candidate for surgery, then a combination of Nd:YAG laser and radiation therapy can afford palliative therapy.

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References

Advertising and Clinical Investigation

To the Editor:

The January 1990 issue of Chest presented a disturbing coincidence. A solid, four-page ad by Wallace Laboratories proclaimed— in large letters, "A Major Multicenter Study Indicates . . . etc." The therapeutic effects of Organidin were advertised and supported by a reference,1 which was at the bottom of the page. The reference read: Petty TL. The National Mucolytic Study: Results of a randomized, double-blind placebo-controlled study of iodinated glycerol in chronic obstructive bronchitis. Chest, January 1990.

There indeed, on page 75, was the article which contained some even more intriguing features. According to Dr. Petty, the steering committee for this study planned the "large multicenter, randomized, double-blind, placebo-controlled, parallel clinical trial (which) was conducted nationwide in the offices of sub-specialists (pulmonologists/allergists) to compare the efficacy and safety of iodinated glycerol vs placebo . . . ."

The multicenter qualification is arresting. The physicians' offices were the centers involved. The "approved investigators" of the "National Mucous Clearance Study" were 74 pulmonologists and one allergist, who were listed alphabetically in Appendix 1. One of the "approved investigators" did his study in a "center" located in my own city of Utica—in his office.

The most truly impressive aspect of this "nationwide study" is the barrage of presumably correct statistical analyses—but based on what kind of data or facts? The whole study rests on detailed, elegant, statistical analyses of completely subjective data. Can any valid conclusions be drawn?

A most disturbing feature of the article is what seems to be the very intimate relationship to the Wallace Laboratories of the whole study and presentation. Well before this article appeared in Chest, an advertisement for the article's appearance on television, October 27, 1989, November 12, 1989 and December 3, 1989, was sent out.

But even more disconcerting is the copy of the symposium faculty given to me by the Wallace Laboratories salesman. Included in this distinguished list is the Vice-President of Medical Affairs for Wallace Laboratories. Why?

The "hype" gets worse. We enclose a copy of the "Dear Colleague" letter from Dr. Petty on the stationery of PSL Center for Health Sciences Education, located in Denver, Colorado. At the bottom of the letterhead page is printed, "Patient Care-Teaching-Research." A telephone call to Denver informed us that, among other things, the center "did research for drug companies."

In this "Dear Colleague" letter, Dr. Petty states he "recently chaired an investigator's meeting to review the results of perhaps one of the most ambitious clinical studies ever undertaken in the field of pulmonary medicine." What modesty! He goes on: "The findings, however, are of such import that I am compelled to submit them for peer review and subsequent publication in a leading medical journal. This, of course, precludes my disclosure of the actual data prior to publication. I can, however, share the conclusions in a more general sense."

He then presents the wonders of iodinated glycerol based on "the quality of the study design and the credentials of participating investigators."

We checked on the number of board certified pulmonologists, but instead of finding 74, we could only tabulate 53. Twenty-one were not board certified pulmonologists, although the allergist was board certified. We realize that many non-board certified pulmonologists and other specialists may be very well-qualified and capable. However, this misrepresentation—we feel—is an example of the strained, promotional, unprofessional nature of the whole presentation.

According to the undated "Dear Colleague" letter, Dr. Petty "chairs an investigator's meeting to review the results . . . ." It seems that Dr. Petty merely reviewed an "investigation" which was organized by the Wallace Laboratories.

One wonders why a "nationwide multicenter" study was chosen. Two or three recognized "centers" could have evaluated the patients under much better and more closely controlled, reliable scrutiny. The authority of Dr. Petty and the high-sounding promotional phraseology of "nationwide" and "multicenters," will add nothing objective to the question involved, but most certainly will increase the sales of Organidin, which is produced by the Wallace Laboratories.

Dr. Petty's study shows that iodinated glycerol seems to help patients more than the placebo. A more important observation might be—does it work any better than a saturated solution of potassium iodine? This is much cheaper, but if it disagrees with the patient then, of course, Organidin could be tried—if the patient can afford it.

The publication of this article raises a question about the peer review of Chest, which, in the past, has been of high quality. Could we have a retrospective peer review, headed possibly by an astute impartial critic like Dr. Eugene D. Robin?

P Ciaglia, M.D., F.C.C.P.; Herman Levy, M.D., and Thomas F. Ryan, Jr., M.D., St. Elizabeth Hospital, Utica, New York

To the Editor:

I am delighted to have the opportunity to respond to Drs. Ciaglia, Levy and Ryan, because it offers an opportunity to emphasize once again the care and objectivity which went into the National Mucolytic Study. It also gives me, on behalf of 75 investigators, an occasion to explain the reasons for the study.

A recent North American and European study published elsewhere (Eur Respir J 1989; 2:702-09) revealed a marked disparity in the practice patterns of European pulmonologists compared with North American pulmonologists in one area only, i.e., the very common use of mucolytic expectorant drugs in Europe, more often than not, compared with the infrequent use of mucolytic agents for COPD by physicians in North America. Few mucolytic drugs available for prescription in this country have received any extensive clinical study. One agent, iodinated glycerol (which has been available for more than 50 years) was the subject of some preliminary and often uncontrolled evaluations. To attempt to better answer the question of the efficacy or lack of efficacy of iodinated glycerol, a steering committee comprised of an internationally-known expert in mucus formation and clearance—Dr. Adam Wanner of the
University of Miami, Miami, Florida—along with three board-certified practicing pulmonologists arrived at the study design that was recently reported in Chest (1990; 97:75-83).

