For clinicians interested in research, the formulation, assessment, and refinement of practice pattern algorithms and studies defining cost-efficient, high-quality care should be a rich field of endeavor. Addressing these issues offers a potential for forging a partnership between academicians and clinicians that can provide the practicing community a unique opportunity to participate in clinical research. The AIDS epidemic has already provided a model for this partnership. AIDS research has been energized by a coalition of academicians, clinicians, and patients coming together to do clinical research. Clinical applications of new technology, standardization of care, and reduction of cost offer opportunities to re-examine most of our daily clinical activity. Who better than the clinician can define the modifications of clinical practice that best achieve these goals? The issues to be addressed are virtually limitless. Medical journals must play a role if these changes are to take place. There has to be acceptance of medical economics and standardization of care as appropriate subjects for inclusion in their pages. Hopefully, studies of this type will find a home in medical journals in the years ahead.

Richard H. Winterbauer, M.D., F.C.C.P.
Seattle

---

Occupational Exposure to Tuberculosis: Risk and Consequences

On October 18, 1993, the Occupational Safety and Health Administration (OSHA) released its “Enforcement Policy and Procedures for Occupational Exposure to Tuberculosis.” This policy requires the use of a high efficiency particulate air (HEPA) respirator as the minimum level of respiratory protection for occupational exposures to tuberculosis. All employees with potential exposure to the exhaled air of an individual with suspected or confirmed tuberculosis will need to wear these HEPA filter respiratory devices.

High efficiency particulate air respirators should not be the minimum respiratory protection required under all circumstances. The risk and consequences of acquiring an infection with tuberculosis varies greatly depending upon the number of infectious particles in the air and whether the infective organism is sensitive to available drugs. Each institution needs to assess the risk and consequences of transmission of tuberculosis within each patient care area and have the flexibility to respond accordingly.

The use of nondisposable HEPA respirators may be quite reasonable in areas of the country where tuberculosis is resistant to multiple drugs and the consequence of infection is greatest or under circumstances when employees are exposed to large numbers of infectious particles, such as with cough-inducing procedures. However, it should be remembered that respiratory protection is only an additive measure to reduce the risk of tuberculosis transmission in most patient care settings. Prompt isolation of the patient in an appropriately ventilated room, and most importantly, treatment of the patient with adequate chemotherapy are much more effective in reducing transmission of tuberculosis within institutions.

In areas of the country where drug-resistant strains of tuberculosis are less than 4 percent, when no cough-inducing procedures are being performed, and when facilities have good ventilation, the less expensive dust-mist (DM) or dust-fume-mist (DFM) respiratory devices should give reasonable protection. For example, in Alabama during the calendar year 1993, the primary resistance rate of Mycobacterium tuberculosis isolates for isoniazid was 0.25 percent, and the acquired resistance rate was 1.8 percent. Additionally, there were no new cases of multidrug-resistant tuberculosis (defined as resistance to both isoniazid and rifampin). Because good drugs are available for preventive therapy, the consequences of acquiring a tuberculous infection under these circumstances remain relatively small. If other tuberculosis precautions are taken, use of the DM or DFM respiratory devices is reasonable. Respiratory devices should never be solely relied upon to protect a worker from tuberculosis.

In fact, there are little scientific data to support the protective efficacy of respiratory devices in tuberculosis. Although HEPA filters (which are 99.7 percent efficient against aerosols of 0.3 μm) theoretically could prevent inhalation of the droplet nuclei of tuberculosis, face-seal leakage can be significant, particularly with the disposable HEPA respirators. The face-seal leakage, which with the disposable HEPA respirator ranges from up to 10 to 20 percent, likely negates any differences in efficiency between the DM, DFM, and disposable HEPA respirators. But the cost of the disposable HEPA respirator is significantly more than that for the DM or DFM respirators. If HEPA respirators are used, it might be more appropriate to use only the nondisposable type that has less face-seal leakage.

