Thorax 1996;51:656–657

Commentary: pulmonary responses to inhaled exogenous agents

Gavin Boyd

The clinical case reports described in this issue illustrate the way in which the lung can react to different abnormal stimuli in terms of specific or non-specific responses.

The case report by Yoshida *et al* on pp 650–1 presents a classical picture of hypersensitivity pneumonitis/extrinsic allergic alveolitis (HP/EAA) related to a smut fungus. This group of organisms is well recognised as a source of aeroallergen associated with symptoms of bronchial asthma. The recognition that the same allergenic material can generate HP/EAA in certain susceptible individuals is an interesting observation but one which is well recognised in routine clinical practice in relation to *Aspergillus fumigatus*. The diagnosis of this type of hypersensitivity reaction hinges on the recognition of exposure to a source of organic materials with a particulate size within the respirable range – that is, below 20 μm – and which is associated with the development of a symptom complex of fever, breathlessness and irritable cough, together with symptomatic upset which occurs some 4–6 hours after contact. In classical cases, interstitial changes are seen on the chest radiograph and a "ground glass" appearance is seen over the lung fields. These changes tend to regress quickly as recovery from the acute state occurs. When soluble antigen is involved as in the case of avian related alveolitis – for example, pigeon fancier's lung – radiological abnormalities are not common and frequently the chest radiograph is unhelpful in assisting with diagnosis.

Immunological evidence of hypersensitivity and the presence of circulating antibody to the offending antigen allows confirmation of the diagnosis and Yoshida and his colleagues have outlined the basic procedures which can be used to clarify the immunological reaction and the presence of appropriate antibody. It is necessary in HP/EAA to identify evidence of appropriate circulating antibody. The simple gel diffusion test remains the easiest and the most convenient way of identifying circulating antibody but it is basically qualitative and, in current clinical thinking, the use of a fluorescent antibody technique allows for some quantification and an ELISA system offers a positive and straightforward way of quantifying the antibody response. Bronchoalveolar lavage (BAL) also permits the identification of the cellular pattern associated with the presence of an active HP/EAA response to the lung with the presence of a high proportion of lymphocytes and pulmonary alveolar macrophages in the lavage fluid in the active phase of the reaction. In routine clinical practice, however, BAL is not readily available and the requirement to perform this test at the appropriate time following exposure to antigen in the development of the clinical reaction makes it less useful as a diagnostic tool where commonly occurring antigens are involved. In the diagnosis of HP/EAA the importance of a carefully taken history cannot be overemphasised, and the presence of circulating specific antibody associated with hypergammaglobulinaemia on routine biochemical screening offers positive serological confirmation of an active hypersensitivity reaction in a case where crepitations are audible on auscultation over the lung field, whether or not radiological or pulmonary function abnormalities are present.

The use of intradermal skin tests in the diagnosis of HP/EAA is not an approach which is helpful in routine practice. Not only is it difficult to prepare sterile endotoxin-free buffered and standardised skin test material, but the responses can be variable. It is interesting that immediate reactions develop to intradermal injections which equate quantitatively with the level of circulating IgG antibody in addition to the occurrence of a delayed Arthus type of reaction which, in classical descriptions of the condition, is the recognised feature of an IgG mediated hypersensitivity response.[1] Although in scientific terms inhalation challenge tests remain one of the gold standards of diagnosis, they frequently pose major logisitic difficulties in normal clinical practice. They have a positive value in occupationally related HP/EAA where appropriate clinical observations and objective measurements can be conducted at the relevant time interval some 4–8 hours following the initial antigenic stimulus. Any investigations of this nature must be related in time to the period of antigen exposure. Thus, in many circumstances, patients who are referred to an outpatient clinic for assessment will attend well after the acute phase of the reaction has settled and, often, no positive findings are available by that stage to allow confirmation of the clinically suspected diagnosis.

