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**Open**

**Vascular thrombosis**

One or more clinical episodes of arterial, venous or small-vessel thrombosis. Thrombosis must be objectively confirmed. For histopathologic confirmation, thrombosis must be present without inflammation of the vessel wall

**Pregnancy morbidity**

- One or more unexplained deaths of a morphologically normal fetus ≥10 weeks of gestation
- One or more premature deliveries of a morphologically normal fetus <34 weeks gestation owing to:
  - Severe preeclampsia or eclampsia defined according to standard definitions
  - Recognized features of placental insufficiency
- ≥Three unexplained consecutive abortions <10 weeks gestation, with maternal and paternal factors (anatomic, hormonal or chromosomal abnormalities) excluded

**Laboratory criteria**

The presence of aPLs on two or more occasions at least 12 weeks apart and no more than 5 years prior to clinical manifestations, as demonstrated by ≥one of the following:

- Presence of lupus anticoagulant in plasma
- Medium- to high-titre anticardiolipin antibodies (>40 GPL or MPL, or >99th percentile) of IgG or IgM isoforms
- Anti-β2GP-I of IgG or IgM present in plasma

Anti-β2GP-I: β2 glycoprotein-I antibody; aPL: Antiphospholipid antibody. Data taken from [22,23].

REACTIVE ERYTHEMAS AND VASCULITIS 97



Fig. 8.4 A classic wheal.



Fig. 8.6 Angioedema of the upper lip.



Fig. 8.5 Severe and acute urticaria caused by penicillin allergy.

**Course**

The course of an urticarial reaction depends on its cause. If the urticaria is allergic, it will continue until the allergen is removed, tolerated or metabolized. Most such patients clear up within a day or two, even if the allergen is not identified. Urticaria may recur if the allergen is met again. At the other end of the scale, only half of patients attending hospital clinics with chronic urticaria and angioedema will be clear 5 years later. Those with urticarial lesions alone do better, half being clear after 6 months.

**Complications**

Urticaria is normally uncomplicated, although its itch may be enough to interfere with sleep or daily activities and to lead to depression. In acute anaphylactic reactions, oedema of the larynx may lead to asphyxiation, and oedema of the tracheo-bronchial tree may lead to asthma.

