# Diagnosis and Management of Thromboembolic Disease During Pregnancy

**Carl P. Weiner, MD**

*University of Iowa College of Medicine*
*Iowa City, Iowa*

Thromboembolic disease (TED), which includes superficial and deep thrombophlebitis and phlebothrombosis, septic pelvic thrombophlebitis and thrombosis, and pulmonary embolus, accounts for almost half of all obstetric morbidity and mortality.[1] The diagnosis and current management of thromboembolic disease, as it relates to pregnancy, will be discussed here.

## Incidence

The propensity for thrombosis during pregnancy can be partially explained. Each element of Virchow's triad (stasis, hypercoagulability, and vascular damage) is present at some time during pregnancy. An increase in venous capacitance produces stasis. Thrombin-mediated fibrin generation increases throughout gestation, directly confirming the long-presumed hypercoagulable milieu of pregnancy.[2] Finally, significant vascular damage occurs at delivery. The reported frequencies of TED vary widely and reflect the diligence with which the diagnoses were sought. The incidence of antepartum disease has been reported to be as high as 0.15% for superficial thrombophlebitis and 0.36% for deep vein thrombophlebitis. The incidence of calf thrombi postpartum as detected by $^{125}$I-fibrinogen scanning was 3% in the only published study[3] (Table 1). Approximately 1 in 2000 pregnancies is complicated by a pulmonary embolus.

## Diagnosis

The signs and symptoms of TED result from obstructed venous return, either singly or in combination with vascular inflammation. Venous thrombi are common in sedentary patients, but most are asymptomatic. Eighty percent lyse spontaneously.[4] Pulmonary emboli occur in 50% of patients with documented deep vein thrombosis; of these, only half are symptomatic.[4] Most clinically significant emboli arise from

Correspondence: Carl P. Weiner, MD, University of Iowa College of Medicine, Iowa City, IA 52242.

**TABLE 1.** Incidence of Thromboembolic Disease in Obstetrics

| Type of Thromboembolic Disease | % Incidence |
|---|---|
| Superficial thrombophlebitis (lower extremity only) | |
| Antepartum | 0.016–0.15 |
| Postpartum | 0.08–1.35 |
| Deep vein thrombophlebitis | |
| Antepartum | 0.11–0.56 |
| Postpartum | 0.15–0.27–3.0 |
| Pulmonary embolus | |
| Postpartum | 0.04–0.05 |

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thrombi deep in the thigh. Occasionally, calf thrombi are large enough to be fatal if they embolize.

A thrombus is likely to extend if the stimulus persists, as it does during pregnancy. Possibly, the overall incidence of TED in the pregnant woman is similar to that in the nonpregnant patient, and the higher incidence of symptomatic disease during pregnancy is the result of a chronic stimulus. It may be more than coincidence that fibrinolytic activity decreases during the third trimester, a time coinciding with an increased incidence of TED.[5]

### *Clinical Diagnosis and Routine Laboratory Studies*

Fifty-eight percent of patients, in a recent study, with suspected acute venous disease had negative results in objective tests for thrombosis. Pain, tenderness, and swelling occurred with equal frequency in patients with and without venous disease.[6] Homans' sign was present in less than a third of symptomatic patients with documented thrombophlebitis and in 50% of those without thrombotic disease. Simply, the clinical diagnosis of venous thrombosis is both insensitive and nonspecific.[7] A good physical examination is still necessary to exclude disorders which may mimic TED. These disorders include rupture of a Baker cyst, muscle strain or hematoma, arterial insufficiency, neurogenic pain, arthritis, lymphangitis, myositis, bone disease, and varicose veins.

Because therapy entails significant risk, treatment for TED should never be initiated solely on the basis of clinical diagnosis. The diagnosis must be objectively confirmed prior to the initiation of treatment. The author has evaluated one patient with ten prior hospitalizations for anticoagulant treatment of clinically diagnosed deep vein thrombosis. Venography had never been performed. On her eleventh presentation with symptoms of deep vein thrombosis, a venogram was done, and fibrinopeptide A measured. The results were normal, and the diagnosis of acute TED excluded.

