**LETTERS TO THE EDITOR**

Cellular mechanisms of acute lung injury: implications for future treatment in the adult respiratory distress syndrome

Although I agree that antibodies to adhesive molecules will have a role in treating the adult respiratory distress syndrome (ARDS), as neutrophil activation by C5a forms the basis of the injury I cannot understand why Drs S C Donnelly and C Haslett (April 1992;47:260-3) fail to give credit to the overwhelming importance of endotoxaemia. Since there are so many mechanisms and mediators concerned in ARDS, just as there are in Gram negative bacterial shock, there has to be a common trigger—that is, lipo-polysaccharide (cf fig 2).

It seems that mistrust has arisen from the results of two sets of experiments conducted by Haslett et al, in particular the one in which a synergistic effect of a small dose of lipo-polysaccharide and C5a was seen. Yet in fact endotoxin itself produces C5a. In my experience in 1970-72 it was clear that endotoxin caused acute lung injury with all the features of ARDS. The details of the mechanisms were reviewed by Brigham and Meyrick in 1986.

In recent years several groups have described endotoxaemia at the onset of ARDS. Thus I feel sure that the emphasis will switch to means of combating endotoxaemia.

E N Wardle
21 Common Road, North Leigh, Oxford OX8 6RD

**AUTHORS’ REPLY**

Dr Wardle’s letter implies that the pathogenesis of ARDS was sorted out in 1970-2. Unfortunately, this is not the case. There is insufficient evidence at present to regard endotoxin as the central mediator of overriding importance in ARDS. Brigham’s group used sheep, which are uniquely sensitive to low concentrations of endotoxin that have little effect as a single agent in other species. Although endotoxin does cause lung oedema due to endothelial damage, this model does not come close to mimicking the complex histological events of full blown ARDS. Although models such as this have proved useful for studies of endothelial injury, most workers would agree that there is, as yet, no ideal model of established ARDS.

The search for a final common mediator in ARDS, as in bronchial asthma, has so far disproved disappointing. Endotoxin is undoubtedly an important mediator and, as we discussed in our article, it may exert both direct effects and important indirect effects in concert with other mediators, which themselves may assume prominence in the near future. Further, should endotoxaemia be a critical event at some stage of ARDS development, the resultant pathogenic mediator cas-

cades may rapidly move on to stages that do not critically involve endotoxin. Thus with our present awareness of the complexity of factors concerned in the initiation of inflammatory tissue injury we cannot subscribe to a blinkered view of the overriding importance of endotoxin, and it would seem premature and imprudent at present to overemphasise combating endotoxin as a single treatment option at the expense of other options (or combinations thereof) that will soon become available.

CHRIS HASLETT
S C DONELLY
Respiratory Medicine Unit, Department of Medicine (RIE), City Hospital, Edinburgh EH10 5SB

**TREATMENT OF RELAPSE OF SMALL CELL LUNG CANCER IN SELECTED PATIENTS WITH THE INITIAL COMBINATION CHEMOTHERAPY WITH CARBOPlatin, Etoposide, and Epirubicin**

I read with great interest, in the May edition of Thorax (1992;47:369-71), the article by Dr Ph Collard and colleagues from Belgium on the treatment of relapse of small cell lung cancer by combination chemotherapy, in particular carboplatin, etoposide, and epirubicin. The general feeling among workers in this area, particularly in the UK, has been that there is little to be gained from repeated courses of chemotherapy in small cell lung cancer, after an initial set of six to eight courses over a similar period of time.

Quality of life has always been an issue in patients with small cell carcinoma of lung and was found similar to those in this article.

In South Lincolnshire I see on average 120 new patients a year with lung cancer, of whom 50-60% have chemotherapy. Although the numbers surviving for long periods with combination chemotherapy are small, none of the less I believe that in selected patients, usually those with limited disease, repeated courses should be considered. In my experience in this group the quality of life has been good, running equally alongside the quantity.

I hope that as a result of the article by Dr Collard and others more patients with small cell carcinoma of lung will be considered for repeated courses.

C R NYMAN
Pilgrim Hospital, Boston, Lincs PE21 9QS

**Barcelona's asthma epidemics**

The article by Dr C Picado about asthma induced by soya bean dust (March 1992;47:197-200) makes intriguing reading. Barcelona’s asthma epidemic has several unusual features, which I believe suggest that attacks might be due to a novel immunological mechanism. These features include the unusually explosive onset of attacks, which were short but short in duration; their occurrence in some with mild asthma or in smokers; the absence of a late response; and the difficulty of reproducing attacks with challenge by standard soy bean allergen.

The seeds of leguminous plants (such as soya beans) are a rich source of lectins, which may be present in order to bind specific carbohydrates present on symbiotic nitrogen fixing microorganisms, but are also potent T cell mitogens. Inhalation of another lymphocyte mitogen (lipopolysaccharide) has been suggested as the cause of bronchoconstriction, mucus secretion, fever, and fibrosis in soybean. Different lectins have subtly different actions, but some are known activators of interleukin-4 producing helper T cells, which are abundant in the bronchial epithelium in patients with asthma. Chronic inflammation of the lung might cause local recruitment of additional T cells, explaining the apparent additive effect of cigarette smoking.

PETER OPENSHAW
Breath Control Unit, Department of Medicine, St Mary’s Hospital Medical School, London W2 1PG

1 Sharon N, Liss H. Lecitins as cell recognition molecules. Science 1989;246:227-34.