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Allergy Testing

Quiz Feedback: Sodium and Potassium Imbalance

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better medicine

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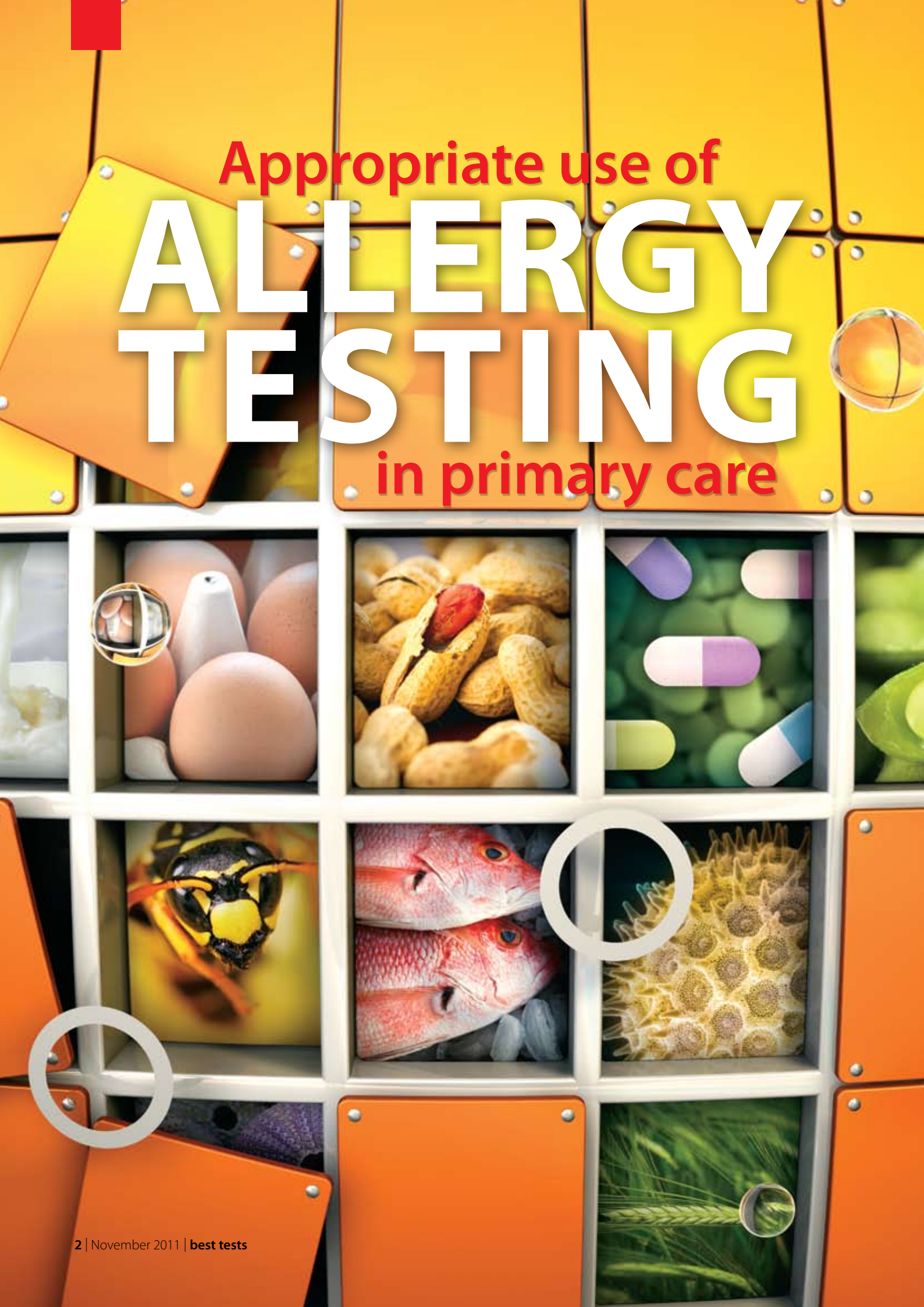

In recent years, the use of serum allergen-specific IgE testing for suspected allergy has increased dramatically. This has created an unsustainable burden on laboratories in terms of the volume and cost of performing these tests. In many cases, testing is not required for a person with symptoms of allergy. If testing is indicated, skin prick testing should be used first-line. In Australia, serum allergen-specific IgE testing is limited to three tests per patient, per year. This approach is supported in New Zealand (although is not policy). General Practitioners need to carefully consider the need for allergy testing before ordering investigations.

Defining allergy

An allergic reaction is a result of hypersensitivity of the immune system to an allergen. Generally, for an allergy to be considered a "true" allergy, there are two factors that need to be present:

- Clinical features – i.e. the development of specific signs and symptoms on exposure to that allergen

AND

- Sensitisation – as shown by the presence of allergen-specific IgE

The exceptions to the definition of true allergy are the non-IgE-mediated food-induced allergic disorders, which are only rarely encountered in general practice, e.g. food protein-induced enterocolitis syndrome.

