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Cover: *The merry mast cell*

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Printed by Tandym Print
Repro by C2 Digital

ISSN 1609-3607

Sponsorship & Support

Current Allergy & Clinical Immunology is the official journal of the Allergy Society of South Africa and is produced as a service for health care workers to improve understanding and communication in the field of allergy. Publication of the journal is made possible by the generous financial and other support offered by the following pharmaceutical and diagnostic companies.

The Allergy Society of South Africa gratefully acknowledges support from these companies:

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GUEST EDITORIAL
ANAPHYLAXIS

It has been my pleasure to edit this, the last edition of the journal for 2008. To all the contributing authors, thank you for your time and expertise.

We discuss anaphylaxis in this edition, which is a condition that often causes anxiety for the health care worker.

The algorithm from the Resuscitation Council (p. 171) gives a practical and simple approach to the treatment of severe anaphylaxis. This can be displayed in all emergency units as well as immunotherapy clinics or any facility undertaking skin testing, where there may be a risk for anaphylaxis.

Dr Sharon Kling has written a fascinating report on anaphylaxis in a paediatric ICU. We leave you to make up your mind whether or not you agree that this was indeed anaphylaxis. If you think it was, it would be the youngest case described in the literature. Mail her and let us know what you think.

Dr Chris Oettle gives us insight into the difficult decisions facing an anaesthetist wishing to prevent anaphylaxis. Her patient, a 4-year-old child with cutaneous mastocytosis, was scheduled for surgery. How does one proceed with elective surgery, in a patient who has an increased risk of mast-cell degranulation? This article may be read in conjunction with Dr Stephanie Fischer's article[1] published in *Current Allergy & Clinical Immunology* last year.

Thank you to Dr Shaunagh Emanuel for the superb cartoons in the story about Angelina. Enjoy the whimsical presentation of this extremely complicated patient. I am happy to report that the patient recovered well from her hysterectomy, and received only IV and oral paracetamol as analgesia. She is back at the convent, where she works as a social worker. She is currently well on her awfully dull diet.

Dr Dave Knight and Prof Mohamed Jeebay have written an excellent account on work-related anaphylaxis, and have outlined the difficulties one has in making this diagnosis. Fortunately criteria exist now to make a clinical diagnosis of anaphylaxis, but there is still no universal definition of work-related anaphylaxis. When discussing the confirmation of the diagnosis, they mention serum total tryptase. I would like to briefly elaborate.

You will find it written that anaphylaxis refers to a life-threatening clinical syndrome following mast-cell degranulation. Tryptase is the most abundant protein found in mast cells.[2,3] Upon mast-cell degranulation, tryptase (along with histamine and other mediators) is released into the blood. Tryptase levels will peak at 1 hour, and remain elevated in peripheral blood for 4-6 hours. It is easy to measure, and is a sensitive and specific marker of mast-cell degranulation. Ideally 2-5 ml of clotted blood is collected within the first hour, 2-3 hours later and again after 12-24 hours for a baseline specimen. Transiently increased levels of mature tryptase serve as a marker of anaphylaxis. A single postmortem specimen would aid in confirming the diagnosis of anaphylaxis, as tryptase is stable in postmortem blood for 24 hours. (Tryptase may also be elevated in certain haematological neoplasms and in systemic mastocytosis.)[2,3]

In Skin focus, Dr Sue Jessop discusses acute urticaria in infancy. Remember that urticaria is often present in anaphylaxis, and may be the first clinical sign to manifest.

In Allergies in the workplace, Dr Fatemah Thawer-Esmail describes a fascinating case of urticaria in an underwater diver. There are many possible triggers for urticaria in a diver, and once identified, one is left with the concern of this progressing to angio-oedema while underwater, as well as the problem of taking medication that may be sedating while working in a hazardous environment.

I hope you enjoy this last edition of the journal for 2008, and I wish you all a great 2009. Enjoy the immune tree (courtesy of Dr Shaunagh Emanuel) .

I look forward to seeing you at the ALLSA Congress in July next year in Durban – one of the main focuses is anaphylaxis.

Di Hawarden

Guest Editor

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ANAPHYLAXIS IN THE PAEDIATRIC INTENSIVE CARE UNIT

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ABSTRACT

Anaphylaxis is uncommonly seen in the paediatric intensive care unit (PICU). Two circumstances under which anaphylaxis could be encountered in the PICU are when a child is admitted for intensive care after an anaphylactic reaction or when a patient in the PICU develops an anaphylactic reaction to his/her therapy. Refractory airway obstruction or refractory hypotension after anaphylaxis are indications for intensive care. The most common causes of anaphylaxis in the PICU are drugs, with antibiotics, anaesthetic agents and muscle relaxants most commonly involved. Anaphylaxis does occur in infants, even as young as 1 month of age, and may be difficult to recognise. Anaphylaxis has even been postulated as an aetiological factor in sudden infant death syndrome (SIDS). The case of a 6-day-old preterm baby who presented with symptoms and signs suggestive of anaphylaxis, but without an obvious trigger is discussed.

INTRODUCTION

Anaphylaxis is rarely seen in the paediatric intensive care unit (PICU), and there is not a single entry for 'anaphylaxis' in the index of a recently published paediatric ICU textbook.[1] There are two potential scenarios where anaphylaxis could be encountered in the PICU: (i) a child who is admitted for intensive care after anaphylaxis; or (ii) a patient who develops anaphylaxis to therapy while in the PICU.

EPIDEMIOLOGY OF ANAPHYLAXIS

The incidence of anaphylaxis in children varies between studies and depends on the setting and country. The incidence of new cases of anaphylaxis is generally considered to be between 8.4 and 21 per 100 000 patient-years, with a lifetime prevalence of 0.05-2%.[2,3] The highest incidence is in children and adolescents.[3] In an Australian study from Queensland the incidence was 1 out of 170 children, which is much more common than in adults.[4] Deaths as a result of anaphylaxis are rare and have been estimated to be approximately 1 per 3 million people per year.[5] In studies based on hospital visits, the mortality rate is 1 per 100-200 cases presenting to emergency units. In children most cases of mortality occur after the age of 10 years. There was only one fatality in a retrospective record review study at the Royal Children's Hospital in Melbourne – in a 7-year-old girl with a background of eczema and asthma and known peanut allergy who developed an anaphylactic reaction to peanut satay sauce.[6] Asthma has frequently been noted as a risk factor for fatal anaphylaxis.

I was unable to find anaphylaxis data for South Africa, but a case report describing an anaphylactic reaction in a 9-month-old boy with severe persistent asthma, eczema and known cow's milk allergy was published in 2005.[7] This child tolerated soy milk but presented to the Red Cross War Memorial Children's Hospital with acute anaphylaxis and respiratory arrest following ingestion of a new brand of soy milk formula. Investigation revealed that the soy milk batch had become contaminated with minute quantities of cow's milk protein, and ingestion of even this small amount of allergen had resulted in a life-threatening event.

CAUSES OF ANAPHYLAXIS IN CHILDREN

The most common causes of anaphylaxis in children are foods, insect venom and drugs. In the Queensland study food was the most common cause of anaphylaxis, with egg and dairy most often implicated.[4] In the Melbourne study, food was also the most common cause of anaphylaxis in young children, but peanuts and tree nuts (cashew nuts) were the most common causative allergens.[6] In older children drugs were more common than food as an initiating factor, with cephalosporins more commonly involved than penicillin.[6]

FEATURES OF ANAPHYLAXIS IN CHILDREN

In both Australian studies respiratory symptoms were more common than cardiovascular manifestations of anaphylaxis. In the Melbourne study the dominant features were shortness of breath, stridor and wheezing (30-56% of children) while hypotension was only present in 11% of the patients.[6] Urticaria (72%) and angio-oedema (55%) were also very common manifestations of anaphylaxis.

ICU MANAGEMENT OF ANAPHYLAXIS

Indications for ICU management of anaphylaxis include persistent airway obstruction or refractory hypotension. The treatment of persistent airway obstruction includes nebulised β_2-agonists and ipratropium bromide.[8] If bronchospasm does not respond to nebulised treatment, then intravenous salbutamol or aminophylline should be administered as a loading dose followed by a continuous infusion. If life-threatening airway obstruction persists, the patient must be intubated and mechanical ventilation commenced. Nebulised adrenaline is standard treatment for the airway obstruction in croup and it has been postulated that the stridor from an anaphylactic reaction may also respond to this therapy.[9] It is not a substitute for systemic adrenaline in the treatment of anaphylaxis, but an adjunct that may decrease the necessity for airway intervention. If the upper airway is obstructed and cannot be bypassed by an endotracheal tube, a surgical airway may be required (cricothyroidotomy).

Severe intractable hypotension is probably the most ominous manifestation of anaphylaxis. The hypotension is as a result of fluid shifts from the intravascular to the extravascular space. The first step is to restore the intravascular volume. This is achieved by the

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administration of large volumes of intravenous fluid. It would appear that rapid administration of fluid is more important than the choice of fluid. If the patient remains hypotensive, ICU admission is indicated for intensive monitoring and vasopressors. If intravenous adrenaline does not reverse the hypotension, dopamine should be administered. Patients who are taking β-blockers may be very resistant to standard vasopressors, and in such cases intravenous glucagon is indicated. Glucagon is a polypeptide hormone and is produced by the pancreas. It is a phosphodiesterase inhibitor and its action is thus independent of catecholamines.[8]

A recent article addresses bee stings in children and when endotracheal intubation should be performed in these patients.[10] The authors point out that insect stings seldom cause life-threatening anaphylaxis in children and systemic reactions are found in less than 1% of children who have been stung. Stings to the mouth and pharynx are uncommon but could cause life-threatening airway obstruction. Three cases are described in which children suffered bee stings to the tongue and one on the lower eyelid, with resultant severe facial oedema and airway compromise in all. All the children were intubated; three had relatively uncomplicated courses and could be extubated between 24 and 48 hours later. The fourth child had a severe reaction with intrathoracic airway obstruction that proved refractory to treatment; he required mechanical ventilation for 10 days. Three of the children had symptoms due to direct toxic effects of the bee venom, while the fourth had an anaphylactic reaction. None of these children was investigated for bee-venom anaphylaxis, but the child who had a prolonged hospital stay was referred to the allergy clinic for further investigation and immunotherapy.

Anaphylaxis occurring in PICU patients

The most common causes of anaphylaxis in the PICU are drugs, with antibiotics, anaesthetic agents and muscle relaxants most commonly involved. Theoretically latex allergy may also be a problem, but even in patients at high risk, e.g. children with spina bifida, the prevalence in South Africa has been found to be low.

The most commonly described antibiotic allergy is to beta-lactams. Drug allergy and anaphylaxis are uncommon in children. In the Melbourne study only 6% of the anaphylactic reactions were caused by drugs, and these presented in older children (median age 13 years, range 6-15 years).[6]

Fischer[11] recently reviewed anaphylaxis in the ICU setting. She pointed out that muscle relaxants are responsible for 60% of anaphylactic reactions in the critical care and peri-anaesthetic setting. A recent case report discussed a 6-year-old child with severe life-threatening airway obstruction following induction with thiopentone and cisatracurium.[12] He had mild pre-existing asthma but no other risk factors for drug anaphylaxis. He developed severe acute bronchospasm 60 seconds after the administration of cisatracurium, an intermediate-acting bis-benzylisoquinolinium neuromuscular blocker. The bronchospasm was unresponsive to halothane, theophylline, salbutamol and steroids; the child developed severe respiratory failure and proved extremely difficult to ventilate. He only responded after the administration of two intravenous boluses of adrenaline followed by a continuous adrenaline infusion.

An extensive work-up was done during this patient's PICU admission. Special investigations revealed slightly raised tryptase and histamine and markedly raised eosinophil cationic protein levels in a blood sample taken 45 minutes after induction of anaesthesia. Specific IgE levels for quaternary ammonium, thiopentone and cisatracurium were also weakly positive.

Muscle relaxants cause anaphylaxis either by means of histamine release by mast cells or IgE-mediated reactions. All muscle relaxants have a common ammonium group that can be bound by IgE, thus causing cross-reactions across all neuromuscular blocking agent groups. The mechanism in this patient appears to be an IgE-mediated reaction to the cisatracurium.

Other agents used in the PICU that may cause anaphylaxis in susceptible children are hypnotics such as barbiturates and propofol, plasma volume expanders such as dextran and hydroxyethyl starch, and local anaesthetic agents. Allergy to egg and soya may predispose children to reactions to propofol, which contains egg lecithin and soybean oil.[13]

CASE REPORT

A 7-week-old baby girl was referred to me for assessment after she had apparently suffered an anaphylactic reaction at the age of 6 days. She had been born at 30 weeks' gestation, weighing 1 350 g, after her mother had suffered an antepartum haemorrhage. She was admitted to the neonatal ICU (NICU) within 24 hours with severe hyaline membrane disease. She was given two doses of surfactant (Curosurf®, Poractant alfa, porcine lung surfactant) and ventilated by means of high-frequency oscillatory ventilation. She responded well to the treatment and was discharged from the ICU at the age of 5 days. She had received penicillin G and gentamicin until the day of discharge from the NICU.

