



# The Sri Lanka Prescriber



September 2014; Volume 22, No. 3



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# The Sri Lanka Prescriber

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Price per copy Rs 50.00 (students Rs 25.00). Personal callers may also obtain copies from the Departments of Pharmacology at the Medical Faculties in Colombo, Galle and Sri Jayewardenepura.

## Published by

Department of Pharmacology

Faculty of Medicine

271, Kynsey Road, Colombo 8, Sri Lanka.

Telephone: + 94 11 2695300 Ext 315

E-mail: phrm\_cmb@hotmail.com

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E-mail: prmanager@spc.lk Web site: www.spc.lk

## Printed by

Ananda Press

82/5, Sir Ratnajothis Saravanamuttu Mawatha,

Colombo 13.

Telephone: + 94 11 2435975

E-mail: anpress@sltnet.lk

## Cover picture

### EUROPEAN AND AMERICAN PHARMACY MEET (1867)

When the Second International Congress of Pharmacy met in Paris, William Procter, Jr., presented a forceful declaration of the free, democratic, American way of Pharmacy, quite different from Old World ways.

One of a series: *A History of Pharmacy in Pictures*, presented by Parke, Davis & Company

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# Allergen immunotherapy

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## Summary

Allergen immunotherapy reduces the symptoms of allergic disease by inducing tolerance to specific allergens. It can be given sublingually or by subcutaneous injection.

Immunotherapy is the only form of treatment which modifies abnormal immune reactivity to a specific allergen, rather than simply suppressing symptoms. It may alter the natural history of atopic disease.

Allergen immunotherapy is effective for respiratory allergy (rhinitis and asthma) and venom allergy such as bee stings. Currently immunotherapy has no role in the routine management of food allergy, but research is ongoing.

**Key words:** allergic rhinitis, anaphylaxis, asthma, venom

*(Aust Prescr 2013; 37: 87-9)*

## Introduction

Allergen immunotherapy was first reported in the successful treatment of pollen-induced allergic rhinitis in 1911. It reduces the patient's abnormal immune-reactivity to harmless environmental antigens (allergens). The repeated administration of the allergen induces tolerance. A reduction of allergen induced symptoms should occur within months. After a 3-5 year maintenance period, this benefit should be long-lasting if not permanent.

For most of its history immunotherapy has been given by subcutaneous injection. As injecting an allergen has the potential to cause anaphylaxis, there is an initial cautious 'updosing' phase followed by a prolonged maintenance phase with regular injections. Recently, sublingual administration of allergen has been found to be effective in allergic respiratory disease.

There is evidence from meta-analyses for the efficacy of subcutaneous and sublingual immunotherapy in the management of allergic rhinitis and

asthma.<sup>1-3</sup> Subcutaneous immunotherapy is also effective for venom allergy.<sup>4</sup> The relative efficacy of sublingual and subcutaneous immunotherapy in respiratory allergy remains unclear.

## Mechanism of action

Several mechanisms are proposed to contribute to the effect of allergen immunotherapy. They include the induction of IgG 'blocking' antibodies (which inhibit binding of allergen to IgE), T cell anergy, switching of T-helper 2 (allergic phenotype) cells to T-helper 1, and the induction of regulatory T cells which suppress the immune response. However, even in clinically successful immunotherapy, allergen-specific IgE is still present and allergy tests usually remain positive.

## Management of allergic diseases

Management of allergen-induced respiratory symptoms starts with the identification of relevant allergens and avoiding them where possible. Oral or topical antihistamines and intranasal corticosteroids can be effective regardless of the specific allergic cause. Immunotherapy is indicated when the patient's symptoms are moderate to severe, symptoms interfere with function or quality of life, avoidance of the allergen is difficult or impossible, and other treatments are unsatisfactory.

It is important to ensure that the allergens used for immunotherapy are the ones that are causing the patient's symptoms. This is established by a history of symptom patterns matching allergen exposure and confirmed by skin prick tests or serum allergen specific IgE tests.