An intolerance is an adverse reaction to a substance, not involving the immune system.

Diagnosis of allergy can often be based on clinical history and examination

It is estimated that approximately 30% of people in New Zealand are affected by an allergic condition during their lives.[1] The symptoms and signs of allergy vary widely from very mild reactions to life threatening situations (anaphylaxis).

The diagnosis of allergy in primary care is often based on the clinical picture rather than on the results of investigations.

Take a detailed history

A detailed clinical history should include information about:

- Type, severity and duration of the symptoms
- Onset of the symptoms and the timing in relation to the presumed allergen
- Relationship of the symptoms to place, time (of day, season), work or hobbies
- What the patient thinks is the likely allergen
- Personal and family history of atopy
- Any exposure to new foods, pets or plants
- Any medicines that are being taken, including all over-the-counter treatments

Physical examination is guided by the clinical history

In general this should include an examination of the:

Skin – for signs of urticaria or other rash, dry skin, eczema or dermatitis, excoriations

Head and neck – in particular eyes (e.g. swelling, tearing, redness, allergic "shiners" in children), nose and sinuses for congestion, mouth and tongue, cervical lymph nodes

Lungs – laboured breathing, wheezing (high-pitched sounds produced by narrowed airways when a person exhales) or the presence of rhonchi (sounds that resemble snoring when air is blocked or becomes rough through the large airways). Abnormal sounds can sometimes be heard without a stethoscope.

Allergy testing in primary care

The majority of patients with allergy can be adequately managed with medicines, appropriate advice and reassurance, without it being necessary to specifically identify the allergen. If medical treatment is inadequate to control symptoms, and it is thought that identifying the likely causative allergens would benefit the management of that patient, then allergy testing for some conditions may be indicated. The two allergy tests that can be requested in general practice for IgE mediated allergies are:

- Skin prick tests *(in vivo)*
- Serum allergen-specific IgE tests *(in vitro)*

The results of both of these allergy tests must be interpreted in the context of the clinical history as a positive result only reflects sensitisation and not necessarily allergic disease if there is no history of symptoms. For example, a patient might display a high response to peanuts when allergy tested, yet have no clinical reaction after eating peanuts. Therefore that person is NOT allergic to peanuts.[2] Positive allergy tests may also be clinically irrelevant if the patient is unlikely to have been exposed to that allergen, in which case it cannot be the cause of their current allergy symptoms.

Patch testing is not available within the primary care setting (but may be available in specialist allergy clinics and within secondary care). It is usually considered for difficult cases of allergic contact dermatitis, e.g. caused by nickel, rubber or cosmetics.

Skin prick testing is the preferred initial test for allergy

If laboratory investigation of allergy is required, skin prick testing is preferred. Skin prick testing should not be requested if the result of the test is unlikely to improve the management of the patient, e.g. confirming an allergy to pollen in a patient with obvious seasonal allergic rhinitis, whose symptoms are well controlled, is unlikely to be helpful.

Skin prick testing detects IgE bound to mast cells in the skin. Small amounts of the suspected allergens are introduced into the epidermis and superficial dermis and interact with any specific IgE bound to skin mast cells. If this occurs, histamine and other mediators are released, leading to a visible "wheal-and-flare" reaction which is maximal after about 15 to 20 minutes.

The extent of the reaction on the patient's skin is assessed to give a positive or negative skin prick test result. If the diameter of the wheal is ≥ 3 mm more than the negative control, this is considered a positive result. The degree of sensitivity of the patient to the allergen is reflected in the size of the wheal, but this should be interpreted relative to the age of the individual. For example, in children aged under five years, a much smaller wheal size can be clinically significant.

The following wheal sizes in adults gives some guidance as to the relative sensitivity to the allergen and the likelihood of being allergic:

Size of wheal	Clinical significance
> 15 mm	Very sensitive
10 to 15 mm	Moderately sensitive
5 to 10 mm	Mildly sensitive
< 3 mm	Negative result

N.B. The size of the wheal (and therefore the degree of sensitivity) is not an indication of the severity of symptoms for that patient.[3] Sufficient clinical information should be included on the request form so that the results of skin prick testing are able to be interpreted appropriately in relation to the patient's symptoms.[3]

In some patients, swelling, heat and itch may develop in the testing spots one to two hours after application of the allergens (rather than within the first 15–20 minutes). This is referred to as a late phase cutaneous reaction. Although these reactions are IgE dependent they do not appear to relate to the clinical situation for the patient and have no diagnostic value.[4]

Negative and positive controls

In addition to application of the suspected allergens, both a positive and negative control are also used.

The negative control is a saline solution, to which no response is expected. If a patient reacts to a negative control, then this will indicate that the skin is extremely

sensitive and that the results may be unreliable, e.g. patients with dermographism can develop wheals to all allergens as well as to the negative control.

