

Complications in Gynecological Surgery

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1. Prevention of Infection Following Gynecological Surgery: The Evidence

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Definition of Infection

Terms such as inflammation, contamination, infection, sepsis, and febrile morbidity may mean different things to different clinicians. It is important, therefore, that in audits of surgical outcomes, reports of research findings, and comparisons of studies, terminology is defined; an example of this process is given in Table 1.1. The definitions of various systemic inflammatory responses and their associated clinical findings and laboratory test results are shown in Table 1.2.

Pathogenesis

The vagina contains more microorganisms than any other site in the body except the bowel. Uterine manipulation through the vagina, e.g., surgical termination of pregnancy (TOP), or operations that open the vagina, e.g., hysterectomy, will result in contamination of normally sterile sites by bacteria that are normally resident in the vagina. Whether these organisms become established and cause infection and inflammation depends on a mixture of surgical and host-related factors, including low socioeconomic status, poor nutrition, smoking, or preexisting medical conditions, such as impaired immunocompetence. These risk factors may be interrelated, e.g., diabetes, obesity, increased blood loss, duration of surgery, and prolonged hospital stay, and many of the measures that can be taken to reduce the rate of postoperative infectious morbidity focus on reducing the impact of these risk factors. The risk of postoperative infection also depends on the virulence and size of the bacterial inoculum. Normal vaginal flora is composed mainly of organisms of low virulence, dominated by lactobacilli species, which, by producing lactic acid from glycogen in vaginal secretions, render the pH of the vagina very acid (<4.5), in which milieu the growth of other potentially pathogenic organisms is suppressed.

At this low-acid pH, lactobacilli are particularly efficient at producing H_2O_2 , which is toxic to bacteria. Under conditions where there is an increase in the

Table 1.1. Definition of Infection—Terminology

	Definition
Inflammation	Localized protective response elicited by injury or tissue damage
Contamination	Pathogenic microorganism(s) in normally sterile tissue without an inflammatory response
Infection	Pathogenic microorganism(s) in normally sterile tissue with a local inflammatory response
Sepsis	Infection with a local and systemic inflammatory response
Febrile morbidity	Temperature of >38.0°C on 2 occasions at least 6 hours apart, excluding the first 24 hours after the procedure

Source: Adapted from and reproduced with kind permission from Tamussino [1].

alkalinity of the vagina (bleeding, semen, douching) or a change in the delicate vaginal ecosystem (few or poor-quality lactobacilli, antibiotics, changes in endocrine status, or phage virus parasitization of lactobacilli), much less H₂O₂ is produced. This results in a 1000-fold increase in other organisms, particularly anaerobes that produce keto acids such as succinate. Succinate blunts the chemotactic response of neutrophils and reduces their killing ability. This

Table 1.2. Definitions of Systemic Inflammatory Responses

	Definition	Clinical Findings, Laboratory Tests
Systemic inflammatory response	Signs and symptoms of disseminated infection or toxins	Fever, tachypnea, tachycardia, leukocytosis, or leukopenia
Sepsis	Infection with a local and systemic inflammatory response	Tachypnea (>20 breaths/min) Tachycardia (>90 bpm) Hyperthermia or hypothermia (>38.4°C or <35.6°C)
Severe sepsis	Sepsis plus evidence of organ dysfunction	Metabolic acidosis, acute encephalopathy, oliguria, hypoxemia, disseminated intravascular coagulation, hypotension
Septic shock	Infection with an overwhelming systemic inflammatory response leading to shock	Hypotension (<90 mm Hg, or 40 mm Hg below baseline)
Sepsis syndrome or multiple-organ syndrome	Sepsis plus evidence of altered organ perfusion	Hypoxia, increased plasma lactate, altered mental state, oliguria

Source: Reproduced with kind permission from Tamussino [1].

results in a synergistic increase in other organisms such as *Mobiluncus* spp and more anaerobes. The result is a polymicrobial imbalance of large numbers of potentially pathogenic organisms, yet no cellular inflammatory response. This condition is called bacterial vaginosis (BV) [2]. As a result, the causative organisms of postoperative infectious morbidity are rarely unimicrobial or exogenous organisms and are more likely to be polymicrobial and endogenous organisms, such as the polymicrobial condition of BV or BV-related organisms, e.g., anaerobes, *Mobiluncus*, mycoplasmas, and ureaplasmas.