Immunotherapy for asthma is problematic because asthma is usually multi-factorial. Moderate to severe asthma is also a risk factor for adverse reactions to immunotherapy. However, there is evidence that subcutaneous immunotherapy improves bronchial hyper-reactivity and reduces symptoms and medicine use for asthma.<sup>3</sup>

In patients who have had anaphylaxis from an insect sting, immunotherapy is highly effective in reducing

the risk of reactions to subsequent stings. In Australia, anaphylaxis most commonly occurs from bee stings, but can also be caused by stings from native and imported wasps and Jack-Jumper ants.

### Allergens for immunotherapy

Allergens are manufactured for both diagnosis and immunotherapy. They are purified protein extracts from allergenic substances. Diagnostic extracts should be from a single species only and contain all relevant allergenic proteins. However, allergen extracts are poorly defined pharmacologically and biochemically and poorly standardised. Extracts from different manufacturers vary considerably and this could influence the effectiveness of diagnosis and treatment. Recombinant allergenic proteins are starting to be used in diagnosis, but not yet for therapy.

Common allergen classes in respiratory disease are pollens (grass, weed and tree), dust mites, moulds and animal danders. Pollens tend to cause seasonal rhinitis although seasonal patterns vary with pollen type and region. Other allergens may cause perennial rhinitis, depending on exposure patterns. Allergens from each of these groups are available for immunotherapy.

The allergens used for immunotherapy may be single extracts from an individual species or mixtures of different allergen species. Mixtures of different allergen classes may not be compatible.<sup>5</sup> The patient's sensitisation pattern and major exposures guide the selection of allergens. Many patients are sensitised to multiple allergens either within one of the main classes (for example pollens) or from several classes. This may be due to cross-reactive allergy or due to separate independent sensitisations. It is unclear whether all relevant allergens need to be included in the mixture for optimal results (some mixtures contain

potentially suboptimal amounts of each allergen) or whether a small number of key or dominant allergens will suffice.

### Treatment

Allergen immunotherapy is usually prescribed by physicians or paediatricians who have received subspecialty training in clinical immunology and allergy. This is to ensure optimal patient and allergen selection and to manage the risks of immunotherapy. Usually therapy begins with weekly injections in an outpatient or clinic setting. Venom immunotherapy may be introduced with a rapid-updosing 'rush' protocol over 2-5 days. This is done in a hospital day-patient setting because of the increased risk of reactions. Most injections can be given by specialists or GPs. Free e-training in immunotherapy is available from the Australasian Society of Clinical Immunology and Allergy.<sup>6</sup> Practitioners need the skill and equipment to be able to manage anaphylaxis (see Australian Prescriber wallchart<sup>7</sup>).

### Subcutaneous immunotherapy

There are two main ranges of injectable immunotherapy products in Australia:

- an aluminium hydroxide conjugated formula which may be ordered in standard preparations or in individual mixtures.
- an aqueous formulation usually prepared by the allergy specialist.

Some allergens are registered therapeutic goods whereas conjugated allergen mixes are available on a named-patient basis. Only certain venom allergens are available on the Pharmaceutical Benefits Scheme. These are for bee, European (*Vespula*) and paper wasp (*Polistes*). Jack-Jumper ant venom immunotherapy is available in some centres (Royal Adelaide



Paper wasp



European Wasp



Honeybee



Jack-Jumper ant

Hospital and Royal Hobart Hospital) at the patient's expense.

Subcutaneous immunotherapy is usually effective for symptom reduction. The responses may be partial rather than total, so it should not be assumed that other treatments and avoidance strategies will no longer be needed. In addition, there is a subgroup of patients who do not improve with immunotherapy. This may be because a suboptimal allergen was used or the symptoms were actually caused by non-allergic disease (for example, chronic rhinosinusitis). Sometimes immunotherapy fails for unknown reasons.

### ***Injection technique***

Injections of allergen are administered subcutaneously, usually in the posterior part of the upper arm, using a fine gauge needle (26/27G) and 1 mL syringe (insulin syringes are ideal). A complete detailed guide to the administration of subcutaneous immunotherapy injections is available at [www.allergy.org.au/healthprofessionals/papers/scit-treatment-plan](http://www.allergy.org.au/healthprofessionals/papers/scit-treatment-plan).

