Bronchoscopy for Hemoptysis

To the Editor:

We read with great interest the letter by Drs Schraufnagel and Margolis concerning the paper by Dr Lederle and co-workers on the issue of whether diagnostic fiberoptic bronchoscopy is indicated for patients with hemoptysis and a negative chest radiograph.

We suggest that disagreement on whether bronchoscopy should be done "routinely" in this setting is often based on two common misunderstandings: considering data from dissimilar patients to be comparable and assuming that showing any difference is the same as proving that such a difference is clinically relevant. Thus, the accuracy of the proposed 16 percent diagnostic yield for bronchogenic carcinoma in this setting depends on exactly which types of patients are included in the analysis (eg, young vs old, first vs recurrent episode of hemoptysis, smoker vs nonsmoker, hemoptysis in the setting of acute bronchitis vs "spontaneous" hemoptysis, and truly negative chest radiograph vs one with borderline or nonspecific abnormalities).

In addition, even if one accepts that immediate bronchoscopy can be used to diagnose some occult bronchogenic carcinomas in patients with truly normal chest radiographs, the value of doing so is by no means automatically proved. Given the high proportion of negative bronchoscopy examinations that would have to be done in this scenario (at least 84 percent), the cost-effectiveness and risk-benefit ratio of such an approach should be considered acceptable only if the following statements are proved to be true:

1. Unless bronchoscopy is performed at once, occult bronchogenic carcinomas will be missed for a long time and will not be diagnosed before it is "too late."
2. Alternatively, even if occult bronchogenic carcinomas are not missed for long, diagnosing them at the time of the first episode of hemoptysis significantly improves prognosis. In other words, even a short delay (days/weeks/months) in making the diagnosis has a definite negative impact on final outcome.

3. Because of the two previous points, the benefits of immediate bronchoscopy clearly outweigh the morbidity/mortality (albeit low) associated with at least 84 percent of "unnecessary" bronchoscopic examinations and justify the definitely not-insignificant added cost.

To our knowledge, no study has ever been published proving any of the above statements to be true. Thus, over the past few years we often have elected to defer bronchoscopy, even in smokers over the age of 40, if all of the following criteria were met:

1. First episode of hemoptysis during a one-year period.
2. Duration of hemoptysis of less than ten days.
3. The hemoptysis developed in the context of a clinically apparent episode of acute bronchitis, or a specific cause of hemoptysis (eg, pulmonary embolism or trauma) is overwhelmingly evident.
4. If hemoptysis is associated with bronchitis, the chest radiograph is completely negative (not suspicious, nonspecific, or unsatisfactory).

5. There are no historical or clinical data suggestive of a possible occult malignancy (eg, unexplained weight loss, anemia, hypercalcemia, or evidence of distant metastasis).
6. Rapid (within seven days) and complete resolution of hemoptysis with medical therapy. If any amount of hemoptysis recurs within 12 months, or if it persists, bronchoscopy is performed at once.

In all cases, close follow-up is provided, and patients are clearly instructed to contact us at once if any amount of hemoptysis (however slight) recurs or if any new symptom develops.

We selected the above criteria based on a review of our clinical experience since 1982 and previously published data, both of which suggested that these criteria may be accurate predictors of underlying bronchogenic carcinoma in this setting. Since 1988, of 17 patients we have seen at our institution who met all of the above criteria, only one was later found to have a bronchogenic carcinoma. In this case, the diagnosis was made within six weeks of the initial episode of hemoptysis due to recurrent blood-tinged sputum. Of course, no conclusions can yet be drawn from our data, since the number of cases is small and many patients have not completed a sufficiently long period of follow-up.

Although routinely performing bronchoscopy in all patients presenting with acute first-time hemoptysis and a negative chest radiograph will eventually result in the diagnosis of a few occult bronchogenic carcinomas, whether this is cost-effective, or even necessary, is far from being definitely established. Consequently, we believe that, until a proper prospective study answers these questions, clinical judgment and close clinical observation, rather than a routine and possibly overaggressive approach, can and should dictate when and if diagnostic fiberoptic bronchoscopy is indicated for a specific patient with hemoptysis.