That night while in the ward she appeared to have an anaphylactic reaction. She developed swelling of the cheeks and neck; this spread rapidly to the head and tongue and subsequently to the abdomen and legs. She developed a bradycardia and became hypoxic. She was intubated, given intravenous adrenaline, promethazine and hydrocortisone, and transferred to the NICU. The oedema and cardiovascular effects resolved rapidly and she could be extubated the following day. At the time of her admission she was on meropenem and vancomycin, aminophylline, vitamin D, caffeine, multivitamin drops, a phosphate mixture and TPN (total parenteral nutrition, intravenous amino acid and lipid mixture). Her condition responded rapidly to therapy; she was extubated the following day and discharged from the NICU. Unfortunately no investigations such as serum tryptase were done, so it is impossible to be sure that this was an anaphylactic reaction.

The other interesting feature from the history is that her maternal grandmother was allergic to bee venom. The family history was negative for hereditary angio-oedema.

At the age of 7 weeks she was clinically well and thriving. Although it was thought extremely unlikely that this was an anaphylactic reaction because of her age, she was investigated for penicillin and latex allergy and C1 esterase inhibitor deficiency. All investigations were normal. Follow-up 6 weeks later revealed a thriving child with no recurrence of her symptoms.

ANAPHYLAXIS IN INFANTS

According to Simons[14] the incidence of anaphylaxis in infants younger than 2 years is unknown, but it has been described in infants as young as 1 month of age. She describes a case of anaphylaxis to cow's milk in a 9-month-old boy. Foods, particularly cow's milk or egg, most commonly trigger anaphylaxis in young infants.

Less commonly anaphylaxis is caused by beta-lactam antibiotics, neuromuscular blockers, latex, insect venoms and vaccinations. Idiopathic anaphylaxis has also been described in this group of children.

Allergen-induced anaphylaxis has been proposed as one of the possible causes of the sudden infant death syndrome (SIDS).[15] SIDS encompasses sudden and unexpected death in infants who have been completely healthy. It is a diagnosis by exclusion with no obvious cause found at autopsy. Certain environmental factors have been implicated in its causation, such as prone sleeping, maternal smoking, and poor socioeconomic status. Allergens may play a role, either alone or in combination with other factors. One theory holds that sensitised infants may suffer an anaphylactic reaction after vomiting and then inhaling cow's milk while sleeping. A postmortem study showed significantly higher serum tryptase levels in infants who died from SIDS compared with other causes of death, thus supporting fatal anaphylaxis as a possible cause of death in these infants.[15]

Infants can obviously not describe subjective anaphylaxis symptoms and so one should have a high index of suspicion in these children. Most of the anaphylactic episodes in infants are IgE-mediated, and the choice of allergens for testing should be determined by the history. Prevention of repeat anaphylaxis is difficult as the adrenaline auto-injectors are designed for bigger children, but a 1 ml syringe and a vial of adrenaline together with detailed instructions can be given to the caregiver.

DISCUSSION OF THE CASE

Did the little girl referred to me have an anaphylactic reaction and, if so, to what? If it was an anaphylactic reaction, this case would probably be the youngest child described. In addition, she was preterm and so her immune system should not have been sufficiently developed to react to an allergen. Unfortunately no tests were done when she manifested the episode and so, unless she has a repeat episode, we will never know whether this was in fact an anaphylactic reaction or not. Any of the antibiotics or other treatments she received could have been implicated in the causation of an anaphylactic reaction.

AVOIDING RISK AFTER ANAPHYLAXIS IN CHILDREN

What advice should one give families after a child has had an anaphylactic reaction to food? Kemp and Hu[16] point out that, since food is essential, it is impossible to completely avoid the risk of exposure. Food allergy and anaphylaxis are 'high-stakes and highly uncertain issues, where the outcome may be the sudden and unpredictable death of a child.' It is difficult to quantify the risk, since we know that labelling of foods is not always accurate and cross-contamination does occur. This leads to uncertainty on the part of the carer – uncertainty about the magnitude of the risk, how to avoid exposure, and when to administer injectable adrenaline. This uncertainty causes stress. Kemp and Hu believe that patients and their parents should not have to deal with unnecessary uncertainty, and that the medical profession as well as policy makers should address concerns about food allergy.

CONCLUSION

Anaphylaxis in the PICU is uncommon, but can pose both diagnostic and management challenges. It is important to have a high index of suspicion in infants as anaphylaxis may be difficult to diagnose in this group of children. The initial management consists of the ABCs of emergency treatment, together with the administration of adrenaline and other therapy as indicated, and is detailed in the algorithm from the Resuscitation Council of Southern Africa (Fig. 1). This is followed by investigations to confirm the diagnosis and establish the cause of the reaction. After this, planning to reduce the risk of future anaphylactic episodes is essential.

Declaration of conflict of interest

The author declares no conflict of interest with regard to the subject matter of this article.

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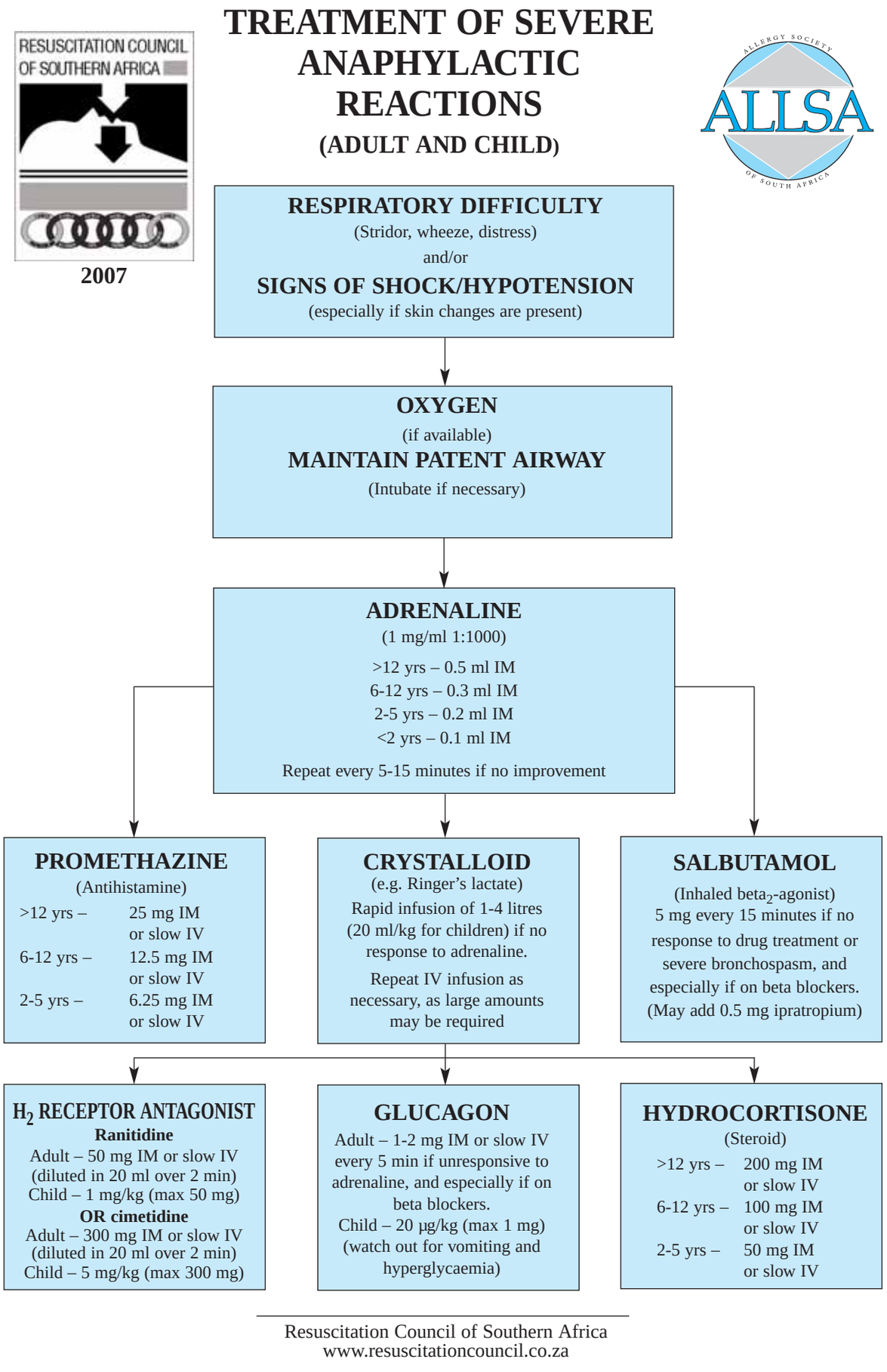

Fig. 1. Algorithm of treatment of severe anaphylactic reactions.

ANAESTHETIC ASPECTS OF CUTANEOUS MASTOCYTOSIS IN A CHILD PRESENTING FOR DAY SURGERY: CASE PRESENTATION

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INTRODUCTION

Cutaneous mastocytosis or urticaria pigmentosa is one of the three major categories of the disease mastocytosis.[1] This is a rare and usually benign disease, presenting with a reddish to brown macular rash, mainly over the trunk, that sometimes spreads to the limbs. The lesions may become itchy and red when rubbed (Darier's sign).[2] The rash usually presents within the first 6 months of life and can be quite prominent, but often fades after a few years. The disease regresses spontaneously in over 50% of affected children. Biopsy shows an increased accumulation of mast cells in the skin lesions. Certain triggers induce release of mediators from the mast cells, causing a range of symptoms including flushing, pruritus, urticarial swellings and even blistering.[3] In rare cases there may be wheezing, syncope and anaphylaxis. Treatment is mainly symptomatic, with control of the rash with H_1 and H_2 blockers and avoidance of physical trigger factors (rubbing, extremes of temperatures) and chemical triggers (histamine-releasing agents such as opiates, codeine, muscle relaxants and insect venom).[1]

The possibility of anaphylaxis during anaesthesia from exposure to certain triggers makes a management plan for the peri-operative period essential. The risk of anaphylaxis is greatly reduced when H_1 and H_2 blockers[4,5] and corticosteroids[5] are administered pre-operatively. Disodium cromoglycate is a mast-cell-stabilising drug and may be of value when used prophylactically.[4] Extremes of temperatures in theatre, as well as contact with cold, rough surfaces should be avoided. There are numerous anaesthetic-related drugs which trigger mast-cell degranulation. These include muscle relaxants, opiates, codeine, atropine, ephedrine and phenylephrine.[6] If any of these agents, especially the muscle relaxants, has to be used, it should be diluted and administered slowly. The agent with the lowest histamine-releasing qualities should be chosen. Intravenous access must be established as soon as possible. Adrenaline should be at hand in case of anaphylaxis, and can be given intramuscularly if there is no vascular access or as an intravenous infusion. Analgesics to be avoided are codeine-containing mixtures, salicylates and opiates. Non-steroidal anti-inflammatory drugs (NSAIDs) may cause a severe reaction, but have been used in the treatment of prostaglandin-induced flushing in cutaneous mastocytosis. If necessary they should be started under close supervision to ascertain if they are tolerated or whether they cause a severe reaction. In the event of an anaphylactic reaction additional resuscitative measures need to be instituted. These include adrenaline, additional intravenous antihistamines, steroids, vasopressors, intravenous fluids, oxygen and respiratory control.

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CASE REPORT

A 4-year-old boy, who had been diagnosed at 3 months of age with cutaneous mastocytosis, presented for elective tonsillectomy and adenoidectomy. His symptoms were occasional extreme flushing and pruritus in response to triggers of heat and pressure. There had been no episodes of anaphylaxis. The rash, which had been quite remarkable when he was a baby, was beginning to fade. His parents were careful, and had never used medications containing codeine, salicylates or NSAIDs. Their internet search (www.mastokids.com) had made them aware of the possibility of anaphylaxis with certain medications and particularly under anaesthesia. Several bouts of tonsillitis had been treated with antibiotics and he had a recurrent wheezy chest, which was treated with montelukast (Singulair). At the time of surgery he was on a short course of Celestamine (betamethasone and dexchlorpheniramine, i.e. a steroid and H_1 blocker) for his chest.

On examination the child was a normal healthy 4-year-old with a faint brownish, macular rash on the trunk. His lungs were clear. Two hours pre-operatively he was given an H_2 blocker (ranitidine 75 mg in 5 ml), an additional H_1 blocker (desloratidine 1.25 mg in 2.5 ml) orally and was nebulised with ipratropium and fenoterol. Anaesthesia was induced with the inhalational agent sevoflurane and intravenous access was secured. A small dose (20 mg) of propofol was given intravenously and the trachea intubated. Anaesthesia was maintained with sevoflurane. Anti-emetics (ondansetron 0.1 mg/kg and dexamethasone 0.15 mg/kg) were given intravenously. Muscle relaxants were not necessary and the child breathed spontaneously throughout the operation. Adrenaline was at hand but not needed. Haemodynamic and respiratory parameters were stable throughout and there was no flushing of the skin. An NSAID in the form of a 25 mg diclofenac suppository was given rectally as medical supervision was deemed optimal. He remained stable throughout the procedure as well as postoperatively, when he was observed in the ward for 6 hours. Paracetamol syrup and diclofenac suppositories were prescribed as analgesia for the postoperative period, which remained uneventful. He was discharged home into the care of his parents.