### ***Adverse effects***

Subcutaneous immunotherapy carries risks which include immediate reactions such as anaphylaxis, and delayed reactions such as local swelling and more rarely, exacerbations of asthma or atopic eczema. The risk of immediate reactions can be reduced by premedication with antihistamines, but medical observation for 30-45 minutes after each injection is mandatory, including during the maintenance phase of treatment even if the injections have previously been well tolerated.

### **Sublingual immunotherapy**

Alternative routes of delivery for immunotherapy have been sought to improve safety and ease of use while retaining effectiveness. Sublingual immunotherapy emerged in the mainstream literature in the 1990s. There is now evidence<sup>2</sup> for the efficacy of sublingually administered allergens in respiratory allergy. Higher doses of allergen are required compared with subcutaneous immunotherapy. The allergen is absorbed through the oral mucosa and studies have shown systemic immunological changes similar to those of subcutaneous immunotherapy. The majority of evidence relates to single allergens or oligo-allergen mixtures, mainly pollen and mite, in allergic rhinitis, but evidence also exists for efficacy in asthma.

Sublingual immunotherapy is available in tablets or in drop form (pump bottles or plastic ampoules). Liquid drops for sublingual immunotherapy are available to order on a named-patient basis as single allergens or allergen mixtures. The only sublingual immunotherapy tablet currently registered is a fixed composition mixture of five pollens from the rye grass family. Sublingual immunotherapy is convenient and can be administered at home. Various protocols are currently suggested, although the default is daily treatment for three years (the same total term as subcutaneous immunotherapy). Alternate daily schedules and pre/co-seasonal-only schedules are also used. While the acceptability of sublingual immunotherapy is high, adherence to the full long-term program is poor.<sup>8</sup>

### ***Adverse effects***

Sublingual immunotherapy has a substantial safety advantage over subcutaneous injections. It has mostly transient local adverse effects with very few reports of systemic reactions.<sup>9</sup>

### **Future developments**

An important finding in both subcutaneous and sublingual immunotherapy is the potential for altering the natural history of atopy. There is evidence for a reduction in the new onset of asthma<sup>10</sup> in those treated for allergic rhinitis and also a reduction in the incidence of new allergic sensitisations.<sup>11</sup> These findings are intriguing and promising, but require further replication. If confirmed, they suggest that immunotherapy may reduce the overall burden of allergic disease and should be used earlier in allergic respiratory disease, not just when other treatments have failed.

Recombinant allergens or modified (peptide) allergens may provide advantages and are currently in development. Peptides and modified proteins may be constructed in such a way as to avoid IgE-binding. This reduces the risk of anaphylaxis while retaining the T cell epitopes which induce regulatory T cells to suppress allergy.

Immunotherapy for food allergy is not routinely practised and hitherto was considered too risky. However, there has been a great deal of recent investigation into inducing specific oral tolerance for egg, milk and nut allergy. This involves gradual introduction of the allergenic food under carefully controlled conditions. It is still considered a research

only procedure. Concerns remain regarding the considerable risk of acute allergic reactions, the induction of eosinophilic enteritis, and whether permanent tolerance (as opposed to temporary desensitisation) can be achieved.

## Conclusion

Allergen immunotherapy is an important modality in the management of respiratory allergic disease and venom allergy. Immunotherapy for respiratory allergic disease has been expanded from the traditional injection method to include sublingual administration which has near-equivalent efficacy

**Conflict of interest:** *William Smith has attended an interstate presentation sponsored by Stallergenes, and while at a conference in London, attended a sponsored visit to the Stallergenes factory in Paris. Stallergenes are manufacturers of allergen immunotherapy products.*

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# Management of allergic asthma

## Introduction

Allergic asthma is the most common form of asthma. About 90% of children with asthma have allergies, compared with about 50% of adults with asthma. Many of the symptoms of allergic and non-allergic asthma are the same (Table 1). However, allergic asthma is triggered by inhaling allergens (Table 2).

