76 Postpartum infections

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Serious postpartum infections remain a significant cause of maternal morbidity and mortality. Some factors that may predispose the puerpera to infection include rapid colonization of the postpartum endometrial surface by vaginal flora (1), contamination of the perineal area by vaginal and fecal flora, introduction of bacteria through manipulations or instrumentation employed to effect delivery, as well as the physiologic adaptation of the breasts for lactation. Despite these risks, the overall incidence of clinical infection in the postpartum period is relatively low (less than 10%). Because postpartum women are generally young and healthy, their general resilience may impede prompt diagnosis if the patient or physician underestimates the risks of infection. Identification and close surveillance of patients at risk allow for timely diagnosis and prompt treatment, which may minimize serious sequelae of infection.

The standard definition of “puerperal fever” as an oral temperature of 38.0°C or more in any 2 of the first 10 days postpartum, exclusive of the first 24 hours, is impractical and may not be a valid indicator of infection. While transient elevations in temperature occur commonly and resolve spontaneously, a temperature greater than 38.4°C or persistent low-grade fever during the first 24 hours postpartum is highly predictive of ensuing infection (2). Disregarding temperature elevations that do not fit into a standard definition or ignoring signs and symptoms of infection not accompanied by fever may delay proper evaluation and therapy.

Time of onset of symptoms may provide a clue to etiology. Infections occurring within 48 hours of delivery commonly involve the uterus and peritoneum following cesarean section, the urinary tract following catheterization, or the respiratory tract. The microorganisms responsible for early infection were frequently present or introduced at the time of delivery, and the rate of bacteremia is high. Abdominal and episiotomy wound infections, breast infections, complications of uterine infection, and uterine infection that follows vaginal delivery usually present later in the postpartum period. The rate of bacteremia is low and the organisms associated with late infection may be anaerobic, chlamydial, endogenous, or introduced after delivery (3).

ENDOMETRITIS

Endometritis, or infection arising from the uterine cavity, is the most common postpartum infection. The diagnosis, classically heralded by a tender uterus and foul lochia, is usually one of exclusion in the febrile postpartum woman without signs of infection from another source.

The pathophysiology of endometritis is similar to that of other pelvic infections—polymicrobial and ascending from the colonized lower genital tract. No risk factor is absolutely predictive; however, when more than one factor is present, risk

is cumulative (4). Endometritis following vaginal delivery occurs in 1% to 3% of patients. Delivery by cesarean section increases the incidence 3 to 30 times when compared with the vaginal route (5,6). Thus, cesarean delivery is the greatest risk factor for endometritis, with baseline rates of 9% following elective and 29% following nonelective procedures (7). Microorganisms from amniotic fluid or vagina directly inoculate the myometrium and peritoneal cavity at the time of surgery. The presence of suture material and surgically devitalized tissue, along with postoperative exudation and fluid collections, creates a favorable environment for subsequent bacterial growth (8). Placement of the uterine incision, however, has no effect on the incidence of postpartum infection (9).

Frank chorioamnionitis is an obvious antecedent of postpartum intrauterine infection, often despite intrapartum antibiotic therapy (10). Risk is compounded by the frequency of dysfunctional labor and failure to progress in women with chorioamnionitis, necessitating delivery by cesarean section (11). A positive amniotic fluid culture, even in the absence of overt signs of infection, is also highly predictive of subsequent endometritis, especially following cesarean section (12,13). Bacterial contamination of amniotic fluid, rare when fetal membranes are intact, is almost always present after 6 hours of ruptured membranes (14). The quantity and virulence of the organisms that colonize the amniotic fluid following membrane rupture are primary determinants of subsequent infection (6,15).

Major risk factors include prolonged duration of ruptured membranes (16), long labor with multiple vaginal exams, low socioeconomic status (17), obesity (17,18), and the presence of bacterial vaginosis (19). Untreated carriers of group B streptococci are also more likely to develop endometritis (20). Administration of glucocorticoids for acceleration of fetal lung maturation does not increase the risk of endometritis or other postpartum infections (21).

The diagnosis of endometritis is usually based upon clinical findings. Fever is the most useful sign and should prompt a physical examination even within the first 24 hours postpartum. In the absence of other signs of infection, continued observation may be appropriate, but further evaluation is indicated if fever persists. Endometritis after cesarean section typically presents within 48 hours of surgery. When endometritis follows vaginal delivery, the diagnosis is made within 7 days in 84% and within 14 days in 98% (6).

The patient may complain of malaise, chills, abdominal pain, or foul-smelling discharge. On physical examination, tachycardia, decreased bowel sounds, lower abdominal tenderness, uterine and adnexal tenderness to bimanual palpation, and purulent or foul lochia may be found, although physical findings may be minimal. A pelvic mass on initial

examination is unusual. Because the differential diagnosis for fever in the immediate postpartum period includes atelectasis, pneumonia, pyelonephritis, viral syndrome, mastitis, and appendicitis, the physical examination should be conducted to exclude these conditions.

If infection is suspected, laboratory evaluation should include complete blood count, urinalysis and urine culture from a catheterized specimen, and blood cultures in most cases. Routine endometrial cultures are rarely useful, as well-chosen antibiotic therapy results in a rapid recovery in most patients despite culture isolates. An endometrial culture may be helpful when hemolytic streptococci or clostridia are suspected or when endometritis develops in patients who are at risk for infection with unusual or resistant organisms (22). Prior to obtaining specimens transcervically, preparation by cervical cleansing is recommended to minimize contamination with lower genital tract flora (8).

