however, attempts to localize IgG4 to the surface of mast cells or basophils have been unfruitful. These cells possess only Fc receptors specific for IgE and not IgG.1,2 Furthermore, antigen-specific IgG4 is thought to play a protective, rather than a detrimental, role, arising after successful immunotherapy.3 For these and other reasons, convincing evidence for an IgG4 reagin is lacking.

In the patient described, a pectin prick test evoked an immediate wheal and flare response, and pectin inhalation challenge induced immediate bronchospasm—strong evidence for an IgE-mediated type I hypersensitivity to pectin. An IgG4-, rather than IgE-, mediated etiology is proposed due to the failure of isolation of pectin-specific IgE by enzyme-linked immunosorbent assay (ELISA); however, without a positive pectin-specific IgE ELISA control, the sensitivity of the test is in question. Even with a sensitive IgE pectin-specific ELISA, nanograms of pectin-specific IgE might well go undetected in the presence of milligrams of pectin-specific IgG4, due to competitive inhibition. Adequate adsorption of IgG from the patient's serum prior to performing the pectin-specific IgE ELISA is required before proclaiming the patient's serum devoid of pectin-specific IgE. Finally, without serum measurement of pectin-specific IgG4 from a pectin-exposed non-atopic coworker control, the pathogenic importance of the patient's pectin-specific IgG4 is, at best, speculative.

In conclusion, although the finding of pectin-specific IgG4 in this patient's serum is interesting, we differ with the authors' conclusion that it is pathogenic. We believe, rather, that the data suggest an IgE-mediated type I hypersensitivity to pectin.

James L. Baldwin, M.D., and Ambrish C. Shah, M.D., Scripps Clinic and Research Foundation, La Jolla, California

REFERENCES


To the Editor:

Drs. Baldwin and Shah feel that our recent report of pectin-associated asthma is more in keeping with an IgE-mediated hypersensitivity reaction than with an IgG4 mechanism, as we postulated. Specifically, they question the sensitivity of our IgG4 ELISA and raise the possibility that because of competitive inhibition by pectin-specific IgG4, we were unable to detect minute amounts of pectin-specific IgE.

In a previous study of patients receiving long-term immunotherapy, ragweed-specific IgE could still be measured in our laboratory in the serum samples of individuals with high ragweed-specific IgG4 and IgG1.1 Since similar methodology was used in this study, we believe that the negative pectin IgE analysis is accurate. We agree that having a pectin-specific IgE positive control would have been useful. As descriptions of pectin allergy, however, are currently still at the case report level, to our knowledge no such control exists.

Although IgE is responsible for type I hypersensitivity and is closely associated with allergy, some clinical problems are not well explained by either the presence or the level of total or specific serum IgE. For example, recent work has shown that antigen-specific IgE does not play a significant role in western red cedar asthma, suggesting that other mechanisms must be causal.2

The role of IgG4 in allergy is controversial. Although IgG4 has been reported to play a protective role in some studies, negative correlations between IgG4 response and clinical improvement were found in two Danish studies of grass and Cladosporium immunotherapy.3,4 A good prognosis was correlated with a low specific IgG4 titer in a study of individuals with dust-mite allergy.5

Our current data suggest that IgG4 may have caused the asthmatic response. Had the individual returned for follow-up, we would have attempted to confirm our impression by passive sensitization of basophils with the patient's serum before and after depletion of IgG. Then, basophils would have been challenged by pectin in different concentrations and histamine release measured.

Our data provide a clue to one of the possible mechanisms of allergy— IgG4-mediated sensitization. It should be noted that in another case of pectin-associated asthma IgG, not IgE, antibodies were detected.4 In this study, the IgG subclass was not documented. Although positive skin and bronchial responses usually suggest an IgE-mediated hypersensitivity, in cases in which serum-specific IgE is not detected, other possible pathogenetic mechanisms should be considered, the most likely in this case being the increased pectin-specific IgG4.

Zhikeng Peng, M.D., Allen Kraut, M.D., Allan B. Becker, M.D., and C. Peter Warren, M.D., Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

RIB BIOPSY

To the Editor:

In an article that appeared in the October 1992 issue of Chest, Dr. Ikard1 stresses that accurate preoperative chest wall localization of the lesion prior to open rib biopsy is crucial. The intraoperative finding of normal-appearing ribs poses perplexing problems to the surgeon, and extramodeleral biopsies are not uncommon.

We would like to describe the method that we use in cases of discrete rib lesions that are not expected to cause gross rib deformity: The osteolytic lesion is localized preoperatively under radiologic guidance. The skin overlying the lesion is marked with a pencil to indicate the site of incision. A 21-gauge needle is brought

CHEST / 104 / 6 / DECEMBER, 1993 1937
in contact with the rib in front of the focal lesion, and a minute amount of methylene blue is injected (0.2 ml). Thereafter, the patient is transferred to the operating theater, and rib biopsy is performed under general anesthesia. The blue spot is readily perceived at dissection.