The parents were concerned that he might still develop an anaphylactic reaction at home. Reassurance was given that this was most unlikely, that the child had a very mild form of the condition and was already outgrowing it. However, they were counselled, shown how to use adrenaline, and supplied with adrenaline (1 ml of 1:1000), a graded 1 ml insulin syringe and a needle.

DISCUSSION

This child presented as a very mild case of cutaneous mastocytosis. Measures were taken to minimise his response on exposure to trigger agents during surgery. He was already covered by steroids and an H_1 blocker because of the Celestamine. An hour before surgery he was given an H_2 blocker (ranitidine) as well as an H_1

blocker (desloratidine), and he was nebulised to lessen airway hyperreactivity in response to tracheal intubation or anaesthetic trigger agents. Although the dexamethasone was used for its anti-emetic qualities, it may possibly be of value for the prevention of non-immune mediated reactions.[5] Adrenaline was at hand. Pethidine is often used as an analgesic after tonsillectomy, but was avoided in this case. After tonsillectomy, the worst pain occurs on day 4 or 5 postoperatively; by this time the child would obviously be at home in the care of his parents. Because an agent more effective than paracetamol might then be needed, an NSAID was given in hospital so that the child's response could be observed; there was no untoward reaction. A severe reaction at a later stage was unlikely, but the parents were instructed how to administer adrenaline correctly should an emergency arise.

Declaration of conflict of interest

The author declares no conflict of interest.

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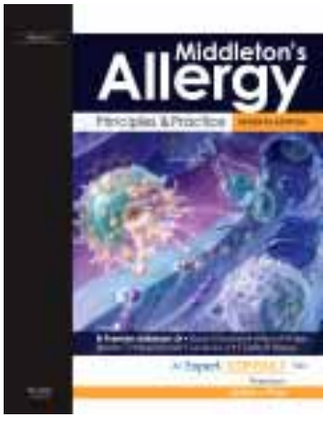

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ANGELINA ANGIO-OEDEMA

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Cartoon case study

Although this case study has been presented in a somewhat jocular style, the account is factual, and tells the story of a patient who was seen at the Allergy Diagnostic and Clinical Research Unit.

The case was presented at the ALLSA congress in 2006, and the presentation graphics have been adapted for this cartoon that illustrates the essentials of the case of a delightful and courageous nun whose name is not really Angelina, but who truly suffers from recurrent angio-oedema.

A kind and gentle nun,
By the name of Angelina,
Suffered something terrible
From recurrent angio-oedema.

She went to see her allergist
In a state of deep despair,
For her life as a result of it
Seemed way beyond repair.
The doctor took a history
And checked her top to toe.
The cause remained a mystery.
For tests she had to go.

A skin prick and a RAST were done
To check the IgE.
Looking at the test results
The doctor did agree;
The wheal was raised,
The flare was wide,
It seemed unequivocally,
That gluten was the obvious cause
Of the malady.

"Lose the morning slice of toast!"
The doctor did proclaim,
"And the sacred heavenly host,
If it's all the same.
'Tis they that start the itchy rash,
And cause your lips to swell.
It's the gluten in the wheat,
Dear one,
That makes your daily hell!"

Wheat-free mass became a hardship,
For Angelina so loved to worship!
Then one day
She made a discovery!
In the UK there is a bakery
That makes hosts
Without wheat entirely!
Right away she had them sent
By express registered mail.
But her efforts, I am afraid,
Came to no avail.
Though it seemed absurd,
The swellings still occurred!
The doctor did deliberate,
And the two of them concurred…
Perhaps those yellow wafers
Were coloured and preserved.
The result of the CAST returned,
And the puzzle, it seemed was solved:
The colourant and the benzoates
Were definitely involved!

And so she made the most
Of mass without the host,
But the daily bouts of swelling
Failed to decline.
Which made them think, perhaps,
There was something in the wine!
The CAST was unequivocal;
Sulphur dioxide was the culprit.
The situation was diabolical
For Angelina at the pulpit.
She still takes communion,
But with neither wine nor bread;
A silver cup of red grape juice
She sips upon instead.

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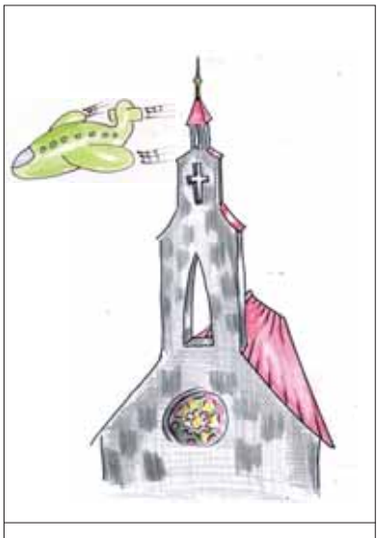
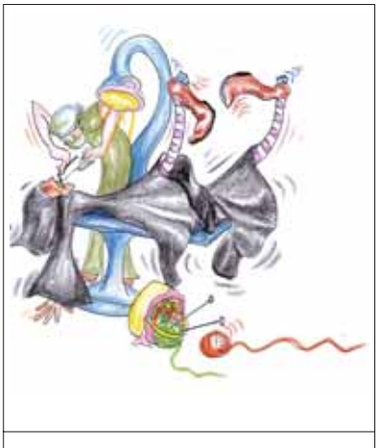
"Avoidance Angelina"
Was the name she soon adopted.
For a simple peasant diet
She reluctantly opted.
But despite her care and diligence,
And new-found label-vigilance,
Angelina could never tell
When next her lip would swell.

One day she developed flu,
Sucked a pink lozenge,
And took pen. V. too,
Lay down on the chaise lounge,
And the next thing she knew…
Her lip was as big
As a size seven shoe!
Even though the tests this time
Revealed no positive finding,
Something in the meds she took
Had got her IgEs binding!



One day she went to Jo'burg
To visit the sisters there.
She had a sip of wine,
And landed on her ear.
She found herself in casualty
Hooked up to lines and gas,
And concluded that for her,
It was not prudent to take mass
In a convent unfamiliar
With a condition so peculiar.



Once she saw a dentist,
And gave the chap a fright!
He had just said: "Open wide"
When she collapsed
And went quite white!
With his own adrenaline running high,
He gave Angelina an amp in her thigh.
Though she made a good recovery,
She still complains of a fair-sized cavity.

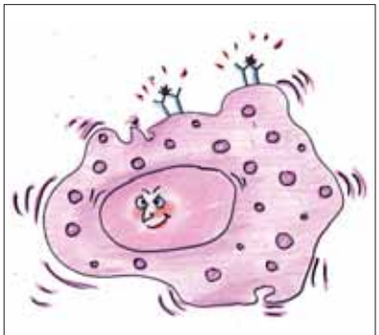
With preparedness and care,
(And some trepidation)
Skin-prick tests were done
As a confirmation
That the local anaesthetic
Caused the prostration
Under the spotlight
In the adjustable chair,
And left the master of dentition
With a shock of white hair!

The result became quite clear
When Angelina fainted,
And slid quietly off her chair,
As she waited in the corner
For the wheals to appear.
Lignocaine is now
No longer an option
If she should need
A minor operation.

Fibroids in her uterus
Were turning her quite pale,
And preservatives in the iron
Made that remedy fail.
She needed them out,
Under the knife,
But the general anaesthetic
Would endanger her life!
A panel of experts
Reached a consensus
That morphine and NSAIDs
Would truly be senseless.

So in an operating theatre,
Free of latex and the rest,
She bravely suffered surgery
On paracetamol IV!
Post-op she was smiling,
Sipping hot sweet tea,
And when asked for a comment,
She stated most humbly:
"Thank you Doc for caring,
I have such faith in thee!"

Armed to the teeth
With an adrenaline gun,
She has to be a careful
And most diligent nun
In avoiding the compounds
Ubiquitous
That threaten her something
Iniquitous!
The sulphurs and the benzoates,
The colourants and the wheat,
And the local anaesthetics
That take her off her feet!



Now she wears a bracelet
With a warning on the disc,
Of her severe condition,
And the potential risk
Of treating Angelina,
Even for a sneeze.
For her mast cells
Are a twitchy bunch,
And can bring her to her knees!

Results of some of the special investigations performed in this case

CAST (cellular antigen stimulation test) **Positive**	**Sodium benzoate** **Tartrazine** **Mivacurium** **Vecuronium** **Atracurium** **Sulphur dioxide**
RAST (radioallergosorbent test) (specific IgE) **Positive**	**Gluten**
Drug challenge **(skin-prick test)** **Positive**	**Mepivicaine** **1: 10 000 dilution**

NOTES ON ANGIO-OEDEMA

- Non-pitting oedema of dermis and subcutaneous tissue
- Face, tongue, lips and eyelids most commonly affected
- May be associated with anaphylaxis of any cause
- Multiple causes:
  - Foods
  - Drugs
  - Insect stings
  - Infections
  - C1 esterase inhibitor deficiency
  - Physical causes
  - Contact reactions
  - Systemic diseases
  - Autoimmune
  - Idiopathic

Declaration of conflict of interest

Drs Shaunagh Emanuel and Diane Hawarden declare no conflict of interest.

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WORK-RELATED ANAPHYLAXIS

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ABSTRACT

A definition of anaphylaxis was recently agreed to at an international symposium on this subject. This article proposes a definition for work-related anaphylaxis that is conceptually consistent with similar classifications for work-related asthma and rhinitis, which defines two major categories – occupational anaphylaxis and work-exacerbated anaphylaxis. The epidemiology and causative agents implicated in work-related anaphylaxis are outlined, with a focus on the most commonly implicated agents such as natural rubber latex, insect venoms, food proteins, disinfectants and pharmaceutical drugs. Diagnosis, management and prevention are discussed. Prevention of work-related anaphylaxis revolves around making a concerted effort to identify the trigger so that more effective primary, secondary and tertiary interventions can be implemented.

DEFINITION

Anaphylaxis is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance.[1] Anaphylaxis and acute allergic episodes manifest clinically with a spectrum of symptoms and signs. This diagnosis has historically been made on a subjective basis with no universally agreed definition or clinical criteria. Recently, a definition of what constitutes anaphylaxis as opposed to other types of allergic reaction was agreed upon at a symposium on the definition and management of anaphylaxis.[2] The symposium proposed the following broad definition useful to both the medical and lay community: **'Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death'**. The clinical criteria in fulfilling this definition are outlined in Table I. Having precise clinical criteria for the diagnosis of anaphylaxis now makes it possible to conduct multicentre trials and evaluate clinical and epidemiological data more accurately. This in turn will also allow for a more accurate understanding of the role that occupational exposures play in anaphylaxis. Finally, this better understanding may allow improved clinical management and workplace control of these exposures, leading to the prevention of serious anaphylactic reactions in at-risk working populations.

There is no universally agreed upon definition of **work-related anaphylaxis.** However, this entity could be classified into two main categories based on the direct causal relationship between work exposure and the development of the disease: (i) occupational anaphylaxis; and (ii) work-exacerbated anaphylaxis. The generally accepted definition of work-related asthma is categorised similarly.[3] *Occupational anaphylaxis* could be defined as 'anaphylaxis arising out of causes and conditions attributable to a particular work environment and not to stimuli encountered outside the workplace'. Work-exacerbated anaphylaxis could be defined as pre-existing or concurrent allergy (e.g. food/pollen allergy) to a particular agent that is precipitated by workplace exposures, possibly as a result of cross-reacting allergens. In occupational anaphylaxis the exposure could be due to a known or unknown allergen as a result of inhalation, dermal contact (in a person with pre-existing skin disease, e.g. dermatitis, skin trauma) or through hand-to-mouth ingestion in workplaces with poor industrial hygiene practices.

Anaphylaxis usually occurs within 20 minutes of exposure to the causative substance, although occasionally with orally ingested substances, there can be a latency of up to 2 hours between exposure and response.[1,4] If anaphylaxis occurs in the workplace, it is therefore highly likely to have been due to a workplace exposure. In contrast, ingestion-related allergic conditions due to

Table I. Clinical criteria for diagnosing anaphylaxis in adults

Anaphylaxis is highly likely when ANY ONE of the following three criteria is present:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (e.g. generalised hives, pruritus or flushing, swollen lips-tongue-uvula) and at least one of the following:
   a. Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxaemia)
   b. Reduced BP or associated symptoms of end-organ dysfunction (e.g. hypotonia (collapse), syncope, incontinence).
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
   a. Involvement of the skin-mucosal tissue (e.g. generalised hives, itch-flush, swollen lips-tongue-uvula)
   b. Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxaemia)
   c. Reduced BP or associated symptoms (e.g. hypotonia (collapse), syncope, incontinence)
   d. Persistent gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting).
3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
   systolic BP of less than 90 mmHg or greater than 30% decrease from that person's baseline.

PEF- peak expiratory flow; BP – blood pressure.