Serological evidence persists for much longer and the advantage of using a quantitative measurement system such as an ELISA allows the change in the level of antibody with time to be monitored. When a sensitised individual with HP/EAA is removed from the source of antigen or when the level of inhaled antigen is reduced by the use of an appropriate respirator system, the level of circulating specific IgG antibody declines and, if this is not seen in certain individuals, the likelihood is that compliance has been poor and/or the respirator system used has been inappropriate. The repeated measurement of IgG antibody following diagnosis is an important method of monitoring the effectiveness of treatment and the clinical management.[2]

Hussain and his colleagues (pp 652–3) have described a case of severe lipoid pneumonia which resulted from what must be an extreme

Department of Respiratory Medicine, Stobhill Hospital, Glasgow G21 3UW, UK
G Boyd

situation of exposure to mineral oil and they have plotted the slow recovery from a major pulmonary insult. Lung disease resulting from the inhalation of mineral oil occurring in the industrial setting often poses no diagnostic dilemma when an appropriate industrial history is available. However, although lipoid pneumonia of non-occupational origin has been recognised for many years, the aspiration of milk, olive oil, codliver oil, or mineral paraffin oil used as a laxative or in nasal drops might not immediately be recognised as a cause of a respiratory disorder in the young, elderly, and chronically sick. The occurrence of lipoid pneumonia in non-industrial settings therefore requires increased awareness of these possible aetiological factors and, where exposure has occurred over a length of time, symptoms and abnormal physical signs may be absent in many cases although productive cough, breathlessness on exertion, and pyrexia may be present. Sometimes lipid droplets can be identified in the sputum using appropriate staining techniques but computed tomographic scanning can reveal opacities of lipid density which offer a more certain diagnostic approach. Transbronchial lung biopsy, however, is specific and the presence of an organising pneumonitis with lipid droplets contained within macrophages is diagnostic. Although in the case described oral prednisolone was included in the therapeutic regimen, the value of steroid therapy in lipoid pneumonia is disputed and the long term prognosis in individuals following severe reactions remains uncertain[3] despite the successful clinical outcome at one year in this instance.

The case described by Anderson and his colleagues on pp 654–5 related to the likely effects of inhalation of toxic material during the course of home renovations poses an interesting diagnostic problem and the possibility that this might be related to silica dust appears to be a tenable hypothesis. Evidence was present from lung biopsy specimens and environmental dust samples that particles of silica appeared to be implicated in the reaction which occurred in the lungs, being present in the air spaces and in adjacent macrophages. Similar particles were also seen in the BAL fluid. Serological and immunological data showed no evidence of any active immune process and, as indicated above in cases of HP/EAA, the relationship between the time from exposure to measurement can encompass the whole span of the immunological reaction that developed acutely at the outset, and this possibility cannot be ruled out in this case. Some support has been identified in the literature for the contention that this clinical syndrome was related to the acute, albeit short term, exposure to silica-containing dust, and the knowledge that freshly fractured silica can result in silicon-based free radicals being released with the consequent enhanced potential for lung tissue injury[4] offers some additional support. It also draws attention to the possibility that acute pulmonary damage relating to the inhalation of free radicals or other potent promoters of acute inflammatory responses my require consideration as aetiological factors in the generation of some "pneumonic" conditions where environmental factors, not necessarily occupationally based, may appear to be relevant.

These three quite different clinical cases draw the attention to variations in the response of the lungs to different exogenous agents and to the value of careful detailed histories, together with the appropriate use of BAL, lung biopsy, and radiological imaging in the clarification of atypical pulmonary reactions.

1 McSharry CP, Banham SW, Lynch PP, Boyd G. Skin testing and extrinsic allergic alveolitis. *Clin Exp Immunol* 1983;**54**: 282–8.
2 Boyd G, McSharry CP, Banham SW, Lynch PP. A current view of pigeon fancier's lung. A model for pulmonary extrinsic allergic alveolitis. *Clin Allergy* 1982;**12**(Suppl): 53–9.
3 Parkes WR. Oil granuloma (lipoid pneumonia). In: *Occupational lung disorders*. 3rd ed. London: Butterworth-Heinemann, 1994:778–82.
4 Vallyathan V, Shi Dalal NS, Irr W, Castranova V. Generation of free radicals from freshly fractured silica dust. *Am Rev Respir Dis* 1988;**138**:1213–9.