With the aim of minimizing infectious morbidity, prevention of endometritis is paramount. Even though instrumental delivery is a risk factor for endometritis following vaginal delivery (23), data are too few and of insufficient quality to recommend routine use of prophylactic antibiotics for operative vaginal delivery (24). Antibiotic prophylaxis for cesarean section, however, reduces the rate of subsequent endometrial infection by more than half after both elective [relative risk (RR) 0.38, absolute risk reduction 4%] and nonelective procedures (RR 0.39, absolute risk reduction 18%) (25,26). The effect is evident even in nonlaboring patients with intact membranes (RR 0.05) (27) with significant cost savings per case (28).

Many antibiotics provide effective prophylaxis. The most recent systematic review (29) showed no benefit in efficacy of either single broad-spectrum agents over ampicillin or first-generation cephalosporins or multiple doses of antibiotics over a single dose. Clindamycin was recommended for penicillin-allergic women. Recent concerns over the rising resistance of Gram-negative organisms have prompted a trend away from ampicillin toward first- and second-generation cephalosporins and ampicillin/sulbactam, although data supporting their superiority are lacking. Adding aztreonam to the clindamycin has been proposed in cases of penicillin allergy.

While delaying administration of the antibiotic until cord clamping was originally touted to avoid clouding the evaluation of the newborn, recent evidence shows significant maternal benefit to administration of the antibiotic 15 to 60 minutes preoperatively. Attaining therapeutic tissue levels of antibiotic before bacterial contamination decreases the risk of endometritis compared with dosing after cord clamping [adjusted odds ratio (aOR) 0.22] without increasing the neonatal length of stay or incidences of sepsis or septic workup in the newborn (30–32). The practice of giving intrapartum prophylaxis to women colonized with group B beta-hemolytic streptococci has also resulted in fewer cases of subsequent endometritis (33).

Other measures of prevention have been studied and warrant consideration. Delivery of the placenta at cesarean section by external uterine massage and gentle traction rather than manually has been shown to reduce the rate of endometritis in several randomized controlled trials (34–36). Administration of methylergonovine 0.2mg q6h following

cesarean section until discharge from the hospital (37) can decrease the rate of endometritis as well as minimize blood loss. A promising measure in the prevention of endometritis is extended spectrum antibiotic prophylaxis. The addition of an antibiotic (doxycycline or azithromycin) targeting *Ureaplasma urealyticum*, which has been shown to be a significant predictor of endometritis despite typical antibiotic prophylaxis and intact membranes, significantly reduced both endometritis and wound infection (38–40). Preoperative intravaginal treatments, such as intravaginal metronidazole gel (41) or a vaginal scrub with povidone–iodine (42), aimed at decreasing the inoculum of vaginal bacteria that may ascend, also show reduced rates of subsequent endometritis in controlled studies. Interventions with no effect on the rate of post-cesarean endometritis include in situ versus exteriorized repair of the uterine incision, glove change after delivery of the fetus before proceeding with the operation, and removal of uterine debris with tissue forceps versus uterine wiping with a laparotomy pad after placental delivery (35,36,43).

Choice of antibiotic therapy for acute endometritis is directed by the bacteriology of the infection. Aerobic organisms are found in about 70% of cultures and anaerobic organisms in about 80% (44). Typically, more than one isolate per culture are identified (45). Gram-negative bacilli, particularly *Escherichia coli*, are the most common aerobes, followed by Gram-positive aerobes such as groups B and D streptococci. Group A streptococci and *Staphylococcus aureus* are recovered in less than 5% of cases. The most common anaerobic isolates are *Bacteroides bivius* and *B. fragilis* as well as the anaerobic streptococci peptococcus and peptostreptococcus. Genital mycoplasmas and chlamydia also may be recovered from patients with acute endometritis (3).

Empirical therapy with parenteral antibiotics should be initiated as soon as the diagnosis of endometritis has been made and cultures have been taken (Table 1). Most patients will show a clear response to treatment within 48 to 72 hours. Following vaginal delivery, 95% respond to initial administration of a penicillin plus an aminoglycoside, despite incomplete anaerobic coverage. With additional antibiotics in those who fail initial therapy, less than 2% develop major infectious complications such as abscess or septic pelvic thrombophlebitis (6). The most recent systematic review (46) did not specifically address endometritis following vaginal delivery due to insufficient data. Recommendations for treatment of endometritis following cesarean delivery are clear: regimens with poor activity against penicillin-resistant

Table 1 First-Line Therapy for Endometritis
After cesarean delivery
Clindamycin 900mg intravenously every 8 h plus
Gentamicin 4mg/kg intravenously once daily ^a , (plus ampicillin 2g intravenously every 6 h) ^b
Clindamycin (as above) plus aztreonam 2g
Intravenously every 6–8 h ^a
Metronidazole 500mg intravenously every 6 h
Plus gentamicin (as above), plus ampicillin (as above)
After vaginal delivery
Ampicillin (as above), plus gentamicin (as above)
^a For penicillin-allergic patients. ^b Depending on the agent used for prophylaxis.

anaerobes (e.g., *Bacteroides fragilis* group) are more likely to fail. The combination of clindamycin and an aminoglycoside remains the gold standard. Although small studies comparing clindamycin/gentamicin with single broad-spectrum agents (such as second- or third-generation cephalosporins, ureidopenicillins, or penicillins combined with a beta-lactamase inhibitor) show them to be equally effective, meta-analysis shows that only 20 women would need to be treated with clindamycin and gentamicin to prevent one failure with other regimens (46). Metronidazole–penicillin–aminoglycoside and clindamycin–aztreonam may be appropriate choices for post-cesarean infection as well (8).