Adapted from Sampson *et al*.[2]

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exposures outside the workplace may manifest while at work, and therefore may require additional evidence before being labelled 'occupational' or 'work-aggravated'. It also needs to be borne in mind that workers may primarily be sensitised from workplace-allergen exposure, and only manifest with anaphylactic reactions in non-workplace contexts. This is the case with health-care workers undergoing surgical/dental procedures or workers ingesting food or medication after they have developed initial workplace sensitisation and minor occupational allergic symptoms (e.g. rhinitis, urticaria, mild asthma).

EPIDEMIOLOGY AND CAUSATIVE AGENTS

The epidemiology of occupational anaphylaxis is difficult to describe, as the condition is uncommon, transient and previously poorly defined.[5] Globally, it is estimated there are about 154 fatal episodes of anaphylaxis per 1 000 000 hospitalised subjects.[6] Based on data from Olmsted County in the USA, it is projected that there are 84 000 anaphylaxis cases and 840 fatalities in the USA annually.[1,7] Of the total fatalities, it is estimated that about 20% are food-induced (mainly nuts), more than 50% are due to β-lactam antibiotics and less than 10% are from insect stings. There are no reliable figures for South Africa. If the American figures are stratified to adults only, and antibiotics and most food-induced reactions are excluded, it is probable that less than 20% of all anaphylactic fatalities in the USA are due to work-related substances.

Any workplace agent capable of causing occupational asthma or generalised urticaria could theoretically cause anaphylaxis.[8] There are a few clinical case series or reports and epidemiological studies that have been reported in the literature, including those related to fatal occupational asthma.[9] These are outlined in Table II.

One of the most common workplace agents reported to give rise to occupational anaphylaxis is natural rubber latex exposure, especially among health-care workers and latex-manufacturing plant workers where it is used in the production process (Fig. 1). Sensitisation to natural rubber latex in the general population ranges between 5% and 10% with the prevalence in health-care workers varying from 0.5% to 17% on either skin-prick testing (SPT) or latex specific IgE immunoassay.[10] Cumulative incidence rates for latex-induced sensitisation from various studies have been reported to be less than 2% per year with incidence rates of latex allergy being far less, in the order of 1-12 per 10 000 workers per year.[10] There are no reliable figures for rates of *occupational latex-induced* anaphylaxis found in the literature, although a recent study of hospital workers at an academic hospital recorded that 3% of respondents (*N* = 277) reported having anaphylactic reactions.[11] There are however a number of case reports and case series of fatal anaphylaxis due to latex-containing products among health-care workers undergoing dental or surgical procedures or wearing gloves over disrupted irritated eczematous skin.[12]

Table II. Causative agents implicated in occupational anaphylaxis

Agent	Industry
Natural rubber latex (NRL)	Health care Other manufacturing plants with NRL in the production process
Insect (e.g. bees, wasps) and arachnid (e.g. ticks) venom	Honey (beekeepers) Agriculture, parks and forestry, gardening and landscaping
Food proteins (e.g. nuts, seafood, spices, cereal grains, soybean, cow's milk powder and hen's egg powder)	Food-processing industry
Pharmaceutical agents (e.g. β-lactam antibiotics, cytotoxics, laxatives)	Pharmaceutical manufacturing plants Health-care institutions (preparation of medication)
Disinfectants (e.g. chlorhexidine, ortho-phthalaldehyde – OPA)	Health-care institutions Other industries using disinfectants
HBTU (o-(benzotriazol-1-yl) -N,N,N',N'-tetramethyluronium hexafluorophosphate)	Peptide synthesis plants

Fig. 1. Natural rubber latex exposure during surgical procedures in theatre.

Agricultural workers and other outdoor workers are at increased risk of insect stings and venom-induced anaphylaxis (Figs 2 & 3). A Spanish case series of 98 patients with anaphylaxis due to wasp stings reported that 18% of these reactions occurred during working hours.[13] A number of studies on beekeepers have also reported increased rates of sensitisation and allergic reactions to hymenoptera venom, with a prospective cohort study in Greece suggesting a threefold increased risk of sensitisation in beekeepers as compared with non-exposed workers,[14] and a Finnish study reporting approximately 30% of a population of 102 beekeepers having had a previous 'systemic' reaction.[15] Tick-bite-induced anaphylaxis due to *Rhiphicephalus* sp. in a goat herder has also been reported.[16]

Fig. 2. Hymenoptera – honey bee.

Food-related anaphylaxis is a potential problem among workers in the food-processing industry. Food-related anaphylaxis in the domestic environment is commonly due to peanut or other tree-nut allergies.[1] Occupational anaphylaxis in the workplace environment is commonly triggered by inhalation of allergenic food proteins, enzymes (e.g. papain), additives (e.g. sulphites) and food colourants (e.g. carmine) in dust particulate (powder, granules) generated during food-processing (e.g. milling, blending) activities. Severe allergic reactions to a range of inhaled allergens from fish, shellfish, soybeans, seeds, beans and cereal grains, as well as cow's milk and hen's egg powder have been reported in the literature.[17] Spices such as garlic[18] and coriander[19] have also been reported to cause anaphylaxis and could be a potential risk in

Fig. 3. Exposure to bees during beekeeping activities.

Fig. 4. Garlic dust exposure during milling, blending and packing procedures in a spice mill.

workers involved with milling, mixing and packaging spices in food-processing plants (Fig. 4).

Pharmaceutical agents are an important cause of anaphylaxis in the general population, but would also be of concern to workers in pharmaceutical plants (e.g. milling, granulation) and health-care workers involved in the preparation of medication for patient administration. There have been reports of severe allergic reactions to β-lactam antibiotics (e.g. penicillins, cephalosporins), antineoplastic agents (e.g. Adriblastina – doxorubicin hydrochloride) and laxatives (e.g. psyllium) where there is the potential for inhalation of powdered dust particulate or hand-to-mouth ingestion.[20,21]

Finally, there have been isolated case reports of occupational anaphylaxis to a variety of other substances found in the workplace, including chemicals such as disinfectants (e.g. chlorhexidine, ortho-phthalaldehyde – OPA) used in health care settings and HBTU (o-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate), which is extensively used for solid and solution-phase peptide synthesis.[22-24]

DIAGNOSIS AND IDENTIFICATION OF TRIGGERS

The diagnosis of occupational anaphylaxis is made according to the criteria set out for the diagnosis of anaphylaxis[2] in the context of an exposure to a suspected workplace agent (Table I). A concerted effort should be made to identify the causative agent because this has major implications for placement of the worker since the removal and relocation of the affected individual from the putative exposure is of prime importance to prevent recurrence. The process to confirm the diagnosis as suggested by Simons *et al.* [25] should be followed: (i) confirm the diagnosis; and (ii) confirm the anaphylaxis trigger.

Confirm the diagnosis

In confirming the diagnosis it is important to work through the following steps:

- Retake a history of the episode, focusing on the antecedent clinical symptoms and signs and obtaining collateral information from fellow workers.
- Review the relevant medical records from the ambulance, emergency department, occupational health clinic, etc.
- Review the laboratory tests (e.g. serum total tryptase, plasma histamine) performed during the episode.
- Review the differential diagnosis, which commonly includes hives, asthma, anxiety/panic attack, fainting, choking.

Identify the anaphylaxis trigger

With regard to confirming the anaphylaxis trigger, there are a number of issues to consider after the episode when the worker has recovered from the acute phase:

- Retake a history of the episode and pay particular attention to questions about inhalational exposures in the 30 minutes prior to the episode and potential ingestion-related exposure within 2 hours. Think about the production process and job tasks the worker performs and create a list of potential exposure agents. In addition review the Material Safety Data Sheets (MSDS) of products the worker may have used.
- Retake a complete medical history, looking for concomitant diagnoses such as asthma, cardiovascular disease, and concurrent medications such as β-blockers, angiotensin-converting enzyme (ACE) inhibitors and others.
- Perform skin tests – skin-prick tests for foods and other agents (e.g latex) and intradermal tests for β-lactam antibiotics. It is preferable for these tests to be done under controlled conditions.
- Perform allergen specific IgE quantitative measurements (Phadia ImmunoCAP Specific IgE) (e.g. insect venoms, cereal flours, spices) and cellular antigen stimulation test (CAST) where appropriate. Identification of cross-reactive allergens may be necessary as well (for instance, latex cross-reactive allergens such as banana, kiwi, pear and avocado; pollen cross-reactive allergens with spices).
- Challenge tests may be indicated that are either allergen specific (e.g. inhalation challenge tests with food products, medication – proceed with extreme caution) or allergen non-specific (e.g. cold and exercise).
- Other assessments as indicated, such as industrial hygiene measurements in the workplace.

It is important to note that SPT and specific challenge tests may precipitate an anaphylactic reaction in sensitised workers and should only be conducted in expert hands if indicated. Specific IgG immunoassays may be a safer, useful alternative if the intention is to rule out exposure to a particular allergen. However, the presence of allergen-specific IgG does not indicate the presence of an allergic cause. The specificity and sensitivity of each allergological test and its correlation with health effects varies between tests. Discussion with the allergologist and laboratory technologist can help the practitioner decide which tests are the most appropriate, taking the clinical context and potential workplace exposures into account. After proper investigation, it would be rare for practitioners to be left labelling the reaction as 'idiopathic' occupational anaphylaxis.

MANAGEMENT

The initial immediate management of an occupational anaphylactic reaction is no different to a non-work-related anaphylactic episode. A recent statement by the World Allergy Organisation concluded that self-administered intramuscular adrenaline is still the mainstay of treatment for anaphylaxis, although it is underutilised and often suboptimally dosed to treat anaphylaxis.[26] Intramuscular adrenaline injection into the lateral thigh is the treatment of choice and it is preferred to intravenous or subcutaneous injection.[27,28] A recent Cochrane review reported that there is no good evidence as to the benefit of antihistamines in the initial treatment anaphylaxis.[29] A more in-depth review of treatment issues of anaphylaxis is dealt with elsewhere in this issue.

Follow-up management of the anaphylactic episode requires relocation and placement of the worker in an area of no exposure after determination of the causative agent in the workplace, so as to prevent repeated exposure of the affected worker. Vigilance regarding other, as yet unaffected, workers is necessary.

Finally, all cases of occupational anaphylaxis must be initially reported to the Compensation Commissioner, Department of Labour, as an occupational disease. The relevant Compensation of Occupational Injuries and Illnesses Act (COIDA) forms should be completed by the medical practitioner and the employer, and the case followed up until finalisation of the compensation process and as the clinical situation dictates. There may be discussion over whether the incident is classified as an occupational injury (a once-off event due to a single exposure) or an occupational disease. If this is the case, the claim is initially managed as an occupational injury and subsequently evaluated as an occupational disease claim should the disease progress to a known compensable entity, such as occupational asthma. Details of this Circular Instruction 176 have previously been published in *Current Allergy & Clinical Immunology*.[30]

PREVENTION

Prevention in relation to the natural history and prognosis of occupational allergy forms a cornerstone of dealing with occupational anaphylaxis. The longer the exposure and delay in diagnosis and treatment, the longer the duration of allergic symptoms, which is ultimately associated with a poorer prognosis and an increased risk of an anaphylactic episode on re-exposure to the offending agent. Risk factors to be considered for modification include environmental factors (exposure to causative or sensitising agents) or host-related factors (atopy, pre-existing food allergies, prior episodes of anaphylaxis, severe uncontrolled asthma, cardiovascular disease).

Primary prevention focuses on prevention of primary or repeated exposure to sensitisers resulting in sensitisation, whether at the source (elimination, substitution, local exhaust ventilation), along the path (enclosure of emission source) or at the worker level (administrative controls, respiratory protective equipment). While respirators may reduce exposure, they are not effective in preventing exposure. All efforts must be aimed at utilising the expertise of experts with insight into the production process, such as engineers and occupational hygienists, to find alternative ways to substitute or eliminate the agent, or reduce exposures to the agent/s concerned. For instance, with natural rubber latex this would entail making the environment latex-free. In some production processes this is not always possible, but attempts to reduce airborne concentrations of the causative agent should always be made. With latex this may involve changing from powdered latex gloves to powder-free low-protein latex gloves to reduce airborne latex particles. While threshold limit values for certain workplace allergens (e.g. latex, flour dust, isocyanates) exist, even low-level exposures have the potential of triggering an allergic reaction in a sensitised worker. In a food-processing worker with a known allergy to the food product, avoidance of the offending food allergen in the diet is another consideration. Similarly, the use of latex-free surgical or dental procedures is indicated in a health-care worker with a known allergy to latex.

Secondary prevention focuses on the prevention of clinical allergy and anaphylaxis in sensitised but asymptomatic individuals. This is effected through early detection of sensitisation to workplace allergens and the presence and degree of impairment of target organs by medical surveillance of workers using questionnaires, SPT, serum-specific IgE, spirometry and other relevant tests to predict future anaphylaxis.