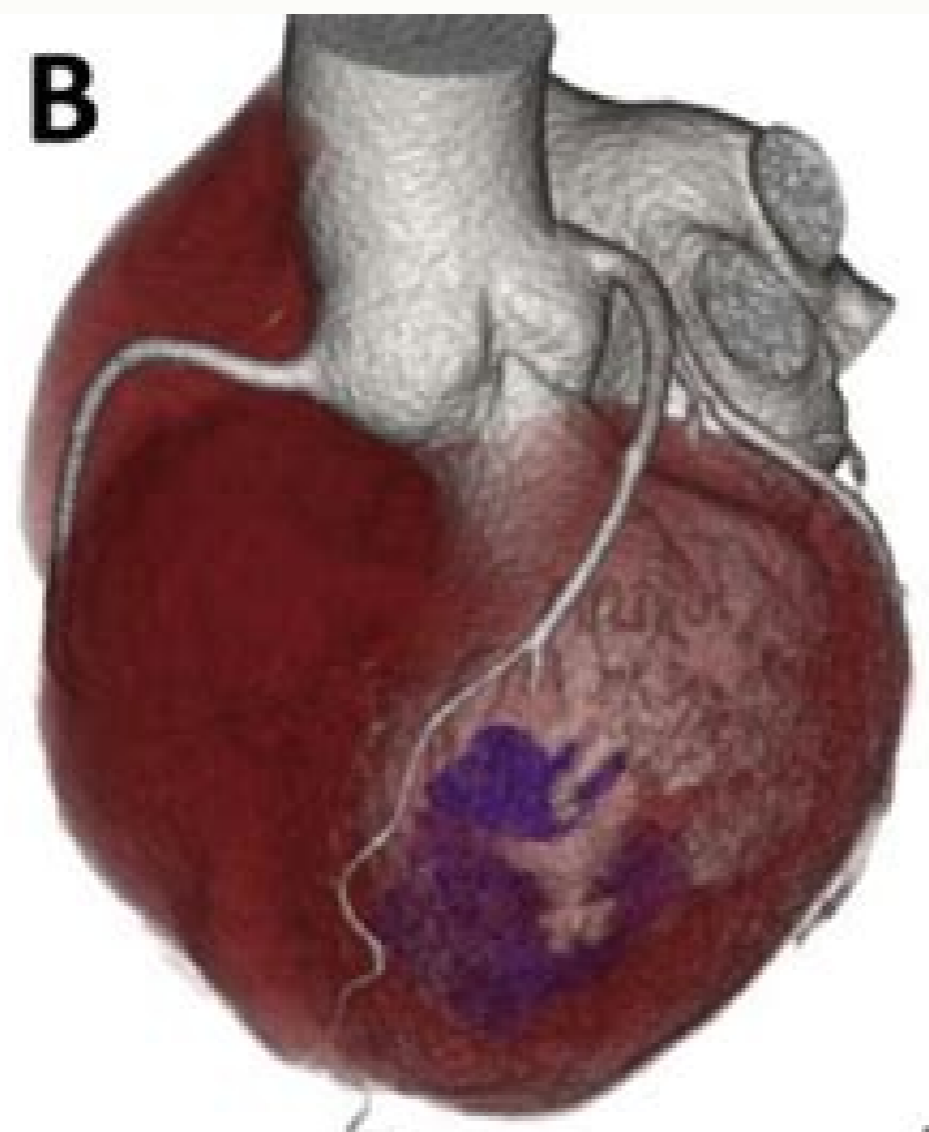