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To the Editor:

Drs Berger and Rehm bring up additional points to consider when answering the important question: Should all patients with hemoptysis undergo bronchoscopy? The problem with a wait-and-see approach is that lung cancer is deadly and only curable surgically. With other cancers that have early warning signs (such as blood in the stool, abnormal cervical Papanicolaou smear, and breast lump), morbidity and mortality have decreased, probably because of an aggressive diagnostic approach. We would not want to wait for "unexplained anemia, weight loss, hypercalcemia, or evidence of distant metastases," which might appear too late for a cure. However, we do not perform bronchoscopy on a patient with another obvious cause of hemoptysis, such as pulmonary infarction. Nor do we perform bronchoscopy more than once on a patient who has bronchitis with recurrent hemoptysis.

Our study was prospective for a 1½-year period. All patients with a first episode of hemoptysis (whom the primary physician had not screened out) underwent bronchoscopy. A better study design might be to randomize patients who meet certain criteria into groups that undergo or do not undergo bronchoscopy. The patients would have to be followed up long enough to learn whether they had cancer and whether the cancer could still be cured. If a life were lost, however, how much the cost savings were worth would be a difficult question to answer.

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Interaction between Carbamazepine and Antituberculosis Agents

To the Editor:

The following is a report of an infrequent drug interaction in a patient being treated for presumptive tuberculosis.

The patient was a 45-year-old white woman who had been treated for years for idiopathic seizure disorder (epilepsy), which had been well controlled with various anticonvulsant agents. For the previous 3 months, she had been given carbamazepine (Tegretol), 300 mg three times a day, and acetazolamide (Diamox), 250 mg three times a day, by her neurologist for the control of her seizures. During this period, trough serum levels of carbamazepine and all active metabolites were 8.5 and 9.5 μg/dl (therapeutic range, 8 to 12 μg/dl). No side effects were encountered.

In addition to these anticonvulsant agents, a daily regimen of isoniazid (INH), 300 mg, rifampin, 600 mg, and pyrazinamide, 1,500 mg, was begun after a pulmonary workup revealed acid-fast bacilli in bronchial washings. Within 3 days of beginning therapy, the patient reported nausea without vomiting. Because early hepatotoxicity was suspected, all antituberculosis medications were discontinued, and the serum SGOT level was determined, which was within the normal range. Three days later, the symptoms of nausea had resolved, and INH alone was re instituted. INH was tolerated without problems for 3 days before rifampin was added. Within 1 day of rifampin use, the patient began to experience nausea, which rapidly progressed to vomiting, ataxia, confusion, and drowsiness over the ensuing 2 days. A neurologic examination performed 3 days after rifampin was reintroduced also revealed nystagmus. The carbamazepine level in a sample obtained 3 h after the last dose of anticonvulsant was 16.9 μg/dl. All tuberculosis medications again were discontinued, with resolution of symptoms within 24 hours.

All first-line antituberculosis drugs depend on hepatic mechanisms for metabolic degradation. The metabolism of carbamazepine is complex but depends on hepatic mechanisms as well. Isoniazid alone is known to slow metabolism of carbamazepine and increase its serum levels. On the other hand, rifampin is known to be an effective inducer of metabolic degradation of many agents, in most cases countering or superseding the inhibition of metabolism of these drugs by INH.

It is interesting that in this patient, no evidence of toxicity to INH alone occurred until 24 hours after rifampin was begun. This makes us speculate that rifampin may have augmented the INH effect on carbamazepine rather than counterbalancing it through enhanced metabolic conversion of carbamazepine to its active epoxide metabolites. Additional pharmacologic studies could help confirm this possible mechanism for enhanced toxicity. In any event, determination of carbamazepine levels early in therapy, when the drug is administered concurrently with INH and/or rifampin, is warranted, and signs and symptoms of carbamazepine toxicity should be monitored closely.

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New Approach for Fluoroscopically Guided Transvenous Catheterization of the Coronary Sinus

To the Editor:

Interest has recently increased in experimental and clinically oriented diagnostic tests and treatments via the coronary sinus, especially in coronary sinus retroperfusion and pressure-controlled intermittent coronary sinus occlusion (FICSO), two modalities used to treat acutely ischemic myocardium, in which the time needed to catheterize the coronary sinus becomes critical.

Recently we performed catheterization of the coronary sinus in 18 patients with coronary heart disease, looking for metabolic markers of ischemia during arterial pacing. In seven of these patients we employed the generally accepted technique, using the anteroposterior projection; in the remaining 11 patients we employed a different fluoroscopic view using the left anterior oblique projection, in which the two ventricles are separated and the direction of coronary sinus projection is toward the spine.