The positive control solution contains histamine, to which everyone is expected to react (i.e. develop a small raised wheal with a red surrounding flare). Failure to react could mean that the patients may have taken medicines that are blocking the response to the histamine and allergens.

Selecting patients for skin prick testing

Skin prick testing may not be reliable for older adults. Skin reactivity (and the size of the wheal) increases with age until age 50–60 years when it begins to decline again.[1, 3] People with darker pigmented skin appear to develop larger wheals than people with paler skin.[1]

If skin prick testing is required for a child aged under two years, this should ideally be performed at a specialist allergy clinic, as it is more difficult to interpret the results in this age group (there is often a small wheal but a large erythematous flare).

Pregnant women should only have skin prick testing if detection of an allergy and subsequent treatment outweighs the risks – in rare cases, uterine contractions may occur as a result of a systemic reaction.[4]

Indications for skin prick testing

Patients who may benefit from skin prick testing include those with:[3, 5, 6]

- Significant asthma, eczema and allergic rhinitis – where avoidance of specific allergens or immunotherapy (desensitisation) may improve the condition
- When major allergen avoidance measures are being considered such as removal of carpets or the family pet or avoidance of specific foods from the diet
- Acute urticaria* and angioedema (often related to food allergy)
- Significant systemic symptoms following a bee or wasp sting (not localised reactions to stings) – especially if immunotherapy (desensitisation) is being considered

* Allergy testing is not usually helpful in the management of chronic urticaria as it is only rarely a manifestation of allergy.

Contraindications for skin prick testing

Skin prick testing is contraindicated in the following clinical situations:[2]

- Patients with a history of recent anaphylaxis. Skin prick testing should not be performed within four to six weeks of an anaphylactic episode because the results may be falsely negative.
- Skin prick testing should be used with caution in people with significant co-morbidities such as cardiovascular disease or arrhythmias and also in elderly people
- Patients with skin conditions such as dermographism, because the results may be falsely positive. Any skin condition, e.g. widespread atopic dermatitis, that affects the skin cell structure or requires topical medicines for treatment may also make interpretation of the results difficult.
- Patients taking medicines that may interfere with skin prick testing and that cannot be discontinued should not undergo skin prick testing (see over page for a list of these medicines)

Choosing appropriate allergens for skin prick testing

It is important that the allergens tested are relevant to both the patient's clinical condition and to their exposure. In general a small number of allergens (e.g. three to four) is required in a patient with a clear history of reactions to specific allergens (e.g. foods) and more allergens (up to 25) in a patient with rhinitis, eczema or asthma.[2, 3]

Considerations when interpreting skin prick testing results

Wheal size results can be affected leading to false positives and false negatives: A positive reaction from one test site may falsely affect the result of a neighbouring test site (this is why test sites need to be at least 2 cm apart). In addition irritant reactions can cause false positive skin prick test results.[3] Negative skin prick test results can occur even in the presence of true IgE-mediated allergy, due to inadequate representation of allergenic proteins in certain extracts,[5] or if the patient has taken antihistamines prior to testing.

Sensitivity does not equal allergy: Positive skin prick test results (sometimes even with large wheal size) can occur without any clinical response occurring on contact with

Medicines that can interfere with skin prick testing

Medicines that may interfere with skin prick testing include:[3, 5]

- Antihistamines (H1-blockers) – decrease the reactivity of the skin and should be stopped at least 72 hours prior to skin prick testing
- Topical corticosteroids – should not be used in the area of the testing site for two to three weeks prior because they have been shown to reduce skin reactivity. Oral or inhaled steroids do not appear to alter the reaction to skin prick testing and can be continued.
- Other medicines – such as tricyclic antidepressants, phenothiazines, benzodiazepines, quetiapine and mirtazapine may also reduce the reactivity of the skin. Skin prick testing should generally only be requested if these medicines are able to be discontinued temporarily.

Histamine receptor -2 blockers (e.g. ranitidine) work mainly in the stomach instead of the skin but have in the past been included among the medicines which should be avoided prior to skin prick testing. However, a recent report showed minimal interference with allergy testing in patients who were taking H2 blockers at the time of testing.[7]

that same allergen. The skin prick test result indicates only whether IgE to a specific allergen is present or not. Therefore a test may be technically positive, but if symptoms do not occur on exposure to that allergen, it is referred to as "clinically silent sensitisation", or a "clinical false positive" test result (however, this individual may still be classified as atopic).[5]

A negative skin prick test result to foods such as peanut has a negative predictive value of >95%, however, the positive predictive value is significantly lower, reaching only 60% in patients with a convincing history of an allergic reaction. A recent study from the United Kingdom reported a 22.4% prevalence of clinical peanut allergy among people with sensitivity demonstrated on testing.[8]