Tertiary prevention focuses on optimal management of a worker with work-related allergy and anaphylaxis to prevent further recurrences and disability. The aim is to reduce the risk of death or reduce the severity of an anaphylactic attack by issuing the worker with an EpiPen for self-administered intramuscular adrenaline injection and a Medic Alert bracelet, and ensuring fellow workers are trained in first aid procedures. Other strategies include removal from ongoing exposure, avoiding exposure to cross-reactive allergens and consumption of food containing the offending allergen or additive, medical monitoring, optimising allergy and asthma treatment, and immunotherapy where appropriate. For bee and wasp venom allergies, desensitisation by means of immunotherapy to hymenoptera venoms has been used with success.[31]

Declaration of conflict of interest

The authors declare no conflict of interest.

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ACUTE URTICARIA IN INFANCY

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Introduction

Urticaria, or hives, is a common disorder in the young child. The characteristic clinical finding in urticaria is a well-circumscribed, raised, erythematous plaque, which is typically evanescent and frequently shows central pallor. The lesions are usually very pruritic. The mast cell is the key cell in urticaria. Its activation causes the release of vasoactive mediators, predominantly histamine, leading to oedema in the superficial dermis. There are many causes of urticaria. However, in many cases the cause remains unknown. The causes of urticaria can be classified as IgE-mediated hypersensitivity reactions, chemically induced mast-cell degranulation, physical urticaria, arachidonic acid metabolism and complement-mediated reactions (Table I). It is important to differentiate urticaria from erythema multiforme, which shows epidermal necrosis, with the characteristic target-like appearance. While urticaria and angio-oedema (in which the oedema is largely in the subcutaneous tissue) are clinically distinct entities, they may be seen in the same patient, either concurrently or at different times during the illness.[1] Urticaria is defined as 'acute urticaria' if it lasts for less than 6 weeks and 'chronic urticaria' if it lasts for more than 6 weeks.

Table I. Common causes of acute urticaria in young children

Drugs
- Penicillins
- Cephalosporins
- Sulphonamides
- Non-steroidal agents
- Narcotics

Foods and food additives
- Milk
- Egg
- Peanut
- Nuts
- Soy
- Wheat
- Shell fish, fish

Infections
- Viruses – adenovirus, Epstein-Barr, enterovirus, Coxsackie
- Bacteria – *Streptococcus pyogenes, Escherichia coli*
- Parasites

Case report

A 6-month-old boy presented to the paediatric dermatology clinic with a 3-day history of a generalised body rash. Prior to this presentation, he had a 4-day history of symptoms suggestive of an upper respiratory tract infection for which he was given amoxycillin and a decongestant containing pseudoephedrine. Twenty-four hours later the rash appeared. He was also feverish and irritable. This was the first episode of such a reaction and he had previously used the medication without any adverse effects.

The child further developed conjunctivitis 1 day after the rash appeared. He had no other medical or dermatological history of note and had no known allergies. His mother is asthmatic.

On examination the child was stable. His temperature was 37.3°C and he had occipital and cervical lymphadenopathy. He had an extensive erythematous rash, which involved more than 80% of the total body surface area, including his scalp (Figs 1 & 2). He also had bilateral conjunctivitis without exudates and bright red lips. However, the oral mucosa was normal. A diagnosis of acute urticaria was made, due to either the

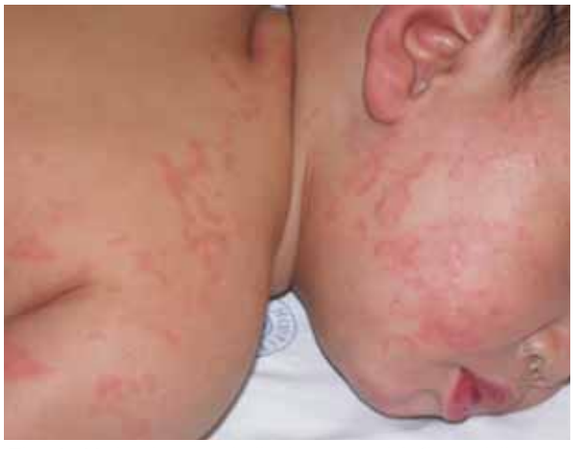

Fig. 1. Urticaria, nasal discharge and inflamed lips on presentation.

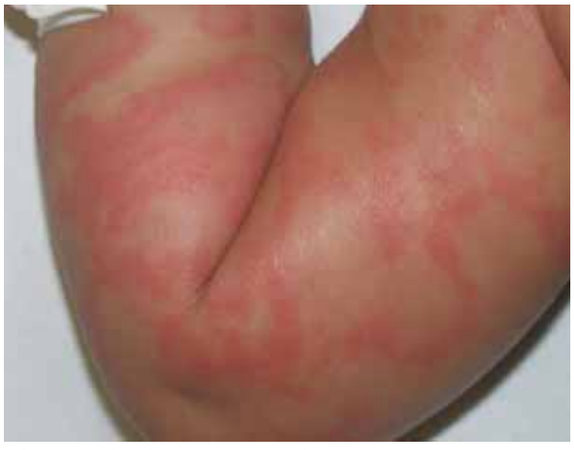

Fig. 2. Urticaria on presentation.

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infection or the amoxycillin or both, and all medication was stopped. In view of the bright red lips, extensive rash, conjunctivitis, fever and adenopathy, Kawasaki syndrome was also considered in the differential diagnosis; however the lack of hand oedema or desquamation, the short duration of fever and rapid clearing of the other clinical signs were thought to be against this diagnosis.[2] The child was admitted and treated with two antihistamine drugs (containing chlorpheniramine maleate and cetirizine dihydrochloride), erythromycin, paracetamol and oxymetazoline hydrochloride nasal drops.

Within the following 4 days the child's skin problem resolved almost completely, leaving a reticular appearance. (Fig. 3).

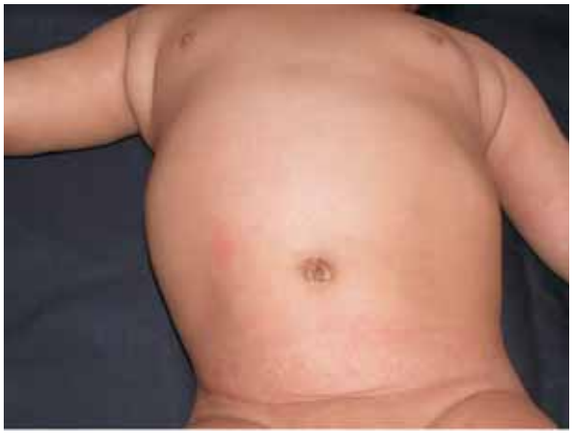

Fig. 3. Clearing of urticaria on day 4.

Discussion

In our case, a 6-month-old infant developed extensive urticaria 24 hours after starting treatment with amoxycillin for a respiratory tract infection. Possible causes for this skin eruption would include both the underlying infection and the therapy.

In a prospective hospital-based study of 56 children (0 to 36 months) with urticaria, Mortureux *et al*.[1] reported the commonest associations to be viral infection (18 cases) and medication (12 cases).[1] Our patient patient probably developed urticaria as a result of the respiratory infection, although the drug may have played a role itself. It may have been due to a combination of infection and therapy, as infection and drug exposure may act synergistically in some cases.

Pure drug allergy is relatively uncommon in young children, but may be commoner in older children.[3,4] In 6 children, food allergy was suspected and in others there were multiple possible causes, including the combination of presumed viral infection and drug therapy. Food allergy is relatively common in babies, but viral infection may again be a cofactor.[1,4] Mortureux *et al*.[1] found that the children with drug-induced urticarias developed the rash 6 to 10 days after starting with the therapy. Some of the children had used the drug previously yet this was their first skin reaction.

The drugs that most commonly cause an urticarial reaction in infants have been shown to be beta-lactam and sulphur-containing antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs may cause urticaria by altering the metabolism of arachidonic acid, which results in increased production and release of leukotrienes. NSAIDs are also implicated in causing angio-oedema.[5] Urticaria with angio-oedema is also relatively common in children with food allergy.

Treatment of urticaria

Medical management is required in the early stages, to alleviate symptoms, although the aim should be to identify and discontinue the offending agent in the case of food or drug allergy. Antihistamines are the mainstay of therapy and should be given in adequate doses to control the symptoms. The main groups of antihistamines commonly used in urticaria are shown in Table II. During the acute phase of the illness, one should give the antihistamines on a regular basis, according to half-life, rather than in response to the severity of symptoms.

First-line therapy should be a non-sedating long-acting H_1 receptor blocker[6] (see Table II). The approach to urticaria in general is dictated by clinical severity and response but one should add further agents until control is achieved, while continuing to try to identify the underlying cause. If a single agent does not control the symptoms, a second antihistamine such as one of the older sedating group may be added at night. There is no evidence to show that one antihistamine is superior to any other in this condition.[7] The addition of an H_2 receptor blocker such as cimetidine or ranitidine is common practice in chronic urticaria and is supported by a controlled trial.[8] Topical antihistamines and steroids have no role in the treatment of urticaria. Oral steroids are generally undesirable, except in the management of severe angio-oedema, as rebound urticarial weals tend to be a problem when the medication is withdrawn.

Table II. Antihistamine therapy for acute urticaria

(Add from each group incrementally if required)

Non-sedating H_1 receptor blocker

- Cetirizine
- Levocetirizine
- Loratadine
- Desloratidine
- Fexofenadine

Sedating H_1 receptor blocker

- Alkylamine, e.g. mepyramine, chlorpheniramine
- Phenothiazine, e.g. promethazine
- Piperazine, e.g. hydroxyzine
- Cyproheptadine

H_2 receptor blocker

- Cimetidine
- Ranitidine

Adverse effects such as drowsiness, dry mouth and urinary retention are frequent with the older sedating antihistamines, although less prominent in children, who may even show paradoxical restlessness and excitement with some antihistamines.

Angio-oedema in children with urticaria will usually respond to the same measures. However when angio-oedema affects the airway or is associated with shock, urgent emergency treatment is required, with adrenaline and intravenous fluids[9] (Table III).

Key points

- Infection is the commonest cause of acute urticaria in young children.
- Drug and food allergy may also occur or may have a synergistic effect.

Table III. Treatment of severe angio-oedema[9]

- Adrenaline (route depends on urgency)
- Intravenous fluids
- Antihistamine
- Steroids and salbutamol if bronchospasm associated (ventilation if inadequate response)
- Identification of cause and future prophylaxis

- First-line treatment is the identification of infection and use of a long-acting non-sedating antihistamine.
- Adrenaline and fluids are first-line treatment for angio-oedema.
- Corticosteroids are not indicated for urticaria or angio-oedema unless laryngospasm is present.

Declaration of conflict of interest

The authors declare no conflict of interest.

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ALLERGIES IN THE WORKPLACE

PHYSICAL URTICARIA PRESENTING AS CHOLINERGIC URTICARIA WITH DERMATOGRAPHISM

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ABSTRACT

About half of the cases of chronic urticaria in the general population are due to physical urticaria. The different types of physical urticaria are: acquired cold urticaria, delayed-pressure urticaria, solar urticaria, vibratory urticaria, urticarial dermatographism and cholinergic urticaria. Physical urticarias are not known to be related to specific occupations, but can present or be aggravated in any occupational setting. This holds true especially for cholinergic urticaria and delayed-pressure urticaria which are the commoner types found in occupational settings requiring heavy work.

Cholinergic urticaria presents clinically in young adults as extremely itchy, pinhead-size wheals on an erythematous background and is due to an increase in body core temperature.

A case of cholinergic urticaria with dermatographism in an underwater diver is presented and discussed.

INTRODUCTION

Urticarias are recognised by itchy, red wheals which develop rapidly and disappear in a short time, leaving skin appearance normal.

The physical urticarias present as localised or generalised urticaria/angio-oedema of the skin and/or mucosa in response to physical stimuli, which may be mechanical, thermal or solar.

Of the 50% of chronic urticarias caused by physical stimuli, dermographic urticaria is the most common, followed by cholinergic urticaria. Physical urticarias are most common in the young adult population between the ages of 16 and 35.[1] The precipitating factor is often not identified and the physical urticaria may persist for years, often resolving spontaneously. Only the rare, familial, autosomal-dominant urticarias persist lifelong.

In most cases urticaria is caused by direct mast-cell degranulation in response to the physical stimuli. Rarely a genetic predisposition to physical urticaria or an associated disease such as atopic dermatitis has been described.

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Specific occupations do not cause physical urticaria; however certain tasks involving heavy work have been associated with occupational cholinergic urticaria (Table I).

CASE REPORT

A 27-year-old underwater diver presented to the occupational dermatology clinic with a 2-year history of an intermittent, itchy, palpable, transient rash which resolved leaving no marks. It was most pronounced on the upper part of the body and the legs were relatively spared.

The patient had worked as a diver in the navy for 2 years prior to the development of the rash. His occupation involved significant, heavy manual labour underwater. He associated the rash with deep diving, hot showers and jogging, and on hot days it appeared in occlusive areas of the body such as around the waist. The rash would appear within 15 minutes of undertaking the triggering activity. The use of regular loratadine had kept the symptoms under control despite ongoing exposure to triggering factors. The patient also reported a lifelong allergy to pork and beef. There were no comorbid conditions.

On examination the patient was generally well and the skin was normal apart from linear discolouration corresponding to areas of scratching on the back.

Investigations showed a normal full blood count, and IgE of 205 (0-158 IU/ml).

