Communications for this section will be published as space and priorities permit. The comments should not exceed 350 words in length, with a maximum of five references, one figure or table can be printed. Exceptions may occur under particular circumstances. Contributions may include comments on articles published in this periodical, or they may be reports of unique educational character. Specific permission to publish should be cited in a covering letter or appended as a postscript.

Severe Pulmonary Hypertension with Diffuse Smooth Muscle Proliferation of the Lungs

To the Editor:

Wagener et al recently reported a 49-year-old man with severe pulmonary hypertension, normal intelligence, absence of epilepsy and no cutaneous lesions. They presumed that this was a form of pulmonary tuberous sclerosis (TS).

Unfortunately, the authors assumed the absence of signs of TS without performing computerized tomography or MRI of the brain or ultrasonography of the kidneys, and without carrying out post mortem examination of these organs. The conclusion that only the lungs were involved in this case cannot be accepted, as relevant organs were not properly examined, neither before nor after death.

Angiomyolipomas of kidneys have been found in almost 80 percent of patients with pulmonary TS, and brain lesions in at least 54 percent. As the pulmonary lesions in TS are morphologically indistinguishable from pulmonary lymphangiomyomatosis, the autopsy in a clinically uncertain case must include examination of brain and kidneys. Otherwise, with the absence of any sign of TS, the diagnosis is less probable.

The hypothesis that the pulmonary lymphangiomyomatosis might be a forme fruste of TS is supported by some investigators and refuted by others. At present, it remains an open question which the case presented does not help to solve.

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Memory Phenotype of Alveolar T Cells in Sarcoidosis

To the Editor:

We read Dr. Rossman’s editorial that stressed the pathogenic and clinical importance of studies on bronchoalveolar lymphocytes in sarcoidosis (Chest 1989; 95:715-16) with pleasure and interest.

We agree with him that our demonstration of a helper-inducer (TQ1 /CD4+) phenotype of lung T cells in patients with sarcoid alveolitis could help explain many of the previously-described functional properties of lung lymphocytes encountered in this disorder. However, we should also like to draw attention to two points arising from these studies. The first regards the mechanisms by which the accumulation of this restricted T-cell subset occurs in the lung. In this respect, it is worth noting that helper-inducer CD4+ cells can also be identified by the anti-4B4 monoclonal antibody that recognizes the CDw29 surface molecule, whereas the reciprocal CD4- subset (with suppressor-inducer activity) displays the CD45R (2H4) membrane antigen. While it has generally been assumed that these reciprocal subsets represent different lineages of T cells, recent data strongly suggest that they correspond instead to different maturational stages. According to this interpretation, naive (or virgin) T cells are found in the CD45R+ subset, whereas activated and memory T cells are confined to the CDw29- subset. A major finding in favor of this concept is the demonstration that peripheral blood T cells of the CD45R+ subset convert to the CDw29 phenotype upon stimulation in vitro, whereas conversion in the opposite direction is not observed. Moreover, functional analysis of the CDw29+ subpopulation of peripheral blood T cells supports the notion that it contains previously-activated cells. Finally, the hypothesis that the CDw29 and CD45R molecules identify primed and non-primed T cells respectively is also supported by the observation that CD45R+ cells predominate in neonatal blood, where the antigenic challenge is very weak. In contrast, the CDw29 phenotype is characteristic of T cells present at sites of inflammation where chronic antigen stimulation occurs, eg, synovial fluid in rheumatoid arthritis and CNS in multiple sclerosis. This is in keeping with our finding that most sarcoid bronchoalveolar T cells are not only of the TQ1 /CD4+, but also of the helper-inducer CDw29+ phenotype. This datum may reflect conversion of non-primed cells to the memory phenotype in the lung and/or the homing of memory cells to the alveoli, where they could both participate in the immune response and facilitate its perpetuation.

The second concern the specificity of these findings and, consequently, their clinical relevance. Although we have insufficient data at present to define the pattern of T-cell distribution in the lung during other immune-mediated conditions, it seems reasonable to assume that accumulation of helper-inducer/memory T cells in the alveoli during sarcoidosis is neither disease- nor organ-specific, but rather a general manifestation of inflammation. Support for this speculation comes from the fact that the great majority of T cells found at the site of inflammation in other immune disorders are TQ1 /4B4+/CD4+. At present, therefore, this datum—perhaps important for diagnosis—lacks the specificity required to make it of value in the diagnosis of sarcoidosis. However, definition of the distribution and enrichment mechanisms of this T-cell subset in the lung should provide both insights into the immunopathogenesis of sarcoidosis and, at least, a target for possible therapeutic intervention.