This method is very straightforward, and we have found it useful for correctly localizing the portion of the rib to be resected.

Philippe Collard, M.D., and
Robert Ponlot, M.D.,
Cliniques Universitaires Saint-Luc, Brussels, Belgium

REFERENCE

To the Editor:

The letter by Drs. Collard and Ponlot addresses one of the difficulties encountered by those doing rib biopsy, that is, accurate preoperative localization. Their method is a variation of an old technique, staining the rib abnormality location with methylene blue. Skin localization alone will not help unless the patient is in the operative position. Changing the patient from the supine to the lateral position will invariably move the marked site and might create more confusion than aid. A technique that predictably marks the bone abnormality would certainly be helpful. Collard and Ponlot do not describe how they locate lesions prior to marking. If their method is reliable, preoperative bone labeling should provide confidence to the surgeon who at operation may see normal-appearing rib.

Robert W Ikard, M.D.,
Nashville, Tennessee

Diffusion Capacity in Heart Transplant Recipients

To the Editor:

We read with interest in the August 1992 issue of Chest the observation made by Groen et al. of a fall in diffusion coefficient (Kco) capacity following cardiac transplantation and their hypothesis that cyclosporine had a causal relationship. The vascular effects of cyclosporine on the kidney are well documented, and it is possible that cyclosporine may affect the alveolar-microvascular structure of the lung. Indeed, a reduced transfer factor (DLco) has also been documented in other solid organ transplant populations, such as renal transplant recipients.

In the setting of an immunocompromised patient, however, variables affecting the alveolar-microvascular structure of the lung other than hemodynamic change and cyclosporine are important. Van Son et al. have documented changes in diffusion capacity in renal transplant patients in the presence of cytomegalovirus (CMV) infection despite a normal chest radiograph. We, like Groen et al., have identified a cohort of heart transplant recipients who had a reduced Dco and Kco following cardiac transplantation. We found no correlation with whole-blood trough cyclosporine levels (either single measurements at lung function or cumulative dose) at a mean of 15 months following transplantation. We found, however, that patients with evidence of CMV infection had a lower DLco than patients free of CMV infection.

Cytomegalovirus infection of the lung may explain why the DLco/Kco was lowest at year 1 in the study by Groen et al., this being closer to the expected time frame for CMV infection. Do Groen et al. have CMV data on their patients? If the impairment in Kco was entirely a result of cyclosporine, one might expect to see a steady decline in Kco with time, rather than the improvement observed at 2 years following transplantation. To say that measurements of Kco reflect changes in cyclosporine dose could only be substantiated by more frequent comparisons of pulmonary function tests and cyclosporine concentrations.

Their data support our belief that the lungs of a solid-organ transplant recipient experience a continuing occult injury. A detailed prospective trial is required to determine the combined influence of cyclosporine and occult viral infection on the lungs of heart transplant recipients.

James J. Egan, M.B., B.Ch., B.A.O.,
Sanja Kalra, M.D., and
Ashley A. Woodcock, M.D.,
Wythenshawe Hospital,
Manchester, England

REFERENCES

To the Editor:

We thank Dr. Egan and his colleagues for their interest in our work. As our computer files did not include data about CMV infections, patient records were reviewed to evaluate the interesting hypothesis that the observed reduction in Kco is associated with CMV infection.

Of our cohort of 34 patients, 15 were CMV-seronegative allograft recipients, 5 of whom received the heart of a CMV-seropositive donor. In one seronegative recipient the serostatus of the donor was unknown. Nine recipient-donor combinations were matched for CMV status. Nineteen recipients were CMV-seropositive before the operation. All CMV-seronegative recipients were treated prophylactically with anti-CMV hyperimmunoglobulin (Cytotect, Biotest GmbH, Dreieich, Germany) for 10 weeks irrespective of the donor status. Cytomegalovirus infection was defined as any appearance of CMV-specific IgM antibodies; isolation of the virus from urine, throat washings, or blood; or detection of CMV antigen. Infection occurred in 12 patients (5 primary and 7 secondary infections). Cytomegalovirus disease was defined as infection coexistent with two of the following symptoms: otherwise unexplained fever (temperature >38°C) for at least 2 days; gastrointestinal, lung, retinal, or central nervous system involvement; leukocytopenia; thrombocytopenia; or elevated aminotransferase levels. Cytomegalovirus disease occurred in three patients (two primary infections) without evidence of pulmonary involvement.

The mean decrease (± SEM) in Kco after 1 year appeared to be 14 (5.5) percent predicted in the group with CMV infection. This figure was 11 (3) percent predicted in the group without such an infection. Both mean decreases were significantly (p<0.05) greater than zero, and did not significantly differ from each other. Using multiple regression analysis to evaluate the relation between Kco...