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What Do We at Present Know about the ALCAT Test and What Is Lacking?

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In many clinical situations, doctors (and patients) find the procedure of performing double-blind, placebo-controlled food challenges (DBPCFC) time-consuming and potentially dangerous and, therefore, try to base the diagnosis on case history supported by one or more *in vivo* or *in vitro* tests. Based on our experience, the validation of such tests varies widely, ranging from the reasonable to the non-existing.

The commercial market for these diagnostic tests for *in vivo* or *in vitro* determination of food hypersensitivity is enormous, and it is, therefore, not surprising that a vast variety of more or less serious companies launch such tests. It is, however, worthwhile bearing in mind that doctors are restricted by the International Code of Ethics, which means that a doctor may only use justifiable methods and tools in diagnosis and treatment of patients.

Basically, the following questions must be addressed before using any new diagnostic test [from 1]:

- (1) Can the test diagnose the parameter in question with sufficient specificity and precision?
- (2) Are abnormal values of the parameter associated with clinical disease, and has an age- and sex-related normal range been established?
- (3) Can other conditions (pathological or physiological) give rise to values outside the normal range?

In food hypersensitivity, any new test *must* be validated against the 'gold standard', i.e., DBPCFC and not against e.g. the most used test – the market leader [2, 3].

The ALCAT Test

Very little information is available regarding the ALCAT test. It has been launched in several countries, and seems to have been promulgated especially for in vitro diagnosis of food intolerance. We have not been able to identify any academic settings or university hospitals using the test, and its penetrance into private practice is not known. The economical profit made on the test may be an integrated part of the total income earned on diagnosing and treating the patient, as is the case in Denmark. Since the test has not been validated, it is not recognized for reimbursement by any Danish health authorities, however. As a consequence, the patient has to pay the full price for the test. This is in contrast to the normal Danish social security system, in which all accepted procedures are free of charge for the patient.

The answers to the above three questions cannot be given based on available data. We therefore instead go through the standard procedure for evaluating in vitro tests in our laboratories and see where data are available.

Technical Validation

The basic principle of the test is measurement of white cell diameter in a Coulter counter before and after addition of a food extract. The company mentions that 'the test is approved by FDA', but it has not been possible for the authors to have this information confirmed by FDA. Whether the company is referring to a possible general improvement of Coulter counters for measurement of cell size is not clear to us.

A number of parameters are listed in table 1 which may influence the outcome of a diagnostic test. In the evaluation of the overall fidelity of a test result, these parameters should be described. For the ALCAT test, only one question in table 1 can be answered, namely the apparatus. No data regarding the other parameters are available. Especially the quality of the reagent (the food extracts) is crucial. The test claims to measure reactions to many foods at a time (100+) including foods (e.g. lettuce or mutton), rarely reported to elicit food hypersensitivity reactions after oral intake. No data are available concerning the source, quality, immunological stability or concentration in the test tubes of any of the food extracts. Another question which cannot be answered is the analytical sensitivity, i.e. the detection limit of the test. The same is true for the measurement range, i.e. the span between the detection limit and the highest amount which can be measured in the assay. Furthermore, nothing is known about the analytical specificity of the test – meaning the ability to distinguish between different foods. Accuracy (correctness) describes the ability of a test to reach the target

Table 1. Parameters influencing the outcome of a diagnostic test [modified from 3]

Design	Choice of detection principle Time and temperature conditions of incubations (often a compromise between speed and analytical sensitivity) Manual, semiautomatic, automated
Reagent quality	Quality of allergen extract
Apparatus	Raw data measurement
The combinations of the above-mentioned parameters produce the <i>inherent</i> analytical sensitivity, accuracy, and reproducibility of a diagnostic test as supplied by the manufacturer, whereas the parameters listed below add further uncertainties which will be experienced by the clinician demanding the test from the laboratory.	
Human factors in laboratory	Educational background Experience
Quality level of laboratory	Monoplicate/duplicate determinations Existence of internal and external quality assurance programs
Biological factors in sample	Numerous

value, i.e. a value which is considered true from other assays or from consensus among a large number of assays. Precision (reproducibility) on the other hand describes the ability to reach the same result in a series of multiple measurements in one assay or in a day-to-day design. An accurate test is not necessarily precise and vice versa.

The only paper describing technical validation reports a poor reproducibility and discourages any use of the test [4]. No other data are available on these parameters. Tests which are analytically sensitive and specific, accurate and precise are said to be reliable. The reliability of a test may be documented by the producer/supplier, but in order to be effective the standards of laboratory employing the tests should also be controlled regularly. An increasing number of quality control programs are now being introduced by suppliers of test kits or by independent organizations, and major improvements are to be expected in the coming years.

In the view of the scarcity of data on reliability of the test, it is not surprising that no data are available on the variation in results when the ALCAT is performed in different laboratories.

Clinical Validation

There is a large amount of theoretical literature on the clinical evaluation of diagnostic tests [reviewed in 5]. We define the true diagnosis of food hypersen-

Table 2. Status of knowledge of the ALCAT test

Parameter	Status
<i>Technical parameters</i>	
Apparatus	Validated
Reagent quality	Data not available
Analytical sensitivity	Data not available
Measurement range	Data not available
Analytical specificity	Data not available
Precision	Data not available
Accuracy	Data not available
<i>Clinical parameters</i>	
Clinical sensitivity	Data not available
Clinical specificity	Data not available
Predictive values	Data not available

sitivity as proven by DBPCFC and the concept of clinical sensitivity, clinical specificity and positive/negative predictive values must be based on patients who have undergone DBPCFC. The most important question to answer before calculating sensitivity, specificity and predictive values for a new test is: 'What is the true diagnosis?' In food hypersensitivity, the 'gold standard' is DBPCFC and any new test must be validated in patients fulfilling this criterium [2, 3].

No data on the above parameters are available regarding the ALCAT test. In Denmark, the specialist using the test used to claim to be investigating the above parameters but has now switched to a position where it is claimed that 'it is unethical to do challenges in these patients'.

Conclusion

In conclusion, no data (table 2) supporting any use of the ALCAT test are available. Until such data become available, the test should not be used outside scientific protocols.

References

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