The clinical diagnosis of pulmonary embolus (PE) also lacks sensitivity and specificity. Most PE are asymptomatic and not life-threatening. Dyspnea and tachypnea are the most common findings; with pleuritic pain, they are present in 70% of patients with a documented PE.[8] Dyspnea may be mild and transient, or severe and persistent. It may resolve with bed rest, only to reappear with activity. Recurrence does not necessarily indicate repeat embolization.

Chest pain, often in the lower chest, may accompany a PE. It is secondary to either infarction or congestive atelectasis. Chest pain is more common after distal obstruction because of poor collateral supply. When pain does occur after proximal obstruction, the onset is often delayed because the infarction takes longer to evolve.

Hemoptysis is uncommon after PE, and represents either infarction or congestive atelectasis. It may begin hours or days after the initial event. The classic triad of dyspnea, pleuritic pain, and hemoptysis is present in only 25% of patients with PE.[8] Syncope occurs only after massive obstruction.

While a decreased arterial oxygen content is common, one in six patients with PE will have a normal $Po_2$.[9] In addition, arterial $Po_2$ is affected by position during pregnancy.[10] It

may be as much as 15 mmHg lower in the supine than in the semirecumbent position because of shunting.

The measurement of serum creatine phosphokinase (CPK), lactate dehydrogenase (LDH), serum glutamic-oxaloacetic triaminase (SGOT), and bilirubin have not been as useful diagnostically as initially hoped. In one study, the triad of elevated LDH, slightly elevated bilirubin, and normal SGOT was present in only 12% of patients with angiographically proven PE.[11] Similarly, elevated fibrin split products lack diagnostic specificity and sensitivity.[12,13]

While a normal chest x-ray is uncommon (7–16%), few findings are diagnostic. A pleural effusion (often associated with other illnesses) is present in 50% of patients with PE. Focal oligemia seems most predictive of PE, but is present in only 2%.[14] A study restricted to patients under the age of 40 found that 25% of PE patients had normal chest x-rays. The finding of a pleural effusion was most predictive of PE in this patient population.[15]

### *Objective Tests for TED*

Objective tests for TED are either invasive or noninvasive. Venography remains the "silver" standard for the diagnosis of deep vein thrombosis–thrombophlebitis. The most commonly used noninvasive tests include impedance plethysmography and pulsed Doppler ultrasound. The invasive tests are more sensitive and specific than noninvasive tests, but entail added patient risk. While the noninvasive tests are usually reliable, their accuracy may be affected by physiologic alterations associated with pregnancy. How much sensitivity and specificity is lost has not been objectively investigated. In general, noninvasive tests aid identification of patients requiring invasive testing. In the nonpregnant patient, a positive noninvasive test is sufficiently accurate as a basis for therapy. In contrast, a positive noninvasive test should be confirmed by venography after 20 weeks' gestation.

### Venography

Ascending venography is the "silver" standard for diagnosis of venous thrombosis. With good technique, the entire lower extremity, including the external and common iliac veins, may be evaluated. Iliac venography is rarely required. Venography is not useful for the evaluation of the pelvic vasculature.

There are limitations to venography, and thus the "silver" rather than "gold" standard status; they include poor technique, errant interpretation, and chemical phlebitis. As the popularity of venography has increased, misinterpretation of the inadequate study, usually as positive, has become more common. The most frequent errors include failure to detect large, nonobstructive thrombi in the common femoral vein (because flow in the external or common iliac veins appears adequate) and the incorrect diagnosis of thrombosis in either the common femoral vein due to a streaming effect or in the iliac veins secondary to inadequate opacification. Injection into a suboptimal site may result in nonfilling of the calf veins.

Approximately 3% of patients with a negative venogram develop a positive $^{125}$I-fibrinogen scan following venography; 1–2% develop clinically significant phlebitis.[16] The risk may be minimized by flushing the dye with saline and elevating the legs.

