In their discussion of drainage systems, the authors do not mention the one-way flutter valve. For patients with pneumothorax, this valve enables the pleural space to be evacuated (expansion of the lung forces the air out) without the encumbrance of a water-seal system.3 Mercier4 has shown that outpatient management with a flutter valve is safe, efficient and economical. These valves are most useful for treatment of primary spontaneous pneumothorax or pneumothoraces occurring after thoracic needle biopsies.

When chest tubes are removed, we believe that it should be done at end-inspiration rather than end-expiration. The rationale for this technique is based on the observation that patients experiencing acute pain (as may occur on tube removal) tend to inhale (rather than exhale), therefore increasing chances of air entry at the drainage site.

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REFERENCES
3 Heimlich HJ. Valve drainage of the pleural cavity. Dis Chest 1968; 53:292

To the Editor:

We are pleased that thoracic surgeons have responded to our article on chest tubes and that it has provided an educational format for their residents. We did not mention aspiration or a small catheter connected to a flutter valve as preliminary alternatives to chest tubes in treatment of pneumothorax as our review discussed standard tube thoracostomy; therefore, we did not address other modalities of therapy. In response to their comments, however, we offer the following observations.

We recommend tube thoracostomy for most secondary spontaneous pneumothoraces and those that are symptomatic, progressing, large or under tension. The series of Stradling and Poole recommending conservative management found their strategy most effective in younger, healthy patients with simple pneumothoraces. However, they suggested admission and active intervention if patients were older, emphysematous, developed respiratory symptoms, relapsed on conservative therapy, or had complications.

The role of aspiration in the treatment of pneumothorax is controversial. The series of Hamilton and Archer, and Raja and Lalor both suffer from small numbers, and the latter from the problem associated with reporting the technique as successful. They selected for aspiration healthy, asymptomatic individuals whose air-leak probably had ceased; those patients likely would have improved regardless of treatment. In the larger series of Spencer Jones, less than half of the patients were treated successfully with aspiration alone. Others question the efficacy of aspiration.14 Aspiration is of no value if the air-leak has not ceased, and the risk-benefit is unclear if the leak has stopped.

There is a place for small chest tubes and flutter valves in the treatment of pneumothorax, as suggested by Mercier,3 but in his study one-third of the patients failed small tube flutter valve drainage and 80 percent of those patients had an open surgical procedure. Tube thoracostomy performed initially might have avoided these failed attempts.

Although usually suggested, large chest tubes (>28 Fr) probably are not necessary to drain malignant effusions and perform pleurodesis. An early report found 18-24 Fr tubes acceptable,1 and recent experience suggests that even small bore 8 Fr catheters can be employed successfully to drain malignant effusions and perform pleurodesis.15,16 We have used the small catheter to perform pleurodesis in malignant pleural effusions and have found it effective in four of five patients. In addition, extensive experience with pleurodesis, both in patients and experimental animals, has shown that fluid generated by tetracycline rarely is hemorrhagic, usually is serous and, despite having protein concentrations of 3 to 4 gm/dl, is drained easily by a small gauge needle or catheter.7

Many attest that drainage of a pneumothorax is equally effective from either the second ICS MCL or the fifth ICS in the MAL.8,9 As mentioned, cosmetic results dictate a midaxillary approach. Following insertion, apical direction can be accomplished from either location. In our review of complications, we did not find a report of internal mammary artery puncture and do not consider it a contraindication to anterior second ICS MCL tube placement. Finally, tubes properly placed and secured in either position do not impede the delivery of respiratory therapy.

Absolute criteria based on pleural fluid characteristics for chest tube drainage of parapneumonic effusions do not exist. Light and colleagues14 suggest a pH <7.00, glucose <40 mg/dl, and LDH >1,000 U as indications for drainage of parapneumonic effusions regardless of gram stain. Sahn11,13 has recommended a more aggressive approach with a pH of <7.20 or a falling pH on serial thoracenteses, in conjunction with the clinical course, as criteria for drainage of these "fibrogenic" effusions to prevent loculation, extensive pleural fibrosis, and trapped lung, and to avoid thoracotomy. There are several reasons not to accept the conservative philosophy of only draining effusions with positive identification of bacteria: 1) antibiotic therapy prior to thoracentesis, 2) inadequately performed gram stains, 3) improper anaerobic culture technique, and 4) sampling a noninfected loculus adjacent to an infected focus. We recommend standard chest tube drainage of complicated parapneumonic effusions if they are purulent, have positive gram stains, or demonstrate profound pleural fluid acidosis.