A diagnosis of physical urticaria was made with a differential of cholinergic and heat-related urticaria.

An exercise-provocative test caused pinpoint follicular papules with surrounding erythema on scattered areas of the trunk (Fig. 1). Linear erythematous urticarial streaks were seen at sites of scratching (Fig. 2). Dermatographism was readily elicited (Fig. 3). Tests for hot and cold temperature provocation were negative after 20 minutes. A diagnosis of cholinergic urticaria with dermatographism was confirmed.

Table I. Epidemiological data on physical urticaria and related occupational activities

Urticaria (descending order of frequency)	Mean disease duration (years)	Occupational activities affected
Dermatographic urticaria	6.5	Heavy manual work
Cholinergic urticaria	5.3	Professions requiring physical exertion
Pressure urticaria	6.0	Heavy manual work
Cold urticaria	4.2	Outdoor work in the cold, freezing industry
Solar urticaria	7.1	Daytime outdoor work
Heat urticaria	1.0	Work in hot environment
Vibratory urticaria	NK	Work on vibrating machines

NK - Not known

(Modified from Kanerva *et al.*[1])

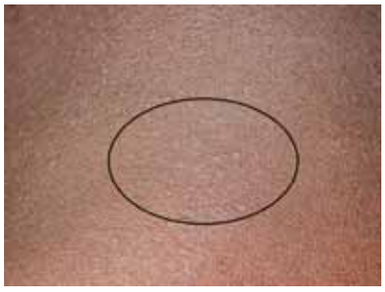

Fig. 1. Pinhead-size papules with surrounding erythema after exercise-provocation test.

Fig. 2. Wheal-and-flare reaction in scratched areas after exercise-provocation test.

Fig. 3. Dermatographism.

DISCUSSION

Cholinergic urticaria is a physical urticaria which is caused by stimulation of the cholinergic sympathetic innervation of sweat glands. The elicitation of symptoms corresponds to an increase of the body core temperature and not an external stimulus. The most frequent causes are a hot bath (69%), sweating (56%), physical exercise (47%) and emotional distress (20%). Sometimes warm or spicy food (9% and 2% respectively) or alcoholic beverages (9%) can also induce a transient rise in body core temperature.[2] People in occupations that require physical exertion that causes sweating are usually affected. A familial tendency has also been reported.[3] It may occur in combination with other physical urticarias such as dermatographism (whealing which is induced by shearing forces on the skin), as in our patient, and cold urticaria. Cholinergic urticaria has a prevalence of 11.2% among the young adult population.[4]

Cholinergic urticaria presents clinically as extremely itchy, pinhead-size wheals on an erythematous background. The lesions develop within 20 minutes of provocation, usually resolve within an hour and rarely persist up to 3 hours. Arms, upper chest, upper legs, back and abdomen are preferentially involved while the palms, soles and axillae are spared, most probably because of adrenergic sympathetic innervation in these areas. In most patients symptoms are mild and 80% do not seek medical advice.[5]

Associated systemic symptoms may include nausea, dizziness and headache and occur in up to 11% of patients.[5] Rarely rhinorrhoea, bronchospasm or gastrointestinal symptoms may occur. Hypotension and anaphylactic shock are extremely rare.

An associated increased incidence of bronchial reactivity on provocation[6] (e.g. exercise) and of atopy have also been observed (45.5%)[1] in cholinergic urticaria.

Diagnosis is usually not missed if a proper history is taken. It can easily be confirmed with provocative tests. Symptoms are provoked during exercise, e.g. climbing stairs, cycling and bending knees. False-negative results may be due to transient refractoriness, antihistamine or corticosteroid use or a cooling effect from evaporation of sweat. A metacholin skin test can also be performed as a provocation test by injecting 0.05 ml of 0.02% metacholin intradermally which elicits the urticarial response.

Exercise-induced anaphylaxis is the most common differential diagnosis, and occurs about 5-30 minutes after physical exertion, usually following intake of certain foods, particularly crab or celery. The wheals are larger and the symptoms persist for about 48 hours.[7,8]

Cholinergic urticaria is thought to carry a good prognosis. Spontaneous remission occurs within 5.3 years, as shown in Table I. Sometimes attacks can be aborted by immediate cooling like taking a cold shower. Non-sedating H_1 antihistamines are the treatment of choice as they suppress itching and whealing.[9] Depending on the severity, the antihistamine can either be taken daily or for prophylaxis before engaging in the activities that provoke the reaction. Severely affected unresponsive patients can be treated cautiously, off-label, with an anabolic steroid such as stanazolol or danazol.

RELEVANCE TO OUR PATIENT

Our patient manifested symptoms 2 years after starting his occupation as a clearance diver which involves removing obstructions underwater by use of explosives in order to make harbours and safety channels for ships. Our patient also reported dealing with heavy items when at work, as well as underwater mining and welding. No clear precipitant was identified. Although it is difficult to ascribe causality to his work environment, the cholinergic urticaria is aggravated by his occupation. It is important to weigh the risks of his continuing his occupation with or without antihistamine cover. There is a small risk of developing angio-oedema underwater. Chronic antihistamine use in a deep-sea diver may lead to drowsiness and disorientation underwater. The final decision should really be left to the patient after explaining all the pros and cons to him and his employers. The best and safest option would be to relocate him to alternative work until the urticaria resolves. He could then consider resuming diving.

Declaration of conflict of interest

The author declares no conflict of interest.

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EVIDENCE-BASED HEALTH CARE

INTRANASAL CORTICOSTEROIDS FOR NASAL AIRWAY OBSTRUCTION IN CHILDREN WITH ADENOIDAL HYPERTROPHY

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Aims

This feature on evidence-based health care (EBHC) aims to present useful practice-related information on topics relevant to readers of *Current Allergy & Clinical Immunology*. The treatment of topics is not comprehensive. The main aim is to illustrate selected aspects of the EBHC process viz. (i) identifying the best evidence and (ii) applying valid and relevant evidence in clinical practice. The box titled 'Some terms explained' enlarges on the technical terms mentioned in the text and marked with an asterisk (*).

Background

Adenoidal hypertrophy is generally considered a common condition of childhood. When obstructive sleep apnoea occurs, adenoidectomy is generally indicated. In less severe cases, non-surgical interventions may be considered; however, few medical alternatives are currently available. Intranasal steroids may be used to reduce nasal airway obstruction.

So what is the question?

What are the effects of intranasal corticosteroids on nasal airway obstruction in children with moderate to severe adenoidal hypertrophy?

The type of evidence to look for, and where to look for it

The best evidence will come from randomised controlled trials (RCTs). If more than one trial has been conducted, the most reliable evidence, if available, is a systematic review of all relevant RCTs. The Cochrane Collaboration (www.cochrane.org) conducts systematic reviews of the effects of healthcare interventions following rigorous methods and processes to reduce bias. You therefore first search *The Cochrane Library* (http://www.thecochranelibrary.com/) for a relevant systematic review.

What was found?

You find a recent systematic review examining the effects of intranasal corticosteroids on nasal obstruction in children.[1]

What did the authors do?

To minimise publication bias* the authors conducted a comprehensive literature search (general approach for a comprehensive literature search is summarised in Box 1) to identify both published and unpublished randomised controlled trials comparing intranasal corticosteroids with placebo or no intervention or other treatment in children aged 0-12 years with moderate to severe adenoidal hypertrophy.

Risk of bias of included studies was assessed independently by two authors.[2] Data were summarised in a narrative format.

Box 1. Approach to a comprehensive literature search to identify studies to include in a systematic review

Attempts must be made to identify all relevant studies regardless of language or publication status (published, unpublished, in press or in progress).[2]

The following sources are recommended:

1. Electronic searching of bibliographic databases using highly sensitive search strategies
2. Conference proceedings
3. Hand searching of relevant journals
4. Contacting individuals working in the field, organisations and pharmaceutical companies for unpublished and ongoing studies
5. Reference lists in other reviews, guidelines, included (and excluded) studies and other related articles should be searched for additional studies
6. Trials registers and trials results registers are important sources of ongoing trials.

Results

Five randomised trials (*N* = 349 children) were included. Two trials were randomised crossover trials.* Interventions included beclomethasone, mometasone and flunisolide. Four of the five trials found significant improvement in nasal obstructive symptoms and adenoid size in the group taking intranasal corticosteroids.

Implications for practice

Limited evidence suggests that intranasal corticosteroids may significantly improve nasal obstruction symptoms in children with moderate to severe adenoidal hypertrophy, and this improvement may be associated with a reduction of adenoid size. The long-term effect of intranasal corticosteroids in these patients remains to be defined.

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*Some terms explained

Publication bias: Publication bias refers to the publication or non-publication of research findings, depending on the nature and direction of the results. Positive results are consistently more likely to be published than negative results. To minimise this in a systematic review authors need to conduct comprehensive literature searches to identify eligible studies.[2]

Crossover trials: Crossover trials allocate each participant to a sequence of interventions. A simple randomised crossover design is an 'AB/BA' design in which participants are randomised initially to intervention A or intervention B, and then 'cross over' to intervention B or intervention A, respectively. Crossover designs offer a number of possible advantages over parallel group trials. Among these are that: (i) each participant acts as his or her own control, eliminating among-participant variation; (ii) consequently, fewer participants are required to obtain the same power; and (iii) every participant receives every intervention, which allows the determination of the best intervention or preference for an individual participant.[2]

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SECRETARY'S REPORT

This is a brief update on the ALLSA Excom activities during the past few months. One of the highlights during this period is the recent recognition by the Health Professions Council of South Africa (HPCSA) of allergology as a sub-speciality in paediatrics, internal medicine and specialist family medicine. This development will no doubt contribute towards the strengthening of training and more specialised service provision for patients with allergic diseases in the country.

Thanks to Robin Green who organised a very successful congress at Sun City in June. We were honoured to have two most distinguished international guests, Prof Thomas Platts-Mills (USA) and Prof Susan Prescott (Australia) and at the same time to celebrate ALLSA's 20th birthday! Ahmed Manjra is convenor of the next ALLSA Congress to be held in Durban in July 2008. This stand-alone congress will have a special focus on 'Anaphylaxis', 'Drug allergy' and 'Food allergy'.

We had two candidates who graduated with the Diploma in Allergology during the last round of exams held in Cape Town (May 2008) under the auspices of the Colleges of Medicine of South Africa. Congratulations to Drs Sarah Karabus and Nilen Chetty!

ALLSA Excom continues its work on developing the ALLSA governance charter, which will be finalised at the strategic meeting planned for January 2009. This is an important development as we bring the organisation's activities in line with its mission, constitution and public benefit organisation status.

On the research front, ALLSA research awards continue to fund allergy- and asthma-related research projects by South African researchers. To date ALLSA has funded over 60 researchers over the last 17 years, with awards in excess of one million rand! These research awards are highly competitive and sought after especially among researchers undergoing master's and doctoral level training. South African researchers continue to present their research at international meetings and win accolades for their work.

On the advocacy front, ALLSA has been involved in developing guidelines for appropriate allergy testing of patients and reviewing the guidelines for childhood asthma and allergic rhinitis.

A considerable amount of time has been spent on updating the membership database so as to ensure effective communication with paid-up members.

We would like to extend special thanks to Ruwayda Adams, Anne Hahn, Shahnaz Arnold and Jean April for their superb work in the Cape Town office and production of the ALLSA journal.

Congratulations to Heather Zar on her appointment as Chair of Paediatrics and Child Health, University of Cape Town, and Vice President of the South African Thoracic Society, and Paul Potter on his election to the Board of the World Allergy Organisation.

Mohamed Jeebhay
Honorary Secretary

ERRATA

We report a couple of gremlins from the August issue and offer our apologies.

In the article 'The history of the Allergy Society of South Africa (ALLSA) – 20 years of service' (p. 148), Prof Cas Motala's name was inadvertently omitted from the list of the first ALLSA Excom. He was co-opted to the Excom at the beginning of 1990 and served as treasurer for 18 months (1990-1991) on that committee.

In the article 'Fixed drug eruption' by Drs N Gantsho and NP Khumalo (p. 138), Nikolsky's sign and phenolphthalein were spelled incorrectly.

DON'T MISS THE

ALLSA CONGRESS

IN 2009!

See p. 191 for details

ALLSA RESEARCH AWARDS REPORT

PREVALENCE AND MOLECULAR EPIDEMIOLOGY OF HUMAN METAPNEUMOVIRUS IN INFANTS AND YOUNG CHILDREN WITH ACUTE LOWER AIRWAY OBSTRUCTION

Primary investigator

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ABBREVIATED SCIENTIFIC REPORT – SUMMARY

Introduction

Acute wheezing and asthma exacerbations in children are commonly precipitated by viral infections. Viruses that have been associated with acute wheezing include respiratory syncytial virus (RSV), rhinovirus, influenza viruses, parainfluenza viruses and enteroviruses. Recently human metapneumovirus (hMPV),[1] human coronavirus NL-63 (HCoV NL-63),[2,3] and human bocavirus (HBoV)[4] have been described, but their role as a trigger in acute wheezing has not been well studied.