Skin prick testing may also be positive when a patient has a previous history of allergy that has since resolved, e.g. hay fever may remit in adults but pollen skin tests often remain positive throughout life.[5]

Lack of sensitivity does not mean that allergy can be ruled out: When the skin prick test result is equivocal or does not correlate with the history, a controlled challenge (by an allergy specialist) with the suspected allergen may be required (if clinically indicated and practical).[5]

Wheal size cannot predict the severity of an allergic reaction: Some patients with anaphylactic sensitivity to insect venom or latex, may have a wheal size as small as 3 mm while, in contrast, others may have wheals of 10 mm or greater to inhalant and other food allergens but show little or no allergic signs if they are exposed to these allergens. In addition, a positive skin prick test result does not predict the nature of the allergic symptoms.[5]

Wheal size has some correlation with likelihood of clinical response: Despite wheal size not automatically correlating with clinical response, wheal size does have some correlation with the likelihood that the patient is clinically reactive to that allergen, i.e. people with a larger wheal size are more likely to clinically react to that allergen upon challenge than those with a smaller wheal size.[5]

Advantages of skin prick testing include:

- The cost – skin prick testing is relatively inexpensive costing approximately $24 for a panel (compared to a cost of $40–$50 per single allergen tested for using serum allergen-specific IgE testing)[6, 9]

- Skin prick testing has a greater sensitivity (and consequently high negative predictive value) than serum allergen-specific IgE tests and is relatively specific
- The results are available quickly (results are known within 15–20 minutes)

Disadvantages of skin prick testing include:

- In rare cases, skin prick testing can trigger anaphylaxis. The risk is higher in younger children and in situations where a systemic reaction has occurred as a result of exposure to, for example, a food, latex or a stinging insect.[10]
- Not all allergens are available for skin testing
- Skin prick testing takes approximately 30 minutes or more to perform at a community laboratory.

Serum allergen-specific IgE testing

Serum allergen-specific IgE tests are used to detect the presence of allergen specific IgE antibodies produced in the serum when it is mixed with a series of allergens.

Serum allergen-specific IgE tests were formerly known as RAST tests (radioallergosorbent test), however, this test is now done by enzyme allergosorbent testing.

Indications for serum allergen-specific IgE tests

Serum allergen-specific IgE tests can be useful when skin prick testing is considered unsuitable, for example:[13]

- When the patient's skin is unsuitable for skin prick testing (e.g. in patients with widespread dermatitis or dermographism)
- When the patient is unable to discontinue a medicine such as an antihistamine (as this does not affect serum testing)
- In rural areas where skin prick testing may be unavailable
- When the suspected allergen is not available for skin prick testing (depending on the clinical need)
- If the history strongly suggests allergy to a specific allergen but skin prick testing is negative
- Where there are specific safety concerns due to past anaphylaxis (e.g. an anaphylactic reaction to nuts)
- For the prediction of allergy persistence or resolution of food allergies in children

Although serum allergen-specific IgE tests are less sensitive than skin prick tests, false positives are less common with serum testing, and so the positive predictive value is greater.[6]

Selecting allergens for serum IgE tests

Serum allergen-specific IgE tests should be requested for an individual allergen or allergen mix (where available). based on the patient's clinical history. They should not be used as general screening tests.[14] The cost for this form of testing is per allergen tested (approximately $40–$50) and therefore testing for multiple allergens incurs a significant cost (to the laboratory). Results of serum allergen-specific IgE tests can take one to two weeks.[9]

Availability of allergens for testing varies throughout the country. Contact your local community laboratory for specific information.

Cross reactivity

Some allergens are related, whereby a patient who is sensitive to one allergen also reacts to other similar allergens, even if they have never have been exposed them. This is known as cross-reactivity.[5]

Common related allergen groups include:[11, 12]

- Brazil nut, walnut, hazelnut, cashew, almond
- Apple, pear
- Kiwifruit, avocado, banana, latex
- Melon, watermelon, tomato

Oral allergy syndrome typically occurs in adults with allergic seasonal rhinitis (hay fever), especially those allergic to birch pollen.[1] It is characterised by allergic symptoms localised to the inside of the mouth after ingesting certain fruits, nuts or vegetables (usually only if raw). This is due to cross reactivity between pollen and pollen remnants found in these foods.

What are the **different types** of **allergy?**

The main types of allergy seen in primary care are:

- Food allergy
- Inhalant allergy
- Stinging insect (venom) allergy
- Medication allergy
- Allergic contact dermatitis

Food allergy

Food allergy is common in children. A United States based study estimated that 4% of children aged under 18 years have a food allergy.[15] Children with food allergy are two to four times more likely to have other related conditions such as asthma, eczema and hay fever (atopy).[15]

Food allergies can be either IgE mediated or non-IgE mediated.

Suspected IgE mediated food allergy – patients usually present with anaphylaxis or symptoms that occur within minutes to hours of ingesting food (Table 1), especially in young children. There may be a history of similar symptoms with prior ingestions of the food.

