Pleurodesis For Spontaneous Pneumothorax
Will the Procedure of Choice Please Stand Up?

In this issue of Chest (see page 1162), Milanez and colleagues describe their experience with thoracoscopic management of spontaneous pneumothorax. They report that after the intrathoracic insufflation of 2 g of sterile asbestos-free talc, only 1 of 18 patients had a recurrence over a period of follow-up ranging from 1 to over 3 years. This is an important observation because the problems presented by recurrent spontaneous pneumothorax are not trivial ones. The estimated incidence in the US alone is about 17,000 cases per year, and the recurrence rate is 23 to 50% after the first episode, and higher after the first recurrence. Thus, the morbidity and even mortality related to this problem are quite considerable, and the potential direct and indirect costs resulting from spontaneous pneumothorax can add up to tens of millions of dollars each year. The search for a rapid, safe, inexpensive, and highly effective way to prevent recurrence has been going on for decades. In general, all proposed approaches have fallen into one of three types: surgical interventions via a standard thoracotomy, intrathoracic instillation (through a conventional chest-tube thoracotomy) of a sclerosing chemical agent, and more recently, thoracoscopic surgery and pleurodesis. Unfortunately, few prospective, controlled studies of any of these forms of therapy have ever been published, and even fewer have directly compared two or more different methods.

The surgical approach to achieve obliteration of the pleural space has traditionally been the gold standard in terms of efficacy, but the inherent risk and expense associated with a thoracotomy have made this a less than ideal first choice. The intrapleural instillation of a suitable chemical agent is easy and far safer than surgery. For these reasons, and because of its low cost (about $48 for 2 g in 1989), the use of tetracycline in this manner, though largely empirical, rapidly became widespread. The publication of the Veterans Administration Cooperative Study and other series eventually confirmed its excellent efficacy and safety in this setting, and intrapleural instillation of tetracycline was widely accepted as the treatment of choice. Its success, however, was short-lived. Since about 1991, the US production and marketing of parenteral intravenous tetracycline hydrochloride was discontinued by the manufacturer because the market source of the sterile tetracycline salt needed for production was no longer available. The disappearance of this form of tetracycline created a vacuum which has yet to be satisfactorily filled. Currently, alternative agents which are commonly used in the US for chemical pleurodesis include bleomycin, minocycline, doxycycline, and talc. Bleomycin is quite expensive (about $15 per unit, or around $1,000 per intrapleural treatment), may not be as effective as tetracycline or doxycycline (Table 1), and is probably not as safe, particularly in the presence of renal insufficiency. Minocycline and doxycycline are readily available in the United States and appear to be reasonably safe when used in this fashion. Minocycline is relatively inexpensive (about $80 for a 300-mg dose), but published experience with its use in human subjects is very small and mostly limited to the treatment of malignant effusions. Clinical experience with doxycycline is somewhat greater, but so can be its price: from about $125 for 500 mg to $500 for a 2,000-mg dose. Finally, injecting a “slurry” of sterile asbestos-free talc through a standard chest tube has been reported to be effective in malignant effusions, but preparing and administering this “slurry” can be cumbersome, and sterile asbestos-free talc may not be readily available in all hospitals.

Thoracoscopy offers a third choice which allows “minimally invasive” access to the chest cavity, and thus, it is associated with significantly less morbidity, shorter hospital stay, and conceivably even lower mortality than conventional thoracotomy. However, because in the United States thoracoscopy is done usually under general anesthesia and in an operating room environment, its direct cost is not substantially lower: about $2,900 vs $3,500, respectively, at our institution. Through the thoracoscope, any accessible bullae or blebs that are identified can usually be resected, sutured, stapled, and/or ablated with electrocautery or laser. Pleurodesis can then be achieved by parietal pleurectomy, by mechanical...
abradion of the pleural surfaces (eg, with the Kittner dissector), by thermally inducing pleural inflammation with laser or electrocautery, or by introducing a chemical agent known to cause pleural irritation and symphysis. Although the ability to resect bullae or blebs would appear to be another obvious advantage of thoracoscopy, I am not aware of any published controlled study showing that such an intervention significantly decreases the incidence of recurrent spontaneous pneumothorax beyond the reduction that would result from performing pleurodesis alone.

On the other hand, published evidence does suggest that insufflating sterile asbestos-free talc may be one of the best methods of achieving pleurodesis through the use of a chemical irritant. In this regard, the 95% success rate reported by Milanez and colleagues in the present issue of Chest compares favorably with the 88% success rate described by van de Brekel and coworkers22 in 356 patients with spontaneous pleurodesis treated in similar fashion. If talc is to be used, thoracoscopy does offer the advantage of allowing its direct insufflation in powder form, and thus, the somewhat cumbersome task of preparing a sterile “slurry” is avoided. However, although talc is very inexpensive (less than $1.00 for 10 g, nonsterile), its availability in sterile form may be limited in certain hospitals, and possible (though rare and/or not yet fully proved) severe toxicity has been reported with its use.23-25 Furthermore, initial studies with doxycycline and minocycline, albeit including few patients, have also shown success rates in the 75 to 90% range (Table 1). Thus, since these drugs also are easier to use, reasonably safe, and readily available everywhere, talc probably cannot yet be proposed as the unquestionable preferred agent for chemical pleurodesis.

