Guest editorial

Responsibility for quality IgE antibody results rests ultimately with the referring physician

In North America, 15 different FDA-cleared assay formats manufactured by seven different companies are used by clinical laboratories to detect and quantify allergen-specific IgE antibodies in human serum as a confirmatory diagnostic test to the clinical history and as an adjunct to the skin test.[1] Alternatively, several clinical laboratories have chosen to manufacture and validate their own assays and allergosorbent reagents. Essentially, all the assay formats are a modification of the original radioallergosorbent test (RAST) that was initially reported by Wide et al[2] in 1967 when IgE was identified as the fifth unique human Ig isotype.[3,4] Most allergists, on occasion, will send a blood sample to either their HMO-preferred or personally selected clinical laboratory for a patient who either poorly tolerates in vivo skin or provocation tests (eg, children); has a surprising negative in vivo test result that is inconsistent with the clinical history; is dermatographic; or has inadvertently taken antihistamines just before his visit. Armed with a reliable serologic result, as well as the patient's clinical history and skin test or other in vivo test results, the allergist will be able to affirm or negate IgE-mediated disease with confidence.

There are two papers by the same group of authors, one published in the *Journal of Allergy and Clinical Immunology*[5] and the other using the same data that are published in this issue of the *Annals of Allergy, Asthma, and Immunology*.[6] These two papers describe the same single-masked proficiency-type study, in which 26 sera containing IgE antibody to 17 dust mite, pet epidermal, grass, tree, and weed pollen, and mold allergens were sent to six laboratories over a period of 6 weeks for allergen-specific IgE analyses. The six laboratories were requested to analyze the test sera using one of three assay designs: the CAP System (Pharmacia Diagnostics AB, Uppsala, Sweden; n = 2), AlaSTAT (Diagnostic Products Corporation, Los Angeles, CA; n = 1) and the paper disc RAST (n = 3) with self-manufactured allergosorbents. Both papers purport to have examined the "accuracy" of these three groups of specific IgE assays. The term "accuracy," however, is defined as the degree to which an analyte concentration estimate from a given assay corresponds to the true value of the analyte concentration. The authors acknowledge that the true value of the allergen-specific IgE antibody concentrations were not known in these 26 challenge sera so they were only able to evaluate relative analytical inaccuracy relating to random errors (precision) and bias (parallelism with dilution recovery). Both papers, however, fall short of actually studying the true assay accuracy and analytical sensitivity for each of the allergen-specific IgE antibody specificities. The authors conclude that one of the assays, the CAP System, performed closest to their ideal. They determine that the CAP assay was the most "quantitative" in detecting changes in IgE antibody content that reflect the actual change in the serum (eg, 2-fold decrease in IgE antibody measured when the serum was diluted 2-fold). This is important because there is increasing evidence that the quantitative level of some IgE antibody specificities can be predictive of more severe clinical allergic disease.[7] The clinician should, however, be careful to not interpret the data in these two papers as reporting on the true accuracy of these IgE antibody assays to detect IgE antibody in an individual who has allergic disease to that allergen specificity. Precision and parallelism are certainly important analytical qualities in a laboratory assay, but analytical sensitivity and true accuracy of the assay are most important in allergy diagnosis. The latter performance measures still need to be more clearly defined for the IgE antibody assays used in clinical laboratories.

The important message of these papers is the unmistakable and obvious, but often overlooked or disregarded, conclusion that commercially reported IgE antibody results are not all equivalent. The physician ordering the test has a ultimate responsibility to the patient to ensure that the blood sample is sent to a laboratory that exhibits the least amount of variability and reports IgE antibody results that are most quantitative and closest to the truth concerning the presence of IgE antibody in the serum.

Selection of the laboratory should consider not only the technical ability and diligence of the laboratory personnel performing and monitoring the assay, but also the assay source used in the laboratory which ultimately determines the overall quality of the reported IgE antibody result. The laboratory should be CLIA-88 certified and should participate successfully in the College of American Pathologists Diagnostic Allergy (SE) Proficiency Survey.[8] The SE survey submits five sera every 17 weeks to participating laboratories. Each serum is analyzed for total serum IgE, specific IgE antibody to five allergen specificities, and a multiaeroallergen screen. By requesting a copy of the CLIA-88 certificate

and reviewing the SE Survey Participant's Summary and the laboratory's actual SE Survey data for the past year, a physician can make an educated decision about the overall performance of the laboratory. When reviewing the laboratory's SE Survey data, the reported semiquantitative class IgE antibody results are grouped by assay method. Actual laboratory data should be reviewed within the context of the SE Survey's critique that provides general expectations for the presence or absence of IgE antibody in each specimen. The frequency of false-positive results with the different assays can be evaluated by examining the data generated with the specimens from individuals identified as nonatopic. Further, the spread in IgE antibody results among the various methods can be evaluated with the IgE antibody-positive sera.

If a patient's serum is sent to a laboratory that uses an assay that has poor precision or displays questionable performance in the SE survey and other studies such as the one in this issue, there is a good chance that bad IgE antibody data will result and lead to a significant potential for misdiagnosis. The requesting physician holds the ultimate responsibility for ensuring the quality of IgE antibody results by making a wise decision about the laboratory that performs his IgE antibody serology.

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