**Table 1. Features of asthma**

<ul style="list-style-type: none"> <li>• Cough</li> <li>• Wheeze</li> <li>• Shortness of breath</li> <li>• Increased respiratory rate</li> <li>• Chest tightness</li> </ul>
---

**Table 2. Common causes of allergic asthma**

Allergens, small enough to be breathed deep into the lungs, include:

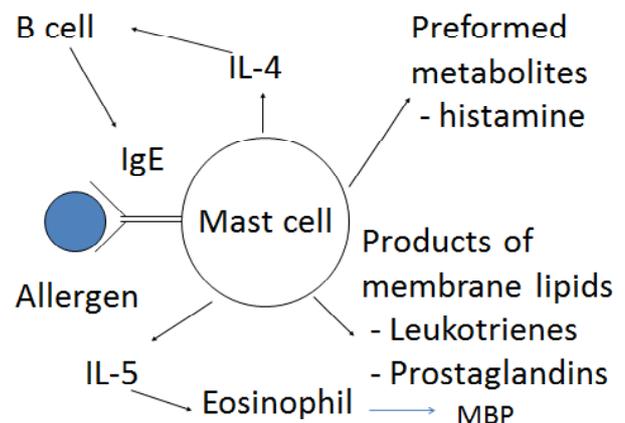
- Windblown pollen from trees, grasses, and weeds
- Mold spores and fragments
- Animal dander (from hair, skin, or feathers) and saliva
- Dust mite feces
- Cockroach feces

Irritants may trigger an asthma attack, even though they do not cause an allergic reaction. These include:

- Smoke from tobacco, a fireplace, candles, incense, or fireworks
- Air pollution
- Cold air
- Exercise in cold air
- Strong chemical odours or fumes

- Perfumes, air fresheners, or other scented products
- House dust

## Immunology of allergic asthma



**Figure 1. Mediators of asthma**

Type I hypersensitivity results in a pathological process leading to lower airway obstruction (Figure 1). Histamine is immediately released by mast cells on exposure to an allergen. Repeated exposure results in inflammation of the lower airway through the action of mediators released from mast cells (Eg; Interleukotriene 1), eosinophils (Eg; Major basic proteins[MBP]) and Th2 cells (IL-4 and IL-5). IL-4 acts on B cells and produce IgE by inducing class switching and IL-5 attracts eosinophils to the site of inflammation. The recognition and avoidance of the allergens that trigger symptoms is the most important step in the management.

Methods of determining the allergens include;

- History of exacerbation of symptoms on exposure to the trigger/allergen
- Skin prick test – pricking the skin with the allergen and measuring the size of the wheal 15 minutes later
- Measurement of specific IgE or sIgE test

## Treatment options for allergic asthma

The British Thoracic Society guidelines for the management of allergic asthma are shown in Table 3.

**Table 3. British Thoracic Society guidelines**

Inhaled SABA	ICS	ICS/LABA	ICS/LABA	ICS/LABA
As required	400µg	ICS to 800µg	+LTRA +Theophylline	+LTRA +Theophylline +Oral Steroids +Others
Step.1	Step.2	Step.3	Step.4	Step.5

\* ICS = inhaled corticosteroids. LABA = Long acting beta agonists. LTRA= Leukotriene receptor antagonist

### Short acting $\beta$ -agonists (SABAs)

These are usually the first medication to be used for an acute attack of asthma. Everyone who has asthma should have a short-acting bronchodilator. The two short acting beta-agonists (SABAs) are salbutamol and terbutaline. There is little difference in the approach to SABAs and there is general agreement that this is a class of medication that needs to be used on a need oriented basis alone. Step one of the two guidelines makes it clear that the SABA is used specifically in step 1 as monotherapy, and thereafter in all other stages as add-on therapy to the existing level of treatment on a need oriented basis. The indiscriminate use of SABAs has become a major hurdle in asthma control as patients who are started on SABAs continue to use them for their rapid onset of action, drop the preventer medication, with a disastrous impact on asthma control. The necessity to communicate this to patients is vital as it could seriously disturb long term asthma control. It is necessary also to educate patients regarding SABA related side-effects such as tremor, tachycardia and cardiac rhythm disturbances. SABAs should never be prescribed as monotherapy, but only on a need oriented basis.

