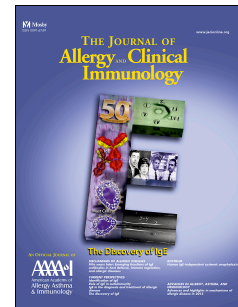


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Allergy terminology: towards a common language and shared understanding

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Summary

Terminology that is used in an inconsistent and ambiguous way by allergists includes the term “cross reactivity” and the use of the word “positive” when referring to allergy tests. This may have serious potential for miscommunication and adversely affect patient care.

To the editor

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

Miscommunication

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)(3)(4)

Of course, members of specialised speech communities (such as the medical community) define words in technical registers differently from lay-people. 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 mis-communication occurs.

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

Negative and positive

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 zero, 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 two distinct "meanings" or "senses" of the word coincide. A "positive" pregnancy test indicates that one is pregnant. However when applied to continuous results along a range of normality, these two senses of the term are not equivalent. A representation along a range of continuous results makes this clear (figure 1)

Thus for continuous variables, the use of the terms "positive" and "negative" are ambiguous. A commonly used resolution for this problem is to refer to results as ordinal categories of negative, low, normal and high, as follows (figure 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 "cut-off levels" that correspond to some level of importance of the test result, e.g. a sodium of less than 135 indicating hyponatraemia or higher than 145 indicating hypernatraemia.

For other tests, however, interpretation is more difficult as “normal ranges” may vary for different individuals and with the clinical situation under investigation. In addition the measured result may reflect an odds ratio which statistically manipulates a pre-test probability to result in a post-test probability.

Allergists are generally comfortable with keeping a good clinical history in mind and thus using a test result to define the post-test probability from a pre-test probability. Although many allergists do this sub-consciously, 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 lead us to put great store in 95% positive predictive values (PPV) often referred to as “cut off levels” despite these being shown to vary between patient populations and thus not to be absolute. (6) (7) (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 “grey zone” as follows (figure 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 sensitisation results in clinically relevant symptoms this would be a false negative test.

In fact, the entire issue of “false positive” and “false negatives” could be removed entirely from our lexicon by not using the terms “positive” or “negative” for continuous test results! (figure 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 CRP 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 “sensitisation” and “allergy”, with almost all patients presuming a “positive”, non-zero test result, requires avoidance of food allergens.

Cross reactivity

In cases where 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”.

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 sensitisation to latex Hevein-like protein domains cause allergen cross-reactivity between latex and banana. Another example is primary sensitisation to cross-reactive carbohydrate determinants (CCDs) causing multiple cross-reactive laboratory results.

Sense 3

While 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 two.

The 3 distinct “senses” of the word “cross reactivity” depend on whether one assumes the perspective of the allergen or antibody, the laboratory test or the patient, as below. (Table 1)

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 to legumes, described by the clinician as cross-reactivity, is necessarily clinically relevant and that s/he should avoid all legumes.

In order 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 two different antigens that bind specifically. Where two laboratory tests are “positive” due to similarity in antigens this is referred to as “cross-reactivity” whereas the presence of two non-similar antigens is often referred to as “co-sensitisation”. The “opposite” of clinical cross reactivity (the lack of a reaction when sensitised to a homologous allergen) is often referred to profoundly unsatisfactorily as a “false positive test result” or occasionally “innocent sensitisation”.

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, viz. cross-binding and cross-sensitisation respectively, and to reserve “cross reactivity” for clinical reactions only. (Table 1)

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 sensitisation and may or may not cause reactions.

A call to action

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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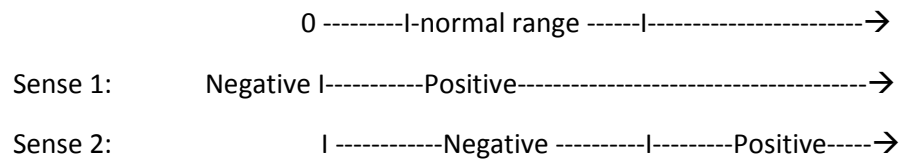
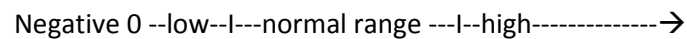
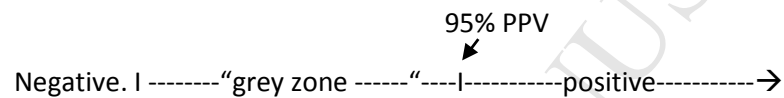
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Table 1: Terminology for 3 senses of the word “cross reactivity”

Allergen / Antibody	Laboratory test	Patient’s clinical reaction
Ambiguous terminology		
Cross reactivity	Cross-reactivity	Cross reactivity
Unambiguous terminology		
Cross-binding	Cross-sensitisation: (Primary sensitising antigen cross-binds to cause secondary sensitisation)	Cross reactivity (Clinically relevant cross-sensitisation)
Opposite		
Specific binding	Co-sensitisation	No cross reactivity (Innocent cross-sensitisation)

Figure 1: Terminology along a range of continuous results

Varying meanings of “positive” and “negative”**Normal ranges as a substitute for “positive”****Grey zones and 95% PPVs as delineators of “negative” and “positive” results****Unambiguous terminology avoiding terms “negative” and “positive”**