Aim

The aim of this study was to investigate the prevalence of novel respiratory viruses, hMPV, HCoV NL-63 and HBoV, in young South African children with acute wheezing.

Methodology

A prospective study of children aged 2 months to 6 years sequentially presenting with acute wheezing at the ambulatory section of Red Cross Children's Hospital, South Africa from May 2004 to November 2005 (two winter seasons) was undertaken. Clinical and sociodemographic information was recorded.

Written, informed consent was obtained from a parent or guardian before a nasal swab was collected. A general shell vial culture using a pool of monoclonal antibodies detecting RSV, influenza A and B viruses, adenovirus and parainfluenza viruses 1, 2 and 3 was performed on every fifth sample by an indirect immunofluorescence assay. Further specific virus identification on pool-positive samples was not undertaken.

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RNA was extracted from the respiratory sample and a reverse-transcription polymerase chain reaction (PCR) followed by a nested PCR was performed targeting the fusion (F) and nucleocapsid (N) genes of hMPV and the 1b (protease) and 1a (RNA polymerase) genes of HCoV NL-63. The extraction procedure also coincidentally isolated DNA which could be used in the detection of the DNA virus, HBoV. A semi-nested PCR was performed targeting the NP-1 (non-structural) and VP1/2 (capsid) genes of HBoV. The PCR products of the hMPV N gene, HCoV NL-63 1a gene and the VP1/2 gene of HBoV were sequenced and phylogenetic trees constructed.

For statistical analysis continuous variables were expressed as median and inter-quartile ranges and compared using the Kruskal-Wallis test. Categorical characteristics were analysed using the Fisher exact test.

Results

Two hundred and thirty eight children were enrolled and 242 nasal swab samples were taken. The median (25th-75th percentile) age of children was 12.4 (6-25) months; 124 (52%) were under 12 months, while 174 (73%) were <24 months.

A novel respiratory virus was found in 44/242 (18.2.%) nasal samples, of which 36 (14.9%) were single infections. hMPV, HBoV and HCoV NL-63 were detected in 20 (8.3%), 18 (7.4%) and 6 (2.5%) samples respectively. Of 59 samples tested for other common respiratory viruses, 15 (25.4%) were positive; 4 of these were dual infections with one of the novel viruses. Dual viral infection was uncommon, occurring in 6/242 (2.5%) cases. However, 5/6 HBoV cases had associated viral co-infection, 3 with other respiratory viruses and 2 with hMPV. The novel respiratory viruses occurred predominantly in children under 2 years of age (38/44; 86.4%) as did other respiratory viruses (14/15; 93.3%). Moreover, infections with hMPV or HBoV were found predominantly in infants, in whom 16/18 (88.8%) hMPV and 9/13 (69.2%) HBoV cases occurred. HCoV NL-63 occurred in children of all ages.

Novel respiratory viruses were detected mainly in the autumn or winter seasons (28/44, 63.6%).

Most children presented with cough (83%), wheezing (83%) or rhinorrhoea (68%). Fever (39%) and gastrointestinal symptoms (23%) were less common. Symptoms were similar in children with and without viral infection.

The illness in most children was mild; only 11 children required hospitalisation, none in the intensive care unit. In 17/44 (38.6%) children this was the first wheezing episode; 15 (34.1%) had a history of two or more prior wheezing episodes.

Phylogenetic analysis showed that children were infected with hMPV and HCoV NL-63 from group A and B lineages. All HBoV positive samples clustered with HBoV strain st2.

Discussion

A novel respiratory virus was detected in 18% of young children with acute wheezing. hMPV was the most common novel virus followed by HBoV and HCoV NL-63. For comparison, in the subset of samples that were also tested for the other common respiratory viruses, 25% were positive. The viral detection rate was lower

than reported in other studies where viruses have been found in up to 90% of cases.[5-8] A number of factors may account for this including patient selection, methodology of viral detection, storage of samples, use of a subset for detection of common viruses and lack of testing for additional respiratory viruses such as rhinoviruses, cytomegalovirus (CMV), other coronaviruses or picornaviruses. Because of resource limitations, only a subset of specimens could be tested for a limited number of respiratory viruses. Furthermore, children with relatively mild illness were studied, which may also account for lower rates of viral identification as infection rates have been reported to be higher in wheezing children requiring hospitalisation compared with an ambulatory population.[9] Nevertheless, the study indicates that respiratory viruses, including the novel viruses, are an important trigger of acute wheezing in young children. Furthermore, this is the first report of the incidence of novel viruses in African children with wheezing.

The prevalence of hMPV is similar to that reported in other studies. In a Finnish study 8% of children with wheezing exacerbations had detectable hMPV.[10] A second study reported hMPV in 9% of wheezing children compared with 1% in a control group without wheezing.[6] Recurrent wheezing was a common diagnosis in almost half of hMPV-infected children compared with 24% in RSV-infected children.[11]

There is accumulating evidence that HBoV can trigger wheezing. Recent studies report HBoV infections in 5-6% of children hospitalised with acute wheezing, similar to the prevalence in our study.[7,8,12-14] In addition, dual viral infection, as occurred in 5 of 6 HBoV-infected children in our study, has previously been reported as a common feature of HBoV infection with co-infection rates ranging from 33% to 80%.[7,14-18]

There are few studies on the role of the newly described coronaviruses in children with acute wheezing although other coronaviruses, HCoV 229E and HCoV OC43, may play a minor role in asthma exacerbations.[5,9] In this study HCoV NL-63 was infrequently detected (2%), a similar rate to that reported from Korea where 1% of young children hospitalised with acute wheezing were HCoV NL-63 infected.[8] HCoV NL-63 infection has been more strongly associated with a clinical presentation of croup.[15,19,20]

The winter predominance of common respiratory and novel viruses is consistent with other studies.[10,12,14,16-18]

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SIGNIFICANT FINDINGS

- Respiratory viruses including the novel viruses are an important trigger of acute wheezing in young children.
- The common respiratory viruses were more frequently detected than the novel viruses (25% v.18%).
- This is the first report of the incidence of novel respiratory viruses playing a role in acute wheezing in young African children.

USEFULNESS OF FINDINGS

The identification of viral infections in young children presenting with acute wheezing is important as it may increase their risk for developing asthma in later life. This is particularly the case in children with persistent wheezing. In this study over a third of children had more than two episodes of wheezing. The low viral detection rate found in this study has resulted in an extension of the study to detect human rhinoviruses, a known trigger of wheezing and asthma exacerbations. Preliminary results show that over 50% of the study group have detectable human rhinovirus.

OUTPUTS

1. Smuts H, Workman L, Zar H. Role of human metapneumovirus, human coronavirus NL-63 and human bocavirus in infants and young children with acute wheezing. *J Med Virol* 2008; **80:** 906-912.
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ACKNOWLEDGEMENTS

We thank the research nurses Ms M Roux and Ms A Joachim as well as the virology laboratory staff at C18, Groote Schuur Hospital, for performing the indirect immunofluorescence and shell vial assays. We are grateful for the support from Dr S Qazi of the World Health Organisation (WHO) and from the staff in the ambulatory section of Red Cross Children's Hospital.

The study was supported by a grant from the WHO and by a GlaxoSmithKline research award from the Allergy Society of South Africa.

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The diagnostic value of IgE antibody measurements to peanut allergen components

Clinical background

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Useful diagnostic tests for food allergy are *in vitro* serum food-specific IgE assays, skin-specific IgE determination, basophil activation tests and oral food challenges.

Currently the only way to assess a peanut sensitisation is the use of native peanut extracts. Because of variability of the raw material linked to its origin and conditions of production and storage, investigators are confronted with a lack of standardisation of the material used both for *in vitro* and *in vivo* testing. Production of recombinant allergens is a promising way to obtain biological material with consistent and standardised properties and will enable further characterisation of the peanut-allergic patient.

Phadia has released a number of new recombinant allergens for peanut.

Utilising these recombinant allergens Ara h 1-3, rAra h 8, a Bet v 1-homologous panallergen, as well as nsLTP (rPru p 3), will be of value in the assessment of peanut allergy.

In particular, rAra h2 is of value in the identification of the high risk of systemic reactions.

- A positive peanut specific IgE and a negative rAra h 2 indicates risk of peanut allergy with severe and/or local reactions.
- A positive peanut specific IgE and a positive rAra h 2 indicates a high risk of peanut allergy with systemic and severe reactions.

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PRODUCT NEWS

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A fact of modern life is the increase in allergies, with more and more adults and children suffering from asthma, rhinitis and hay fever. Allergies are made worse by household pets, and dust mites in carpets, mattresses and soft furnishings. In response to the growing need for appliances that can help alleviate the problems suffered by allergy sufferers Miele have developed a number of features and accessories to ensure excellent levels of cleanliness in the home.

The S5281 MedicAir Vacuum Cleaner is supplied with all the features and accessories to meet the specific needs of allergy sufferers. The unit is equipped with an innovation that offers additional security and comfort; the Allergotec Sensor floorhead for visible hygienic cleanliness.

Miele offers a choice of three filters placed behind the motor. Because of the airtight design, any air leaving the vacuum cleaner only leaves via the final filter. The **Miele Super AirClean filter** removes nearly 94% of the particles as small as 0.3 µ and, for this reason is the most suitable for everyday households. The **Miele Active AirClean filter** incorporates the Super AirClean filter and is designed for customers who have to vacuum up items with unpleasant odours. A tight-fitting filter cassette with a rubber seal prevents any air escaping. The active charcoal component absorbs and neutralises odours. The **Miele Active HEPA filter** solves the problems of allergy sufferers. The Active HEPA filter retains 99.5% of particles.

For the true pet lover – the S5261 in Capri Blue and S5361 in Tayberry Red are Miele's Cat & Dog range of vacuum cleaners. Stubborn pet hairs do not stand a chance with the Miele Cat & Dog's Turbo Brush. This special floorhead is driven by the suction of the cleaner and rotates evenly to pick up hair and dirt from most types of carpets, while the smooth running floor head SBD takes care of most hard floor surfaces. The Miele Cat & Dog vacuum cleaner is specially fitted with an ActiveAirClean filter. The activated charcoal filling ensures any smell arising from the contents of the dustbag is absorbed before it leaves the cleaner and that the exhausted air is always fresh too.

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FURTHER ACCEPTANCE FOLLOWS GLAXOSMITHKLINE'S SERETIDE PRICE REDUCTION

GlaxoSmithKline's decision to reduce the price of its flagship asthma medication, Seretide, is showing encouraging signs of success. Seretide is used in the treatment of chronic asthma and was already one of the most prescribed chronic medications in South Africa at the time of the 20% price reduction. Medical schemes, as well as medical practitioners and healthcare professionals, are also starting to adopt Seretide as the medication of choice, now that it is more affordable. Medical institutions are following suit and the cumulative effect is that more and more chronic asthma sufferers in South Africa are gaining access to the medication.

Following the price reduction, one of South Africa's leading medical aid schemes, Medscheme, included Seretide in its Restrictive Formulary from 1 February 2006. The result is that all Medscheme-administered asthma patients now have access to Seretide. Restrictive formularies are primarily used to determine prescriptive needs of the lower to middle income groups, which means that the use of Seretide is likely to be extended to asthma sufferers who previously would have had no means of gaining access to the medication. In the light of the Department of Health's drive towards creating lower income medical schemes, the inclusion of Seretide in a major health scheme's Restrictive Formulary gains extra significance. It is still too early to ascertain the extent to which chronic asthma sufferers in previously disadvantaged communities are now able to acquire Seretide, but as time elapses this should become easier to determine.

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PRODUCT NEWS

NEW DESIGN FOR SYMBICORD

AstraZeneca is proud to introduce a new design for Symbicord boxes and packaging. The purpose of the packaging change is to standardise the colours and design globally, so that wherever in the world you may be, the Symbicord packaging will look the same.

In line with these changes, we are also keeping these colours for our promotional and educational material, so that the design is standardised throughout. The new look is bold, positive, professional and modern, with an emphasis on clinically relevant and clear information. The approach is future-focused, to reflect the constant innovation and challenging of conventions that is the basis of our approach to medicine at AstraZeneca.

Please note that the ingredients and doses of Symbicord will remain the same.

In conjunction with the new look, AstraZeneca intends to introduce user-friendly educational and support material to assist and support people with asthma.

The new material is aimed at providing the busy physician and his/her patients with the tools that they need so that people with asthma can take responsibility for their own asthma control.

S 3 **Symbicord® Turbuhaler® 80:4,5 µg/dose (Inhaler),** Reg No. 35/21.5.1/0404. Each delivered dose contains as active constituents: Budesonide 80 micrograms and formoterol fumarate dihydrate 4,5 micrograms.

S 3 **Symbicord® Turbuhaler® 160:4,5 µg/dose (Inhaler),** Reg No. 35/21.5.1/0405. Each delivered dose contains as active constituents: 160 micrograms and formoterol fumarate dihydrate 4,5 micrograms.

S 3 **Symbicord® Turbuhaler® 320:9 µg/dose (Inhaler),** Reg No. 38/21.5.1/0187. Each delivered dose contains as active constituents: Budesonide 320 micrograms and formoterol fumarate dihydrate 9 micrograms

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HEALTHWAY EMF AIR PURIFIER

World's most advanced medical grade air purifiers

Studies have shown that indoor pollution is five times more dangerous than outdoor pollution and we spend 90% of our time indoors. It seems we live in an environment tailored to creating allergy sufferers.