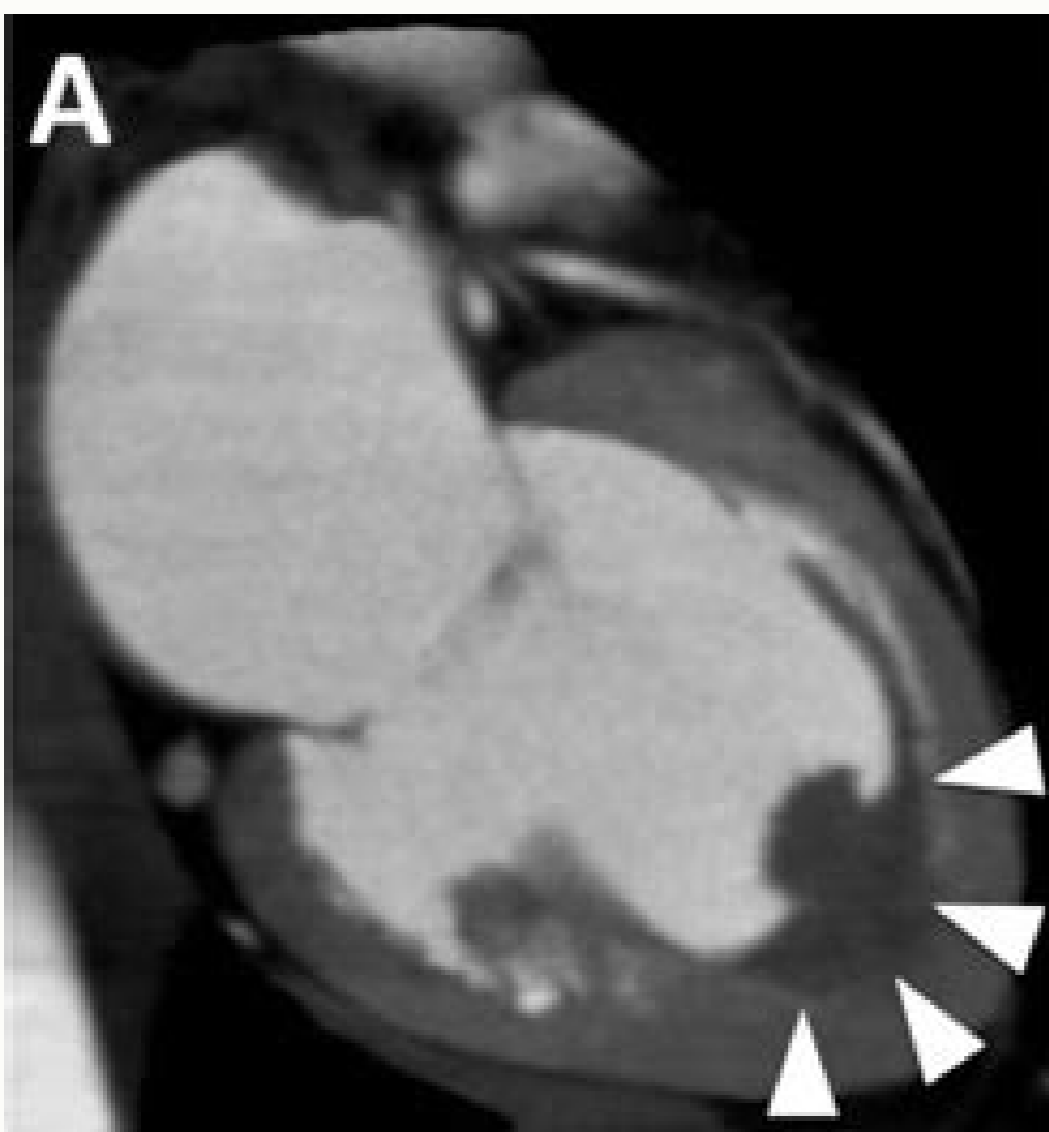