In 2001, the Clinical Effectiveness Group of the Association for Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases produced national guidelines for the management of BV. They listed the complications associated with BV as postabortal sepsis, post-hysterectomy vaginal cuff cellulitis, and abscess post-vaginal hysterectomy. They concluded (level of evidence A) that treatment was indicated for symptomatic women, some pregnant women, and women undergoing some surgical procedures. Most of the evidence pertaining to the use of antibiotics in women undergoing surgery relates to hysterectomy and surgical TOP as an example of transvaginal manipulation of the uterus.

Prophylactic Antibiotics for Hysterectomy

Vaginal Hysterectomy

Hirsch [3] reviewed those studies in which antibiotics were used prophylactically in women undergoing vaginal hysterectomy. As early as 1985, Hirsch was able to find 48 studies of 5524 patients, of whom 3037 had been treated and 2487 were used as controls. Febrile morbidity occurred in 444 (15%) of 3037 women who received antibiotics compared to 988 (40%) of 2487 women who did not receive antibiotics (relative risk [RR] = 0.37; 95% confidence interval [CI] = 0.33–0.41; $P < 0.01$). Similarly, pelvic infections occurred in 105 (5%) of 2099 women who received antibiotics compared to 354 (25%) of 1391 women who did not receive antibiotics (RR = 0.2; CI = 0.16–0.24; $P < 0.01$).

Abdominal Hysterectomy

As part of the same review [3], Hirsch reviewed those studies in which antibiotics were used prophylactically in women undergoing abdominal hysterectomy. Hirsch found 30 studies involving 3752 patients, of whom 2165 had been treated and 1587 were used as controls. Febrile morbidity occurred in 348 (16%) of 2165 women who received antibiotics compared to 444 (28%) of 1587 women who did not receive antibiotics (RR = 0.57; CI = 0.51–0.65; $P < 0.01$). Pelvic infection occurred in 57 (5%) of 1196 women who received

antibiotics compared to 114 (10%) of 1144 women who did not receive antibiotics (RR = 0.48; CI = 0.35–0.65; $P < 0.001$). The nature of the abdominal hysterectomy procedure provided a third outcome category—wound infection—for analysis. In this category, 45 (3%) of 1434 women who received antibiotics developed a wound infection compared to 98 (8%) of 1194 women who did not receive antibiotics (RR = 0.38; CI = 0.27–0.54; $P < 0.01$).

Vaginal Versus Abdominal Hysterectomy

Around the time of the Hirsch review [3], 2 studies [4,5] reported on postoperative complications of vaginal versus abdominal hysterectomy. Shapiro et al. [4] found that a higher incidence of infection at the operation site was associated with increased duration of the procedure, lack of antibiotic prophylaxis, younger age, and an abdominal approach. Correcting for these associations, there was no predictive value of the following: obesity, preoperative functional and anatomical diagnosis, postoperative anatomical and pathological diagnosis, estimated blood loss, menopausal status, or surgeon who performed the procedure. Dicker et al. [5] studied 1851 women from 9 institutions. They found that vaginal hysterectomy when compared to abdominal hysterectomy was associated with significantly fewer complications but more unintended surgical procedures. Vaginal hysterectomy was associated with less febrile morbidity, less bleeding requiring transfusion, and less hospitalization and convalescence. Bearing in mind the results of these studies [4,5] and the review by Hirsch [3], in which there were more studies (48 versus 30) and more patients (5524 versus 3752) in which prophylactic antibiotics were used for vaginal hysterectomy compared to abdominal hysterectomy, it seems likely that up to 1985, antibiotics were used preferentially for vaginal hysterectomy compared to abdominal hysterectomy, though the logic of this choice is unclear. This is emphasized by the conclusion of Dicker et al. [5], who claimed that while vaginal hysterectomy with antibiotics had a better outcome than abdominal hysterectomy, the differences were probably attributable to the prevalence and efficacy of antibiotic usage in vaginal hysterectomy.