### Inhaled corticosteroids (ICS)

- If the rescue inhalers are too often used, that is a sign that asthma is not under control. It is an

indication to take medications such as inhaled steroids every day.

- ICSs work by curbing inflammation in the airways.

The inhaled corticosteroids (Table 5) form the foundation of asthma therapy, and their introduction has revolutionised the approach to asthma control. The use of ICS begins with step 2 in the BTS, opting for a starting dose of 400µg beclomethasone equivalent. Combination of ICS and long-acting  $\beta$ 2 agonist (LABA) results in faster asthma control. LTRAs are usually added if there is an element of rhinitis and background atopy in association with asthma. This could achieve better control of both rhinitis and asthma, and appears to have been well established in clinical practice. However, not all patients will respond to LTRAs, and serious consideration should be given to withdrawing the LTRA if there is no substantial clinical benefit after 12 weeks.

The guidelines do not talk about individual inhaled corticosteroids (ICS). Beclomethasone is the oldest ICS in use and is still a very useful drug. The problem is that it is extremely short-acting and needs to be used three to four times a day. Fluticasone is a good topical anti-inflammatory agent and is probably best suited for once daily use. Budesonide is also a useful ICS, preferably used twice daily. The concept of single inhaler therapy for both prevention and rescue is a simple and practical way of achieving asthma control and this will be dealt with on the section of LABAs. The side-effects of inhaled steroids are emphasized in the BTS guidelines, where side-effects such as hypertension, diabetes, osteoporosis and linear growth in children need to be monitored on a regular basis. The evidence for the side-effects of low dose of inhaled steroids is scanty, and it can be safely assumed in clinical practice that doses below 800µg beclomethasone equivalent are safe. It is now well established that long term ICS use not only gives better control, but also reduces asthma mortality.

### Long acting $\beta$ -agonists (LABAs)

LABAs work as rescue inhalers, but the effects last longer, usually about 12 hours. Hence they are used regularly, twice a day. These should only be used along with inhaled steroids, never as the only medication to control asthma.

**Table 5. Inhaled corticosteroids**

- 
- Fluticasone
  - Budesonide
  - Mometasone
  - Beclomethasone
- 

LABAs are a major advance in rapid asthma control, and they will continue to play this pivotal role in the future. Safety of ICS-LABA combinations has been well established and will probably form the cornerstone of asthma therapy. The use of ICS-LABA combination inhalation especially after an exacerbation has been a subject of much research. The ICS-LABA combinations have made asthma control goals easier to achieve. A combination of mometasone and the once daily LABA indacaterol, if approved for asthma, could herald a new era of once daily therapy and greatly improve compliance. The expectation of once daily medication for long term asthma control appears to be within striking distance at present.

### **Leukotriene receptor antagonists (LTRA)**

Leukotriene receptor blockers zafirlukast and montelukast, have opened up a new approach to a segment of the asthmatic population. The use of montelukast has found acceptance and efficacy in patients with concomitant allergic rhinitis and asthma, and has also become popular and effective medication among paediatric patients. The safety of LTRAs has been established. LTRAs are recommended at step 3 in the BTS guidelines as additions to the ICS-LABA combination. The side-effects of LTRAs are seldom seen in clinical practice. There is, however, a clear set of non-responders and it would be pertinent to identify these patients and withdraw the drug early. The use of LTRA as monotherapy in established asthma is not recommended.

### **Theophylline**

Theophylline is a weak bronchodilator. Theophylline is recommended at step 3 in the BTS guideline. Intravenous theophylline is no longer recommended routinely as it has a very narrow therapeutic spectrum, and the toxic range produces a variety of adverse effects such as restlessness, irritation and tachyarrhythmias. Theophylline is cheap, reasonably effective, and has been around for a very long time.

### **Oral steroids**

Oral glucocorticoids continue to be the mainstay of severe exacerbations and are placed at step 5 in the BTS guidelines. The most commonly used oral steroid is oral prednisolone, which is usually started at 5 to 10 mg daily and stepped up gradually. Steroids related side-effects such as muscle cramps, osteoporosis and cushingoid features are seen mainly in patients who abuse steroids by using them long term without medical supervision. Steroids are the most effective anti-inflammatory therapy available for asthma. It is essential to weigh the benefits and side-effects of oral steroids when prescribing them. The advent of methylprednisolone and deflazocort have probably made a marginal change in regard to steroid-related side-effects. Side-effects of steroids are minimised by using the smallest effective dose for the shortest possible period.

