Laboratory Allergy Testing

General

Laboratory allergy testing measures immunoglobulin E (IgE) specific to allergen(s) in serum.

Allergen-specific IgE testing (sIgE) is an important tool in the diagnosis of IgE mediated food allergy, insect venom allergy, as well as some forms of drug and latex allergy. It may also be helpful in the management of patients with allergic conditions such as asthma, eczema or allergic rhinitis, assisting with identification of relevant allergic triggers that can exacerbate symptoms.

sIgE testing is generally not helpful in the evaluation of non-IgE mediated food allergy, intolerance reactions, chronic urticaria and non-specific symptoms such as headache or fatigue.

Historically, sIgE was measured using a RAST (radio-allergo-sorbent test), however many years ago, the RAST was superseded by newer immunoassays. The term RAST is still commonly used but we would like to encourage the use of the more accurate term specific IgE or sIgE. Dorevitch Pathology provides sIgE testing on the ImmunoCAP platform and this is considered the benchmark method used in the majority of current allergy clinical trials.

Allergy is not an all-or-nothing phenomenon. The development of an allergic response starts with initial sensitisation to an allergen, at very low levels of sIgE. Later, as the level of sIgE increases, the patient may progress from asymptomatic sensitisation to the development of clinical allergy, with symptoms such as urticaria, anaphylaxis, rhinoconjunctivitis or asthma.

Interpretation of allergen-sIgE

In clinical practice, 0.35 kUA/L has commonly been used as a cut-off for allergen-specific IgE to separate positive from negative results. Nevertheless, a positive allergen-specific IgE test (which indicates detection of allergen-specific IgE) does not necessarily indicate clinical allergy. In general, low sIgE antibody levels indicate a low probability of clinical disease, whereas high antibody levels to an allergen show better correlation with clinical disease. Clinical history is the best indicator of possible allergy. A positive allergen specific IgE is used together with the clinical history to support and confirm the diagnosis of clinical allergy.

Food allergy

Correlation of sIgE level and risk of allergic reaction

For foods such as peanut, egg and milk, allergen-specific IgE levels correlate with the likelihood of an individual having an allergic reaction to that substance. The higher the level of sIgE, the more likely the patient is to experience symptoms of allergic disease upon exposure to that substance. Threshold values of sIgE that indicate 95% likelihood of clinical allergy have been established for ImmunoCAP sIgE results to egg, milk, peanut, fish, soy and wheat (Sampson, HA. Journal of Allergy and Clinical Immunology 2004;113:805).

In contrast, the level of allergen-specific IgE does not correlate with the severity of an allergic reaction. For example, anaphylaxis to an allergen can occur with low levels of sIgE to that allergen, while high levels of sIgE may be seen in patients who only experience mild allergic reactions on exposure to the relevant allergen.

Interpretation of positive sIgE results (≥0.35 kUA/l) to food allergens

- If there is a clear history of immediate allergic reaction to a food, a positive sIgE test confirms the presence of allergy to that food.
- However, if the patient has not previously ingested the food or there is an unclear history of reaction, the finding of a positive sIgE test does not necessarily indicate allergy – it only indicates sensitisation that may or may not be associated with clinical allergy.

Interpretation of negative results (<0.35kUA/l)

Negative allergen-specific IgE does not exclude clinically significant allergy:

- Allergen-specific IgE have no clinical utility in non-IgE mediated food allergy, delayed-type hypersensitivity reactions or other non-IgE mediated allergic disorders.
- Allergen-specific IgE tests to allergen panels (mixes) may be less sensitive than allergen-specific IgE tests to single allergen (e.g. " staple food mix" vs "egg").
- Skin prick tests with fresh food or allergen extracts may be more sensitive than ImmunoCAP for some allergens, for example fruits and vegetables.
- Therefore, if clinical suspicion of allergy is strong and sIgE to the suspected allergen is negative a referral to a specialist for further evaluation including skin prick testing may be warranted.

