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Thinking Outside the Box

TO THE EDITOR: Farzaneh-Far et al. (June 1 issue)¹ describe a case of massive pulmonary embolism, stating that in more than 80 percent of patients with acute pulmonary embolism, echocardiography reveals abnormalities. However, others report that most patients with pulmonary embolism have normal echocardiographic results.² For that reason, echocardiography has not been recommended as a routine imaging test for the diagnosis of suspected pulmonary embolism.³

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TO THE EDITOR: Farzaneh-Far et al. state that “although this is the patient’s first thromboembolic event, testing him for a hypercoagulable state would be reasonable.” This statement requires clarification.

There is currently no consensus regarding whom to test for the inherited thrombophilias. Each year, approximately 250,000 patients receive a diagnosis of acute venous thromboembolism. It has been argued that testing of all patients with an initial episode of venous thromboembolism is not cost-effective.¹ For patients with an initial episode of idiopathic venous thromboembolism, routine testing for an inherited thrombophilic defect would only be warranted if the results changed the treatment approach. However, Farzaneh-Far et al. later state that they “favor providing long-term anticoagulation with warfarin.” If the decision has already been made to provide long-term anticoagulation, then the clinical utility of testing for a hypercoagulable state is limited.

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THE AUTHORS REPLY: Dr. Jaitovich correctly points out that many patients with pulmonary embolism do not have echocardiographic abnormalities; we wish to clarify that the high rate of echocardiographic abnormalities we noted would apply to patients with massive pulmonary embolism. Nevertheless, echocardiographic evidence of right ventricular dysfunction in patients with unexplained hemodynamic instability can suggest the diagnosis of pulmonary embolism and may warrant further diagnostic testing by spiral computed tomography of the chest with intravenous contrast.¹ The primary role of echocardiography in acute pulmonary embolism is risk stratification. As we noted in our commentary, right ventricular hypokinesis is a powerful independent predictor of 90-day mortality in patients with submassive pulmonary embolism (defined as a systolic arterial pressure greater than 90 mm Hg).²

Dr. Itskowitz makes an important point regarding the lack of consensus about indications for testing for inherited thrombophilias. We agree that routine testing of all patients with idiopathic venous thromboembolism is not cost-effective. However, one could argue that a patient who has an idiopathic venous thromboembolism before 50 years of age has thrombophilia, and therefore, laboratory investigation is warranted.³ Given that abnormalities predisposing patients to venous thromboembolism, including protein S deficiency, are more common in patients with HIV infection, testing a 35-year-old man with HIV is not unreasonable, albeit costly. Although long-term anticoagulation was favored in this patient regardless of the test results, because of the life-threatening nature of his pulmonary embolism, such results could influence the intensity of anticoagulation. If the patient were found to have clinically significant titers of antiphospholipid antibodies, for example, his target international normalized ratio might be higher than that of a patient without this finding.

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Life-Threatening Asthma during Treatment with Salmeterol

TO THE EDITOR: Although the addition of a long-acting β_2 -agonist such as salmeterol to an inhaled corticosteroid has been demonstrated to provide greater control of asthma than does a substantially increased dose of the inhaled corticosteroid,¹ this medication was associated with an increased risk of asthma-related death in a large population study.² We have identified two adolescent boys with poorly controlled asthma and a history consistent with sudden asphyxial episodes during mod-

Table 1. Results of Four Exercise Studies in Two Patients Receiving Inhaled Corticosteroids, with and without Concurrent Administration of Salmeterol.*

| Patient No. | Day | Maintenance Medication | Medication Taken before Exercise | FEV ₁ before Exercise | Decrease in FEV ₁ during Exercise | Exercise Duration and Symptoms |
|-------------|-------------------------|--|--|----------------------------------|--|--|
| | | | | liters | % | |
| 1† | 1 day after admission | Budesonide (Pulmicort Turbuhaler), 200 μ g twice daily, and salmeterol (Serevent MDI), 50 μ g twice daily | Pirbuterol (Maxair Autohaler), 2 inhalations | 2.83 | 42 | Highest heart rate, 157 beats per min; target heart rate not attained because of dyspnea after 4 min |
| | 5 days after admission | Budesonide, 200 μ g twice daily, and salmeterol, 50 μ g twice daily | Pirbuterol, 4 inhalations | 3.26 | 55 | Highest heart rate, 158 beats per min; target heart rate not attained because of dyspnea after 4 min |
| | 9 days after admission | Budesonide, 200 μ g twice daily, and SR theophylline, 225 mg twice daily (serum theophylline concentration, 15 μ g/ml) | Pirbuterol, 4 inhalations | 3.60 | 1 | 9 min, with highest heart rate of 173 beats per min and no dyspnea |
| | 18 days after admission | Budesonide, 200 μ g twice daily, and SR theophylline, 225 mg twice daily | Pirbuterol, 4 inhalations | 3.56 | 1 | 10 min, with highest heart rate of 172 beats per min and no dyspnea |
| 2‡ | Before admission | 2 Inhalations twice daily of fluticasone, 500 μ g, in combination with salmeterol, 50 μ g (Advair 500/50) | Albuterol, 4 inhalations from a metered-dose inhaler | 1.43 | 71 | 3 min, with severe dyspnea and hypoxemia (oxygen saturation, 82%) |
| | Day of admission | 1 Inhalation twice daily of fluticasone, 250 μ g, in combination with salmeterol, 50 μ g | Albuterol, 4 inhalations from a metered-dose inhaler | 1.88 | 68 | 3 min with severe dyspnea and hypoxemia (oxygen saturation, 74%) |
| | 2 days after admission | Budesonide, 200 μ g twice daily, and SR theophylline, 250 mg twice daily (serum theophylline concentration, 9 μ g/ml) | Albuterol, 4 inhalations from a metered-dose inhaler | 1.98 | 51 | 9 min, with highest heart rate of 168 beats per min, no hypoxemia, and rapid spontaneous improvement |
| | 3 days after admission | Budesonide, 200 μ g twice daily, and SR theophylline, 300 mg twice daily (serum theophylline concentration, 16 μ g/ml) | Albuterol, 4 inhalations from a metered-dose inhaler | 1.93 | 14 | 11 min, with highest heart rate of 172 beats per min, no dyspnea, and no decrease in oxygen saturation |

* FEV₁ denotes forced expiratory volume in one second, MDI metered-dose inhaler, and SR sustained release.

† The predicted FEV₁ for Patient 1 was 3.45 liters.

‡ The predicted FEV₁ for Patient 2 was 1.69 liters.