With limited healthcare resources, the efforts and costs of implementing an indiscriminate policy of requiring expensive respiratory devices in areas where this level of protection is unwarranted will
Non-Small-Cell Lung Cancer

Toward the Next Plateau

For many years, the role of chemotherapy in the treatment of advanced non-small-cell lung cancer (NSCLC) has been controversial. In patients with unresectable stage III or stage IV disease, a number of clinical trials have compared single-agent or combination chemotherapy with best supportive care only, usually defined as including radiation therapy to painful lesions. Three of these trials individually showed a statistically significant benefit for chemotherapy-treated patients,1-3 while several other studies indicated a trend for improved survival, but lacked statistical significance.4-7 In 1991, we had an opportunity to write an editorial regarding chemotherapy for stage IV disease.8 At that time, we suggested that, although not all individual trials had achieved statistical significance, all had shown at least a trend for improved survival in chemotherapy-treated patients. It appeared to us that, collectively, these trials supported the use of chemotherapy in some patients with metastatic NSCLC, although they left undefined the precise preference of chemotherapy regimen. We also suggested that a meta-analysis of all randomized trials might prove this point more conclusively.

Since that time, three meta-analyses have been published fully,8,10 including the meta-analysis by Marino et al in this issue of Chest (see page 861). Grillo et al10 analyzed six studies1,2,4-7 and found a 24 percent reduction in the probability of death when compared with supportive care alone. The beneficial effect of chemotherapy decreased after the first 6 months. The mean potential gain in survival was 6 weeks. These authors concluded that future randomized trials should still include an untreated control group. Souquet et al10 included one additional trial15 in their meta-analysis. Again, a reduction in mortality at 3 and 6 months was shown. These authors concluded that chemotherapy should be given to patients with nonresectable NSCLC.

In this issue of Chest, Marino et al report their findings when analyzing a total of eight randomized trials comparing chemotherapy with best supportive care. They include in their analysis the same seven trials analyzed by Souquet et al10 and add a paper by Buccheri et al.11 This is somewhat problematic, since Buccheri et al treated all patients initially with chemotherapy and only following up two to three cycles of therapy assigned patients to continuation of chemotherapy or observation only. Thus, this trial does not meet the same stringent design criteria as the other seven. This meta-analysis of eight trials also supports the use of chemotherapy in NSCLC with an estimated increase in median survival from 3.9 months for best supportive care to 6.7 months for chemotherapy, and an absolute difference in survival at 6 months estimated at about 20 percent. A recent individual trial, not included in any of these three meta-analyses, also showed significant improvement in survival through the use of polyagent chemotherapy.12

A fourth meta-analysis is currently available only in abstract format.13 In this analysis, the updated individual data from 11 randomized trials were used, 8 using cisplatin-based regimens. A preliminary report of this analysis also suggests benefit from the use of chemotherapy in NSCLC. For cisplatin-based trials, the improvement in survival at 1 year was estimated at 16 vs 26 percent of patients with an increase in median survival from 6 to 8 months.

Therefore, when analyzing survival data in patients with NSCLC, some individual randomized trials, as well as four currently available meta-analyses, support the conclusion that survival is prolonged as a function of the use of chemotherapy.

What about quality of life? It is frequently feared that quality of life is decreased as a function of receiving polyagent chemotherapy. No firm data exist to support these concerns. While all chemotherapy regimens result in objective and subjective toxicity, it is not clear that such toxicity results in a greater decrease in quality of life than the use of no therapy at all. This is supported by theoretic assumptions of the psychological benefits of receiving a “cancer treatment,” as well as the potential benefit of having a tumor response, and the objective benefit of more frequent contact with healthcare professionals and a repeated focused assessment of tumor status. The Canadian trial showed a decrease of costs in chemotherapy-treated patients because of a lower incidence of disease-related complications.14 Furthermore, of currently used agents, it is cisplatin that results in the highest degree of subjective toxicity.