Summary of The Aspen Conference

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The 1978 Aspen Conference was perhaps more concerned with fundamental mechanisms of inflammation in the lung than with topics more conventionally regarded as within the scope of classic immunology. Thirty-two fascinating papers were presented; many were concerned with mediators of inflammation, including histamine release (into the blood and bronchoalveolar secretions), slow release substance of anaphylaxis, prostaglandins and chemotactic factors for neutrophils, monocytes and even for alveolar macrophages themselves. Many workers described their studies on individual living cell types obtained using the technique of bronchoalveolar lavage. Qualitative and quantitative aspects of these were described in smoking and non-smoking volunteers, as well as from patients with a range of diseases, notably sarcoidosis, interstitial pulmonary fibrosis and hypersensitivity pneumonitis. In view of the predominance of the alveolar macrophage in bronchoalveolar lavage, this cell came under particular scrutiny. Indeed, the new information about the characteristics and function of tissue macrophages which has now become available will be of fundamental importance throughout the whole of pathology.

Some of the specific contributions to our knowledge of the macrophage should be mentioned. The surface appearance of macrophages using scanning electron microscopy were described, as well as the changes induced by various drugs. Important studies on the possible heterogeneity of macrophage populations were suggested using a number of histochemical techniques to identify various types of secretory and phagocytic macrophages. Several workers described important secretions from these cells, including the production of prostaglandins, perhaps exerting a controlling influence on other types of inflammatory cells, especially lymphocytes; complement components and other small molecular weight materials possessing chemotactic properties and cytoplasmic enzymes potentially augmenting the inflammatory response.

The distinctive characteristics of cell populations obtained from bronchoalveolar lavage samples in smokers (with increased macrophage numbers), in sarcoidosis (with a relative increase in lymphocytes) and in interstitial pulmonary fibrosis (with a relative increase in neutrophils) was described. The diagnostic potential of such studies is obvious and with further refinement may well lead to the use of these techniques in place of more invasive biopsy procedures. Before this can be done, further comparisons between biopsy material, elution of cellular elements from histologic material with lavage samples, must be studied. However, preliminary reports presented to the Conference suggest that differential counts from lavage may be reasonably similar to those obtained from elutions of lung biopsies. The value of lung lavage in the identification of desquamative interstitial pneumonia (DIP) is an obvious and important one, but disappointingly, cell yields from these patients are not apparently increased above normal as much as might be expected, and diagnostic indicators of this histologic pattern in lavage fluid have not yet been identified. There has perhaps been a somewhat unrealistic attempt to polarize interstitial pneumonias into substantially fibrotic and substantially cellular types when, in reality, many pathologists observe that the majority of cases have mixed features. Thus, correlates with other factors such as steroid responsiveness or the presence of circulating or tissue-fixed immune complexes may be more difficult to make than has sometimes been suggested.

New developments in the field of host defenses were also discussed and the multiplicity of the defense mechanisms of the lung were emphasized. The fact of this multiplicity goes some way to explain those cases in which gross depletion of an individual defense component can be identified, but in spite of this, many patients remain remarkably free from serious infections. A good example of this was described in patients with C2 deficiency showing impaired protection against those antigens normally handled by the classic pathway of complement activation but not interfering with the normal handling of agents by the alternative pathway. The possibility of a neutrophil defect in a group of children with recurrent infections but without obvious immunologic defects was described; the abnormality apparently occurred as a transient event, recovering with time.

In this program, only selective aspects of asthma were included and these related especially to a study of mediators and various types of receptor sites. The identification of histamine and evidence of complement conversion in arterial blood following bronchial challenge was described and, interestingly, in a single case having apparently a dual asthmatic response to rat serum, these two components disappeared at the time of the late reaction. A study of beta adrenergic receptor sites (as measured on lymphocytes) in asthmatics demonstrated a correlation with the degree of reduction in the forced expiratory volume in one second. This deficiency appeared to be corrected by administration of corticosteroids and might well account for the facilitation effect of steroids on beta adrenergic responsiveness, as well as beta adrenergic refractoriness in severe asthma. These studies certainly need to be extended to look at various clinical patterns of asthma in less acute cases and in...
relation to various types of drug responsiveness. An interesting observation was made in a group of workers exposed to toluene diisocyanate (TDI) and showed that some patients, symptomatic on exposure during work, had no evidence of increased airways resistance on bronchial challenge; these patients did, however, show evidence of changes in their small airways, thus emphasizing the importance of studying flow-volume relationships in addition to conventional spirometry when investigating occupational respiratory diseases.

Many other fascinating papers were presented, stimulating much lively discussion and summaries of these can be found on the foregoing pages. Perhaps the most important outcome of the Conference was to emphasize the potential of the technique of bronchoalveolar lavage, both in terms of its practical clinical application and as a powerful research tool. This relatively noninvasive technique can be undertaken repeatedly to follow progress in response to therapy and it can also provide living cells for a wide range of in vitro studies, including cell interaction, assessment of a large range of secretory functions, assessment of phagocytic and killing capacity, as well as the influence of drugs and noxious agents on all of these processes. The opportunities provided by what might be termed “a living biopsy” must be almost unique in the field of clinical medicine. However, for this technologic advance to achieve a major breakthrough in respiratory medicine, it must be matched by clinical applications or therapeutic advances of similar magnitude. Analogy with the development of cardiac catheterization reinforces this statement. Cardiac catheterization alone would perhaps not have transformed the status of cardiology in the way that has obviously occurred had it not been for the parallel advance of cardiopulmonary bypass and open heart surgery. Thus, the magnificent and carefully conducted laboratory studies reported at the Conference must now be applied to the detailed assessment of clinical problems, particularly focusing on opportunities to develop new forms of prevention or therapy.

I believe that this Conference has provided the first phase of development of a new and exciting approach to respiratory medicine. The challenge lies in whether the future can fulfill our expectations.