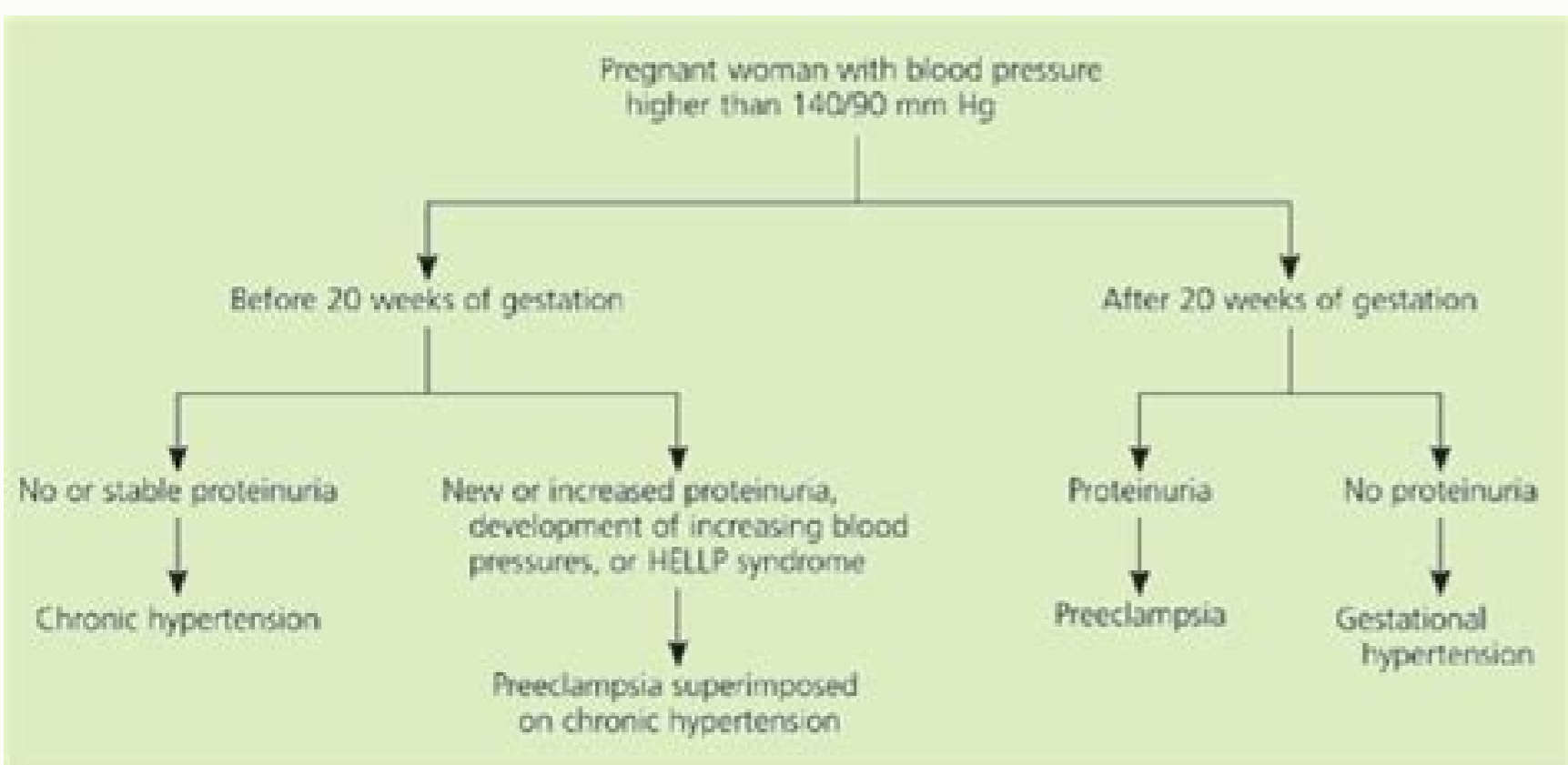
**Differential diagnosis**