Fewer failures occur with once-daily gentamicin dosing (46). Advantages of once-daily dosing include a superior bactericidal effect with higher peak serum concentrations, time for recovery of bacterial sensitivity between doses (post-antibiotic effect), lower trough levels resulting in less accumulation of the drug in the cochlear system, and cost savings (47,48). Typical formulas for calculating the daily dose may be inadequate in the postpartum woman due to greater renal clearance, increased volume of distribution, and obesity. The pharmacokinetics has been investigated with the following recommendations: 4mg/kg actual body weight, or 5mg/kg adjusted body weight, or substituting a volume of distribution of 0.4 to 0.43L/kg in the formula pharmacies usually use to calculate the dose (49).

Changes in endometrial flora have been demonstrated following administration of prophylactic antibiotics and may affect treatment of subsequent infection. The use of cefazolin and other cephalosporins is associated with increases in infections with enterococci (17,22,50,51), and the use of penicillin or ampicillin has resulted in an increased risk of infections caused by Gram-negative organisms (50,52) and mycoplasmas (50). Unfortunately, no evidenced-based recommendations exist for treatment of women who develop endometritis after receiving antibiotic prophylaxis for cesarean section. In one study (53), only 54% of women, who had received cephalosporin prophylaxis and developed post-cesarean endometritis, responded to clindamycin and gentamicin within 48 hours. An additional 40% responded to the addition of ampicillin or vancomycin. Thus, it seems prudent and pragmatic to consider initial treatment with clindamycin and once-daily gentamicin if a penicillin has been used for prophylaxis, but treatment with ampicillin, clindamycin, or metronidazole, and once-daily gentamicin if a cephalosporin has been used for prophylaxis.

Common sense guidelines and important caveats warrant mentioning. When the diagnosis of endometritis is suspected, it is unwise to extend the prophylactic agent for a longer time as the causative organism is likely resistant. In general, do not use an antibiotic for treatment to which the patient has been recently exposed (52). When high fever but no localizing signs are present, consider group A streptococcus infection (52) as two-thirds of patients present with a fever only (54). Similarly, group B streptococcal cultures are not 100% predictive; if a patient has an early-onset endometritis with high-spiking fever, group B streptococcus may be the causative organism even if her culture within 5 weeks was negative (33).

The appropriate duration of therapy has not been well established. Typically, parenteral antibiotics have been

continued until the patient has been afebrile for 48 hours and the physical examination is benign. Discontinuation of treatment in a nonbacteremic patient when the patient's temperature has been $\leq 37.5^{\circ}\text{C}$ for at least 24 hours has been shown to be safe and cost-effective in both private and indigent populations (55,56). After treatment of uncomplicated endometritis, follow-up oral antibiotics, except in patients with known chlamydial infection, are generally unnecessary (3,17,46,57).

Failure to respond within 48 to 72 hours warrants reevaluation of the patient. Common causes of failure include wound infection and resistant microorganisms. Culture results should be reviewed, if available, and cultures of blood, endometrium, and wound collected. Antibiotic therapy should be assessed. Increases in dose or frequency of administration may be required, as pregnancy-related changes in renal function, blood volume, and total body water affect elimination and volume of distribution of drugs, usually toward lower serum levels (58). In patients receiving clindamycin plus an aminoglycoside, aminoglycoside levels should be drawn and ampicillin added to provide coverage against enterococci (22). Anaerobic coverage should be added if lacking. Single-agent therapy may be changed to clindamycin plus an aminoglycoside plus a penicillin. For proven staphylococcal infection, specific therapy should be added (e.g., nafcillin 1–2g intravenously every 4–6 hours, cefazolin 2g intravenously every 8 hours, or vancomycin 1g intravenously every 12 hours). Wound infection, of course, warrants drainage.

If antibiotic therapy requires no modification, or if changes fail to produce response (80% respond) within another 48 to 72 hours, the case should be scrutinized for sources of continued fever. The differential diagnosis must be broadened to include wound infection, pelvic cellulitis, pelvic abscess, venous thromboembolism, drug fever, septic pelvic thrombophlebitis, enterocolitis, retained placental fragments, as well as viral or connective tissue disorders. Pelvic ultrasound may be helpful in visualizing retained placenta or a fluid collection. A computed tomographic (CT) scan may identify ovarian vein thrombosis, abscess, hematoma, or other masses.

The incidence of documented bacteremia following cesarean section is 3% to 4%, compared with 0.1% to 0.4% in patients who have delivered vaginally. Endometritis accounts for the majority of cases, but wound, respiratory and urinary infections, as well as endocarditis may be responsible (59,60). Bacteremia is more commonly found in post-cesarean endometritis (8–30%) compared with endometritis following vaginal delivery (5%) (5,6). Risk for positive blood cultures is correlated with length of labor, number of vaginal exams, duration of ruptured membranes, estimated blood loss, and intra-amniotic infection (61). Bacteremia is rare ($<1\%$) in the postpartum woman with a temperature peak $<38.8^{\circ}\text{C}$, but occurs in more than 20% of those with higher fevers (61). Organisms isolated from the blood reflect organisms infecting the endometrium and are found in similar proportions (57). While blood culture results may guide antibiotic therapy for endometritis, failure to respond to initial therapy does not correlate with a resistant organism in blood culture (59). Identification of a pathogenic organism resistant to the antibiotics administered warrants broadening the antibiotic coverage despite apparent clinical response. Prolonged therapy may be indicated when *S. aureus* is isolated from the blood to

avoid metastatic infection (8,44). Mortality among obstetric bacteremic patients is extremely low (<1%) compared with other medical or surgical populations (60).