Suspected non-IgE mediated food allergy – usually in children diagnosed with conditions such as moderate to severe atopic dermatitis, eosinophilic oesophagitis, enterocolitis, enteropathy and food protein-induced allergic proctocolitis, and adults with eosinophilic oesophagitis.

What are the common food allergens?

Food allergens are components of food (typically proteins) that cause specific immunologic reactions (involving IgE), resulting in characteristic symptoms (Table 1). More than 170 foods have been reported to cause IgE-mediated reactions.[16] The seven most common are; cows' milk, egg, peanut, soy, wheat, fish and cashew and these allergens account for 90% of identified food allergies. Approximately 75% of allergies in young children are caused by cows' milk, egg and peanut.[17]

People with an allergy to a food may be able to tolerate the allergen in a different form. For example, some allergens (mostly from fruits and vegetables) cause allergic reactions only if eaten raw, because the cooking process denatures the allergen. Other allergens are heat stable, e.g. peanut and fish, so cooking does not denature or reduce the allergenicity.[11] As fruits and vegetables ripen, they generally become more allergenic.[11]

Table 1: Signs and symptoms of possible food allergy[16, 18]

IgE mediated (often acute, rapid onset)	Non IgE mediated (often delayed onset)
Skin	
Pruritus	Pruritus
Erythema	Erythema
Acute urticaria (localised or generalised)	Atopic eczema
Acute angioedema (most commonly in the lips and face and around the eyes)	
Gastrointestinal	
Angioedema of the lips, tongue and palate	Gastro-oesophageal reflux
Oral pruritus	Loose or frequent stools
Nausea/Vomiting/Diarrhoea	Blood or mucous in stools
Colicky abdominal pain	Abdominal pain/ infantile colic
	Food refusal or aversion
	Constipation
	Perianal redness
	Pallor and tiredness
	Failure to thrive (in association with other symptoms)
Respiratory system (usually in combination with the above signs and symptoms)	
Upper respiratory tract symptoms – nasal itching, sneezing, rhinorrhoea or congestion (with or without conjunctivitis)	Lower respiratory tract symptoms – cough, chest tightness, wheezing or shortness of breath
Lower respiratory tract symptoms – cough, chest tightness, wheezing or shortness of breath	
Other	
Signs or symptoms of anaphylaxis or other systemic allergic reactions e.g. tachycardia (occasionally bradycardia in anaphylaxis), hypotension, fainting, loss of consciousness	

N.B: this list is not exhaustive – the absence of these symptoms does not exclude food allergy.

Cows' milk protein allergy

Cows' milk protein allergy (CMPA) has a prevalence of approximately 2% in infants aged under two years, and can be IgE or non IgE mediated with a wide spectrum of presentations from immediate anaphylaxis to delayed effects such as atopic eczema.

CMPA is a cluster of syndromes including:

- Immediate allergic reaction, anaphylaxis and food protein-induced enterocolitis
- Gastrointestinal syndromes such as CMPA induced gastro-oesophageal reflux disease, constipation, enteropathy and allergic eosinophilic gastroenteritis
- Food protein-induced enterocolitis syndrome (FPIES)
- Eosinophilic oesophagitis

As many of these syndromes have overlapping symptoms, diagnosis can be difficult. However, eczema and a family history of atopy increase the risk of CMPA, while blood in stools accompanied by vomiting and diarrhoea is suggestive of FPIES. Complete elimination of cow's milk from the diet for two to three weeks and observing if symptoms resolve will usually confirm suspected cases. Allergy testing is not generally required.

For further information see: "Allergy to cows' milk protein and the appropriate use of infant formula" BPJ Special Edition (May, 2011).

Diagnosing a food allergy

Diagnosis of a food allergy requires:

- A history of allergic symptoms after ingesting a particular food (ask the patient or their caregiver to keep a diary of foods eaten and symptoms observed)
- A detailed medical history and physical examination
- Consideration of allergy testing (with skin prick testing or serum allergen-specific IgE tests) and a food elimination diet or food challenge (usually done in secondary care) to confirm a diagnosis or to help with management

Testing for food allergy in children

If food allergy is suspected in a child aged less than two years, referral to an allergy specialist should be the first option. A food elimination challenge is usually the preferred method for diagnosing an allergy in a young child. However, if coeliac disease is suspected, it is important not to suggest any elimination of gluten from the diet before investigative tests are done. Food elimination challenges should be performed in a controlled setting, as there is a risk of anaphylaxis on re-challenge.

Food allergy testing may be considered for children who have moderate to severe atopic dermatitis, thought to be related to a food, which has persisted despite optimised management and topical steroid treatment.[16]

Tolerance

Tolerance is a term used where a person has naturally outgrown the food allergy or they have received treatment and they now no longer develop clinical symptoms following ingestion of the food.

