transplant remains a possibility for younger patients with severe, intractable heart failure. However, transplantation can be avoided by diagnosing the disease early and treating with corticosteroids.

To deal successfully with the menace of myocardial sarcoidosis, one must first learn to think of the entity not only in patients with multisystem sarcoidosis but in any patient with a complex and undiagnosed arrhythmia, conduction disease, myocardiopathy, or unexplained congestive heart failure in a young or middle-aged person. Once the presence of the wolf is suspected, further diagnostic studies should be aggressively pursued to establish the extent and severity of the illness. Finally, the beast needs to be tamed with high-dose corticosteroids and immunosuppressive drugs. Surgical intervention and cardiac transplantation are the last resort.

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Chemotherapy and Survival in Non-Small Cell Lung Cancer

Locally advanced or metastatic non-small cell lung cancer (NSCLC) is, notoriously, a therapeutic dilemma to solve. Although radiotherapy has a palliative effect and cytotoxic combination chemotherapy produces a definite number of objective responses, their overall clinical value remains uncertain. A controversy, in particular, already strong in the early 1990s, is still topical today. It pertains to the suitability of encouraging widespread use of chemotherapy at the community hospital level.

Three years ago, arguments against such use were essentially of two types: one was basically scientific, the other rather moral and philosophical. The first argument, moved in the most cautious commentaries, was that the scientific evidence suggesting a beneficial effect of chemotherapy on survival was scarce or incomplete. Is such an objection still valid?

By the end of 1991, at least ten trials of chemotherapy vs support care alone had been peer-reviewed and published. These studies are quite inhomogeneous as to years of publication, drugs and regimens used, planned duration of chemotherapy, and characteristics of the populations studied. For example, one study was limited to patients with metastasis, whereas in other studies, locally advanced disease (stage IIIb) was usually included and consisted of varying proportions of the sample. Only one element, ie, the prolongation of the median survival recorded after chemotherapy, was constant in each of the studies. One of them, the Canadian trial by Rapp et al, showed significantly improved survivals after two different programs of chemotherapy; the study was large enough, used active drugs (cisplatin, vindesine), and had a study design good enough to be convincing. Three older studies, dating back to the 1960s and early 1970s, had shown a similar significant difference, or suggested a trend toward a prolongation of survival in the group of patients treated with chemotherapy. However, minimally active drugs (alkylating agents, methotrexate) and only single-agent chemotherapy regimens were used in these studies. Two other trials showed statistically significant survival differences favoring chemotherapy with MACC (methotrexate,
doxorubicin, cyclophosphamide, and lomustine), but they were quite small,11 or had some other weakness in their study design.17 The remaining four studies found various increases in the duration of survival in patients treated with chemotherapy, but the differences did not reach statistical significance.13-15 To this date, an additional good-quality trial of chemo-therapy vs supportive care alone in metastatic NSCLC has been published,18 and at least three meta-analyses have been reported.19-21 In the study by Cartei and colleagues,18 a modest but highly significant survival prolongation was observed in patients receiving cisplatin-cyclophosphamide-mitomycin therapy. Confirming a previous suggestion based on the observation of the unique direction of results,4 all the meta-analyses consistently concluded that chemotherapy did give a survival advantage.19-21 These new facts, when added to the prior data, constitute a body of evidence that should be no longer questioned.

As a matter of fact, almost all the arguments currently raised against chemotherapy belong to the second type, ie, they are mainly ethical, and concern the question: Is chemotherapy worthwhile?26 Considering the reports published to date,5-17 one should agree on the following three points: (1) the survival benefit of chemotherapy is real, although of short duration; (2) the impact of chemotherapy on health costs and the quality of life of patients are extremely important and nearly unknown (however, indirect and incomplete evidence would suggest no detrimental effect on the patient’s quality of life,7,9,14,22 nor on the costs of hospitalization25); and (3) a strategy focusing on the discovery of new drugs, new combination of drugs, and new biochemical modulators of established regimens should be enforced. In spite of the possible agreements, however, no easy consensus can be anticipated. This is essentially because of the subjectivity which is intrinsic in any moral judgment. Clinicians, who face the therapeutic decision of treating patients out of the reassuring investigational framework, will continue, probably for a long while, to weigh the modesty of the survival gain and the scarcity of information on psychosocial and economic factors. They will reach different conclusions and will give different therapeutic advice to patients, depending on their personal preferences (or prejudices).

Perhaps, it is time for doctors to be less personally involved in the therapeutic decisions. As previously suggested,4 a compromise to respect the patient’s personality and rights may consist in offering the palliation of chemotherapy to any patient with unresectable NSCLC and no contraindications, while explaining the nature, facts, and potential benefits and harms of the treatment proposed, and leaving the final decision to the patient.

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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 intrapleural 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, intrapleural 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...