N-glycans with core xylose together with core α-1,3-fucose and modifications have been identified in the egg stage of schistosomes.[9] In our study, *S haematobium* infection, mainly in urban low SES subjects, was significantly associated with raised IgE to core xylose. Although some *S haematobium* positives had elevated IgE to structures with core α-1,3-fucose only, similarly raised levels to these structures were observed among *S haematobium* negatives, suggesting that these may not have been driven by schistosome infection. Therefore, our observations link schistosome infection in IgE cross-reactivity involving core xylose.

Overall, our findings suggest that cross-reactive IgE among Ghanaian children may be directed against both core xylose and core α-1,3-fucose independently. Further investigations are needed to explore factors aside from helminths such as insects that may drive reactivity to these motifs. Recently, protein microarray technology has revolutionized allergy diagnostics by allowing the simultaneous assessment of specific IgE to multiple allergens with a small amount of serum. Our investigation illustrates how glycan microarrays can further improve molecular diagnosis of specific IgE to allergenic motifs by providing additional information on IgE profiles of patients.

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Allergy terminology: Toward a common language and shared understanding

To the Editor:

The practice of allergy centers on 4 main pillars, namely, patient education, allergen avoidance, pharmacological intervention, and immunotherapy. Central to all these interventions is the need for shared understanding between patients and doctors, which, in turn, relies on effective communication. Communication is, however, adversely affected by time constraints, language of communication, and the understanding of practitioners of the

difficulties in communication and effective strategies to mitigate against them. The responsibility for ensuring accurate communication resides with health practitioners and learned intermediaries not patients or laypeople, and thus accurate use of terminology between ourselves and between us and our patients deserves close attention. Furthermore, the terms we use affect our own understanding of disease entities and have an impact on our patients.

In medical settings, modes or styles of communication, educational level, and cultural systems may all adversely affect communication, but differences in lexical meanings may be the most common and important mechanism whereby miscommunication occurs.[1] In addition, terminology may be used differently in different countries and by different specialities and even within a speciality terms may be used inconsistently, or ambiguously where multiple senses of a term occur. Patient and practitioner miscommunication affects allergy care in profoundly important ways.[2-4]

Of course, members of specialized speech communities (such as the medical community) define words in technical registers differently from laypeople. Where terminology is logical, consistently understood, and used by medical professionals and understood in an equivalent (or similar) way by patients, it can be considered as "good" for communication. However, close scrutiny of terminology that is used inconsistently by medical professionals or is not equivalently understood by patients may enhance professionals' understanding of how and why miscommunication occurs.

Two examples of terminology that cause significant miscommunication in the sphere of allergic sensitization are considered.

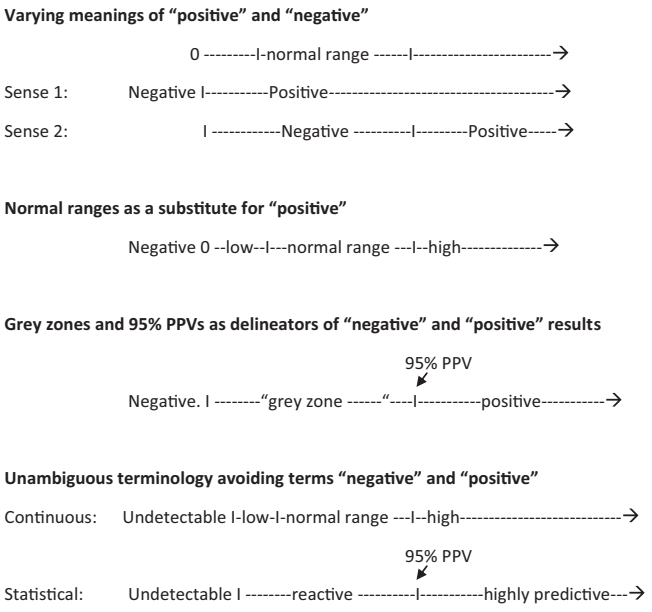
What is a "positive" test result? A positive test result means that the substance or condition being tested for was found. A positive test result may also mean that the amount of a substance being tested for, although not 0, is higher than normal. A negative test result means that the substance or condition being tested for was not found. Where a test result is a categorical variable, the 2 distinct "meanings" or "senses" of the word coincide. A "positive" pregnancy test result indicates that one is pregnant. However, when applied to continuous results along a range of normality, these 2 senses of the term are not equivalent. A representation along a range of continuous results makes this clear (Fig 1).

Thus, for continuous variables, the use of the terms "positive" and "negative" is ambiguous. A commonly used resolution for this problem is to refer to results as ordinal categories of negative, low, normal, and high (Fig 1).

This resolves the problem for laboratory measurements with direct correlation between the test result and what is "truly" being measured, and in which a low value or a high value correspond to abnormal states. Examples of this include a glucose test or a sodium level. It is thus easy to allocate "cutoff levels" that correspond to some level of importance of the test result, for example, a sodium of less than 135 indicating hyponatremia or higher than 145 indicating hypernatremia.

For other tests, however, interpretation is more difficult because "normal ranges" may vary for different individuals and with the clinical situation under investigation. In addition, the measured result may reflect an odds ratio that statistically manipulates a pretest probability to result in a posttest probability.