How to order allergy laboratory tests

The clinical utility of sIgE testing is greatly enhanced by provision of clinical information. This allows the pathologist to provide more meaningful results, and as a result enable you, as the clinician, to appropriately tailor management for the patient.

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Dorevitch® PATHOLOGY

Food allergy

Requests for sIgE should clearly indicate the specific allergens you wish to test for - eg sIgE to milk, egg, peanut.

Requests for "RAST" or "Allergen test" do not provide sufficient information and will result in delayed testing while our staff contact you for more information.

Specific IgE testing to single food allergens are recommended in preference to sIgE tests to food panels (mixes) as a positive test to a sIgE food allergen panel (eg 'staple food mix') does not provide information on which specific food the patient may be sensitised to.

Allergic rhinitis or asthma

In patients with asthma or allergic rhinitis, sIgE testing to inhaled allergens can help with investigation and management. sIgE testing to food allergens is rarely indicated. Although food allergy reactions may cause airway symptoms similar to asthma, foods do not trigger asthma exacerbations and food-sIgE testing is not indicated in the management of asthma. Inhaled allergens such as house dust mite, pets and pollen are potential triggers for asthma and allergic rhinitis, and the selection of sIgE testing should be guided by clinical history. For example house dust mite allergy typically results in year round symptoms particularly when settling into bed, through the night or first thing in the morning, while pollen allergy typically presents with symptoms in spring/summer although pollen seasons may be extended in warmer regions (and with global warming).

- Identification of specific allergen triggers (eg house dust mite) can assist with management as patients may benefit from implementation of avoidance measures.
- Detailed sIgE testing is required when prescribing immunotherapy for allergic rhinitis or asthma so that treatment can be tailored to each individual patient.

There are certain clinical situations where sIgE testing to inhalant allergen panels may be helpful.

- For establishing the presence or absence of atopy, testing for a limited number of common environmental allergens is appropriate (eg dust mite, grass pollens, animal epidermals).
- Testing to tree mix, grass mix and weeds can guide when treatment should be implemented for seasonal allergic rhinitis and asthma. Tree pollens are generally prevalent in spring, grass pollens in spring/summer, and weed pollens in summer/autumn.

Changes to standard allergy testing panels.

- For requests that state "RAST test" or "allergy test" without stipulating specific allergens of interest, we will run a standard panel of tests that covers the common allergens (Australian grass and weed pollens, and house dust mite) which are relevant to the most common allergic disorders (asthma, allergic rhinitis).
- We encourage clinicians to specify allergens of interest when ordering allergy tests. This change took effect in May 2013. If there is a clinical suspicion of allergy to an allergen(s) that has not been tested, serum will be held for 7 days in the event that add-on testing for additional allergen specific IgE is required.

Laboratory Testing – your questions answered

Why test for specific IgE?

Allergen-specific IgE has a central role in immediate (Type 1) hypersensitivity reactions. In this type of reaction, clinical manifestations usually develop acutely following exposure to the allergen and may include acute urticaria, angioedema, rhinitis, vomiting, diarrhea, hoarse voice, wheeze, stridor, hypotension, tachycardia. Testing for sIgE is recommended in this setting to confirm suspected allergen triggers based on history. It is not recommended in patients with non-specific chronic symptoms, fatigue, headaches, chronic gastrointestinal symptoms and chronic urticaria.

Allergic disorders (including allergic rhinitis, asthma, eczema) are among the most common problems seen by the medical practitioners, and their incidence continues to increase. The demonstration of allergen-specific IgE is an essential adjunct to diagnosis of atopic diseases and can identify relevant allergic triggers that exacerbate symptoms. Results of sIgE testing can assist in formulation of an effective management strategy for patients with such disorders.

In some situations, monitoring of allergen-specific IgE can be used as a guide to the efficacy of immunotherapy for treatment of allergic disease, or a change in an individual's allergy status over time (especially for food allergy in children).

What does the test measure?

The sIgE test measured by ImmunoCAP is a quantitative, in vitro assay for the measurement of sIgE in human serum. Unlike skin testing, it is not affected by medications.