Bacterial Vaginosis and Post-hysterectomy Infectious Morbidity

Two studies [6,7], in neither of which antibiotic prophylaxis was used, highlighted the association between BV and post-hysterectomy vaginal cuff cellulitis. Soper et al. [6] found that 11 (34%) of 32 women with BV developed post-hysterectomy vaginal cuff cellulitis compared to only 11 (11%) of 102 of women with normal flora (RR = 3.2; CI = 1.5–6.7; $P < 0.005$). Larsson et al. [7] found that 7 (35%) of 20 women with BV developed post-hysterectomy vaginal

cuff infection compared to 4 (8%) of 50 with normal flora ($R = 4.4$; $CI = 1.4$ – 13.3 ; $P < 0.01$).

Choice of Antibiotics

With the important association of BV and BV-related organisms and the development of post-hysterectomy infectious morbidity, it is important that the antibiotics used prophylactically are active against those organisms, particularly anaerobes. In a metaanalysis, Mittendorf et al. [8] identified 25 randomized controlled trials of antibiotic prophylaxis that used vigorous protocols. They performed metaanalyses and cumulative metaanalyses for all the trials. Separate metaanalyses were performed for cefazolin, metronidazole, and tinidazole. Overall, 21% (373/1768) of patients who did not receive antibiotic prophylaxis had serious infection after abdominal hysterectomy. In comparison, of women who received any antibiotics, only 9% (166/1836) had serious postoperative infections ($P = 0.00001$). Among those who received cefazolin, metronidazole, or tinidazole, 11.4% (70/615; $P = 0.00021$), 6.3% (17/269; $P = 0.015$), and 5% (5/101; $P = 0.034$), respectively, had serious postoperative morbidity. The metaanalyses for individual studies and a cumulative metaanalysis are shown in Figure 1.1. Mittendorf et al. concluded that randomized controlled trials of antibiotic prophylaxis in abdominal hysterectomy that used controls who received no treatment are no longer justified. Moreover, they concluded, if the results of the various studies had been pooled at an earlier date, the inappropriateness of controls who received no treatment would have been discovered in 1980 for cefazolin, in 1984 for metronidazole, and in 1986 for tinidazole.

The Swedish National Study of Infection after Hysterectomy (1996), which took place before publication of the Mittendorf metaanalysis, involved 1060 women from 42 centers, yet included only 236 women (22%) who were given preoperative or postoperative antibiotics [9]. Not surprisingly, the postoperative infection rate was high, at 23%, 9.4% of whom had an infection that was situated either in the wound, in the vaginal cuff, or deep in the pelvis. Thirteen percent had a urinary tract infection (UTI), and 4% had infections distant from the site. Only 50% of the wound, cuff, and deep-pelvic infections were detected before discharge from the hospital. An increased risk of postoperative infection was associated with Wertheims-Meigs hysterectomy (21.4%; $RR = 3.0$; $P < 0.03$), intraoperative blood loss of >1000 mL (15%; $RR = 2.4$; $P < 0.001$), and BV (17%; $RR = 2.3$; $P > 0.05$). Admitting that the publication of Mittendorf et al. (1993) [8] had not been drawn to their attention until after preparation of their manuscript, Henriksson et al. (1998) [10] reported that 500 mg of metronidazole administered intravenously to 134 women immediately before total abdominal hysterectomy resulted in a significantly lower erythrocyte sedimentation rate on day 6 (50 mm/hr vs 56 mm/hr; $P < 0.05$), rate of infection (9% vs 17%; $P < 0.04$), and duration of postoperative hospitalization (7.9 vs 8.8 days; $P < 0.02$).