### **Anti-IgE**

The advent of the Anti-IgE monoclonal antibody (omalizumab) has provided a different approach for the management of asthma. This therapy has so far shown moderate results in step 5, and may be of particular use in reducing the requirement of oral steroids. The dose of this drug is based on the level of IgE and has a clear regimen that needs to be followed, taking into consideration the IgE level and the weight of the patient. The real problem with this therapy is its cost-benefit ratio. With the high cost of omalizumab this becomes a major consideration.

### **Immunotherapy**

Immunotherapy helps treating asthma by gradually reducing the immune system response to certain allergy triggers. Immunotherapy involves getting regular injections of the allergens that trigger symptoms. The immune system builds up a tolerance to the allergens over time, resulting in reduction of the allergic reactions. This treatment generally requires regular injections over a period of three to five years under supervision.

### **Co-morbidities of asthma**

Asthma is often associated with co-morbidities, mainly gastro-oesophageal reflux disease and allergic rhinitis. ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines highlight the importance of managing rhinitis with adequate doses of nasal steroids for better control of asthma. Diseases such

as obesity, depression, some cardiovascular diseases and obstructive sleep apnoea may affect the clinical intensity and severity of asthma.

## Conclusions

Management of allergic asthma needs a holistic approach taking triggers and co-morbidities into consideration. Anti-inflammatory drugs in the form of inhaled steroids in adequate doses, when administered early, prevent airway remodelling and progression to chronic asthma, while reliever medications decrease morbidity.

## Further reading

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Email <weerasingheanura@gmail.com>. *I have no conflicts of interest regarding this article.*

## Notices of Meetings

1. **Ninth World Congress of the International Society of Physical and Rehabilitation Medicine (ISPRM), Berlin, Germany 19-23 June 2015**  
Information: [www.isprm2015.org/weitere-navigation/contact/](http://www.isprm2015.org/weitere-navigation/contact/)
2. **The Fifth International Conference on Clinical and Experimental Dermatology, New Orleans, USA 13-15 July 2015**  
Information: <http://dermatology.conferenceseries.com/>
3. **Third International Conference on Epidemiology and Emerging Diseases, Valencia, Spain 4-6 August 2015**  
Information: <http://conferenceseries.com/epidemiology-emerging-diseases-virus-bacteria-infections.php>
4. **World Congress on Infectious Diseases (Infectious diseases - 2015), London, United Kingdom 10-12 August 2015**  
Information: <http://conferenceseries.com/infectious-diseases-skin-infection-ebola-viral-infection.php>
5. **Fourteenth Congress of the Asian Society of Transplantation, Singapore 23-26 August 2015**  
Information: [www.cast2015singapore.org/](http://www.cast2015singapore.org/)
6. **The Seventeenth Asia-Pacific League of Associations for Rheumatology Congress, Chennai, Tamil Nadu, India 6-9 September 2015**  
Information: V. Krishnamurthy, APLAR 2015 Organising Committee, 17th APLAR Congress Secretariat, PICO Creative Centre, 20 Kallang Avenue, Singapore 339411; [www.aplar2015.com](http://www.aplar2015.com)
7. **Fourth World Congress of Clinical Safety, Vienna, Austria 28-30 September 2015**  
Information: <http://www.iarimm.org/4WCCS/>
8. **WAME International Conference for Medical Journal Editors 2015, New Delhi, India 2-4 October 2015**  
Information: *The National Medical Journal of India*, All India Institute of Medical Sciences. New Delhi 110029; [india.editors@gmail.com](mailto:india.editors@gmail.com), [www.meeting.2015wame.org](http://www.meeting.2015wame.org)
9. **International Congress on Trauma and Prehospital Care, Dubai, United Arab Emirates 5-7 October 2015**  
Information: <http://emergencymedicine.globol-summit.com/>
10. **Indo Global Diabetes Summit and Medicare Expo, Bengaluru, Karnataka, India 19-21 October 2015**  
Information: <http://diabetesexpo.com/india/organizing-committee.php>