### Impedance Plethysmography

Plethysmography measures volume change within the leg. Impedance plethysmography (IPG) is based on the observation that changes in blood volume are reflected by changes in electrical resistance. Sensitivity and specificity are high for proximal thrombosis, but low for distal thrombosis. In comparison with venography, the sensitivity and specificity of IPG for the detection of proximal venous thrombosis is 90%.[17] Accuracy is dependent upon the degree of vein filling obtained during the application

of a pressure cuff. A technical error can lead to a false-positive test (as may involuntary muscle contractions). In addition, small, nonocclusive thrombi and larger proximal thrombi may be missed if the collateral supply is well developed. This is uncommon in the usually young obstetric patient.

Thrombotic and nonthrombotic occlusion cannot be differentiated by IPG. Therefore, compression of the common iliac vein and/or the vena cava by the gravid uterus may yield false-positive results. Even when clinical symptoms of vena caval compression are alleviated by manual displacement, some clinically undetectable impediment to blood flow may remain. Hence, unless displacement of the uterus results in a positive test becoming negative, a positive IPG after 20 weeks' gestation or within the early puerperium should be confirmed by venography prior to initiation of treatment (see Venography).

### Doppler Ultrasound

The presence or absence of venous flow may be detected by directional Doppler ultrasound. Loss of the phasicity of flow is consistent with a nonocclusive thrombus. Like IPG, Doppler is sensitive for occlusive proximal thrombi, but less sensitive for nonocclusive and distal thrombi. Unlike IPG, Doppler studies are extremely subjective. Technique, technician experience, and patient positioning are extremely important. An accuracy of 90% is feasible, but more difficult to obtain than with IPG.

Doppler ultrasound is more reliable than IPG in the rare obstetric patient with raised venous pressure or arterial insufficiency. Like IPG, Doppler is sensitive for occlusive vein or vena cava by the gravid uterus may result in false-positive results. A positive Doppler study after 20 weeks' gestation should be confirmed by venography.

### $^{125}$I-Fibrinogen Scanning

Identification of thrombi by $^{125}$I-fibrinogen scanning depends upon the incorporation of radioactive fibrin into the developing thrombus. It is the only noninvasive technique accurate for calf and lower thigh thrombi; here sensitivity exceeds 90%. Sensitivity in the proximal venous collecting system ranges between 60% and 80%.[18]

Unbound $^{125}$I crosses the placenta; a small amount enters the fetal circulation.[18] Postpartum, radioactivity can be detected in breast milk.[18] For these reasons, $^{125}$I-fibrinogen scanning is contraindicated during pregnancy, lactation, and the immediate puerperal period. Venography is the only available technique for evaluating the distal collecting system during those times.

Noninvasive tests are used alone, or in combination, to confirm or exclude the clinical diagnosis of deep vein thrombosis/thrombophlebitis. In the nonpregnant patient without evidence of congestive heart failure or severe peripheral vascular disease, a positive IPG or Doppler study is sufficient for proceeding with anticoagulation. If symptoms persist despite a negative study, two alternatives are left: repeat the tests serially, or perform either a venogram or an $^{125}$I-fibrinogen scan. One to two per hundred will become positive. As a screening device, the $^{125}$I-fibrinogen scan identifies 80% of venographically confirmed thrombi. Little added sensitivity is acquired by the addition of an IPG.[19]

During pregnancy or early puerperium, the option of $^{125}$I-fibrinogen scanning is unavailable. A negative IPG or Doppler study all but precludes an occlusive proximal vein thrombus (assuming an adequate technique). Serial studies might identify a developing calf thrombus after extension above the knee. Venography is indicated to evaluate the calf or to confirm a positive IPG or Doppler study. Exposure of the fetus to radiation can be minimized by use of a lead shield and by limiting the study to the affected limb.

It may on occasion be difficult to differentiate chronic obstructive venous disease (postphlebitic syndrome) from active thrombotic disease. The venogram may be abnormal in each. In the nonpregnant patient, $^{125}$I-fibrinogen scanning would be

useful. During pregnancy, an indirect route must be taken. A normal fibrinopeptide A level is incompatible with an active, thrombotic process. In addition, normal antithrombin III activity during pregnancy would also be inconsistent with the diagnosis of active thrombotic disease.