Table 1 summarizes some of the published data regarding the efficacy of different methods of pleurodesis. When available, data have been included on both spontaneous pneumothorax and malignant effusions. Excluded are published data on the use of nitrogen mustard, methylprednisolone, mitomycin-C, doxorubicin, etoposide, fluorouracil, interferon-β, cisplatin, and others, because these agents have been used mostly or exclusively for malignant effusions, the total number of patients treated with each of them is very small, and their efficacy (at least in this clinical scenario) has been low, ranging from 0% for etoposide to about 40% for interferon-β and mitomycin C.

In conclusion, I believe that the current study and other published data22 clearly support the use of thoracoscopy for the prevention of recurrence of spontaneous pneumothorax. Although issues of safety and cost prevent this approach from being the ideal routine, thoracoscopy probably is the best available option for those patients in whom a previous attempt at chemical pleurodesis through a conventional chest-tube thoracostomy has failed, and/or for those in whom any recurrence of pneumothorax is judged likely to be life threatening. As Milanez and coworkers point out, however, whether it is best to attempt thoracoscopic pleurodesis by pleurectomy, by mechanical or thermal abrasion, by insufflation of asbestos-free talc, or even by the use of intrapleural tetracycline, minocycline, or doxycycline, it remains an unresolved issue. Until properly controlled clinical trials are funded and carried out, the choice of

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**Table 1—Reported Efficacy of Different Methods of Pleurodesis**

<table>
<thead>
<tr>
<th>Procedure*</th>
<th>Method of Pleurodesis</th>
<th>Dose Used</th>
<th>No. of Patients</th>
<th>Failure Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP</td>
<td>Thoracotomy with bleb/bulla resection and pleural abrasion</td>
<td>Not Applicable</td>
<td>747</td>
<td>0 to 6 (mean 2.4)</td>
</tr>
<tr>
<td>SP</td>
<td>Thoracoscopy+insufflation of talc powder</td>
<td>Exact dose not reported in all cases</td>
<td>380</td>
<td>11</td>
</tr>
<tr>
<td>ME</td>
<td>Talc powder</td>
<td>2 to 10 g</td>
<td>242</td>
<td>6</td>
</tr>
<tr>
<td>ME</td>
<td>talc slurry</td>
<td>2 to 10 g</td>
<td>48</td>
<td>10</td>
</tr>
<tr>
<td>SP</td>
<td>Tetracycline</td>
<td>500 mg to 30 mg/kg</td>
<td>173</td>
<td>20</td>
</tr>
<tr>
<td>ME</td>
<td>Tetracycline</td>
<td>500 mg to 30 mg/kg</td>
<td>381</td>
<td>33</td>
</tr>
<tr>
<td>SP</td>
<td>Doxycycline</td>
<td>500 mg</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>ME</td>
<td>Doxycycline</td>
<td>500 mg</td>
<td>87</td>
<td>26</td>
</tr>
<tr>
<td>ME</td>
<td>Minocycline</td>
<td>300 mg</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>SP</td>
<td>Silver nitrate</td>
<td>2 mL 10% solution</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>SP</td>
<td>Quinacrine</td>
<td>100 mg</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>ME</td>
<td><em>Corynebacterium parvum</em></td>
<td>3 to 15 mg of dried, killed <em>C parvum</em></td>
<td>169</td>
<td>24</td>
</tr>
<tr>
<td>ME</td>
<td>Bleomycin</td>
<td>15 to 240 units</td>
<td>199</td>
<td>46</td>
</tr>
</tbody>
</table>

*SP=spontaneous pneumothorax; ME=malignant effusion.
†A list of individual series combined to construct this table is available from the author.
‡"Failure" means persistence/recurrence of the pneumothorax or effusion in the treated side. Follow-up ranged from months to years, but in most series ≥12 months were reported.
sclerosing agent will remain largely a matter of physician preference and local availability.

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ACCP-SEEK Board Review Question of the Month: A New Feature of Chest

In 1990, the American College of Chest Physicians conceived the idea of the Assessment in Critical Care and Pulmonology: Self-Education and Evaluation of Knowledge (ACCP-SEEK) program. The goals of the program were four-fold: (1) to provide a self-assessment program for practicing specialists in pulmonary and critical care medicine designed to reinforce training and experience; (2) to disseminate important new knowledge in the field; (3) to assist both the practicing specialist and individuals in training in preparing for certification and recertification examinations sponsored by the medical specialty boards; and (4) to publish in alternating years practice specialty board question and answer booklets in pulmonary medicine and critical care medicine.

Dr. John Weg was recruited as the first Chair of the ACCP-SEEK program with the charges of assembling committees of experts with diverse clinical interests, developing a self-education and evaluation program, and identifying an experienced and skilled medical examination publisher. He developed the format of 200 peer-reviewed questions of a type and quality similar to actual board examinations; each question would be followed by a peer-reviewed concise, thoughtful, critical, and occasionally controversial answer/discussion well supported by current references. American College Testing of Iowa City, Iowa initially acted as the publisher and provided psychometric support, including confidential report-