Late postpartum endometritis, with onset from 7 to 42 days after delivery, is a clinically mild disease, which typically occurs in women who have delivered vaginally. Lower abdominal pain and an increasing vaginal discharge with odor are the presenting symptoms; systemic signs are rare. *Chlamydia trachomatis*, uncommon in acute endometritis (45), is isolated from the cervix or endometrium in 30% to 67% of cases (62). In women with chlamydial infection detected in the antepartum period, late postpartum endometritis develops in 30% to 60% if untreated (62). When late-onset infection is suspected, a cervical or endometrial culture for chlamydia should be obtained. Azithromycin (1 g orally in a single dose), tetracycline (doxycycline 100 mg orally twice a day for 7 days), or erythromycin (500 mg orally four times a day for 7 days) therapy is clinically effective. Treatment in the antepartum period may prevent late postpartum infection.

WOUND INFECTIONS

Abdominal wound infections occur in 1.6% to 10% of women delivered by cesarean section (4,63,64). Antibiotic prophylaxis has been shown to reduce the rate of wound infection after both nonelective (RR 0.36) and elective (RR 0.73) cases (25). Extended spectrum prophylaxis with doxycycline and/or azithromycin (covering for *Ureaplasma*) reduces the risk even further (38,40). Other basic measures, such as preoperative showering with chlorhexidine, clipping hair rather than shaving the area for incision, and preparation of the skin with an alcohol-based agent, are also advocated (65). Risk factors identified by prospective surveillance include skin closure with staples rather than subcuticular suture and maternal obesity (66), particularly in women with subcutaneous tissue thickness greater than 3 cm (67). One randomized trial showed a reduction in wound infections using the Joel-Cohen rather than Pfannenstiel incision (68). No effect on rate of infection has been demonstrated with prophylactic subcutaneous drainage (69).

The diagnosis of wound infection is based on the findings of local advancing erythema, induration, and/or drainage from the wound. Fever is not always present. Clinical signs typically manifest 4 to 8 days following delivery; 71% occur after discharge from the hospital (66). Many patients have had endometritis and present with recurrent fever after the initial response to treatment for the uterine infection. The majority of wound infections result from extension of polymicrobial contamination of the endometrium and amniotic fluid to the incision site (70), but the skin may also be the source of bacteria (65). Staphylococcal wound infections, accordingly, typically develop in women without obstetric risk factors. If wound infection presents with fever and spreading cellulitis within the first 48 hours after operation, a single bacterial pathogen, such as group A or B beta-hemolytic streptococci or *Clostridium perfringens*, may be responsible. A Gram stain of material aspirated from the active margin of infection may identify the causative organism.

Treatment for early-onset infection consists of antibiotic therapy such as penicillin 4 million units intravenously every 4 hours or cefazolin 2 g intravenously every 6 hours, and

prompt debridement of necrotic tissue (71). Later infections usually respond to simple incision and drainage. Antibiotics are required only if there is extensive cellulitis, bacteremia, or failure to defervesce within 12 to 24 hours of opening the wound (71). Debridement under anesthesia is sometimes required (70). Fascial dehiscence of the wound occurs in 0.5% of post-cesarean patients and may be more common when wound infection is present (64,70). Fascial repair under anesthesia may be necessary. Modern management of open wounds, including secondary closure within 1 to 4 days of disruption, negative pressure wound therapy (vacuum-assisted closure), or healing by secondary intention with dressings that keep the wound moist and absorb drainage, has been shown to be superior to frequently changed, traditional "wet-to-dry" dressings and cleansers that disrupt wound healing (65).

Complications of wound infection such as necrotizing fasciitis, synergistic bacterial gangrene, and clostridial gas gangrene are extremely rare after cesarean section but should be suspected if the patient fails to respond following incision and drainage of the wound. Early recognition is essential to prevent mortality from these life-threatening conditions. Necrotizing fasciitis should be suspected if the patient appears critically ill or if the edema and induration surrounding the wound worsen rapidly despite treatment or are accompanied by local anesthesia or crepitus. At surgical exploration, there is undermining of the involved skin surrounding the wound and the superficial fascia lacks resistance to a blunt instrument. Synergistic bacterial gangrene is recognized by a central ulcer, a surrounding deep red zone, and peripheral erythema. The process is slowly progressive and is often marked by inordinate pain. Clostridial gangrene presents with sudden onset of severe pain, mild local edema, thin watery drainage from the wound, and systemic toxicity. In advanced stages, the skin appears bronzed with bullae, gangrene, and crepitation. Gas may be evident on X-ray (71). These destructive processes require extensive surgical debridement. Aerobic and anaerobic cultures and broad-spectrum parenteral antibiotics are appropriate in the management of these polymicrobial infections. Delays in treatment may lead to maternal mortality.

SEPTIC PELVIC THROMBOPHLEBITIS

Septic pelvic thrombophlebitis is a potentially life-threatening complication that occurs most commonly after obstetric procedures. The diagnosis is typically suspected in a woman with persistent fever after several days of adequate antibiotic therapy for presumed endometritis with no wound infection apparent (72). This persistent fever occurs in about 1 in 650 deliveries (72) or 0.5% to 2% of patients with postpartum endometritis (73).

The pathogenesis of pelvic thrombophlebitis rests on Virchow's triad of venous stasis, endothelial damage, and alterations in coagulation factors. Damage to the intima of pelvic veins may result from direct surgical trauma or from the inflammatory response to an infected uterus. The velocity of blood flow through the dilated ovarian veins declines sharply postpartum. The long veins have multiple valves, which are major sites of venous pooling and their thin walls make them subject to external compression. Pregnancy-related increases in levels of clotting factors and platelet adhesiveness, along

with possible thromboplastin release from placental fragments and necrotic tissue, may generate a thrombotic process (73).