Investigators were selected from directories of the American College of Chest Physicians and American Thoracic Society without any effort to confirm board certification by checking with the Pulmonary Disease Subspeciality Board of the American Board of Internal Medicine in Philadelphia (the only accurate listing of certification). In our report, the common protocol followed by each physician plainly states in two places: "The following large, multicenter randomized double-blind placebo controlled parallel clinical trial was conducted nationwide in the offices of subspecialists (pulmonologists/allergists). . . . " The term "center" is proper English according to Webster. Center literally means point or focus.

It should be emphasized that the data analysis, which has been reviewed on several occasions, was done by a third party (Clinical Sciences, Inc, Bethesda, Maryland). Coded forms were received by Wallace and checked for adverse reactions. They were then sent to the data center for statistical analysis.

That 75 subspecialists could enroll such a large number of patients in 37 states and bring the project to completion is indeed remarkable. In fact, a report about the design and discipline involved in this study is being readied for the journal, Clinical Trials. Since it is generally agreed by mucus experts that no clinically applicable measure of mucus clearance exists, and since patients are the only ones who know how they feel, the steering committee wisely chose symptomatic parameters, but these were evaluated in an objective fashion. As is the case with studying responses to analgesic drugs, the patient must grade his/her own symptoms. Only the patient knows whether or not a symptom has improved. Since symptoms impinge on the quality of life of a patient, they are of key importance in judging efficacy of many drugs.

Before this paper was submitted for peer review and final publication, results of the study were presented to five additional experts, who are all academically-based pulmonologists. Their advice was unanimous that the results were of great importance to patients who suffer symptoms of mucus retention. We were urged to disseminate the results as quickly as possible, but we waited until our peer-reviewed paper was in print before revealing the details, which is standard publication policy.

This was a Phase Four clinical trial and, as such, was properly sponsored by industry, as is the case with the great majority of such studies. We did not study SSKI because of the known unacceptable incidence of side effects from this agent.

The Presbyterian/St. Luke's Center For Health Sciences Education is a not-for-profit Colorado corporation, which is a consortium of academic programs. All are affiliated with one or more universities; all physician programs are affiliated or integrated with the University of Colorado Health Sciences Center. The Research Division is actively involved in evaluating a variety of drugs and medical devices, all with approval of the Human Subjects Committee, and all are done with the strictest scientific scrutiny. We do not promote products, but do disseminate our scientific findings as widely as possible, so that practitioners can evaluate the data and scientific study design and draw their own conclusions from our findings.

Thomas L. Petty, M.D., F.C.C.P., Director of Academic and Research Affairs, President, PSL Center for Health Sciences Education; Professor of Medicine, University of Colorado School of Medicine, Denver

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ARDs Treated with Sustained Adrenocortical Steroids

To the Editor:

With interest and a certain surprise I read the article of Hooper and Kearl (Chest 1990; 97:138-43) on the successful treatment of ARDS with steroids.

This paper does never mention what type of "adrenocortical steroids" were given, nor the route it was administered—IV or orally.

For comparison of the treatment results, only a historic control group, published from another hospital with a different type of ARDS patients,' was used.

Also, the selection of patients for this report is interesting: for instance, case 2 is described as having "prolonged ventilator dependence. By the seventh hospital day, there had been no improvement in the ARDS." Pulmonary artery wedge pressure was 19 mm Hg. Looking at figure 2 (which illustrates this case), the reader realizes that this ARDS patient was extubated on day 6, indicated by "CPAP mask" treatment. Can the diagnosis of ARDS be retained in this patient? How do the authors explain the successful extubation despite "no improvement in the ARDS"? Interestingly, subsequent "progressive deterioration . . . consistent with ARDS" did not require endotracheal intubation nor mechanical ventilation in this case, but motivated reinstitution of steroid therapy.

It is certainly interesting to read that steroid therapy may be efficient in certain forms and phases of ARDS, but it would be even more helpful to know in what stages this can be considered, and which form of steroids have been given, ie, cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone or dexamethasone. At the very end of the manuscript, this reader finds what he would like to see in the title or the abstract: "this limited, uncontrolled, anecdotal experience." Indeed, "controlled investigations are indicated," but in the report of Hooper and Kearl more precise information on all patients treated, precipitating events and severity of their disease, and the therapy administered would be helpful. It could be that case 2 reflects the majority of the patients included, which in turn could explain the benign prognosis in this series as compared to other, larger groups studied.1

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REFERENCE


To the Editor:

There are many issues surrounding the use of any treatment for a complex condition such as ARDS. Dr. Suter's letter raises some of these issues and asks important questions regarding our work. This letter will address three points he raises: 1) role of stage or classification of disease, 2) role of study design, and 3) specific questions regarding our paper.

Separating, classifying, staging, or employing any method to subdivide a heterogeneous population is critical to understanding a clinical condition, its pathophysiology, treatment, and prevention. The definitions of the clinical patterns of ARDS need to be refined. Most authors and investigators recognize this need. The process is evolving with each new contribution to the literature.14 An ARDS