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Carotid Body Resections

To the Editor:

I want to congratulate the editorial board on publishing the two articles by Drs. Stubbarg and Severinghaus concerning carotid body resections and COPD in the May issue. I read them both with great interest. Since this procedure was tagged in the early sixties as "unethical," many of us ceased its application as a treatment for breathlessness (asthma) as it was introduced by Dr. Nakayama. His lack of definition of "asthma" added to the confusion of its understanding by physicians at large.

Knowing that hyperventilation worsens the respiratory function of an emphysematous lung, it follows therefore that the respiratory reflex to hyperventilate, in the presence of O2 and CO2 abnormality, is actually counterproductive. Since the threshold for a discharge of efferent action is quantitive, the thought of reducing efferent impulses by removing half of its sensors (unilateral cervical glomemoty) is appealing in its logic. This is the rationale behind my employment of unilateral resection of carotid body, as I have reported. Also, of course, since this is an untried territory, the danger of total removal of an important safeguard against altered blood O2 and CO2 level is ameliorated by the "half a loaf is better than none" adage.

Perhaps with the acceptance today of acupuncture, which has no scientifically demonstrable logic as yet, time has come to reevaluate cervical glomemoty for breathlessness, particularly for pink puffers. To me, it is always unseemly and nearsighted to brand any inexecutable procedure due to lack of technologic wherewithal as unethical.

I am writing to support any new consideration by the National Heart Institute of a study regarding the proper place for this procedure. It is difficult to believe that this procedure, which could be done under local anesthesia with the patient in semi-Fowler's position, should stress the financial resources of the parties concerned. In addition, the impression we received of the patients' improved ability to take care of their daily toiletry after such a procedure, though perhaps "bluer," is indelible.

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Evaluating Ventilator Therapy

To the Editor:

I have recently read the editorial by Dr. Matthay entitled, "New modes of ventilation for ARDS: how should they be evaluated?" and must take issue with his viewpoint. In fact, he appears to be guilty of the same offense that he accuses some investigators of committing. Advocation of the termination of feasibility studies is an untenable position. Research is very expensive and patients' well-being is at stake. Are we to apply any animal-tested treatment to a whole group of patients in a random manner if we have no inkling of whether it has any chance of success in a human subject? The cost differential between a feasibility study and a randomized prospective study is quite substantial. What needs to be addressed is the conclusions that authors draw from such a study. This burden must fall on journal reviewers and staff. When I review a paper for Chest, in addition to critiquing the text I do a power analysis on the data (when sufficient data is presented) to be certain that the results that do reach statistical significance can be translated to the greater population at large. I also evaluate the conclusions reached by the investigator to be certain that the experimental design and results support these conclusions. In the article discussed at length by Dr. Matthay, two shortcomings of the editorial staff come to the forefront. First, the data presented do not suggest that inverse I:E ratio ventilation in the patients in whom it was applied is efficacious or safe. Thus, the editors allowed the investigator to publish a study with a conclusion that is not borne out of the facts in the paper. It is the responsibility of the editorial staff to prevent unsupported conclusions from appearing in their journal. Second, although statistically there were some improvements in certain parameters, many of these were not clinically significant. Once again, it is up to the editorial staff of the journal to insist that this be pointed out in the paper.

Dr. Matthay is guilty of the same offense as the authors of the article. Based on a retrospective review of a few articles, he concludes that there is no utility in feasibility studies. The only conclusion that he should have reached is that, in this feasibility study, the conclusions reached by the authors are not tenable from the data presented. If he were in an appropriate position he might continue that, based on this feasibility study, further financial support for a prospective study is unwarranted. There have been many reviews of the medical literature by statisticians and the results have been appalling. Many studies are analyzed incorrectly, conclusions are made which are not warranted, and insufficient numbers of subjects were employed.1 None of the reviews have ever stated that feasibility studies are inappropriate if the information obtained is handled in an appropriate manner. In fact, it has been suggested that feasibility studies precede randomized studies in order to determine the magnitude of the intervention's effect so as to predict the number of patients needed in the randomized prospective trial to reach a valid conclusion. Certainly, feasibility studies are one of the mainstays of industrial manufacturing companies. If done correctly and reported honestly, feasibility studies serve to focus attention on a potentially useful modality of therapy. The results of a feasibility study then determine if further investigation of the modality is appropriate. The burden falls on the editorial staff and clinical investigators to assure that misinformation is not distributed to clinicians. Scientific honesty and editorial tenacity must exist if we are to continue to evaluate future modalities of treatment even if it results in the publication of significantly fewer scientific articles.

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