Finally, there is no consensus on the time in the respiratory cycle at which to remove a chest tube.8,15,16 We think that a patient who can successfully perform a Val-Salva maneuver following expiration will be at less risk to have air enter the pleural space than one who has created negative intrapleural pressure by inspiration.

With a common procedure such as chest tube insertion, personal preference will continue to be advocated based on local experience and observations. However, it was the intention of this review to put into perspective the scientific knowledge that exists so that optimal and cost-effective patient care can be delivered.

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REFERENCES
5 Talamonti WJ, Victor LD, Signori EE, Signori OR. Small bore
Human Placental Alkaline Phosphatase and Acute Lung Injury

To the Editor:

A specific and sensitive marker for acute lung injury is not available.1 We believe that serum human placental alkaline phosphatase (hPLAP) is a possible candidate.

For three years we have been involved in research on hPLAP, an oncofetal protein, as a possible marker for gonadal cancer, using several monoclonal antibodies for its specific detection.2-4 In this context, it was essential to explore the occurrence and localization of this enzyme in normal non-cancerous tissues. hPLAP could be localized on the plasma membrane of some type 1 pneumocytes and in the unciliated epithelial cells of respiratory bronchioi.5 Since an increase of serum hPLAP was sometimes observed in heavy smokers, its behavior in several other conditions of acute lung injury was investigated using an enzyme-antigen immunoassay (Innogenetics, Gent, Belgium).

In 88 percent of patients with adult respiratory distress syndrome (n = 17), a significant rise of serum hPLAP could be observed within a 24-hr span before or after clinical onset. The same observation was made in bacterial or viral pneumonia (n = 10), where 100 percent positivity for hPLAP occurred within the same time period. Furthermore, three cases of paraplu/ operation all showed a distinct elevation in serum hPLAP at the moment of, or shortly before, overt lung damage. Artificial ventilation also induced serum hPLAP elevation in 88 percent of the patients (n = 8). In these four clinical settings, serum hPLAP levels correlated well with disease progression or regression.

No elevated serum hPLAP levels occurred in 14 patients with chronic aspecific respiratory disease, except for two smokers. We believe that further evaluation of hPLAP as a marker of acute lung injury is worthwhile.

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REFERENCES


Measuring Protease Inhibition

To the Editor:

The report by Fera et al5 again draws attention to the unresolved issue of inactivation of alpha-antitrypsin (A,AT) by tobacco smoke in vivo, an effect that was found by some investigators, among them Fera et al,1 but not by others.1 Two types of measurements are usually made to demonstrate the inactivation of A,AT: 1) functional assay to determine the complete or partial loss of activity to inhibit elastase and/or trypsin; and 2) immunologic measurement of A,AT, usually radial immunodiffusion or nephelometry, that determines the antigenically-reactive protein regardless of its functional state. By dividing the functional activity by the immunologically-determined A,AT concentration, the specific activity can be calculated.

When these measurements are made in serum or plasma, it is important to realize that the protease whose inhibition is measured interacts with other inhibitors besides A,AT. The interaction that is of major consequence for the apparent inhibition of a protease is that with alpha-macroglobulin (A,M). A,M forms complexes with proteases that remain enzymatically active against small molecular size substrates such as benzoyl-arginine-p-nitroanilide (BAPNA) and

Table 1—Elastase Inhibition by Alpha-antitrypsin in the Presence of Alpha-macroglobulin

<table>
<thead>
<tr>
<th>A,M (ug)</th>
<th>0</th>
<th>25.4</th>
<th>63.5</th>
<th>127.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibitory activity of 100 ug A,AT (units of elastase inhibited)*</td>
<td>2.03 ± .06†</td>
<td>1.9 ± .06</td>
<td>1.67 ± .03</td>
<td>1.31 ± .04</td>
</tr>
</tbody>
</table>

*One unit of elastase is defined as the amount of elastase that solubilizes 1 mg of elastin in 20° at pH 8.8 at 37°C.
† Mean of three measurements ± standard deviation.

Elastase assay was as follows: To 1 ml of Tris buffer (1 M, pH 8.0) was added 20 μl of SAPNA (10 mg/ml in dimethylformamide) and 2.07 units of porcine pancreatic elastase (Sigma) in .1 ml of Tris buffer. The color development at 405 nm was followed for 5' in a Gilford spectrophotometer with recorder at 25°C. For the inhibition measurements .1 mg of A,AT in 0.1 ml of Tris buffer containing either no A-2M or the amounts indicated was added to the cuvette with the elastase (2.07 units) mixed thoroughly and allowed to remain at room temperature for 3'; then 20 μl of SAPNA was added and the reaction was followed by spectrophotometer for at least 5'.