How does this Dorevitch Pathology test compare with alternative methods?

The technology used in the ImmunoCAP method offers dramatic improvements over earlier in vitro technologies (RAST) for the measurement of sIgE. Results obtained with ImmunoCAP technology correlate better with skin prick.

The unique ImmunoCAP technology provides high binding capacity of clinically relevant allergen proteins, including those present in very low levels. This provides accurate results, and increased sensitivity, specificity and reproducibility and is the most advanced in vitro allergy testing available today. The ImmunoCAP method is globally considered the gold standard for quantitative in vitro measurement of sIgE for precision, accuracy and reliability (Williams PB et al, Journal of Allergy and Clinical Immunology, 2000 Jun; 105:1221-30).

Billing for allergy testing

Requests for up to 4 standard allergens or allergen mixes per request will be bulk-billed for up to four episodes within a 12 month period. Patients will be subject to an out-of-pocket charge if more than 4 standard allergens or allergen mixes are requested in a single request or if more than four episodes of allergy testing are requested within a 12 month period. Requests for recombinant or component sIgE testing will be charged to the patient. Out-of-pocket payments are summarised below (Table 1).

SCENARIO	GAP PAYMENT	COMMENTS
> 4 allergens or mixes/ episodes	$40.00 per episode	Non-specialist referrals only
> 4 episodes/12 months	$60.00 per episode	
Recombinant or component allergens	$40.00 per episode	

Table 1: Gap payment scenarios for allergy testing at Dorevitch Pathology.

Introduction of molecular allergy testing

Dorevitch Pathology is now offering a broad array of molecular allergy tests. Component-resolved diagnostics , based on well-characterised individual allergen molecules, is a new development in allergy diagnosis, that may allow clarification of the nature and severity of allergic reactions, and allergen cross-reactivity. The clinical significance of these tests continues to be studied. These specialised recombinant and component allergens are unfortunately expensive, so in order to provide a comprehensive repertoire of these useful tests, out-of-pocket charges will be introduced for each allergen requested. Examples are listed in the table.

CODE	NAME	COMMON REQUEST TERM
f423	Peanut (rAra h 2)	Ara h 2
f416	Wheat (rTri a 19, Omega-5 Gliadin)	Omega 5 gliadin
f232	Egg (nGal d2, Ovalbumin)	Ovalbumin
f233	Egg (nGal d 1, Ovomucoid)	Ovomucoid
f76	Milk (nBos d 4 a-lactalbumin)	Lactalbumin
f77	Milk (nBos d 5 B-lactoglobulin)	Lactoglobulin

Allergen – Specific IgE (sIgE) Available.

The following allergen-specific IgE tests are available at all times. These represent the commonest allergen triggers and are the most relevant to patient care. Note: sIgE to allergen mixes are available – clearly state the components of mix to ensure the correct test is performed.

A more comprehensive range of allergen sIgE tests are also available – if you wish to perform an allergen sIgE test that is not on the common allergen list, please contact our scientists or immunopathologists to discuss – call (03) 9244 0326 Mon – Fri 8am-4pm.

DRUGS

- Amoxicilloyl (c6)
- Ampicilloyl (c5)
- Cefaclor (c7)
- Chlorhexidine (c8)
- Gelatin bovine (c74)
- Morphine (c260)
- Penicilloyl G* (c1)
- Pholcodeine (c261)
- Suxamethonium (c202)

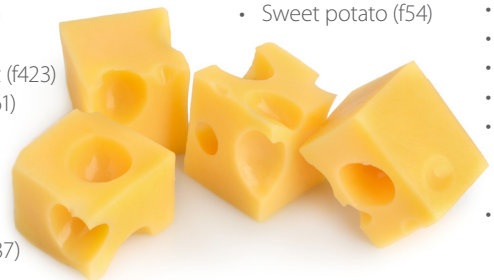
* This detects sIgE against the major determinant Benzyl penicilloyl. sIgE to minor determinants not available.