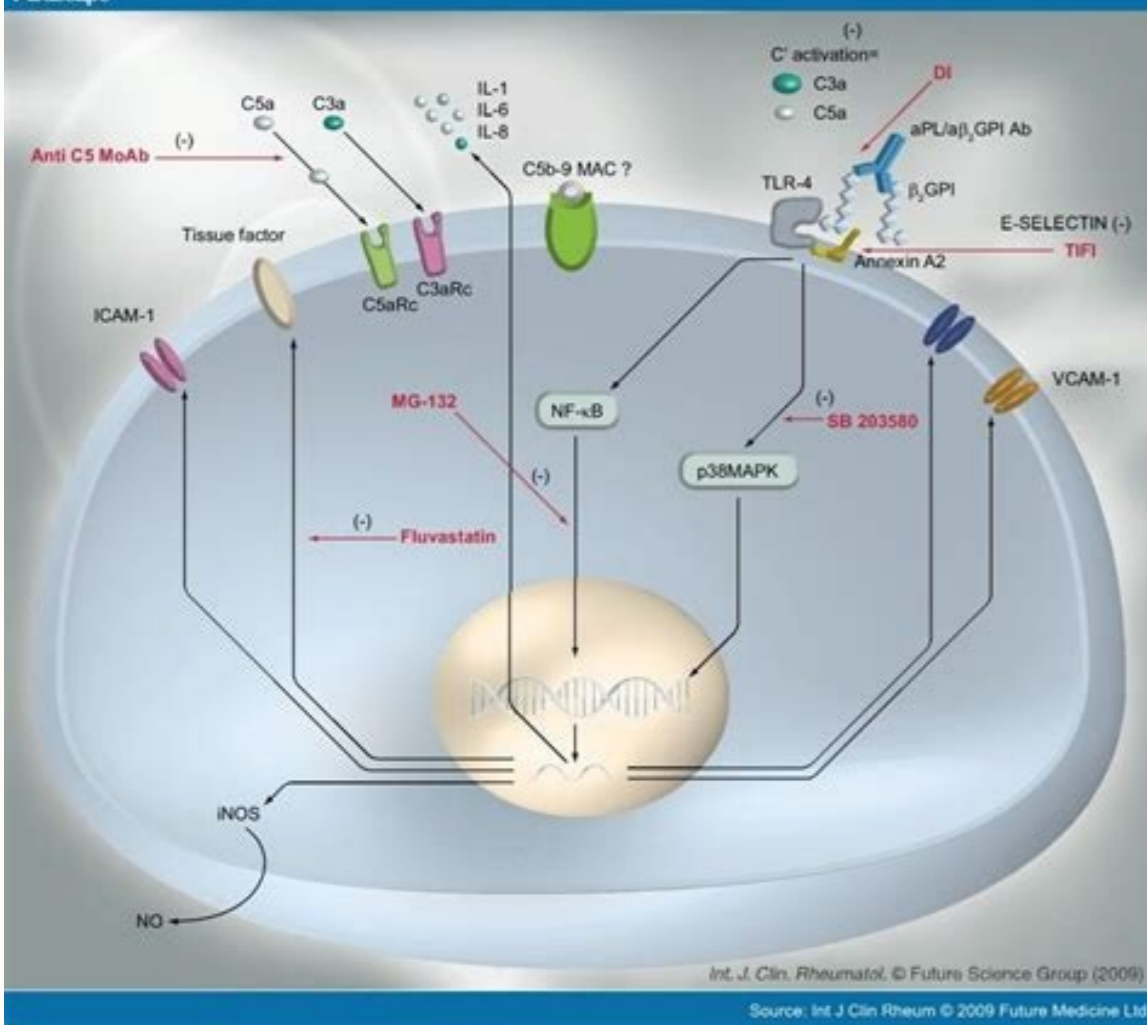
There are two aspects to the differential diagnosis of urticaria. The first is to tell urticaria from other eruptions that are not urticaria at all. The second is to define the type of urticaria, according to Table 8.1. Insect bites or stings (Fig. 8.7) and infestations commonly elicit urticarial responses, but these may have a central punctum and individual lesions may last longer than 24 h. Erythema multiforme can mimic an annular urticaria. A form of vasculitis (urticarial vasculitis, p. 103) may resemble urticaria, but individual lesions last for longer than 24 h and may leave