### Perfusion/Ventilation Scanning

A perfusion scan (Q) is performed by the administration of intravenous technetium-99 microspheres. After mixing in the right ventricle, the microspheres are distributed according to blood flow and entrapped within the pulmonary capillaries. Almost all emboli occluding vessels larger than 3 mm and 90% of emboli occluding vessels between 2 and 3 mm are detectable by a perfusion scan.[20] However, the specificity is quite low. Any process disturbing the lung architecture or blood flow will alter the perfusion scan.

A ventilation scan (V) is performed with an isotope of xenon inhaled either just prior to or after the perfusion study. Perfusion/ventilation mismatches are consistent with PE. By applying Baye's theorem of probability to data obtained from angiography, the various V/Q scan patterns may be classified as having a low, average, or high risk for PE. A matching defect carries a near zero probability of a PE. A mismatched segmental or lobar defect has at least a 54% chance of PE; with an average or high probability scan, the likelihood of PE exceeds 80%.[15] No further evaluation is necessary in the latter category. Patients with high-risk subsegmental mismatched defects require angiography. Only 10-15% of patients who undergo a V/Q scan because of suspected PE will require angiography.

## Treatment of TED During Pregnancy

While warfarin and heparin remain the anchors of anticoagulant therapy, the regimens and indications have evolved over the last decade. With few exceptions, *heparin is now the anticoagulant of choice during pregnancy.*

Heparin is a heterogeneous, mucopolysaccharide organic acid. The distribution of high- and low-molecular-weight fragments, and possibly the anticoagulant efficacy, differs from preparation to preparation.[21] Its half-life is proportional directly to dose and the extent of active thrombosis, and inversely proportional to renal function.[22,23] The activity of antithrombin III (AT III), a serine protease inhibitor of most intrinsic cascade factors (see Brandt, this symposium), is profoundly increased by small amounts of heparin.[24] In contrast to warfarin, heparin neither crosses the placenta nor is excreted into breast milk.

Two heparin regimens are commonly employed. Each has a different indication. Full-dose, that is, sufficient heparin to prolong the PTT 1.5–2-fold over baseline, is the treatment of choice for acute thrombotic disease. It is rationalized that once the thrombus has formed, enough heparin to neutralize formed thrombin is necessary to prevent extension or recurrence.[24] Heparin is equally effective whether administered intravenously or subcutaneously.[25,26] Subcutaneous heparin is associated with a lower rate of bleeding complications and thrombus extension than intravenous heparin.[25] A third advantage of subcutaneous heparin is its simplicity and economy. When administered intravenously, nously, a continuous heparin infusion rather than an intermittent bolus should be used.[27]

The second therapeutic regimen is low-dose heparin, utilized primarily for the prevention of TED. Patients at risk for TED benefit from the accentuation of AT III activity. A low dose of heparin permits widescale application with minimal patient risk. Routine use of low-dose heparin in hospitalized patients could save 4000–8000 lives each year.[28] These regimens, with occasional modification, are applicable to all thrombotic events.

### Thromboembolic Prophylaxis During Pregnancy

Thromboembolic prophylaxis is indicated for three settings during pregnancy: 1) high risk for TED, but no prior history; 2) prior history of TED, acute or remote; 3) AT III deficiency. A list of possible high risk characteristics is offered in Table 2. Women with preeclampsia or delivered via cesarean section or midforceps are at particular risk for TED.

While the efficacy of low-dose heparin (5000 units subcutaneously every 12 hours) for the prevention of TED in the postoperative gynecologic patient with benign disease is well established,[28,29] similar studies are unavailable for the pregnant woman. Preliminary reports from both prospective and retrospective studies indicate that heparin effectively prevents TED in the situations cited.[30–34] Long-term, subcutaneous heparin injections during pregnancy are well tolerated, and the complications minimal.[32,33] However, the dose required is increased. Whether secondary to the increased plasma volume, renal clearance, the presence of a placental heparinase, or, during labor, an increase in low-density lipids,[35] 5000 units of heparin sustains a prophylactic level only during the first trimester.[34] An obstetric patient should receive 7500 units of heparin every 12 hours, beginning at about 13 weeks' gestation, and 10,000 units every 12 hours after 30 weeks' gestation. The PTT is not usually prolonged at the cited gestational ages. One group believes that the PTT should be prolonged 5–10 seconds above baseline for prophylaxis, but further study is necessary for determination of whether the higher dose of heparin has any advantage.[33] Postpartum, the dose of heparin should either be reduced to 5000 units or substituted with ultra-low-dose heparin. The latter consists of a constant heparin infusion at 1 U/kg/hr.[36] This regimen is ideal for the patient in labor. Finally, the anticoagulant effect of heparin may be enhanced by aspirinlike drugs. These should be avoided.

