sudden cough and immediately after described intense left pleuritic pain and dyspnea. The procedure was interrupted and a chest x-ray examination confirmed left pneumothorax of two-thirds of the hemithorax. Thoracic drainage tube was placed. Seven days later the lung was reexpanded.

Pneumothorax is an occasional complication of transbronchial biopsy but has not been described during BAL. We think this case shows that patients with obstructive lung disease can suffer pneumothorax if they present sudden cough when the tip of the bronchoscope is wedged. High intraalveolar tension during cough with no flow could cause bleb rupture and pneumothorax.

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Syncope Caused by Methacholine in a Patient with Exercise-Induced Anaphylaxis

To the Editor:

In their editorial, Pratter and Irwin discuss the usefulness and safety of pharmacologic bronchoprovocation challenges (Chest 1988; 93:898-900). I have seen a patient with syncope who reacted to methacholine PBPC.1

The patient was a 34-year-old Miller who suffered exercise-induced anaphylaxis (EIA) with cholinergic urticaria, which were also triggered by sauna bath. He suffered chest tightness, wheezing and cough from flour dust and had positive skin test reactions to some allergens. Spirometry values were normal. There was no eosinophilia.

A methacholine challenge was performed as follows. The patient successively took five breaths of 0.025 and 0.25 percent, 20 breaths of 0.25 percent and five breaths of 2.5 percent methacholine solution, which was delivered by a DeVilbiss nebulizer at an oxygen flow of 3 L/min. He lost conscious after five inhalations of the initial methacholine concentration. Before syncope he felt weak and was sweaty. He woke up 3 min after intravenous administration of methylprednisolone (300 mg), after being unconscious for 8 min. Placebo methacholine challenges with saline solution and aque distillata caused dizziness and slight vertigo.

Two months later methacholine and exercise challenge tests were performed under premedication with either 40 μg ipratropium bromide given 15 min before the tests, or 20 mg disodium cromoglycate (DSCG) given 30 min before the tests, which were on consecutive days. The exercise tests were performed on an ergometer, increasing the work load by 50 W every fourth minute until maximal pulse rate (190/min) and profound sweating were achieved at 150 W. This effort would anamnestically have caused EIA. Both medications almost prevented the previous reactions. During methacholine challenge under DSCG protection the patient felt vertigo, visual disturbance, fatigue and sweating from the last concentration of methacholine (2.5 percent). A similar 5-h delayed reaction occurred after the exercise test under ipratropium bromide protection. Methacholine challenge after ipratropium bromide and exercise challenge after DSCG protection caused no symptoms. An intradermal skin test with 0.01 mg methacholine was weakly positive.

Since 1983, the patient has successfully used either ipratropium bromide or DSCG in preventing EIA. This, and the observations by Sheffer and coworkers6 that marked morphologic alterations of cutaneous mast cells occur and serum histamin levels rise in patients with EIA, indicate that mast cell degranulation is involved in the pathogenesis of EIA. According to Errington and coworkers,8 exercise can alter the threshold for mast cell mediator release in a subset of EIA patients. In this case, serum histamin concentrations did not correlate with symptoms during challenge.

The patient's reaction to methacholine, the cholinergic urticaria, also through sauna bath-induced symptoms and the inhibitory effect of ipratropium bromide indicate cholinergic hyperreactivity as another possible cause of the symptoms.

In cases of EIA it is advisable to be careful with methacholine PBPC. Ipratropium bromide and/or DSCG could be worth trying in such cases.

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To the Editor:

Dr. van Assendelft's report of a patient who developed syncope during methacholine bronchoprovocation challenge (BPC) is of great interest. Although, BPC is considered safe,1 a history of cholinergic hypersensitivity is an absolute contraindication to its performance.2 It is the policy in our laboratory that patients be questioned about any history of cholinergic hypersensitivity (eg, cholinergic urticaria); if it is present, the challenge is not done. Based on the fact that the patient described by Dr. van Assendelft had known cholinergic urticaria, methacholine bronchoprovocation challenge should not have been performed. The importance of this policy is reinforced by his experience.