Allergists are generally comfortable with keeping a good clinical history in mind and thus using a test result to define the posttest probability from a pretest probability. Although many allergists do this subconsciously, the use of the Fagan's nomogram[5] has been widely recommended as a more rigorous way of determining the



clinical utility of a test result. Despite this, the desire for simplification of a test into a positive and negative result (in the sense where negative means the condition is absent or unlikely, and positive means it is present or likely) has led us to put great store in 95% positive predictive values (PPVs), often referred to as "cutoff levels," despite these being shown to vary between patient populations and thus not to be absolute.[6-8] Some authors refer to levels above the 95% PPV as "positive" and the range between a low value and the 95% PPV as the "gray zone" (Fig 1).

However, in this setting, both the words positive and negative are still not truly accurate. A "positive" result will still be wrong (false positive) in approximately 5% of cases, and a "negative" result may be found with small amounts of the substance being measured that are not detectable by the lower detectable limit of the instrument. If this very low level sensitization results in clinically relevant symptoms, this would be a false-negative test result.

In fact, the entire issue of "false positives" and "false negatives" could be removed entirely from our lexicon by not using the terms "positive" or "negative" for continuous test results (Fig 1)! Although this sounds complex, it is actually very clear and intuitive to refer to laboratory results simply as undetectable, low, normal, and high for continuous/ordinal variables or as undetectable, reactive, and highly predictive for variables that are statistically related to outcomes such as C-reactive protein and IgE levels.

Advantages of removing "positive" and "negative" from laboratory reporting would be reduction of confusion for the patient that a test can be falsely positive or falsely negative. For patients, the need to correlate a test result with a clinical meaning is strong. Patients find it nearly impossible to understand our differentiation between "sensitization" and "allergy," with almost all patients presuming that a "positive," nonzero test result requires avoidance of food allergens.

In cases in which different senses of a word exists, there is great potential for miscommunication. A potent example of this is the multiple senses of the word "cross-reactivity."

TABLE I. Terminology for 3 senses of the word "cross-reactivity"

Allergen/Antibody	Laboratory test	Patient's clinical reaction
Ambiguous terminology		
Cross-reactivity	Cross-reactivity	Cross-reactivity
Unambiguous terminology		
Cross-binding	Cross-sensitization: (primary sensitizing antigen cross-binds to cause secondary sensitization)	Cross-reactivity (clinically relevant cross-sensitization)
Opposite		
Specific binding	Cosensitization	No cross-reactivity (innocent cross-sensitization)

Sense 1: In immunology, cross-reactivity has a narrow meaning of the reaction between an antibody and an antigen that differs from the immunogen. Cross-reactivity measures the extent to which different antigens appear similar to the immune system.

Sense 2: In medical tests, cross-reactivity indicates a test result that is reactive due to the presence of a closely related molecule. Examples include a laboratory result where primary sensitization to latex Hevein-like protein domains causes allergen cross-reactivity between latex and banana. Another example is primary sensitization to cross-reactive carbohydrate determinants (CCDs) causing multiple cross-reactive laboratory results.

Sense 3: Although a CCD "cross-reactivity" will not manifest with clinical allergy, a latex "cross-reactivity" may result in the latex-fruit syndrome. Thus, the patient's clinical condition itself may be referred to as "cross-reactive." Cross-reactivity in allergic reactions occurs when a patient allergic to one substance experiences a reaction to a different substance due to the similarity between the proteins in the 2.

The 3 distinct "senses" of the word "cross-reactivity" depend on whether one assumes the perspective of the allergen or the antibody, the laboratory test, or the patient (Table I).

This has potential for serious miscommunication. For example, a patient with allergy to peanuts who is told that peanuts cross-react with legumes may assume that their "positive" test result to legumes, described by the clinician as cross-reactivity, is necessarily clinically relevant and that he or she should avoid all legumes.

To assess possible solutions for the problem of multiple sense of the word "cross-reactivity," it may be useful to reflect on what the "opposites" are of each sense of the word.

The "opposite" of immunological cross-reactivity is 2 different antigens that bind specifically. Where 2 laboratory test results are "positive" due to similarity in antigens this is referred to as "cross-reactivity," whereas the presence of 2 nonsimilar antigens is often referred to as "cosensitization." The "opposite" of clinical cross-reactivity (the lack of a reaction when sensitized to a homologous allergen) is often referred to profoundly unsatisfactorily as a "false-positive test result" or occasionally "innocent sensitization."

These opposites suggest possible substitutions for the different senses of the term "cross-reactivity," which may allow easier differentiation between them by coining new terms for the perspective of the antigen and the laboratory result, namely, cross-binding and cross-sensitization, respectively, and to reserve "cross-reactivity" for clinical reactions only (Table I).

The coining of additional terms would simplify matters by allowing one-to-one correlation between words and concepts. In addition, it would be clear whether we are discussing the nature of an antigen, the result of a test, or the relevance to the patient, and it places the patient at the end of a process that reflects physiological reality in which binding causes sensitization and may or may not cause reactions.

Many specialities have embarked on processes to refine terminology. In 1991, the American College of Chest Physicians and the Society of Critical Care Medicine convened a consensus conference to establish recommendations for the terminology to be used when describing sepsis. In 2001, several North American and European intensive care societies agreed to revisit the definitions for sepsis and related conditions.[9] A similar process may be needed to assess whether terminology commonly used in allergy actually does cause significant miscommunication and whether alternative terminology should be recommended.

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Autoinflammatory phenotypes in Aicardi-Goutières syndrome with interferon upregulation and serological autoimmune features

To the Editor:

Recent advances in molecular genetics have revealed that polymorphisms in the genes implicated in innate immunity via nucleic acid metabolism and type I IFN production underlie a subgroup of autoimmune diseases, such as systemic lupus erythematosus.[1] In addition, mutations in the same genes cause