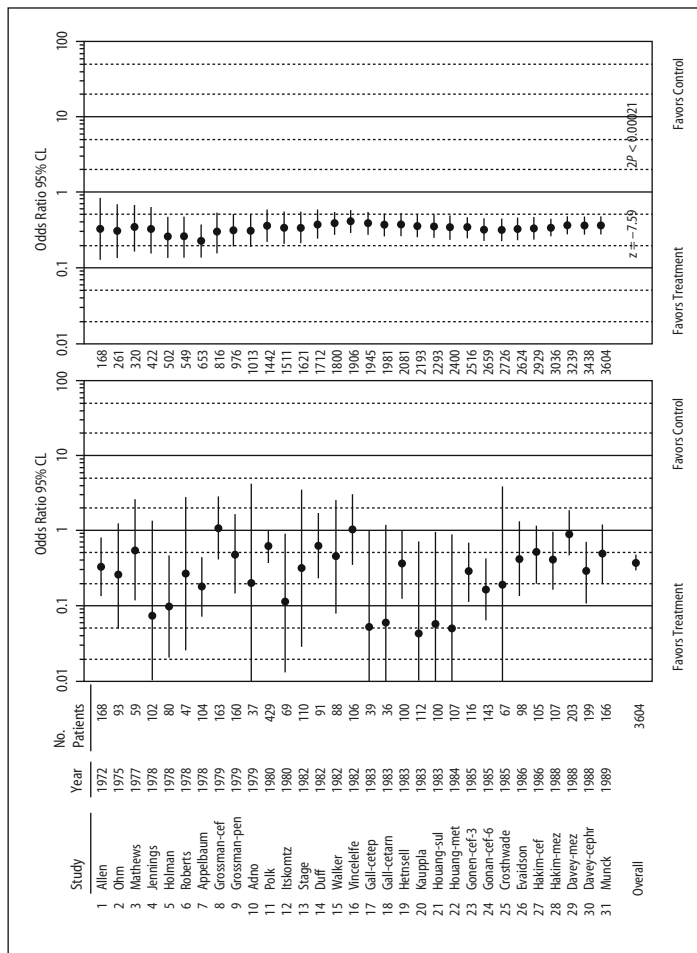


Figure 1.1. All antibiotic prophylaxis studies combined. Odds ratios for occurrence of serous infection after hysterectomy, DerSimonian and Laird random-effects model. In the left-hand graph, point estimates and 95% confidence intervals are given for each individual study, with pooled result at the bottom. On the right-hand side, the same data are presented as a cumulative metaanalysis.

Prevention of Infection Associated with Termination of Pregnancy

Following an unpublished pilot study in Swansea, Wales, in women presenting for TOP, in which the rate of pelvic infection was higher than expected, a larger, more formal study was performed. The study recruited 400 women attending for termination of pregnancy. One hundred twelve women (28%) had BV, 95 (24%) had candida, 3 (0.75%) had *Trichomonas*, and 1 (0.25%) had gonorrhoea. Of 32 women (8%) with chlamydia, 63% developed postabortal pelvic infection, requiring 7 to be readmitted to the hospital. As a result, the authors recommended that, since the estimated cost of hospital admission due to chlamydia was twice the estimated cost of screening for and treating chlamydia, screening for chlamydia was essential, and prophylactic antibiotics should cover both chlamydia and BV [11].

The incidence of postabortal sepsis (PAS) is estimated to be between 4% and 12%. Those women with BV have a 3-fold increased risk of PAS compared to women with *Lactobacillus* spp–dominated flora [12]. Prophylactic metronidazole reduces PAS by 66% [13,14]. In a randomized, double-blind, placebo-controlled trial of 231 women attending for TOP who were given either 500 mg of metronidazole or placebo for 10 days starting the week preoperatively, the incidence of PAS was 3.8% in the metronidazole group compared with 12.2% in the placebo group ($P < 0.05$) [13]. The incidence of PAS can also be reduced by the administration of 2% clindamycin vaginal cream preoperatively in women with abnormal flora [15]. Penney et al. [16] found that prophylaxis against PAS was as good as screening and treatment and more cost-effective.

