

Labnews

Serum Testing for Allergies

Serological testing correlates with IgE mediated hypersensitivity but should be interpreted in conjunction with the clinical history and should not be considered definitive.

Serum Testing for Allergies

Serum testing for the detection of allergies using Pharmacia's UniCAP™ test system is now available from MDS Laboratories. This methodology, also known as SAIGE testing (Specific Allergen IgE), identifies the presence of circulating IgE antibodies which are the basis of allergic hypersensitivity reactions to specific allergens.

General Approach to Allergy Testing

The first step in identifying an allergy is completion of a detailed clinical history with particular attention to the effect of environmental factors such as grass, weeds, trees, animal and foods.

For more specific answers it has been traditional to use skin prick tests however these have generally been restricted to specialists and are subject to certain limitations. Skin tests demonstrate the presence of IgE antibodies on the surface of mast cells in the skin. These tests are affected by the patient's propensity to react to an allergen or irritant exposure and are subject to several variables which cannot all be readily controlled.

Serum Testing

The UniCAP™ test system utilizes a solid phase immunoassay procedure to detect IgE antibodies to specific allergens. The utilization of purified allergens allows for quantitative and highly reproducible results. UniCAP™ testing has demonstrated greatly improved sensitivity and specificity compared to older serological method known as the RAST test. Agreement between allergists' diagnoses and serum test results for common allergens in a large European study demonstrated sensitivity and specificity levels of 93% and 89% respectively¹.

It may also be an appropriate testing approach in young children in whom skin reactivity is lower and compliance with testing may be difficult or for elderly patients, in whom there is a decrease in skin reactivity to histamine².

Food Allergens

Food allergies affect a significant proportion of the pediatric population with cow's milk allergy affecting about 2.5% of newborn infants. Although most infants outgrow this allergy, 15% of infants retain their IgE mediated allergic sensitivity

Clinical situations where serum testing is recommended³

1. Atopic dermatitis and other skin disorders
2. Patients on medication which may affect skin test results
3. Pre-desensitization
4. Evaluation of cross reactivity to insect venoms
5. Food allergies
6. Evaluation of allergic parasitic disorders
7. High risk of anaphylaxis
8. Cannot cooperate with skin testing

until the second decade and 35% have allergic reactions to other foods. Egg allergies occur in about 1.3% of young children and peanut allergies in about 0.5%. In total these three allergens account for about 85% of all food allergies seen in children and adolescents⁴.

UniCAP™ tests can predict clinical reactivity to egg, milk, peanut and fish with greater than 95% certainty. This is similar to skin prick tests, however neither of these tests can be solely relied on to exclude allergies to foods. The definitive test for exclusion is the double-blind placebo controlled, oral food challenge (DBPCFC). Negative exclusion is important in determining whether a child has outgrown sensitivity to food allergens, including peanuts⁵. In these circumstances a diagnostic approach may include:^{4,5}

1. Skin test:

This may continue to be positive even though the patient is no longer sensitive.

2. UniCAP™ serum allergy test

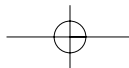
If the result is low then this may mean that the patient is no longer allergic. Confirmation by oral challenge is required.

3. Oral challenge test

This double-blind, placebo controlled, oral food challenge (DBPCFC) must be done in a controlled medical environment, usually by an experienced allergist, due to the risk of a hypersensitivity reaction. If negative the patient may be considered to no longer be sensitive to the allergen. *(continued on page 4)*

In This Issue

Serum Testing for Allergies	1
Drugs of Abuse Urine Testing	2
Lab Notes	
New MDS Cytology Requisition	3
Reporting of Enteric Parasitology Results	3
Serum 5' - Nucleotidase and Aldolase: Obsolete Tests	3





Drugs of Abuse Urine Testing

How long after use will a urine sample test positive for a drug? This is a commonly asked question and one that is difficult to answer as there are many physiological and analytical factors that determine the presence of a drug in urine. Physiological factors include the drug's half-life, the individual's ability to metabolize and excrete the drug and the frequency and amount of drug used. Other considerations

include the cut-off value used to denote positive or negative results, as well as the analytical sensitivity and specificity of the method used.

MDS performs initial drugs of abuse testing using class specific immunoassays which will detect compounds of similar chemical structures. Drugs are typically excreted in the urine as the free drug, metabolites and as conjugates with glucuronic acid. Consequently, the length of time a urine sample will test positive after drug use may vary depending on whether the method used will detect all excreted forms of the drug. For example, the MDS benzodiazepine assay detects all

excreted forms of benzodiazepine in urine and may give a positive result while the same sample may test negative by another immunoassay that does not detect the conjugate.

