classifications, especially when the patients had nondilated left atria, and how they resolved those conflicts.

In conclusion, we want to highlight that in the echocardiography laboratory, it is not always easy to grade diastolic dysfunction. In respiratory patients, the absence of an important parameter such as dilatation of the left atrium can make classification even more complicated.

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REFERENCES

1. Tonelli AR, Plana JC, Heresi GA, Dweik RA. Prevalence and prognostic value of left ventricular diastolic dysfunction in idiopathic and heritable pulmonary arterial hypertension. *Chest*. 2012;141(6):1457-1465.
2. Barr RG, Bluemke DA, Ahmed FS, et al. Percent emphysema, airflow obstruction, and impaired left ventricular filling. *N Engl J Med*. 2010;362(3):217-227.
3. Unzek S, Popovic ZB, Marwick TH; Diastolic Guidelines Concordance Investigators. Effect of recommendations on interobserver consistency of diastolic function evaluation. *JACC Cardiovasc Imaging*. 2011;4(5):460-467.

Response

To the Editor:

We agree with the important remarks by Dr Claver and colleagues pertaining to our article in *CHEST*.¹ There is a strong relationship between left atrial (LA) enlargement and the degree of left ventricular (LV) diastolic dysfunction.² The increase in left atrial volume reflects the cumulative effects of elevated filling pressures over time. In patients with pulmonary arterial hypertension (PAH), a mitral filling pattern of impaired relaxation is commonly observed.^{1,3} However, this degree of diastolic dysfunction is not related to elevated left-sided filling pressures because they are normal or low.^{1,3} The abnormal mitral inflow pattern is likely explained by ventricular interdependence.^{1,3,4} Because the pericardium limits the space available for the ventricles to expand into, right ventricular pressure overload leads to leftward bowing of the interventricular septum, with a decrease in LV chamber size and filling.⁵ This reciprocal relation of the ventricles is also observed at the auricular level, given that there is also limited room for the right atrium (RA) to expand. This "atrial interdependence" leads to displacement of the interatrial septum and reduction of the volume of the left atrium.

In our study, the LA volume index was lower in patients with diastolic dysfunction grade $\geq$ I (18 ± 8 mL/m² vs 26 ± 12 mL/m², $P = .03$).¹ This phenomenon was likely due to a compression of the left atrium by the right one, because these patients had higher RA pressure (12 ± 6 mm Hg vs 6 ± 3 mm Hg, $P = .04$) and larger RA to pulmonary artery occlusion gradient (2.3 ± 6.6 mm Hg vs -6.7 ± 3.7 mm Hg, $P = .001$). In support of our findings, Kasner et al⁴ recently described the presence of impaired LV diastolic function due to ventricular interaction in patients with mild idiopathic PAH. They compared patients with idiopathic PAH with subjects who had isolated LV diastolic dysfunction and found that LA volume was larger only in the latter group.

In our cohort, we did not take into account the atrial size to make decisions regarding diastolic dysfunction in these patients. Nevertheless, we found discrepancies between the initial read and the subsequent echocardiographic review in five out of 61 cases (8%). A third physician reviewed these cases and a consensus was achieved. Of these five cases, an initial grade I diastolic dysfunction was reclassified as normal, a grade II was changed to grade I, and no changes were made in the remaining three patients. In summary, although LA size determination is part of the grading scheme for diastolic dysfunction,³ this particular criterion should not be used in patients with PAH.

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REFERENCES

1. Tonelli AR, Plana JC, Heresi GA, Dweik RA. Prevalence and prognostic value of left ventricular diastolic dysfunction in idiopathic and heritable pulmonary arterial hypertension. *Chest*. 2012;141(6):1457-1465.
2. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. *Am J Cardiol*. 2002;90(12):1284-1289.
3. Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr*. 2009;22(2):107-133.

4. Kasner M, Westermann D, Steendijk P, et al. Left ventricular dysfunction induced by nonsevere idiopathic pulmonary arterial hypertension: a pressure-volume relationship study. *Am J Respir Crit Care Med*. 2012;186(2):181-189.
5. Gan CT, Lankhaar JW, Marcus JT, et al. Impaired left ventricular filling due to right-to-left ventricular interaction in patients with pulmonary arterial hypertension. *Am J Physiol Heart Circ Physiol*. 2006;290(4):H1528-H1533.

Can Omalizumab Be Effective in Chronic Eosinophilic Pneumonia?

