The Efficacy/Cost Ratio of New Therapy
What is the Physician’s Fiduciary Responsibility?

The FDA Pulmonary and Allergy Drug Advisory Committee recently approved the new drug to treat cystic fibrosis, Pulmozyme (Genentech), a recombinant DNA-ase. Although formal approval is still pending, approval by the advisory committee is generally followed by approval from the FDA Commissioner, Dr. David Kessler.

The committee meeting is noteworthy for several reasons. First, the drug went from concept to advisory committee in 5 years, half the normal development time. Furthermore, the advisory committee meeting came only 4 months after Genentech’s application was received. The expedited process is part of Dr. Kessler’s laudable goal for the FDA to more quickly review drugs for life-threatening ailments.

Also noteworthy was the members’ discussion of the drug’s efficacy vs its cost. With regard to efficacy, much of the committee’s consideration was based primarily on one unpublished study in cystic fibrosis patients. Other preliminary data are available. The considered study was a large, 6-month placebo-controlled trial of once- and twice-daily administration of Pulmozyme. The subjects were “stable” outpatients with a lung capacity of at least 40 percent of normal. Outcome criteria included documented respiratory tract infections as determined by the attending physician, pulmonary function tests (spirometry), and morbidity parameters (days of hospitalization, antibiotic therapy, and general well-being). Compared to placebo, those taking a once-daily dose of Pulmozyme over a 6-month period had a statistically significant decrease in respiratory infections, spent an average of 1.4 fewer hospital days, 2.7 fewer days on an antibiotic regimen, and 1.5 fewer days home from work or school. Spirometry improved only 5.8 percent, while mortality was unchanged.

Several disquieting aspects of this study regarding efficacy were also discussed. First, long-term patient benefit could not be ascertained due to the relatively short duration of the study. Second, 3 percent of patients receiving the once-daily dose and 5 percent of those receiving the twice-daily dose produced antibodies to the drug. Third, concern was raised regarding the necessity of delivering this inhalation drug with a “dedicated” nebulizer. Fourth, when the results were analyzed by age, those patients over 20 years of age appeared to obtain greater benefit from a twice-daily dose, although the results were statistically inconclusive. Finally, an open continuation of the controlled trial did not show continued statistical benefit in decreased respiratory tract infections for the once-a-day dose.

Regarding cost, the question of the drug’s price was raised in the meeting, “How much will Genentech charge for Pulmozyme?” The answer has huge financial implications for a drug that cost millions to develop but which treats a patient population of only 30,000 in the United States and 55,000 worldwide. The patient population may be expanded as Genentech is reported to be also testing the drug in chronic bronchitis.

The answer given by Genentech was equivocal. They indicated the cost of the drug had not been set, although it is widely reported that the company is considering charging about $10,000 a year for the drug. In an unusual public statement during the committee meeting, Dr. Kessler reminded the committee that its decision had reimbursement consequences. At the end of 8 hours of discussion, the committee supported the approval of Pulmozyme in a once-daily dose.

In this day and age of fiscal restraints and ever-increasing healthcare costs, physicians should address the issue of therapeutic efficacy vs cost. As a member of the advisory committee, I was concerned about approving a drug with limited efficacy but potentially huge costs that will be borne by all of us. The question arises, “How much is some efficacy worth?” The question is even more poignant when the relatively young age of cystic fibrosis patients and the life-threatening nature of their illness is considered.

I cannot pretend to have the answers. In the best of all worlds, physicians would be totally immune from the impact of finances on therapeutic decisions. Now, however, in the real world, we are not, nor showed we be immune from these decisions. Physicians have a fiduciary responsibility not only to the patients for whom the new therapy is being considered, but also to other patients whose care will be diminished by the use of expensive therapy. Indeed, use of expensive new therapy might also limit other therapies in the same patient population for whom the new therapy is being considered (eg, lung transplantation).

This is not an isolated case. Another example is thrombolytic therapy of acute myocardial infarction where the much more expensive tissue plasminogen activator (tPA) was recently found to have a small but significant effect as compared to the much less expensive streptokinase therapy. My belief is that prioritization of
therapy based on efficacy as well as in part by cost will have to take place. I doubt that any new health care policy will entirely remove the need for this debate in which physicians should be included.

Regarding Pulmozyme, after the likely formal approval, physicians should review the available data and prescribe the drug according to FDA guidelines. Unlike the healthcare industry's too frequent extrapolation of some data to cover all circumstances, we should use this very expensive drug based on available data. Because of the limited benefit and huge cost, it is incumbent for physicians to be fiduciarily responsible in the use of this drug.

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REFERENCES

How is Respiratory Medicine Growing in Europe?

There is nothing that can testify to the well-being of a scientific society better than its annual congress. When after a few successive congresses and either spontaneous participation or participant enthusiasm decline, we can assume that something is going wrong.

This is not occurring within the European Respiratory Society (ERS), at least not according to the data coming from the Third Annual Congress held in Firenze, Italy, from September 25 to the 29, 1993. With respect to the Second Annual Congress (Vienna, Austria, 1992), the data are really exciting, considering ERS was born only 3 years ago after the merger of two pre-existing European societies, the more than 25-year-old Societas Europaea Physiologiae Clinical Respiratoria (SEPCR) and the 10-year-old Societas Europea Pneumologica (SEP).

More than 5,700 members attended the Congress with an increase of 30 percent compared with the attendance at last year's Vienna Congress. More than 2,400 abstracts were submitted and about 1,800 were accepted (37 percent and 29 percent more, respectively). Three hundred ninety-seven members from Eastern European countries attended the Congress, most of them having an abstract accepted for presentation.

Of course, not only the quantitative but especially the qualitative features of the meeting were happily surprising. The Saturday preceding the official opening of the Scientific Sessions, eight postgraduate courses in English and four in Italian were held and most of them were fully booked. During the Congress, the 24 Major Symposia devoted to general topics and the 12 Assembly Symposia, dealing with more specific items, were of exceptionally high quality and were held in fully packed auditoriums. On three different days, 12 Satellite Symposia sponsored by the pharmaceutical industry were organized in the afternoons at the end of the Scientific sessions. Content was overseen by the ERS Scientific Committee and was excellent. Every room during the 4 days of the Congress was filled to capacity; the discussions after each session were pertinent and constructive, and they offered an exchange of wide ranging, stimulating ideas.

During the Congress, many other initiatives took place, such as a symposium jointly organized by ERS and the American Thoracic Society, two joint meetings with the European Society of Intensive Care Medicine, a postgraduate course organized in collaboration with the European Academy of Allergy and Clinical Immunology, and a special symposium organized with the cooperation of the World Health Organization and the National Heart, Lung, and Blood Institute. Particular attention was given also to the educational programs of the ACCP, whose experience in this field can be very helpful to European respiratory medicine.

Language problems were faced and partly solved by broken English, the language of Scientific Communication, spoken with Italian, Polish, Portuguese, Greek, and many other accents. A happy few were able to completely solve their language problems, after having attended the special linguistic course devoted to "Scientific Communication in English."

Of course, the masterpieces of the Florentine Renaissance, the European musical tradition, and the delights of Italian cooking easily created the warm and friendly atmosphere so helpful to scientific discussion and the promotion of new study projects.

If on the basis of the Annual Congress we can argue about the health of ERS, we can also be reassured and should conclude that European respiratory medicine is growing rapidly and well. In a short time, it will come of age, furthered by the enthusiasm of the young scientists and professionals who have themselves matured and benefitted by the wisdom of the old European tradition.

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