In the summary of recommendations, section 5.5 of the national evidence-based clinical guidelines for the care of women requesting induced abortion, evidence (level A) states that “abortion care should encompass a strategy for minimizing the risk of post abortion infectious morbidity.” Level-B evidence states that “appropriate strategies include: antibiotic prophylaxis or screening for lower genital tract organisms with treatment of positive cases.” An example of metronidazole 1 g per rectum at the time of TOP plus doxycycline 100 mg twice daily for 7 days commencing post-TOP is given.

Despite this and other recommendations, such as the Government Chief Medical Officer’s Expert Advisory Group [17] and the 31st Study Group for the Royal College of Obstetricians and Gynaecologists (RCOG) on the Prevention of Pelvic Infection [18], for the prevention of pelvic infection following TOP and uterine instrumentation there still appears to be lack of uniformity in the United Kingdom. Skinner et al. [19] sent an anonymized questionnaire to gynecologists in the North and South Thames region of the United Kingdom requesting information on case load, screening policies for infection, and the use of prophylactic antibiotics for women undergoing TOP, insertion of intra-uterine contraceptive device, laparoscopy, and endometrial sampling and/or hysteroscopy. Respondents were asked about screening procedures for genital infections, antibiotic regimes used, and advice given to women on referral to

genitourinary medicine clinics. Only 55% fulfilled RCOG guidelines for the prevention of chlamydial infection prior to TOP. Only 40% followed guidelines for other uterine instrumentation procedures, and when antibiotics were used, only 42% administered antibiotics that were active against both *Chlamydia trachomatis* and BV. The authors concluded that there were marked inconsistencies and lack of uniformity and that antibiotic regimes were frequently inadequate or inappropriate [19].

Infections Postoperative Hysteroscopy

While accepting the recommendations and guidelines from national bodies, clinical effectiveness groups, professional bodies, RCOG study groups, and expert advisory groups concerning the use of antibiotic prophylaxis to prevent infection when uterine instrumentation is involved, a recent report of 1952 operative hysteroscopies from Marseille, France, recorded a remarkably low incidence of postoperative infection despite the fact that no antibiotic prophylaxis was used. Following 782 resections of leiomyomata, 422 endometrial polypectomies, and 90 uterine septa resections, together with 623 endometrectomies and 199 lyses of intrauterine synechiae, the incidence of endometritis and UTI was extremely low at 18 (0.9%) of 1952 and 12 (0.6%) of 1952, respectively [20].

Conclusion

On July 3, 1909, at the age of 47, Herman Pfannenstiel (1862–1909), the Berlin gynecologist who gave his name to the low transverse incision so commonly used in obstetrics and gynecology, died of septicemia 1 week after a needle-stick injury to his left middle finger, sustained while operating on a patient with a tubo-ovarian abscess. With the introduction of antibiotics, postoperative infections are no longer the danger they were for patients or their surgeons but are still common, potentially life threatening, and a drain on health care. The following bullet points represent the evidence available for the prevention of infection following gynecological surgery.

- Prophylactic antibiotics significantly reduce infectious morbidity following hysterectomy and termination of pregnancy.
- Vaginal hysterectomy is associated with less infectious morbidity than total abdominal hysterectomy, but all hysterectomies should have antibiotic prophylaxis.
- Consensus guidelines also recommend antibiotic prophylaxis for other procedures that involve uterine instrumentation.
- Prophylactic antibiotics for TOP are as good as screening and treatment and probably more cost-effective. The possible exception to this rule is among women under the age of 20 years in whom screen-