Pelvic thrombophlebitis encompasses two fairly distinct forms—ovarian vein thrombosis and thrombosis of multiple small pelvic vessels. In the acute ovarian vein syndrome, onset is usually within 2 to 4 days postoperatively, but may be weeks after delivery. The patient usually appears ill with a low-grade fever, tachycardia, flank or lower abdominal pain with guarding, and ileus with abdominal distention. Nausea and vomiting may be present. A tender, rope-like, abdominal mass originating near the uterine cornu and extending cephalad and laterally, palpable in one-half to two-thirds of patients, represents the thrombosed ovarian vein. Ovarian vein thrombosis commonly occurs in association with pelvic infection, but the patient's symptoms worsen, rather than improve, with continued antibiotic therapy. The syndrome may present in the absence of clinical infection, sometimes prompting laparotomy to exclude other disorders. The differential diagnosis includes acute appendicitis, broad ligament hematoma, degenerating fibroid, adnexal torsion, pyelonephritis, ureterolithiasis, and abscess.

Postpartum ovarian vein thrombosis is predominantly right sided (80%), with bilateral and left-sided lesions unusual (14 and 6%, respectively) (74,75). The preponderance of right-sided involvement is explained by venous drainage, which, in the upright position, flows from the left ovarian vein and uterine venous plexus into the right ovarian vein, increasing venous stasis and the inoculum of pathogens on the right (3). Incidence is approximately 1 in 3000 deliveries, following 1 in 800 cesarean and 1 in 9000 vaginal deliveries (72). Although, when studied, 50% of women who had postpartum ovarian vein thrombosis were found to have inherited prothrombotic factors (76), no clinical risk profile could be established—prior thrombosis was rare, many had taken oral contraceptives without complication, and none had a family history of clots.

Septic pelvic thrombophlebitis with diffuse thrombosis of multiple small pelvic vessels usually presents with enigmatic fever and typically follows the diagnosis of endometritis or other pelvic infection. After several days of antibiotic therapy, recurrent high-spiking fevers occur despite resolution of other signs and symptoms of infection. The patient generally feels well when not febrile and may need to be convinced that she has a serious complication. Imaging techniques do not demonstrate the small uterine and vaginal veins, which have been shown at laparotomy to be involved (77). The diagnosis is usually presumptive, based on defervescence within 48 to 96 hours (average 37 hours) after addition of heparin to the antibiotic regimen (78). The incidence is estimated at 1 in 2000 deliveries, following 1 in 400 cesarean and 1 in 10,000 vaginal deliveries (79).

Diagnostic imaging may be helpful in evaluating patients with suspected septic pelvic thrombophlebitis as thrombus in ovarian and larger veins may be visualized by CT scan, ultrasound, or magnetic resonance imaging (MRI). Sonography has been suggested as a screening examination for postpartum ovarian vein thrombosis, but sensitivity is only 56%, with imaging hampered by intervening bowel gas or obesity (80). CT and MRI are also superior to sonography at evaluating for other conditions in the differential diagnosis. CT remains the imaging procedure of choice (sensitivity

78–100%), as MRI (sensitivity 92–100%) offers no clinical advantages to balance its increased cost (80,81). All imaging techniques are helpful only if positive and are inadequate in excluding the diagnosis.

Serious complications of pelvic thrombophlebitis are mainly due to extension of thrombus or embolization. About 45% of ovarian vein thromboses imaged are seen to extend to the inferior vena cava (76); extension to femoral, iliac, mesenteric veins, and even the right atrium is possible. Extension of clot from the ovarian to the renal vein may result in renal vein thrombosis with subsequent nephrotic syndrome and renal insufficiency. Clots in pelvic vessels may fragment, possibly owing to the presence of bacteria, and embolize. Showers of small infected emboli are characteristic with resulting septicemia and metastatic abscesses (82) (Fig. 1). Massive involvement of ovarian veins or the vena cava may precipitate large pulmonary emboli with symptoms of venous occlusion; in fact, respiratory distress from pulmonary embolism may be the presenting symptom (75). Mortality from pulmonary embolism or metastatic abscesses is estimated at 18 deaths per million (80). Ventilation–perfusion or CT scanning of the lung may be indicated to determine whether pulmonary embolization has occurred. Classic papers report evidence of emboli in one-third or more of patients tested (73,82,83), even though symptomatic pulmonary embolism was rare (84). No modern reports contain a systematic assessment for emboli.

The diagnosis of pelvic thrombophlebitis, in either form, may not be confirmed by radiographic study. Clinical response to heparin may secure the diagnosis in both the acute and the enigmatic syndromes. Full anticoagulation should be instituted along with broad-spectrum antibiotics (Table 2) as microorganisms have been isolated from resected venous specimens and require treatment to promote resolution of the thrombus (73,85). Resolution of the fever does not imply resolution of the clot, so a full course of anticoagulation is necessary. Substitution of low molecular weight for unfractionated heparin seems reasonable, but has not been systematically studied. Primary surgical ligation of ovarian veins and vena cava, employed 50 years ago, decreased mortality from 50% to 10% (86), but is fraught with risks of significant hemorrhage, embolization, and death (74). Today, a surgical approach should be reserved for patients who do not respond to anticoagulation plus antibiotics, who experience pulmonary

Figure 1 Septic emboli are seen as multiple peripheral and hilar infiltrates on the computed tomographic scan without contrast.

Table 2 Treatment of Septic Pelvic Thrombophlebitis

Continuation of antibiotic therapy
Until the patient is afebrile for 48–72 h
Full anticoagulation with heparin
5000–10,000 units loading dose, followed by 800–2000
Units/h to maintain the PTT at 1.5–2.5 × baseline value
Duration of anticoagulation therapy
Ovarian vein thrombosis
6 weeks to 6 months (no fewer than 3 weeks)
May change to oral anticoagulation after the first 5–7 days
Suspected thrombosis of smaller pelvic vessels (enigmatic fever)
7–10 days
<i>Abbreviation:</i> PTT, partial thromboplastin time.

embolism while on therapeutic anticoagulation, or in whom the diagnosis is uncertain. If pelvic vein thrombosis is found unexpectedly at postpartum laparotomy, closure of the abdomen without vein ligation and institution of medical therapy is probably the treatment of choice. Need for anticoagulation during or after subsequent pregnancy is probably not required.