Specimen adulterants may affect the length of time a urine sample is positive for a drug. For example, diluting the urine with water or adding common household products, such as soaps, to the urine may result in a negative test even when the drug is present at levels above the analytical cut-off value.

MDS reports a presumptive positive result if the level of drug is above the cut-off point. The cut-off values are those recommended by the Substance Abuse and Mental Health Services Administration (SAMHSA, USA) formerly the National Institute on Drug Abuse. All positive results by immunoassay are "presumptive positives" until confirmed by an alternate technique, preferably gas chromatography with mass spectrometry (GC/MS). Confirmatory testing may be requested by telephoning MDS at 416-675-3637 or toll free 1-877-849-3637.

Table 1 contains a summary of approximate time periods, since last use, that a sample will test positive for some of the common drugs of abuse. Values should be used as general guidelines only. MDS



Table 1.
Approximate time periods, since last use, for a positive urine drug test by routine immunoassays

Drugs	Long-Term Use	Occasional Use	Cut-off Value, ug/L (test is positive at value > cut-off)
Amphetamines/ Methamphetamines	7 -10 days	1 - 2 days	1000
Benzodiazepines	7 -10 days	3 - 5 days	200
Cannabinoids	3 - 6 weeks	1 - 5 days	50
Cocaine Metabolite	10 - 15 days	2 - 4 days	300
Opiates	1 - 3 days	1 - 2 days	300
Phencyclidine	2 - 4 weeks	3 - 8 days	25

References

1. Mandatory Guidelines for Federal Workplace Drug Testing Programs 1998, SAMHSA, Division of Workplace Programs, US Department of Health and Human Services, Rockville, Maryland.
2. Cone EJ and Weddington WW, Prolonged Occurrence of Cocaine in Human Saliva and Urine after Chronic Use, *J Anal Toxicol* 1989; 13: 65 - 68.
3. Cody JT and Schwarzhoff RH, Impact of adulterants on RIA analysis of urine for drugs of abuse, *J Anal Toxicol* 1989; 13: 277 - 284.

LAB NOTES

New MDS Cytology Requisition

A new MDS Cytology requisition has been designed in collaboration with the Ontario Association of Medical Laboratories. You will start to receive the new requisition when your existing supply is depleted in the early Fall.

A tear-off patient fact sheet titled "You and your Pap Test" will be part of the new form. It enables you to quickly inform women how they should participate in the screening program and to realize the limitations of a single Pap Smear. You can also indicate when the next regular Pap test is due at the bottom of this sheet.

Serum 5' - Nucleotidase and Aldolase: Obsolete Tests

Serum 5' - Nucleotidase activity is measured as an indicator of liver disease and has been used in the differential diagnosis of hepatobiliary disorders. Assessment of liver diseases associated with biliary tract obstruction is more effectively completed using measurement of gamma glutamyl transpeptidase and alkaline phosphatase (ALP). 5' - Nucleotidase has also been used to confirm the origin of an unexplained elevated ALP.

Aldolase activity is sometimes measured as an indicator of skeletal muscle, liver and cardiac disease. Elevated levels of serum aldolase are associated with cancer, muscular dystrophy, hepatitis and myocardial infarction. Due to its ubiquitous nature, aldolase is not particularly helpful in such assessments. Tests which provide more diagnostic information for these pathologies include total creatine kinase (CK), CK-MB and the transaminases, AST and ALT.

Therefore, effective October 30th, 2001, MDS will no longer perform routine testing for serum 5' - NT and aldolase activity. For further assistance, please consult a MDS Clinical Biochemist at 416-675-3637.

References

1. Moss DW and Henderson AR, *Enzymes, Tietz Fundamentals of Clinical Chemistry*, 4th edition, Burtis CA and Ashwood ER, eds. WB Saunders Co, 1996; 283-335.
2. Jacobs DS, DeMott WR, Strobel SL and Fody EP, *Aldolase, Laboratory Test Handbook*, 2nd edition, Jacobs DS, Kasten Jr. BL, DeMott WR and Wolfen WL, eds. Lexi-Comp Inc, 1990.