INSECTS

- Cockroach (i206)
- European Paper Wasp (i77)
- Honey bee (i1)
- Yellow jacket (European or common) (i3)

FOODS

- Abalone (f346)
- Almond (f20)
- Ara h 2 Peanut (f423)
- Asparagus (f261)
- Avocado (f96)
- Banana (f92)
- Barley (f6)
- Beef (f27)
- Blue mussel (f37)
- Buckwheat (f11)
- Cashew (f202)
- Chicken (f83)
- Clam (f207)
- Crab (f23)
- Crayfish (f320)
- Egg white (f1)
- Fish (cod) (f3)
- Goat milk (f300)
- Hazelnut (f17)
- Kiwi (f84)
- Lentil (f235)
- Lobster (f80)
- Lupin (f335)
- Macadamia (f345)
- Mackerel (f206)
- Maize, corn (f8)
- Milk (cows) (f2)
- Mutton (f88)
- Oat (f7)
- Octopus (f59)
- Oyster (f290)
- Pea (f12)
- Peanut (f13)
- Pecan (f201)
- Pine nut (f253)
- Pistachio (f203)
- Pork (f26)
- Potato (f35)
- Pumpkin (f225)
- Quinoa (f347)
- Red snapper (f381)
- Rice (f9)
- Rye (f5)
- Salmon (f41)
- Sardine (f308)
- Scallop (f338)
- Sesame seed (f10)
- Sheep milk (f325)
- Shrimp (f24)
- Soya bean (f14)
- Squid (f258)
- Sweet potato (f54)
- Trout (f204)
- Tuna (f40)
- Turkey meat (f284)
- Walnut (f299)
- Wheat (f4)
- White fish (f384)
- Yeast (f45)
- Cereal mix (wheat, oat, maize, sesame seed, buckwheat) (fx3)
- Citrus mix (orange, lemon, grapefruit, and mandarin) (fx29)
- Meat mix (pork, beef, chicken) (fx73)
- Nut mix 1 (peanut, hazel, brazil, almond, coconut) (fx1)
- Nut mix 2 (pecan, cashew, pistachio, walnut) (fx22)
- Seafood mix (cod fish, shrimp, blue mussel, tuna, salmon) (fx2)
- Staple food mix (egg white, milk, fish, wheat, peanut, soybean) (fx5)



INHALANTS

Animals

- Cat epithelium & dander (e1)
- Dog dander (e5)
- Guinea pig (e6)
- Horse dander (e3)
- Mouse epithelium (e71)
- Mouse urine proteins (e72)
- Rabbit epithelium (e82)
- Animal mix (Dander's: cat, horse, cow, dog) (ex1)

Moulds

- Alternaria alternata (m6)
- Aspergillus fumigatus (m3)
- Cladosporium herbarum (m2)
- Mould mix 1 (penicillium chrysogenum, Cladosporium herbarum, Aspergillus fumigatus, Alternaria alternata) (mx1)

Grasses

- Bahia grass (g17)
- Bermuda grass (Couch) (g2)
- Rye grass (g5)
- Timothy grass - wild oats (g6)
- Aust pollen mix (bermuda, rye, bahia, common ragweed, plantain, lamb's quarters) (rx3)
- Grass mix (bermuda, rye, timothy, kentucky, johnson, bahia) (gx2)

TREES

- Acacia (t19)
- Australian Pine (t73)
- Cedar (t212)
- Cypress (t222)
- Eucalyptus (t18)
- European Ash (t25)
- London Plane (t11)
- Melaleuca (t21)
- Olive (t9)
- Privet (t210)
- Silver birch (t3)
- White Pine (t16)
- WillowTree mix 1 (Boxelder, Common silver birch, oak, walnut, Elm) (tx1)
- Tree mix 2 (Box-elder, oak, Elm,Cottonwood, Pecan/ Hickory) (tx2)
- Aust tree mix (Olive, Eucalyptus, Acacia, willow, white pine, melaleuca) (tx7)

Weeds

- Common Ragweed (w1)
- Plantain (w9)
- Weed mix (common ragweed, mugwort, plantain, lamb's quarters, saltwort) (wx1)