Most children with food allergy eventually will tolerate milk, egg, soy and wheat, however, fewer children will eventually tolerate tree nuts and peanut. Resolution of food allergy in children varies with the type of food and may not occur until the child is in their teenage years. A high initial level of IgE against a particular food is associated with a lower rate of resolution of clinical allergy over time.[16]

Food intolerance

The diagnosis of food allergy can sometime be difficult because non-allergic food reactions such as food intolerances can be often mistakenly classified as food allergies.

An example of food intolerance is lactose intolerance when a person is intolerant to cows' milk because of an inability to digest lactose. This inability to digest lactose can lead to abdominal pain and diarrhoea. However, lactose is not considered an allergen because the response is not immune based (i.e. IgE based).

In contrast to this would be a person who is allergic to cows' milk protein. In this scenario the cows'-milk protein is considered an allergen because it triggers an adverse immunologic reaction (i.e. it results in high levels of cow's-milk protein IgE).

Inhalant allergy

Seasonal allergic rhinitis (hay fever) is commonly encountered in general practice, especially over the spring and summer months when pollens from trees and grasses are prevalent. Usually patients with hay fever are managed well with symptomatic measures and pollen avoidance advice.

Perennial allergic rhinitis is when symptoms are encountered all year round, triggered by house dust mite, pets and mould (indoor allergens).

Indications for testing in patients with allergic rhinitis

Testing for possible underlying allergy is rarely indicated but may be considered in patients with significant rhinitis or asthma if it is likely to assist or change management.

If testing is indicated, skin prick testing is the preferred method. This may be considered if:

- The diagnosis is in doubt
- Identification of sensitivity to a particular allergen is desired
- Expensive avoidance measures or immunotherapy are being contemplated

For further information see: "Seasonal allergic rhinitis", BPJ 24 (Nov, 2009).

Stinging insect (venom) allergy

Most insect stings produce a transient local reaction that can last up to several days but resolves without treatment. Marked local swelling extending from the sting site is usually an IgE-mediated late-phase reaction.

It has been estimated that severe life threatening reactions to insect stings occur in only 0.4% to 0.8% of children and 3% of adults.[19] The risk of a systemic reaction in patients who experience large local reactions is approximately 5% to 10%.[19] Signs and symptoms of a systemic reaction are characterised by any combination of urticaria, angioedema, bronchospasm, oedema of the large airway, hypotension or other clinical manifestations of anaphylaxis.[19]

Patients who have a history of a systemic reaction to an insect sting should:[19]

- Carry emergency adrenaline for self-administration (and be instructed on its use)
- Carry medical identification for stinging insect hypersensitivity

For further information see: "The management of anaphylaxis in primary care", BPJ 18 (Dec, 2008).

Indications for testing in patients with a systemic reaction to insect stings

Patients who have had a systemic allergic reaction to a bee or wasp sting and are considering immunotherapy (desensitisation) need to have skin prick testing or serum allergen-specific IgE tests in order to ensure that appropriate immunotherapy is administered. Testing is not indicated for patients who have only had local reactions to stings, as immunotherapy is not indicated.

Allergy testing for bee and wasp stings may require intradermal tests, which are usually only available through some specialist laboratories and specialist allergy clinics.

Medicine allergy

Patients with allergies to medicines do not usually require allergy tests because:[4]

- Test results will not change management
- There are only a limited number of medicine allergens available for testing
- Skin prick tests to detect the presence of IgE antibody are available for penicillin and insulin, but are of limited accuracy (approximately 80%)
- Serum allergen-specific IgE tests for possible penicillin allergy presently lack sufficient sensitivity

Allergic contact dermatitis

Allergic contact dermatitis is a delayed inflammatory reaction that occurs more than 12 hours after contact with an allergen – known as a delayed hypersensitivity reaction. Perfumes, chemicals, plant resins and lipids are the most common causes of allergic contact dermatitis. Allergic contact dermatitis is more prevalent among people who are hairdressers, florists, nurses, printers, cleaners or mechanics.

The immunological skin reaction can be detected by patch testing, however, this is usually done in secondary care or specialist allergy clinics.

Differentiating allergic contact dermatitis from irritant dermatitis

Irritant dermatitis is caused by the direct exposure of the skin to an irritant agent without any immunological response involved. It is sometimes difficult to differentiate between irritant and allergic contact dermatitis as they can have very similar clinical features and histology (when skin biopsy is performed).

In irritant dermatitis, the edges of lesions are usually well demarcated, and do not extend beyond the site of contact. In allergic contact dermatitis, the affected area can often extend beyond the site of contact. Pruritus is not usually a feature of irritant dermatitis.

