lactobacilli, may also support the diagnosis of endometritis but have not been rigorously assessed.

**One of the central questions in the management of endometritis is whether endometritis and PID are different aspects of the same disease, or separate clinical entities requiring different treatment and having a different prognosis**

Endometritis is commonly found in women who have otherwise uncomplicated lower genital tract infection. Around a quarter of women with cervical gonorrhoea or chlamydia will also have endometritis on endometrial biopsy, as do 15% of women with bacterial vaginosis.<sup>4</sup> Predicting which women will have endometritis as opposed to infection limited to the lower genital tract is difficult. The presence of endometritis is not associated with behavioural or demographic features such as age, ethnicity, condom use, or sex during menstruation.<sup>5</sup> The use of the oral contraceptive pill does not itself increase the risk of endometritis,<sup>6</sup> but it

does appear to increase the risk of endometritis being asymptomatic.<sup>7</sup>

One of the few features that has been linked to endometritis is the phase of the menstrual cycle.<sup>6, 8</sup> In women presenting with lower abdominal pain, in whom a diagnosis of PID is being queried, almost 80% have endometritis when they present in the first 3 weeks of the menstrual cycle, compared to around 20% if they present in the final week of their cycle, just before menstruation.<sup>8</sup> This suggests that women are at highest risk of infection ascending and causing endometrial inflammation just following their period, possibly because of loss of the cervical mucous plug or hormonal changes affecting local immune function. It also raises the possibility that endometritis may, at least in a subgroup of women, be a transient phenomenon with spontaneous clearance occurring within a few weeks.

Vaginal douching has been linked with a higher incidence of endometritis, but only in those women who have douched recently or give a history of frequent douching.<sup>9</sup> It has been postulated that douching “washes away” the normal vaginal flora, increasing the risk of bacterial vaginosis, which in turn predisposes to endometritis. Interestingly, the association between douching and endometritis is only seen in those who do *not* have bacterial vaginosis, which is somewhat against this theory.<sup>9</sup> This highlights the difficulties of interpreting the relation between upper genital tract infection and douching since, until recently, the studies have all been retrospective and therefore unable to attribute cause and effect. More recently, prospective data have been presented suggesting that women who douche are at no higher risk of upper genital tract infection than those who do not (ISSTD Meeting Ottawa, 2003, oral presentation 0052). It therefore seems possible that PID itself may make women more likely to douche (rather than vice versa), with women using douching to try to reduce the symptoms (vaginal odour, discharge) associated with their PID.<sup>10</sup>

One of the central questions that needs to be addressed in determining the correct management of endometritis is whether endometritis and PID are different aspects of the same disease, or separate clinical entities requiring different treatment and having a different prognosis. Endometritis is associated with abdominal pain<sup>6</sup> and also with vaginal discharge, cervical tenderness, and pyrexia, albeit at a lower rate than is seen with salpingitis.<sup>8</sup> Endometritis also leads to elevations in the peripheral white blood count and erythrocyte

sedimentation rate, which suggests that it is of clinical relevance. The presence of endometritis on endometrial biopsy correlates well, although not completely, with salpingitis—its positive and negative predictive values are around 90%.<sup>1</sup> Thus, endometritis is commonly associated with salpingitis but either can occur in isolation.

Does endometritis require treatment? Antimicrobial therapy of endometritis has been assessed most thoroughly in the PEACH study.<sup>11</sup> This large randomised controlled trial primarily compared the efficacy of PID treatment in symptomatic inpatients and outpatients, but also includes data from endometrial biopsies taken at baseline and after 30 days in a subset of patients. Almost half the patients in the study failed to clear their initial endometritis despite a good clinical response, and no correlation was found between the failure to resolve endometrial inflammation and subsequent symptoms. Also, the presence of endometritis at initial diagnosis did not have an adverse effect on subsequent long term outcomes, such as pregnancy, infertility, and chronic pelvic pain. Indeed, the trend was towards the presence of endometritis improving these outcomes.<sup>12</sup>

Endometritis can be defined on the basis of histopathological appearances and appears to occur commonly in

women with asymptomatic lower genital tract infections. It is often associated with salpingitis but can cause abdominal pain and systemic signs of infection even in the absence of classic PID. Some reassurance regarding the long term sequelae of symptomatic endometritis is provided by the PEACH study which suggests that failure to clear endometritis following antibiotic therapy is not associated with an increased risk of long term sequelae. Endometritis can be a distinct clinical syndrome requiring treatment in those women who are asymptomatic, but evidence for or against active screening and treatment of asymptomatic women in the absence of lower genital tract infection is currently lacking.

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