**TABLE 2.** Possible Obstetric Indications for TED Prophylaxis

1. Prior history of TED during or prior to pregnancy
2. Anemia (≤9.9 g)
3. Operative delivery
4. Concurrent malignant disease
5. Preeclampsia-eclampsia

Complications of low-dose heparin include thrombocytopenia, osteoporosis, thrombosis, and fat necrosis.[37–43] Heparin-associated thrombocytopenia occurs in 0.8–26% of patients; rarely, it may be associated with arterial thrombosis. Both osteoporosis and fat necrosis have only been reported in patients receiving greater than 15,000 units per day for more than 3 months.[41–43] Osteoporosis, which apparently reflects heparin inhibition of 1α-hydroxylation of 25-hydroxyvitamin D in the kidney, has been reported during pregnancy.[42,44] The earliest clinical sign of osteoporosis is back pain. While these complications have been rare to date, the denominator, or the number of patients receiving a high dose of heparin for a prolonged period of time, has been small. The incidence of osteoporosis and fat necrosis will probably increase dramatically as the number of patients using heparin for long periods increases. It may be necessary to follow these women with some parameter of bone density.

About 75 pregnant women who have received long-term prophylaxis have either been reported or are known to the author. There is no evidence that heparin treatment, as described, results in an overall increase in preterm delivery, placental abruption, or blood loss at delivery. In general, conduction anesthesia has been avoided in these patients.

A thrombotic episode within 3–6 months of conception or during pregnancy necessitates prolongation of the clotting time. Whether secondary to vascular endothelial damage or to the persistence of an underlying thrombotic stimulus, the risk of

acute recurrence is high (greater than 30% without prophylaxis). In the past, a warfarin type of agent was utilized for long-term treatment. The risks of warfarin during pregnancy are well known. They include a unique embryopathy, fetal hemorrhage, and a high likelihood of maternal hemorrhage. Recent studies demonstrate that 1) low-dose heparin is as effective as warfarin in patients whose thrombotic disease has been restricted to the distal venous segments[45,46]; 2) subcutaneous heparin administered every 12 hours at a dose sufficient to maintain a midinterval partial thromboplastin time (PTT) at 1.5–2 times baseline is as effective as warfarin in patients with proximal venous disease[47,48]; 3) the frequency of bleeding complications is 4–8-fold greater in patients treated with warfarin when compared with that of heparin-treated patients.[49,50] While other investigators have since shown that bleeding complications may be reduced with less warfarin while effective prophylaxis is maintained,[51] it is clear that warfarin can be avoided during pregnancy. A previous report that the fetal salvage rates from pregnant patients treated with warfarin and heparin were similar is misleading.[52] Pregnancy loss in the warfarin group was usually related to placental abruption, fetal anomalies, or fetal/neonatal intracranial hemorrhage—each warfarin-related. In contrast, pregnancy loss in the heparin group was predominantly secondary to preterm delivery. Analyses of the individual case reports reveal that the sickest patients were continued on heparin.

The administration of aspirin for venous TED prophylaxis during pregnancy is without foundation and should be avoided. Aspirin has reduced the incidence of TED only in men undergoing hip replacement.[53,54] No benefit was noted in women. The efficacy of aspirin alone for the prevention of arterial thromboses is also suspect.[55] At best, aspirin is ineffective prophylaxis against venous thrombosis; at worst, aspirin may increase the rate of maternal and neonatal complications.[56]

## Treatment of Acute TED During Pregnancy

### *Superficial Venous Thrombosis–Thrombophlebitis*

Anticoagulants are rarely necessary for superficial venous disease. The risk of subsequent embolus is low. Treatment consists of moist heat applications to the affected vein, four times a day, and elevation of the involved extremity. Ambulation should be minimized until the inflammation has begun to resolve, but absolute bed rest is usually unnecessary. Healing occurs within 1–3 weeks. In resistant cases, anti-inflammatory agents may provide symptomatic relief.