The subject of anticoagulation has recently become controversial. The observation that some fevers eventually resolve without heparin has led some to argue that the superior efficacy of today's antibiotics may obviate the need for heparin. One trial in 14 women with CT-proven ovarian vein thromboses, randomized to receive either antibiotics and heparin or antibiotics alone, showed no difference in durations of fever or hospitalization and no evidence of symptomatic emboli (72). Unfortunately, the numbers were too small to preclude possible protection from embolization by heparin.

EPISIOTOMY INFECTIONS

Postpartum infection arising from an episiotomy site is a rare but potentially fatal condition. An episiotomy is a contaminated wound; yet clinical infection manifests in only 0.035% to 3% of patients (63,87). In a randomized controlled trial, use of prophylactic antibiotics (second-generation cephalosporin) for repair of third- and fourth-degree tears was shown to decrease the rate of infectious complications (88). Life-threatening infection associated with episiotomy has occurred in 0.5 to 2 per 100,000 live births, accounting for 20% of maternal mortality. Perineal infection has been classified according to the depth of soft-tissue involvement (89). Successful management depends on accurate assessment of the infected tissues.

Infection limited to the skin and superficial fascia along the episiotomy incision may be managed conservatively. Episiotomy dehiscence or perineal pain may be the presenting complaint, with edema and erythema confined to the area immediately adjacent to the episiotomy (89). The previous repair should be taken down to allow careful inspection of the wound to exclude hematoma, abscess, or unsuspected rectovaginal communication. Following cleansing and debridement, the wound may be allowed to heal secondarily. With surrounding cellulitis, a course of broad-spectrum parenteral antibiotics (such as suggested in Table 1), in addition to local wound care, may be required. Early repair of episiotomy dehiscence, while contrary to traditional practice, has produced excellent anatomical and functional results (90).

Superficial fascial infection presents with erythema and edema, which extend beyond the area of episiotomy to the thigh, buttock, or abdominal wall. Appropriate therapy is dependent upon determination of associated necrotizing fasciitis. Diagnosis by inspection is unreliable, thus surgical exploration may be necessary to rule out fascial necrosis. In the absence of obvious signs of necrotic fascia, frozen-section biopsy has been employed to expedite diagnosis and avoid a possible lethal delay in treatment (91). In the absence of fascial necrosis, severe systemic involvement is uncommon and response to broad-spectrum antibiotics should occur within 24 to 48 hours. Lack of response or progression of the infection during antibiotic therapy may indicate a more severe infection.

When necrotizing fasciitis is present, aggressive management is necessary to avert mortality. Both Camper's and Colles' fascial layers become necrotic with this infection, which spreads along these fascial planes, undermining the skin, and eventually involves all tissues external to the deep fascia (92). The onset is acute with a rapidly progressive clinical course, systemic toxicity, and a fatality rate of 21% to 76% (89). Although the condition is classically described in patients with diabetes or atherosclerosis, affected obstetric patients are usually otherwise healthy (93). The patients appear severely ill, usually with fever and leukocytosis. Erythema with indistinct margins that gradually fade into normal areas may be present. As the disease progresses, skin color becomes blue or brown, with subsequent formation of bullae and gangrene. Progressive brawny edema and induration are evident; vulvar edema, especially unilateral, is characteristic (93). Marked local tenderness is common initially, but the lesions become hypesthetic or anesthetic as cutaneous nerves become ischemic (92). Crepitation may be detected. Exudate is serosanguinous "dirty dishwater" rather than purulent. Anemia due to hemolysis is common (92), but may be masked by massive fluid shifts into the extravascular compartment with resultant hemoconcentration (89). Hypocalcemia may develop due to saponification of liquified subcutaneous fat (92). At surgical exploration, the superficial fascia does not bleed and lacks resistance to blunt probing; the skin is easily separated from the underlying deep fascia.

Prompt surgical resection of the involved tissues is essential for effective management of necrotizing fasciitis. Mortality is 100% in patients treated with antibiotics alone or with incision and drainage only (94). Debridement should extend to where the subcutaneous tissues cannot be separated from the underlying deep fascia or from normal skin. Any tissue that is indurated, edematous, or crepitant, or that does not bleed readily when incised, should be removed (92). More than one surgical debridement may be necessary if subcutaneous necrosis is not arrested. Hyperbaric oxygen is an adjunctive measure and should not substitute for surgical debridement.

Similar to most pelvic infections, necrotizing fasciitis is a polymicrobial disorder. The pathophysiology involves bacterial synergism among various combinations of aerobic and anaerobic organisms (92,94). Comprehensive antibiotic coverage with a penicillin, clindamycin, and an aminoglycoside is recommended as an adjunct to operative intervention until a healthy bed of granulation tissue is apparent. After extensive debridement, these patients resemble those with severe burns.

Management in an intensive care setting with invasive monitoring, aggressive fluid management, and hemodynamic support may be required (92). The wound may be allowed to heal secondarily.