Latex allergy

It is estimated that 2.5% of the general population and 15% of healthcare workers have a latex allergy.[1]

Latex products contain two types of compounds that can cause allergic reactions:

- Chemical additives causing dermatitis
- Natural proteins that induce immediate allergic reactions (anaphylaxis in severe cases)

Latex is most commonly associated with medical products, e.g. disposable gloves, IV tubing, stethoscopes, catheters, dressings and bandages. Other latex products include; balloons, elastic bands, elasticsed garments, mattresses, condoms and diaphragms.

Testing for latex allergy using skin prick testing or serum allergen-specific IgE testing is necessary if the diagnosis is in doubt. Skin prick testing should be done in a controlled setting due to the possibility of anaphylaxis occurring.

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QUIZ FEEDBACK

Sodium and potassium imbalance

Introduction

This quiz feedback provides an opportunity to revisit Best Tests, September 2011 which looked at the primary care approach to investigating sodium and potassium imbalance. All general practitioners who responded to this quiz will receive personalised online feedback and CME points

1.	**In which of the following scenarios would immediate referral to secondary care for treatment of hyponatraemia be warranted?**	Your peers	Preferred
☐	Serum sodium 130 mmol/L, no specific symptoms	1%	
☐	Serum sodium 120 mmol/L, some neurological symptoms	98%	✓
☐	Serum sodium 135 mmol/L, deteriorating to 125 mmol/L the following day	82%	✓
☐	Any level of hyponatraemia in association with dehydration	15%	

Comment:
The majority of respondents correctly identified the indications for urgent referral to secondary care, which is recommended for patients with a serum sodium <120 mmol/L, if the levels are rapidly decreasing or if neurological symptoms are present.

Often patients with mild hyponatraemia are either asymptomatic or may have non-specific symptoms, e.g. nausea and lethargy. Patients with dehydration will often display signs and symptoms consistent with hypovolaemia, e.g. dizziness.

As a general rule, mild, asymptomatic hyponatraemia does not require corrective measures except for the treatment of the underlying factors. When a patient has symptoms, addressing the underlying cause will often help address both the symptoms and the hyponatraemia.

2.	**If a patient with hyponatraemia is hypervolaemic (i.e. has fluid overload), which of the following are possible causes?**	Your peers	Preferred
☐	Hypothyoidism	14%	
☐	Pancreatitis	4%	
☐	Congestive heart failure	99%	✓
☐	Liver cirrhosis	96%	✓

Comment:
The majority of respondents correctly identified that the possible causes of hyponatraemia in a hypervolaemic patient were liver cirrhosis and congestive heart failure. Other causes are renal failure and nephrotic syndrome.

Pancreatitis tends to be associated with hypovolaemia. Hypothyroidism is a possible cause of hyponatraemia but is not necessary associated with hypovolaemia.

3.	Which of the following medicines are reported to cause hyponatraemia?	Your peers	Preferred
☐	Bendrofluazide	98%	✓
☐	Citalopram	98%	✓
☐	Naproxen	89%	✓
☐	Nortriptyline	83%	✓

Comment:
All four medicines are reported to cause hyponatraemia. Diuretics cause hyponatraemia in approximately 20% of people who take them, and severe hyponatraemia is more commonly seen in thiazide rather than loop diuretics. SSRIs cause hyponatraemia in up to one-third of people who take them. Serum sodium levels should be checked before and several weeks after starting a SSRI in older patients and those taking other medicines associated with hyponatraemia. NSAIDs can cause hyponatraemia by promoting water retention (by increasing water permeability across the renal collecting ducts). Tricyclic antidepressants are one of a number of other medicines that are associated with hyponatraemia.

4.	Which of the following statements about hypernatraemia are true?	Your peers	Preferred
☐	A patient with serum sodium of 148 mmol/L should be referred to secondary care immediately for treatment	4%	
☐	A serum osmolality test should be ordered to investigate a high sodium level	10%	
☐	The signs and symptoms of hypernatraemia are primarily neurological	92%	✓
☐	Diabetes insipidus is a possible cause of hypernatraemia	92%	✓

Comment:
A patient should be referred to secondary care for treatment if their serum sodium is ≥ 155 mmol/L, if levels are rapidly rising, if neurological symptoms are present or the patient is systemically unwell, or if oral rehydration is not possible. The signs and symptoms of hypernatraemia are primarily neurological and can include lethargy, weakness and irritability. With more severe hypernatraemia or a rapid rise in sodium level, this can progress to twitching, seizures, coma and death.

The cause of hypernatraemia is usually derived from the clinical assessment and history. When associated with a net water loss, diabetes insipidus (either neurogenic or nephrogenic) can be a cause. Osmolality tests (serum or urine) are only rarely required to be requested in the primary care setting.