To the Editor:

We have recently read with interest the article by Kaya et al¹ in *CHEST* (August 2012) reporting on a patient suffering from chronic eosinophilic pneumonia (CEP) who responded successfully to omalizumab. Five years ago, we attended a 43-year-old nonsmoking man who complained of cough, fever, dyspnea, and wheezing. On the basis of his clinical presentation, peripheral blood and BAL eosinophilia, and the presence of bilateral peripheral infiltrates on the chest radiograph, the diagnosis of CEP was made. As in the Kaya et al¹ case, oral corticosteroids (OCs) were started with an initial successful response. After 3 months of therapy, the dose of OCs was progressively tapered. When the dose reached 10 mg prednisolone, a relapse occurred that forced us to increase the dose of OCs. The patient improved, and bronchospasm and chest infiltrates disappeared.

During the process of OC tapering, a new relapse occurred, bronchospasm being the most relevant clinical symptom that forced us to increase again the dose of OCs. A skin prick test was performed that was positive for mite dust. Total blood IgE level was 253 IU/mL. Omalizumab treatment was started at the dose calculated according to the patient's weight and IgE concentration. The patient progressively improved, and after 18 months of treatment (6 months to check clinical response followed by 12 months of stabilization), according to our decreasing-dose protocol of omalizumab,² the dose of omalizumab was progressively tapered by 50% every 6 months. The patient's tolerance was excellent, and omalizumab treatment could be safely quit 12 months later. The patient has remained free of symptoms of CEP for > 2 years, requiring only two short courses of OCs for his asthma.

The IgE-dependent inflammatory phenomena have been studied in depth and are clearly recognized in atopic subjects, and the anti-IgE blocking effect of omalizumab has been clearly shown. Additional benefits can be provided by the findings of Kalesnikoff et al,³ who observed that by binding to its high-affinity receptor, FcεRI, IgE was able to induce intracellular signaling pathways, resulting in the production of cytokines and the enhancement of mast-cell survival on its own, without cross-linking by allergens. In addition, IgE can directly bind and activate receptors present on eosinophils, neutrophils, and monocytes. As a result, the rationale for the use of omalizumab in diseases other than allergy is based on its blocking effect on IgE, which inhibits part of the T helper cell type 2 immune response, thus, reducing recruitment and activation of effector cells of the inflammatory process, including eosinophils. Because IgE effector cells (ie, mast cells and basophils) are a source of proinflammatory molecules, anti-IgE therapy may have antiinflammatory properties that reduce circulating and tissue eosinophils⁴; indeed, this role has been suggested in other diseases, such as eosinophil-associated GI disorders.⁵ More recently, Noga et al⁴ demonstrated an increase in eosinophil apoptosis and a decrease in granulocyte-macrophage colony-stimulating

factor. All this information can help to explain the benefits of omalizumab in CEP.

In their report, Kaya et al¹ communicate that their patient remains free of symptoms 15 months after omalizumab treatment began, but they do not state future treatment options. We believe some of these patients can benefit from a decreasing dose protocol.²

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REFERENCES

1. Kaya H, Gümüş S, Uçar E, et al. Omalizumab as a steroid-sparing agent in chronic eosinophilic pneumonia. *Chest*. 2012; 142(2):513-516.
2. Domingo C, Pomares X, Casabon J, Garcia A, Veigas C, Monton C. Decreasing dose protocol for omalizumab treatment in oral corticosteroid allergic asthma patients. Paper presented at: European Respiratory Society Annual Congress; September 24-28, 2011; Amsterdam, The Netherlands.
3. Kalesnikoff J, Huber M, Lam V, et al. Monomeric IgE stimulates signaling pathways in mast cells that lead to cytokine production and cell survival. *Immunity*. 2001;14(6):801-811.
4. Noga O, Hanf G, Kunkel G. Immunological and clinical changes in allergic asthmatics following treatment with omalizumab. *Int Arch Allergy Immunol*. 2003;131(1):46-52.
5. Foroughi S, Foster B, Kim N, et al. Anti-IgE treatment of eosinophil-associated gastrointestinal disorders. *J Allergy Clin Immunol*. 2007;120(3):594-601.

Response

To the Editor:

We read the correspondence by Drs Domingo and Pomares about our case report¹ with interest. The case described by the authors, and probably some other unpublished cases, support the potential benefits of omalizumab in chronic eosinophilic pneumonia and other hypereosinophilic states.

The mechanism of the effect of omalizumab on hypereosinophilia is unclear; however, the defective expression of CD23 on B cells, as in our case, might be an explanation.¹ The low-affinity receptor for IgE, FcεRII, also known as CD23, is expressed on