Infection beneath the deep fascia produces myonecrosis. A clostridial infection is the most common cause, although myonecrosis can occur from a neglected necrotizing fasciitis, which invades deep fascia. Clostridial infection may present early in the postpartum period with severe pain disproportionate to the physical findings. A wound or blood culture positive for clostridia should raise the index of suspicion for myonecrosis. Crepitation or clinical deterioration in the presence of an episiotomy infection warrants surgical exploration and radical excision of involved tissues, supplemented with antibiotic therapy. For clostridial infection, high-dose penicillin (4 million units intravenously every 4 hours) is indicated. Polyvalent gas gangrene antitoxin is thought to be ineffective (89). *C. perfringens* is the most notorious organism associated with myonecrosis. *Clostridium sordellii* has also been identified in serious episiotomy infections, but presents with massive malignant vulvar edema thought to be caused by toxin production and results in death from cardiovascular collapse (95).

MASTITIS

Lactation mastitis is a cellulitis of the interlobular connective tissue within the mammary gland that usually occurs within the first 6 weeks postpartum (96). Mastitis occurs in up to 9.5% of breastfeeding women (96,97), but may rarely occur in women who are not nursing. Most cases are sporadic, presenting commonly in the second or third week following delivery (98,99). The onset of symptoms is usually abrupt with chills, malaise, generalized achiness, and fever as high as 39 to 40°C. The affected breast is tender, hot, swollen, and erythematous in a wedge-shaped segment (96) with its apex at the nipple and its base toward the periphery, demarcated by the divisions between the lobes of the breast. Decreased milk secretion may be noted (100), but expression of pus from the ducts is uncommon (99). Poor breastfeeding technique with attachment difficulties, injury to the nipple, nipple fissuring, and milk stasis (101) is considered to be the primary etiologic factor, along with lowered immune status from stress or sleep deprivation (96), but the cause of most cases is unclear (97). One study found fewer than 10 feedings/day to be protective (96), contrary to common belief. Mastitis is no more common among women who are nursing for the first time than among women who have previously nursed. Previous mastitis is a risk factor for recurrence in successive pregnancies (96), perhaps due to persistence of poor practices (102).

Breast infections should be distinguished from segmental breast inflammation due to milk stasis or focal engorgement. Milk contains pro-inflammatory cytokines, which may leak into the circulation when not drained and elicit a systemic response in the absence of infection (101). Fever and erythema are less marked in the absence of infection and will resolve with rest, frequent, complete emptying of the breast, and without antibiotics (101,103). Local hot wet compresses or prone soaks in a hot tub may soften the indurated breast and allow drainage (99). Change in feeding position may permit drainage of blocked ducts. Antibiotics are indicated if

symptoms do not resolve. Patients with obvious signs and symptoms of mastitis should be treated immediately with antibiotics, as delay in institution of antibiotic therapy is associated with abscess formation (98,104). Diagnostic criteria based on leukocyte counts from the milk and quantitative bacterial cultures, helpful in differentiating mastitis in dairy cows, are not always valid in women, as bacterial counts have not been reliable (101).

Appropriate therapy for mastitis includes routine emptying of the breast and administration of antibiotics. Breastfeeding from both breasts should continue. If the infected breast is too sore for nursing, gentle pumping may be employed to reduce congestion. Weaning may increase the risk of abscess formation (97,99,105). Choice of antibiotic may be empirical or based on culture of expressed breast milk. *S. aureus* is the organism isolated in 35% to 50% of breast infections, and 50% to 70% show penicillin resistance in vitro (97,100,104,106). Other common pathogens include coagulase-negative staphylococci, streptococci, *E. coli*, *Klebsiella pneumoniae*, and *Bacteroides fragilis* (100). Cultures of breast milk may be prudent, since methicillin-resistant *S. aureus*, primarily community-acquired, is emerging as a pathogen in mastitis (107), even in those without predisposing factors (108).

Therapy with a penicillinase-resistant penicillin, such as dicloxacillin (250–500 mg orally four times a day) or amoxicillin/clavulanic acid (500/125 mg three times a day), or a first-generation cephalosporin (cephalexin 500 mg orally four times a day) should be started immediately after cultures are obtained. Erythromycin or azithromycin is the alternative in penicillin-allergic patients. In most cases, antibiotics may be given orally, and hospitalization is not required. Therapy should be continued for at least 10 days. Most patients become afebrile and asymptomatic within 36 to 48 hours of beginning treatment (97). If the patient is not improved within 48 hours, examination for abscess formation is warranted.

Breast abscesses develop in 4% to 11% of patients despite appropriate treatment (96,97,106). An indurated, fluctuant area may be palpable, usually peripherally, and should be aspirated for culture if suspected. Axillary lymphadenitis is not typical, but the patient may be febrile and tachycardic, with leukocytosis. Bacteremia may occur (109). *S. aureus* is recovered from 38% of abscesses (104). Ultrasound is a useful adjunct when there is clinical suspicion of abscess or in cases of mastitis that do not promptly respond to appropriate therapy (110). Ultrasound imaging excludes abscess in one-third to one-half of suspected cases (104) and may allow guided aspiration of those that are confirmed (110). Serial aspiration has emerged as first-line therapy for abscesses, with a 91% cure rate. Aspiration and irrigation are performed with follow-up every 2 to 3 days for re-aspiration until the abscess is no longer visible by ultrasound (110). Incision and drainage have been the standard treatment, but risks ductal damage and a poor cosmetic result (110). If incision and drainage are required, radial or circumferential incision is made over the site of maximum tenderness and loculi are broken down, followed by insertion of a dependent drain or pack. Rapid resolution is invariable.

Antibiotic coverage is recommended preoperatively and susceptibility-directed antibiotic therapy is continued

postoperatively (109). Milk stasis should be prevented by complete emptying of the breast with pumping to avoid secondary abscess formation. Continuation of breastfeeding from the affected breast is controversial. In the past, the presence of a staphylococcal breast abscess has been associated with infant deaths from lung abscesses, presumably due to aspiration of a large inoculum (3). Certainly, breastfeeding may continue from the unaffected breast and resume from the affected breast once the abscess has resolved.