Reporting of Enteric Parasitology Results

Please note that MDS Laboratories has changed the reporting of enteric parasitology results to reflect recently developed consensus guidelines¹. While all helminths will continue to be reported, only protozoa with pathogenic (see table), potential will be listed on the final report. The presence of nonpathogenic protozoa will be reported without specific identifications since this may be of clinical value to some physicians.

Pathogenic Protozoa	Non-Pathogenic Protozoa
<i>Entamoeba histolytica</i>	<i>Endolimax nana</i>
<i>Giardia lamblia</i>	<i>Entamoeba coli</i>
<i>Cryptosporidium spp.</i>	<i>Entamoeba dispar</i>
<i>Cyclospora cayetanensis</i>	<i>Entamoeba hartmanni</i>
microsporidia	<i>Entamoeba polecki</i>
<i>Dientamoeba fragilis</i>	<i>Enteromonas hominis</i>
<i>Balantidium coli</i>	<i>Iodamoeba butschlii</i>
<i>Isospora belli</i>	<i>Retortamonas intestinalis</i>
<i>Eimeria spp.</i>	<i>Trichomonas hominis</i>
<i>Sarcocystis spp.</i>	<i>Blastocystis hominis</i> *

* Inclusion of *Blastocystis hominis* in this group may change as its pathogenic potential is clarified by well-controlled studies.

Please be reminded that microscopic differentiation between pathogenic *E histolytica* and nonpathogenic *E dispar* is not possible. Currently, serological testing is the only available test to aid in the discrimination between these species. Specific stool antigen and PCR testing may become available as more performance data emerges. ^{MDS}

References

1. Quality Management Program - Laboratory Services, Guidelines for Reporting Enteric Parasitology Specimens, April 3, 2001.
2. Pillai DR, Keystone JS, Sheppard DC, MacLean JD, MacPherson DW and Kain KC, *Clin Infect Dis* 1999; 29: 1315-1318.



A Canadian study indicates that even in symptomatic or high risk patients, less than 5% of *E histolytica/dispar* antigen positive

stools are actually antigen positive for *E histolytica* specifically.²

(continued from page 1)

General Selection of Tests

With over 450 allergens available, test selection begins with the clinical history. In the first instance it is recommended that a "mix test" be selected which includes five or six allergens commonly associated with hypersensitivity to grasses, animal, food types etc. The "mix test" for children's foods includes, for example, egg white, milk, wheat, peanut and soybean, while the animal allergen "mix test" includes allergens related to cat, dog, horse and cow dander. "Mix test" results are reported as positive or negative.

In other circumstances, selection of single allergens with a high probability of being positive may be more appropriate. Depending upon the results of the first round of tests a second round may be ordered using the original sample.

Interpretation of results

Numeric results are graded based on the level of the antibody detected in the serum. The quantitative results may be used longitudinally to determine the effectiveness of therapeutic interventions. It is important to note that the level of antibody elevation will not necessarily correspond to the clinical situation since the IgE antibody is only one factor involved in the induction of symptoms.

A positive result will generally indicate an allergic response and may sometimes be seen in the early phases of sensitization before development of inflammation and hence not correlate with symptoms.

A positive result for a "mix test" indicates that there is reactivity to one or more of the allergens included in the mixture.

A negative result in the presence of allergic symptoms is most likely due to testing an incorrect target. Alternatively, a molecule not included in the allergen extract may be the offending allergen. For example, the patient may be allergic to a biological metabolite or a by-product of food processing rather than the "pure" substance tested.

Availability of Testing

To request these tests please use the MDS Allergy requisition which lists many of the more common single allergens and combinations of allergens ("mix tests"). For a more detailed list of allergen testing options please contact MDS at 1-877-849-3637.

Serological allergy testing is not covered by OHIP but may be covered by a patient's private insurance plan. Patients will be charged at the time of specimen collection. 

References

1. Paganelli R *et al.* *Allergy* 1998; 53: 763-768.
2. The Allergy Report. NIH Guidelines for the diagnosis and management of allergies. Washington DC, NIH Publication.
3. Bernstein L and Storms WW, *Ann Allergy Asthma and Immuno*, 1995; 75: 553-625.
4. Sampson HA, *J Allergy Clin Immunol.* 2001; 107: 891-896.
5. Skolnick HS, Conover-Walker MK, Koerner CB, Sampson HA *et al.*, The natural history of peanut allergy, *J Allergy Clin Immunol*, 2001; 107: 367-74.



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