## Self-assessment questions

Select the **best** response in each question

### Question 1

A 62-year old woman was admitted to the ETU of a General Hospital with a history of tremor and ataxic gait for 2 weeks. She was on a high dose of beclometasone DPI and salbutamol DPI via inhaler for chronic asthma, lithium carbonate for manic depressive disorder, losartan potassium and atorvastatin. A medical officer had recently prescribed furosemide 80 mg mane daily for mild bilateral pedal oedema. In the ETU the initial findings were BP 160/95 mm Hg, and a 12-lead ECG showing sinus rhythm with left ventricular hypertrophy. Her gait was ataxic, and she had finger tremor and nystagmus. The laboratory data were:

Glucose 5.4 mmol/l	(4.5 - 5.5)	PaO <sub>2</sub> 10.4 kPa	(10.6 - 13.3)
Urea 6.9 mmol/l	(2.5 - 6.5)	PaCO <sub>2</sub> 4.6 kPa	(4.8 - 6.1)
Creatinine 130 µmol/l	(80 - 120)	[H <sup>+</sup> ] 34 nmol/l	(35 - 45)
Na <sup>+</sup> 128 mmol/l	(135 - 145)	Bicarbonate 23 mmol/l	(22 - 26)
K <sup>+</sup> 4.9 mmol/l	(3.5 - 5.0)	ALT 35 U/l	(< 40)

The most likely reason for her presenting complaints is

- (A) anxiety
- (B) salbutamol overdose
- (C) hyponatraemia
- (D) cerebellar ataxia
- (E) lithium toxicity

### Question 2

A 50-year old bank executive with no relevant medical history consulted a specialist physician because he felt occasional palpitations or a “thump” in his praecordium during his morning walks, but no chest pain. The last occasion he had this sensation was ten weeks ago. He was not taking any prescription drugs, and had never smoked.

His blood pressure was 140/82 mmHg, and the pulse rate was 68 b.p.m. The rest of his cardiovascular system and physical examination was clinically normal. A 12-lead ECG showed sinus rhythm with occasional unifocal ventricular ectopics. A 24-hour Holter recording showed sinus rhythm and normal pulse rate, with normal QRS complexes, normal PQ intervals and a normal QTc. However, there were 692 isolated unifocal ectopic beats.

The best therapy for this man is

- (A) atenolol
- (B) verapamil
- (C) amiodarone
- (D) disopyramide
- (E) no medication, only appropriate advice

### Question 3

A 48-year old man taking enalapril and atorvastatin on prescription had epigastric pain and vomiting during a bout of drinking arrack with friends. The vomitus became tinged with blood. On admission to a General Hospital ETU at 11.30 pm he was confused, his blood pressure was 145/90 mmHg, the pulse rate was 105 b.p.m,

and the general examination of the systems was normal. Initial tests showed a normal 12-lead ECG with sinus tachycardia, and normal urea, glucose, haemoglobin and troponin. The ALT was 70, AST 63 and gamma-GT 88. He had no icterus, pedal oedema, or parotid enlargement. What is the most likely diagnosis?

- (A) duodenal ulcer
- (B) Mallory Weiss tear
- (C) bleeding from oesophageal varices
- (D) alcoholic hepatitis
- (E) raised prothrombin time

### Answers to self-assessment questions

- Question 1. **(E).** The clinical features are those of lithium toxicity, probably precipitated by inappropriate furosemide. Anxiety and salbutamol do not cause ataxia or nystagmus, and adult onset cerebellar ataxia is unlikely in view of the short history and timing of furosemide.
- Question 2. **(E).** No medication is indicated for occasional unifocal ventricular ectopic beats in an otherwise healthy person.
- Question 3. **(B).** The history physical examination and laboratory data do not support a diagnosis of either oesophageal varices or alcoholic hepatitis. The raised ALT and AST are likely to be the result of regular alcohol ingestion in a patient taking atorvastatin.

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