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Primary Biliary Cirrhosis and Sarcoidosis

To the Editor:

In a recent review of primary biliary cirrhosis (PBC), the possible association of this disease with sarcoidosis is not mentioned.1 Although most patients with sarcoidosis have no clinical evidence of liver disease, hepatic granulomas occur in 60 percent of patients with this disease.2 Rarely, patients with sarcoidosis may develop chronic intrahepatic cholestasis, which may progress to biliary cirrhosis and liver failure. Since many patients with PBC show hepatic granulomas, the question arises of the relation between these two disorders. Similarities between PBC and sarcoidosis with chronic intrahepatic cholestasis were described more than 25 years ago. In 1969, Karlish et al3 reported the case of a 47-year-old woman with enlarged hilar and paratracheal lymph nodes, a positive Kveim test, circulating antimitochondrial antibodies and progressive cholestatic liver disease. Maddrey et al,4 in a study of 20 patients with sarcoidosis and chronic hepatic disease, described two patients who had features of PBC: they subsequently described two other patients with pulmonary granulomas and progressive cholestatic liver disease.4 Antimitochondrial antibodies were positive in one of two patients tested in this group of four. Stanley et al5 described two middle-aged women with pruritus, liver findings compatible with PBC, and positive antimitochondrial antibodies. Both patients had pulmonary infiltrates; after they died from liver disease, autopsy showed pulmonary granulomas. Rudzki et al6 described a series of five young men who had evidence of systemic granulomatous disease with clinical and biochemical data similar to those of PBC. Antimitochondrial antibodies were not found; survival exceeded the usual survival of patients with PBC and the authors considered sarcoidosis as the most likely diagnosis. Fagan et al7 described four women with high titers of antimitochondrial antibodies and hepatic granulomas, in addition to prominent pulmonary signs and symptoms. Kveim test was positive in one of the three patients tested; all patients had abnormal chest radiographs and three of them had lung granulomas on biopsy. The authors stressed that their patients' disorders were not discrete entities, but had clinical, serologic and histologic findings that overlapped those of Sjögren's syndrome, celiac disease and mixed connective disease as well as sarcoidosis and PBC. About 95 percent of patients with PBC have positive antimitochondrial antibody tests, as opposed to 1 percent of patients with sarcoidosis. It therefore seems reasonable to use this finding as a defining characteristic for PBC. The absence of antimitochondrial antibodies would identify patients with chronic intrahepatic cholestasis complicating sarcoidosis. Patients with chronic intrahepatic cholestasis, extrahepatic granulomas and circulating antimitochondrial antibodies would be considered to have both sarcoidosis and PBC. Sarcoidosis should be added to the list of diseases that may be associated with PBC.

Interaction of Rifampin and Glyburide

To the Editor:

Numerous clinically significant drug interactions have been reported with the use of rifampin, including the sulfonylureas, tolbutamide and chlorpropamide.8,9 We recently observed a case suggestive of an effect of rifampin on serum glyburide concentrations. To our knowledge, this is the first report of this interaction in the literature.

A 67-year-old woman was diagnosed with renal tuberculosis in March, 1988 on the basis of a urine test positive for acid-fast bacilli and positive urine cultures for Mycobacterium tuberculosis. On March 10, therapy was begun using rifampin (600 mg daily), isoniazid (300 mg daily), and pyridoxine (50 mg daily). The patient's past medical history included adult onset diabetes mellitus, hypertension, gout, and mild renal insufficiency. Medications for these problems included allopurinol (100 mg daily), glyburide (5 mg daily), pentoxifylline (400 mg three times daily), furosemide (120 mg in the morning and 80 mg in the evening), nifedipine (20 mg three times daily) and methyldopa (250 mg twice daily). Glyburide dosage was increased to 10 mg in the morning and 5 mg in the evening in July, 1988. In August, insulin therapy (10 units in the morning and 5 units in the evening) was added to help control serum glucose levels. Insulin dosage was further increased in October, 1988 to 15 units in the morning and 5 units in the evening. In October, 1988, furosemide was replaced with metolazone (5 mg daily).

Using a modification (unpublished) of the method of Adams et al,10 serum glyburide concentrations were determined twice before rifampin therapy was discontinued on December 10 and then three times after rifampin was stopped. Morning trough glyburide serum concentration rose dramatically upon discontinuation of rifampin therapy (Fig 1). Renal and hepatic function remained stable throughout this period.

This case is strongly suggestive of a glyburide and rifampin

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