### *Deep Vein Thrombosis–Thrombophlebitis*

Once the diagnosis of DVT has been confirmed, a sufficient quantity of heparin should be administered to prolong the PTT 1.5–2-fold over baseline for 7–10 days. (There is some controversy concerning the optimal laboratory parameter for monitoring the adequacy of anticoagulation. However, experience has demonstrated that a prolongation of the PTT as cited is satisfactory.[57,58]) Heparin may be administered either subcutaneously or by continuous infusion with similar results.[25,26]

If the intravenous route is selected, a loading dose (110 U/kg) is given, followed by a continuous infusion of heparin (initially 1000 U/hr). The PTT should be monitored every few hours, and fine adjustments made in the infusion rate until a stable prolongation is achieved. Further testing is not required over the next 36–48 hours. Heparin resistance is associated with extensive thrombosis.[23] There is a drop in the heparin requirement with the cessation of thrombin production. This reduction should be identified and the infusion adjusted so that the risk of hemorrhage is minimized. There is no need to obtain a prothrombin time (PT) measurement at any time during heparin treatment.

If the subcutaneous route is selected, a loading dose of 150 U/kg is given intravenously followed by 20,000 units of calcium heparin every 12 hours; the PTT is check at midinterval. The plasma heparin level achieved with subcutaneous injection is stable. Though there is no difference in efficacy between 8- and 12-hour dose intervals, the 8-hour interval may be preferred when the volume of heparin injected exceeds 1 ml, or when the history suggests that hypocoagulability should be maintained at the lower therapeutic limit as much as possible. Subcutaneous therapeutic heparin has lower rates of thrombus extension and bleeding complications than does continuous infusion.[25] It is advisable to check the platelet count prior to beginning heparin and periodically thereafter to detect developing thrombocytopenia. Complications from full-dose heparin include hemorrhage (mucosal, gastrointestinal, and retroperitoneal) in addition to those already discussed under "Prophylaxis."

When the thrombus involves the proximal venous system, prolonged anticoagulation (the PTT 1.5-fold over baseline) is necessary to prevent recurrence. If limited to the distal collecting system, routine heparin prophylaxis as previously outlined is adequate. Subcutaneous heparin should be continued for a minimum of 3 months, or until 6 weeks postpartum. The patient should be instructed not to inject her heparin once regular uterine contractions have begun. If delivery appears likely within 12 hours of the last heparin injection, an episiotomy should be avoided. Uterine hemostasis is unaffected by heparin. If the PTT is greater than 60 seconds in the second stage, protamine sulfate reversal may be considered for minimization of bleeding from lacerations. One milligram of protamine for every 100 units of heparin will quickly shorten the PTT. Larger doses should be avoided, since excess protamine may act as an antithrombin. *As soon after delivery as feasible, the patient should receive her next subcutaneous injection, because 2–4 hours will pass before a therapeutic plasma level of heparin is obtained.*

The continued use of heparin postpartum must be weighed against the risk of osteoporosis, and the ease of oral warfarin administration against the increased frequency of bleeding complications. Warfarin is initiated after 4–7 days of heparin. A Simplastin time of 15 seconds (equivalent to a PT of 25 seconds) will usually prevent a recurrence of thrombosis. More extensive anticoagulation increases the risk of a bleeding complication. A progestational contraceptive should be considered for the anticoagulated ovulating women to reduce the risk of a hemorrhagic corpus luteum and menorrhagia.[59]

If heparin is continued postpartum because of an antepartum or postpartum thrombosis, low-dose heparin (5000 units subcutaneously every 12 hours) is adequate if the thrombus was limited to the distal collecting system. Low-dose heparin is not associated with osteoporosis. If the thrombus involved the proximal venous system, the PTT should be prolonged 1.5-fold.

Many physicians advocate either calf- or thigh-high support hose for prophylaxis. It appears that the custom-made, waist-high hose are effective adjuncts. However, there is little to support the use of others for prophylaxis. While logical, they tend, in practice, to gather at the thigh or knee in an ambulating patient and reduce venous return.