Mites

- Blomia tropicalis (d201)
- D. farinae (d2)
- D. pteronyssinus (d1)
- Glycphagus domesticus (Storage mite) (d73)
- Dust mix (Hollister-Stier labs, D. pteronyssinus, D. farinae, cockroach) (hx2)

MISCELLANEOUS

- Anasakis (p4)
- Latex (k82)
- rHev b 5 Latex (k218)

Meet our Immunopathology Team

Dr Katherine Nicholls

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Dr Katherine Nicholls graduated with a Medical degree from the University of Tasmania, and following several years working in the United Kingdom and in Queensland, she undertook her postgraduate training in Clinical Immunology/Allergy and Immunopathology in Brisbane and then Melbourne. She joined Dorevitch Pathology in early 2010 where she is the Head of Immunopathology. She has practiced clinical medicine at the Royal Melbourne Hospital since 2010 and is Deputy Head of the Department of Clinical Immunology and Allergy.

Dr Nicholls is interested in all areas of immunology, with immunodeficiency and autoimmunity being of particular interest. She enjoys the complexity of this specialty and takes a keen interest in clinical teaching, both of basic physician and specialist trainees. Dr Nicholls is a member of the Royal Australasian College of Physicians and Royal College of Pathologists of Australasia joint training committee, and is currently an examiner for Immunopathology with the RCPA. She is a member of the Australian and New Zealand Anaesthetic Allergy Group, having recently completed her tenure as the Immunology Liaison representative for this group, and is active in clinical research at the Royal Melbourne Hospital.

Professor Mimi Tang

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Professor Tang graduated from Medicine (with Honors) at The University of Melbourne in 1986, where she also completed her PhD in 1995. She went on to complete her Allergy and Immunology training through the Royal Australasian College of Physicians and Royal College of Pathologists Australasia in 1997. Today, in addition to her consultant Immunopathologist role at Dorevitch Pathology she is a Paediatric immunologist allergist at the Royal Children's Hospital in Melbourne, Group Leader of Allergy and Immune Disorders Research at the Murdoch Children's Research Institute; and a Professor in the Department of Paediatrics at the University of Melbourne.

Professor Tang has received national and international awards in recognition of her achievements in allergy immunology research and clinical care, including the prestigious Victorian Department of Health Public Health Care Silver Award (Category – Most Appropriate Care), the Pharmacia International Allergy Fellowship and the American Academy of Allergy Asthma and Immunology President's Grant-in-Aid Award.

Professor Tang has authored more than 230 peer reviewed journal articles, invited reviews, and book chapters. She has been invited to speak at major international scientific meetings in the field of Allergy and Immunology including the American Academy of Allergy Asthma and Immunology (AAAAI), European Academy of Allergy Asthma and Clinical Immunology (EAACI), and World Allergy Congress (WAC).

Dr Sam Mehr

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Dr Sam Mehr completed his MBBS at the University of Melbourne in 1999 along with his BMed Sci. He completed his internship at St Vincent's Hospital in Melbourne before moving to the Royal Children's Hospital. Dr Mehr moved to the Children's Hospital at Westmead where he completed his fellowship in Clinical Allergy and Immunology and in Immunopathology. He is a Fellow of the Royal College of Pathologist of Australasia in Immunopathology and a Fellow of the Royal Australasian College of Physicians.

His current appointments include Immunopathologist at Dorovitch Pathology (joining in mid 2016), Consultant Staff Specialist in Allergy and Immunology at the Royal Children's Hospital, Honorary Medical Officer at the Children's Hospital at Westmead, Sub-editor of the Journal of Paediatrics and Child Health and he sits of various committees (Allergy working party for Immunology QAP, Immunotherapy working party of ASCIA, Paediatric subcommittee of ASCIA, AusEE patient support group, and Centre for Food & Allergy Research).

Dr Mehr has a strong interest in research, having published peer-reviewed papers published in both local and international journals. His immunopathology interests include autoimmune serology and allergy testing.