**Presentation**

Most types of urticaria share the sudden appearance of pink itchy wheals, which can come up anywhere on the skin surface (Figs 8.4 and 8.5). Each lasts for less than a day, and most disappear within a few hours. Lesions may enlarge rapidly and some resolve centrally to take up an annular shape. In an acute anaphylactic reaction, wheals may cover most of the skin surface. In contrast, in chronic urticaria only a few wheals may develop each day.

Angioedema is a variant of urticaria that primarily affects the subcutaneous tissues, so that the swelling is less demarcated and less red than an urticarial wheal. Angioedema most commonly occurs at junctions between skin and mucous membranes (e.g. peri-orbital, peri-oral and genital; Fig. 8.6). It may be associated with swelling of the tongue and laryngeal mucosa. It sometimes accompanies chronic urticaria and its causes may be the same.





Antiphospholipid syndrome pregnancy guidelines acog. Acog guidelines antiphospholipid antibody syndrome.

Ann N Y Acad Sci. Committee on Practice Bulletins-Obstetrics ACOG Practice Bulletin No. 132: Antiphospholipid Syndrome, December 2012 (Replaces Practice Bulletin No. 118, January 2011). Shamonki JM, Salmon JE, Hyjek E, Baergen RN. 2007;1108:505-514. 3. Other hemostatic sequelae of the disorder include the presence of antiphospholipid antibodies (APA) in around 5% of stroke victims younger than 50 and the 40% to 50% prevalence of thrombocytopenia among APS patients. To test or not to test? Obstetrical sequelae include fetal loss after 10 weeks, recurrent (>2) embryonic losses, and an association with preeclampsia and uteroplacental insufficiency.1 The Bulletin recommends testing women for APS only if they have had an unexplained fetal loss (>10 weeks) or 3 or more unexplained embryonic losses. Low-dose aspirin may be added in both cases. ACOG also opines that, "For women with APS who have not had a thrombotic event, expert consensus suggests that clinical surveillance or prophylactic heparin use antepartum in addition to 6 weeks of postpartum anticoagulation may be warranted." This recommendation would apply if the diagnosis of APS was made based on the occurrence of 1 or more preterm births associated with eclampsia, severe preeclampsia, or features consistent with placental insufficiency, since ACOG does not recommend treatment for these indications. Looking back-and forward This unusual condition fascinated me as a young maternal-fetal medicine fellow and led to my career-long interest in the study of uterine hemostasis. However, it is frustrating to realize what little progress has been made in understanding APS in the ensuing 25 years. Melamed N, et al. 2003;12(7):535-538. 4. Excessive complement activation is associated with placental injury in patients with antiphospholipid antibodies. Despite the prevalence and clinical significance of APS, there is controversy about the indications for and types of antiphospholipid tests that should be performed in order to diagnose the condition. Antiphospholipid Syndrome Antiphospholipid syndrome (APS) is an autoimmune disorder defined by the presence of characteristic clinical features and specified levels of circulating antiphospholipid antibodies. Di Simone N, Luigi MP, Marco d, et al. The mystery of the antibodies still awaits a solution By Charles J. 2021 Mar;152 Suppl 1(Suppl 1):3-57. PMID: 33740264 Free PMC article. doi: 10.1002/tjgo.13522. Lockshin MD. 2012;120(6):1514-1521. 2. Used with permission. Antiphospholipid antibody. Activation of complement mediates antiphospholipid antibody-induced pregnancy loss. We still do not know how these antibodies arise, how they trigger losses, or how heparin prevents such losses. Practice bulletin no. Am J Obstet Gynecol. Testing is also indicated in previously untested patients with current or prior venous or arterial thrombosis. The tests to be employed have not changed-they are a lupus anticoagulant assay and a screen for anticardiolipin and anti-beta-2-glycoprotein I antibodies. Committee on Practice Bulletins-Obstetrics, American College of Obstetricians and Gynecologists. 2012;120(6):1514-1521. 2007;196(2):167.e1-167.e5. ACOG Abstract Reference 1. The purpose of this document is to evaluate the data for diagnosis and treatment of APS. Babies, blood clots, biology. 132: antiphospholipid syndrome. However, thrombosis is rarely observed with embryonic losses, and whether it is a cause or consequence of later losses is unclear.2 There is even recent evidence that inflammation and complement activation, not clotting, may be at the heart of the disease process.3,4 Thus, there is much left to be discovered about these mysterious antibodies. Commentary References 1. Antiphospholipid antibodies are a diverse group of antibodies with specificity for binding to negatively charged phospholipids on cell surfaces. Salmon JE, Girardi G, Holers VM. Lupus. Diagnosis requires that at least one clinical and one laboratory criterion are met. FIGO (international Federation of Gynecology and obstetrics) initiative on fetal growth: best practice advice for screening, diagnosis, and management of fetal growth restriction. Copyright the American College of Obstetricians and Gynecologists. Because approximately 70% of individuals with APS are female (1), it is reasonably prevalent among women of reproductive age. Melamed N, Baschat A, Yinon Y, Athanasiadis A, Mecacci F, Figueras F, Berghella V, Nazareth A, Tahlak M, McIntyre HD, Da Silva Costa F, Kihara AB, Hadar E, McAuliffe F, Hanson M, Ma RC, Gooden R, Sheiner E, Kapur A, Divakar H, Ayres-de-Campos D, Hiersch L, Poon LC, Kingdom J, Romero R, Hod M. Full text of ACOG Practice Bulletin available to ACOG members at .JAMA. Much of the debate results from a lack of well-designed and controlled studies on the diagnosis and management of APS. Pregnancies complicated with antiphospholipid syndrome: the pathogenic mechanism of antiphospholipid antibodies: a review of the literature. Int J Gynaecol Obstet. Pregnancy loss was long assumed to be due to uteroplacental thrombosis. Obstet Gynecol. 2021. Lockwood, MD, MHCM Dr. Lockwood is Dean of the College of Medicine and Vice President for Health sciences, the Ohio State University, Columbus, and Editor in Chief of Contemporary OB/GYN. The American College of Obstetricians and Gynecologists' Practice Bulletin Antiphospholipid Syndrome (No. 132, December 2012) replaces the original bulletin from November 2005.1 That there is little difference between these 2 documents should not be surprising, since there has been little progress in research into this still-quiet-mysterious disorder during that interval. The new Practice Bulletin reviews the association of antiphospholipid syndrome (APS) with thrombosis, noting that most thrombotic events are venous and that among untreated APS patients, risk of recurrent venous thromboembolism (VTE) may be as high as 25% per year.1 Pregnancy poses a particular risk of clotting (5% to 12%). 1997;277(19):1549-1551. These tests must be positive on 2 occasions 12 weeks apart. Complexities of treatment. According to ACOG, therapy with prophylactic anticoagulation is indicated in women with APS and prior thrombosis during pregnancy and for 6 weeks postpartum.1 Similar therapy is warranted for women with APS associated with fetal loss or recurrent embryonic loss.

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