### Pulmonary Embolus

Confirmation of the clinical diagnosis by objective testing is mandatory. The best treatment for PE is prevention. Two-thirds of patients who ultimately die from PE do so within 30 minutes of the acute event,[60] too soon for anticoagulants to have any effect on mortality.

Treatment of an acute PE requires both cardiovascular support and anticoagulation. The latter is necessary to prevent recurrent embolus. Whether or not heparin

actually speeds resolution is unclear. A loading dose of intravenous heparin (110-120 U/kg) is administered and followed by a continuous infusion adequate to maintain the PTT at twice normal. The subcutaneous route is best avoided initially because of the delayed absorption (2-4 hours). If the embolus occurred during the postpartum period, warfarin may be initiated after 7-10 days of heparin. The PT should be kept twice control. A patient who experiences recurrent emboli despite adequate anticoagulation should be considered for surgical interruption of the vena cava distal to the renal veins. If the location of the thrombus is unknown, the left ovarian vein must also be ligated. Caval ligation should not be undertaken lightly. Long-term sequelae are not uncommon.[61]

Anticoagulation of some form is required for 3 months, or until 6 weeks after delivery. As with deep vein thrombosis, the 30% incidence of all bleeding complications in patients receiving warfarin[49] should be balanced against the ease of administration. Full-dose heparin may be utilized after delivery, but the incidence of osteoporosis is unknown. If the embolus occurred antepartum, the patient should be anticoagulated with heparin until delivery. At that time, warfarin may be utilized if desired. In addition to the well-known embryopathy occurring in about 10% of fetuses exposed to warfarin during the first trimester, complications of warfarin in the second and third trimesters include fetal and placental hemorrhage. After delivery, a progestogen for contraception should be considered to prevent menorrhagia or a hemorrhagic corpus luteum.[59]

### Septic Pelvic Vein Thrombophlebitis

Septic pelvic thrombophlebitis (SPT) occurs in approximately 0.1% of all deliveries.[62] Though uncommon, SPT is a potentially life-threatening complication of puerperal endometritis. Septic pulmonary emboli have been reported in 31-39% of untreated patients.[63] The notable lack of specific physical findings for SPT necessitate that the diagnosis be made retrospectively, when defervescence of a patient with persistent puerperal fever resistant to adequate aerobic and anaerobic therapy follows therapeutic anticoagulation.

Sufficient heparin to prolong the PTT 1.5-2-fold is indicated in women who remain febrile after an adequate trial of antibiotics whose coverage includes the enterococcus and the anaerobes, and in the absence of a detectable abscess, ureteral damage, or drug fever. The diagnosis of SPT is presumed when defervescence occurs within 12-36 hours of inititating therapeutic anticoagulation. Heparin is continued for 10 days. Failure of the patient to respond to heparin strongly suggests the presence of an abscess, and operative intervention should be considered.

During the delay necessary to differentiate SPT from fever of another cause, progressive thrombosis of the vena cava or renal veins and/or pulmonary embolus may result. Unfortunately, identification of a suitable diagnostic aid to shorten or eliminate this delay has proved elusive. Computerized axial tomography (CAT scan) has been recommended, but the sensitivity and specificity of tomography for the diagnosis of SPT is unknown. Fibrinopeptide A (FPA) may be of value. It has been reported that an FPA in excess of 12 ng/ml in a nondiabetic, puerperal patient is found only with thrombotic disease.[64]

### Ovarian Vein Thrombosis

Acute ovarian vein thrombosis has been reported postpartum in 1 per 4000 deliveries.[65] It presents as severe pain 2-3 days postpartum localized to the involved adnexa (usually the right). Fever is consistently present; flank or abdominal pain may be noted.[65,66] Therapeutic heparinization is indicated once ureteral obstruction has been excluded. In practice, the diagnosis is often made at laparotomy for suspected appendicitis; however, the obstruction is detectable by CAT scan.[67] If the clot has extended into

the inferior vena cava, ligation should be performed. Heparin is continued for 10–15 days.

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