5.	Which of the following medicines are reported to cause hypernatraemia?	Your peers	Preferred
☐	Lithium	82%	✓
☐	Furosemide	84%	✓
☐	Prednisone	61%	✓
☐	Amoxicillin	1%	

Comment:
The majority of respondents correctly identified the medicines that can cause hypernatraemia, which include lithium, loop diuretics (e.g. furosemide) and corticosteroids (e.g. prednisone). The most common complication of chronic lithium therapy is nephrogenic diabetes insipidus (causing a net water loss). Medicines such as loop diuretics, mannitol, urea, corticosteroids and high protein supplements can also result in hypernatraemia (by causing hypotonic fluid losses). Amoxicillin is not known to be associated with hypernatraemia.

6.	In which of the following statements about the cardiac effects of hypokalaemia are true?	Your peers	Preferred
☐	Hypokalaemia is not associated with cardiac signs and symptoms	3%	
☐	ECG changes are not typically seen with hypokalaemia	4%	
☐	Cardiac symptoms do not become apparent unless serum potassium is < 2.5 mmol/L	12%	
☐	Mild hypokalaemia can cause life-threatening cardiac arrhythmias in people with underlying cardiac disease	94%	✓

Comment:
Hypokalaemia can be associated with hypotension, bradycardia or tachycardia, premature atrial or ventricular beats, ventricular arrhythmias and cardiac arrest. Characteristic progressive ECG changes can be seen as the serum potassium level drops but there is no cut-off level at which they become apparent. However, it is recommended that an ECG be performed in patients with a serum potassium < 3.0 mmol/L.

Mild hypokalaemia is often well tolerated in otherwise healthy people, however, in people with co-morbidities, particularly those with hypertension, underlying heart disease or liver cirrhosis, it is associated with an increased incidence of life-threatening cardiac arrhythmias, sudden death, and rarely hepatic coma.

7.	Which of the following clinical scenarios is a potential cause of hypokalaemia?	Your peers	Preferred
☐	Acute gastroenteritis	98%	✓
☐	Test-tube haemolysis (of the blood sample)	3%	
☐	Use of a diuretic for one week	78%	✓
☐	Inadequate potassium in the diet	84%	✓

Comment:
Hypokalaemia can be caused by increased losses from the gastrointestinal tract such as acute gastroenteritis, and by increased urinary potassium excretion with the use of medicines such as diuretics. Diuretic induced hypokalaemia usually occurs within the first two weeks of treatment.

Reduced dietary intake of potassium is a rare cause of hypokalaemia, but may be an important factor in patients concurrently taking diuretics, e.g. an elderly patient on a "tea and toast" diet, or in a person aiming to achieve rapid weight loss on a diet of low calorie liquid protein drinks.

Test–tube haemolysis tends to be associated with pseudohyperkalaemia, not hypokalaemia.

8.	If no obvious cause is found for hypokalaemia, which of the following blood or urine tests may be appropriate?		
		Your peers	Preferred
☐	Serum magnesium	93%	✓
☐	Urine magnesium	3%	
☐	Serum bicarbonate	95%	✓
☐	CRP and ESR	1%	

Comment:
If no obvious cause for the hypokalaemia can be found, additional blood and urine tests may be useful. Measuring urinary potassium excretion (although rarely done in general practice) and serum magnesium concentrations (to investigate for hypomagnesaemia) can be appropriate. Serum bicarbonate levels may help determine if an acid-base disorder is present e.g. metabolic alkalosis. Unexplained hypokalaemia is not an indication to request both CRP and ESR together.

9.	Which of the following statements about hyperkalaemia are true?		
		Your peers	Preferred
☐	Urgent referral to secondary care is required for an asymptomatic patient with serum potassium 6.0 mmol/L	5%	
☐	Pseudohyperkalaemia, caused by sampling or analysis error, is a common cause of a high serum potassium result	96%	✓
☐	An ECG is recommended for patients with serum potassium > 6.0 mmol/L	98%	✓
☐	Medicines are rarely the cause of a raised serum potassium level	2%	

Comment:
Urgent referral to secondary care is recommended for patients with serum potassium ≥ 7.0 mmol/L or potassium ≥ 5.5mmol/L with any ECG changes or symptoms.

Pseudohyperkalaemia is a common reason for an isolated raised potassium level. It is advisable to contact the laboratory for any level of potassium > 6.0 mmol/L, especially if unexpected, to discuss potential reasons such as haemolysis that may explain the raised level.

An ECG is recommended for patients with serum potassium levels > 6.0 mmol/L. ECG changes are not usually seen below this level in hyperkalaemia. A raised serum potassium level is most commonly caused as an adverse effect of a medicine or secondary to a disease process.

10.	Which of the following ECG changes may be seen with hyperkalaemia?		
		Your peers	Preferred
☐	Peaked T waves	98%	✓
☐	Absence of P waves	91%	✓
☐	U waves	6%	
☐	Sine waves	85%	✓

Comment:
ECG changes that can be seen with hyperkalaemia include: progressive abnormalities including peaked T waves, flattening or absence of P waves, widening of QRS complexes and sine waves (which can indicate that arrest is imminent).

U waves are one of the characteristic ECG changes seen with hypokalaemia.

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