Epidemic mastitis is a hospital-acquired infection caused by *S. aureus*. During the 1940s and 1950s, when lengthy postpartum hospitalization was practiced, up to 20% of women became infected (3). The infection involves the lactiferous glands and ducts of the breast, in contrast to the interlobular connective tissue in the sporadic form, and may affect multiple lobes. Abscess formation is common. Epidemic mastitis usually originated in hospital nurseries and was traceable to attendant carriers of the specific phage type that caused the infection (3,98). Infants suffered significant mortality from staphylococcal pneumonia, meningitis, osteomyelitis, and pyoderma during these outbreaks (98). Fortunately, infection control measures and superior antibiotics have made epidemic mastitis an unlikely occurrence today.

URINARY TRACT INFECTION

Immediately postpartum, bacteriuria is found in up to 40% of women (111), but resolves spontaneously in most (112). By the third postpartum day, bacteriuria is found in 1.7% to 4% by suprapubic aspiration. Only one-fourth of women with bacteriuria complain of dysuria, but the symptom is more common following catheterization. Conditions and procedures that are associated with bladder catheterization—cesarean section, vaginal operative delivery, epidural anesthesia, tocolysis, pre-eclampsia, abruption, renal disease—significantly increase the risk of bacteriuria (113,114). Antibiotic prophylaxis decreases the incidence of post-cesarean bacteriuria (115).

Treatment for urinary tract infection is similar to that for the nonpregnant woman. High rates of cure are achieved even with a short (3 days) course of therapy (113). The causative organism is *E. coli* in 80% to 90% of infections, but may be another coliform or staphylococcal or enterococcal species (3,113). Culture and susceptibility testing may guide therapy, especially in patients who have recently received antibiotics. Suprapubic aspiration from a full bladder or urethral catheterization may be necessary to obtain samples of urine, as clean-catch midstream collections are frequently (46–69%) contaminated (113).

Treatment of persistent asymptomatic bacteriuria, perhaps unwarranted in the nonpregnant patient, is recommended in the postpartum period (111). Decreased bladder tone, increased capacity, and incomplete emptying, along with a dilated collecting system and an enlarged uterus, capable of mechanical obstruction, may be present for weeks to months postpartum. These pregnancy-related changes predispose to vesicoureteric reflux and development of pyelonephritis. Infection of the urinary tract can be minimized by avoiding routine urethral catheterization of laboring or postpartum women. High-risk patients, who have received antibiotic suppression during the antepartum period to prevent

pyelonephritis, should probably continue the regimen for at least 2 weeks postpartum.

UNUSUAL INFECTIONS

Infections resulting from spinal or epidural anesthesia occur following less than 1 in 10,000 blocks (116). The diagnosis should be considered in the febrile patient with backache and pain radiating from the spinal area. Evaluation may include neurologic examination, cerebrospinal fluid analysis, and myelography. Weakness, numbness, and finally paralysis will develop if the infection goes untreated (117).

Subgluteal or retropsoal infections have been reported following paracervical or pudendal block (116,118). Patients presented with poorly localized severe hip pain and limited range of motion. Associated organisms were normal vaginal or bowel flora. Gas in the soft tissues was seen in half the cases, and abscess formation was common. Treatment may be delayed, owing to failure to suspect the diagnosis. In addition to antibiotic therapy, surgical drainage, debridement, and diverting colostomy may be necessary for appropriate treatment. Sequelae from these serious infections include persistent discomfort, impaired ambulation, and death.

Toxic shock syndrome has been reported in women with puerperal mastitis (119), postpartum endometritis (120), and abdominal wound infections (3) and may occur from several days to weeks after delivery. The organism responsible is typically *S. aureus* producing toxic shock syndrome toxin-1, but may alternatively be group A *Streptococcus* producing pyrogenic exotoxin A. Toxic shock syndrome presents with high fever, hypotension, rash, and multiorgan dysfunction. With proper antibiotic treatment and aggressive supportive care, most cases resolve in 48 to 72 hours, but mortality is 10% in cases of persistent hypotension, renal failure, or adult respiratory distress syndrome (ARDS) (120).

SEPTIC SHOCK

Rarely, septic shock may complicate a postpartum infection. Septic shock is characterized by hypotension and inadequate tissue perfusion, owing to overwhelming infection. The hypotension may be preceded by chills and fever and associated tachycardia, tachypnea, oliguria, or mental obtundation. Theories of pathogenesis and treatment of septic shock are reviewed elsewhere (121) (see further discussion in Chapter 11).

Microorganisms causing sepsis incite the formation or release of vasoactive and inflammatory mediators that lead to peripheral vasodilatation, regional microembolization, and endothelial cell injury. Severe multiorgan dysfunction involving the lungs, kidneys, liver, heart, and central nervous system may result from inadequate perfusion. Aggressive management strategies incorporate broad-spectrum antibiotic coverage, volume replacement, invasive hemodynamic monitoring, inotropic agents, and peripheral vasoconstrictors to maintain afterload. Rapid reversal of organ hypoperfusion, improvement in oxygen delivery, and correction of acidosis must be achieved for successful stabilization of the patient. A careful search for infected or necrotic foci that may be responsible for persistent bacteremia is warranted. Surgical intervention is sometimes required to remove the underlying cause of sepsis.

Associated complications include ARDS, pulmonary edema, disseminated intravascular coagulation, thromboemboli, and cardiac arrest. The risk of maternal mortality increases as associated complications become superimposed on the septic hypotension. Fortunately, mortality due to septic shock is thought to be considerably lower than that in the nonobstetric population. Early identification of sepsis, prompt institution of antibiotic therapy, volume administration, and cardiopulmonary support when needed are essential to prevent complications and minimize mortality.

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