One of the best ways to combat allergies is to remove airborne allergens in the first place. Until recently, this was not possible for the average man on the street as it required expensive, advanced equipment.

Healthway has pioneered the quest for smaller air purification units that are packed with all the required technology but packaged into an affordable product.

The Healthway EMF Air Purifier is one of the most advanced air purification systems in the world. It is certified by FDA as a class 2 medical device and defined as a medical air purification system.

Independent laboratory testing certified that bacteria were reduced by 98-100%, virus by 99-100% and mould and fungi by 94-100%.

The system includes dual cleanable pre-filters for larger particulate collection. It also includes 4 pounds of granule carbon and zeolite filter for high-capacity multiple gas/chemical scrubbing.

The EMF system is 99.97% efficient at collecting 0.3 microns size particulate. The 12 inch diameter EMF filter is 100% sealed so no air can bypass around the filter, to ensure 100% of the air passing through the system is treated by the EMF germ-killing zone.

H2O International is proud to be the exclusive distributor of this product. With a 13-year history of great service,

over 70 branches nationwide and a central warehouse stocked with maintenance staff and parts, you can rest assured that you are buying from a well-established company that can back you up on any after-sales service you may need.

Call H2O toll free on 0800 492 837 and receive a free indoor quality test valued at R495.00.

PRODUCT NEWS

BOEHRINGER INGELHEIM LAUNCHES THE NEW INFLAMMIDE® 200 NOVOLIZER®

The prevalence of asthma is continuing to rise throughout the world and South Africa. Guidelines still recommend inhaled corticosteroids as the cornerstone of asthma therapy.[1] Despite the availability of numerous treatments the disease remains poorly controlled.[2]

Inappropriate and incorrect use of inhaler devices contribute to the lack of adequate asthma control; **71%** of patients misuse their MDIs and up to **47%** of patients cannot co- ordinate on activation and inspiration.[3] It is now well recognised that improvement in drug delivery will continue to be paramount in improving asthma management.[4]

Boehringer Ingelheim has launched the new **Inflammide® 200 Novolizer®**. This product combines the proven efficacy of **Inflammide® 200** with the innovative technology of the **Novolizer®** delivery system.

The Inflammide® 200 Novolizer® is designed in such a way that it is virtually impossible to use incorrectly, closely meeting the characteristics sought in an 'ideal' inhaler. [5]

The Inflammide® 200 Novolizer® is breath actuated and can only be successfully activated once the threshold PIFR of 35-50 litres/min is generated. At this level the complete dose is delivered to the patient. The Novolizer® has a triple feedback that tells the patient when each dose has been successfully inhaled,[5] thus optimising dosing.

In healthy volunteers the median lung deposition of budesonide administered via the Novolizer® was 19.9 - 32.1% at mean PIFR of 45 - 90 litres/min.[6]

The Inflammide® 200 Novolizer® contains 200 µg of budesonide per inhalation in a 200-dose cartridge. The product will be available in 2 forms:

- The **Inflammide® 200 Novolizer® Complete** which contains the Novolizer device and a cartridge.
- The **Inflammide® 200 Novolizer® refill** which contains the cartridge only.

In line with the Montreal Protocol manufacturers were compelled to switch their asthma inhalers, which contain CFC propellants, to more environmentally friendly products by December 2005. The Inflammide® 200 Novolizer® is a multidose dry powder inhaler (MDPI) and does not contain any propellants, making it not only patient-friendly but environmentally friendly too.

The Inflammide® 200 Novolizer® offers substantial advantages over metered dose inhalers making it an ideal replacement product for patients using budesonide MDIs.

For further information please contact Greg Zurnamer (Inflammide® 200 Novolizer® product manager) at 011-886-1075 or e-mail: zurnamer@jnb.boehringer-ingelheim.com

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Managing the Allergic Patient

John H. Krouse, M. Jennifer Derebery, and Stephen J. Chadwick
2008, hardcover, 400 pp, 300 illus., 265 x 195 mm, R1 850
This new reference provides up-to-date, disease-specific diagnostic and treatment protocols in a new, full-colour, heavily illustrated reference. This is the most current allergy management information at your fingertips – regardless of your medical specialty.

Key features

- The most up-to-date guidance from trusted experts in the field.
- Quickly locate key anatomy, tests, and management protocols in the clinical setting.
- Find everything you need in one place with diagnosis and management included in each chapter.
- Compare common presentations and quickly reference the latest in diagnosis and treatment options with over 300 clinical and diagnostic algorithms, photographs, charts, and tables.

Contents: 1 – Introduction to Allergy. 2 – Principles of Allergy Management. 3 – Management of the Patient with Rhinitis. 4 – Management of the Patient with Rhinosinusitis. 5 – Management of the Patient with Asthma. 6 – Management of the Patient with Ocular Allergy. 7 – Otitis Media: Background and Science. 8 – Management of the Child with Otitis Media. 9 – Management of the Patient with Inner Ear Allergy. 10 – Management of the Patient with Laryngitis. 11 – Management of the Patient with Drug Allergy. 12 – Management of the Patient with Occupational Allergy. 13 – Management of the Patient with Atopic Skin Disease. 14 – Managing the Allergic Child. 15 – Management of the Patient with Anaphylaxis.

Orders: Jackie Strydom of the Medical Bookseller Tel 083 303 8500 Fax (021) 975-1970

PRODUCT NEWS

SINGULAIR 4mg
(montelukast sodium, MSD)

MSD (Pty) Ltd is proud to announce the introduction of SINGULAIR 4 mg. Studies have shown that asthma in children under the age of six is on the increase worldwide.[1] SINGULAIR 4 mg is the first asthma controller therapy, that is not a steroid, to be approved in South Africa for children as young as 2 years old.[2]

Studies have shown improvements in symptom and activity scores from as early as day one, affirming the efficacy of SINGULAIR 4 mg in this age group.[3] The current guidelines for treatment of asthma in children, as compiled by the Allergy Society of South Africa (ALLSA), call for the introduction of a leukotriene antagonist as a controller agent in this age group at step 2, after the use of short-acting reliever medication has proven to be inadequate in controlling asthma symptoms. In other words using leukotriene antagonist as a first line controller agent.[4] At present, of the leukotriene receptor antagonists, only SINGULAIR is indicated for use in children under the age of 12.[2]

SINGULAIR 4 mg is indicated for the prophylactic treatment of mild to moderate asthma in the 2-5 year old age group. SINGULAIR 4 mg is presented in a 28-day pack and one tablet should be taken once daily at bedtime.[2] To date worldwide use is more than 2.2 million children in more than 90 countries. This puts SINGULAIR in the unique position of being the only controller therapy to be registered and indicated for asthmatic patients from 2 years old and up.[2]

The FREEDOM to be a Child!

REFERENCES:

1 Ehrlich, R. The Prevalence of Asthma in South Africa. *Current Allergy and Clinical Immunology* March 2002; Vol 15: 4-8.

2 Data on File.

3 Knorr B, Franchi LM, Bisgaard H, *et al.* Montelukast, a leukotriene receptor antagonist, for the treatment of persistent asthma in children aged 2 to 5 years. *Pediatrics* 2001;**108**(3):1-10.

4 Motala C, Kling S, Gie R, *et al.* Guidline for the management of Chronic Asthma in Children – 2000 Update. *SAMJ.* 2000; **90**: 524-539.

MSD (Pty) Ltd (Reg. No. 1996/003791/07), Private Bag 3, Halfway House 1685.

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Reg. No: 35/10.2.2/0397, SINGULAIR 4 mg S3

MSD

Foratec HFA

Foratec HFA is another exciting addition to Cipla's range of respiratory products, emphasising our commitment to offering solutions for Total Asthma Control!

Foratec HFA (formoterol fumarate 12µg) is:

- a long-acting β_2-agonist, giving up to 12 hours bronchodilation[1]
- as fast-acting as salbutamol,[2] between 1-3 minutes[1]
- the only available formoterol fumarate MDI
- a 120-dose MDI; 2 months' supply (at 1 puff b.d.)
- CFC-free, re-enforcing our global commitment to preserving our planet within our sphere of influence
- indicated as add-on therapy to inhaled corticosteroids in patients with chronic persistent asthma (GINA step 3)[3] and for prophylaxis and treatment of symptoms in patients with COPD[1],
- priced at R69.60 SEP (excl VAT), the most cost-effective long-acting β_2-agonist in SA![5]

Isn't this enough reason to prescribe **Foratec HFA**?

Cipla offers you **Total Asthma Control through choice of molecules, choice of devices and a choice to treat cost-effectively!**

Prescribing information available on request. Please contact Beverley Kruse on 021-917-5620.

1. Foratec HFA Package Insert
2. Van Noord J, *et al*. Salmeterol versus formoterol in patients with moderately severe asthma: onset and duration of action. *Eur Respir J* 1996; **9:** 1684-1688
3. Asthma Guidelne Iimplementation Project. Primary care management of adults with chronic asthma. Revised 2006. *SA Family Practice Journal.* June 2007; **49:** 19-31
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5. SEP (excl. VAT) as per PCD, July 2008

PRODUCT NEWS

NASONEX IS NOW INDICATED FROM THE AGE OF 2 YEARS!

Nasonex Aqueous Nasal Spray is indicated for use in adults, adolescents and children between the ages of 2 and 11 years to treat the symptoms of seasonal allergic or perennial allergic rhinitis.

In patients who have a history of moderate to severe symptoms of seasonal allergic rhinitis, prophylactic treatment with Nasonex Aqueous Nasal Spray is recommended prior to the anticipated start of the pollen season.

Dosage and directions for use

Adults and adolescents: The usual recommended dose for prophylaxis and treatment is two sprays (50 µg/spray) into each nostril once daily (total dose 200 µg). Once symptoms are controlled, dose reduction to one spray into each nostril (total dose 100 µg) may be effective in some patients for maintenance.

Children between the ages of 2 and 11 years: The usual recommended dose is one spray (50 µg/spray) in each nostril once daily (total dose 100 µg).

For more information contact
Gary Vine,
Schering-Plough (Pty) Ltd,
011-922-3300.

Schering-Plough
Complete Allergy Control

PIMECROLIMUS CREAM 1% IN ATOPIC DERMATITIS: A 6-MONTH, OPEN-LABEL TRIAL IN PAEDIATRIC PATIENTS

Pimecrolimus, a new, non-steroid, inflammatory-cytokine inhibitor, has been shown to prevent progression to flare in atopic dermatitis (AD) and to improve long-term disease control when applied as a 1% cream. In this 6-month, open-label, multinational study, 177 infants aged 3-23 months and 489 children aged 2-17 years, with mild to severe AD, were included. The study was designed to evaluate the efficacy and safety of pimecrolimus cream 1% used as a first-line treatment. Treatment consisted of an initial bid regimen, for as long as signs and symptoms of disease persisted; this was followed by treatment as required at the first signs and symptoms of AD. Emollients were allowed as per the physician's normal practice, and topical corticosteroids could be used to treat severe flares at the discretion of the physician. Efficacy was assessed by evaluations of pruritus, and total-body and facial Investigators' Global Assessment (IGA). Results from the first return visit (day 7) showed an improvement from baseline of ≥ 1 in total-body and facial IGA for infants (59.1% and 72.8% of patients, respectively) and children (59.3% and 62.2%, respectively). Pruritus was absent or mild in 67.8% and 65.4% of infants and children, respectively. This level of improvement in the patient population was maintained throughout the 6-month study. Adverse events occurred in 75.7% of infants and 71.1% of children. Most adverse events were common childhood illnesses that would be expected in this population (e.g. nasopharyngitis (infants 22.0%, children 12.8%), upper respiratory tract infection (infants 18.6%, children 11.9%) and cough (infants 8.5%, children 10.1%)). Concerning pimecrolimus's local tolerability, application-site burning occurred in 2.3% of infants and 7.0% of children, and local pruritus occurred in 0.6% infants and 1.0% children. Application-site reactions were most frequently reported during the first 6 weeks of treatment and were mild to moderate in intensity. In conclusion, pimecrolimus cream 1% was effective in the treatment of the early signs and symptoms of AD (including pruritus) in infants and children, and demonstrated a good safety profile.

Reference available on request. Contact Thoko Nzama, 011-929-9111

NOVARTIS

CPD QUESTIONNAIRE

Earn 2 CPD points after you have read the journal by completing the following questionnaire online on the ALLSA website at www.allergysa.org/cpd or follow the links from the home page. To earn points, you will need to register and fill in personal details (make sure you have your HPCSA number handy and decide on a password beforehand). Once you have registered, you can answer the questionnaire. If you have registered for a previous questionnaire, you'll need your HPCSA number and password to logon. Please note that there is only one correct answer per question, and you will have only one opportunity to submit the questionnaire, so please check answers carefully. You will be able to change answers if you click the wrong one by mistake, but once you click 'Submit Answers' the test will be submitted and marked.

Points will be submitted electronically to the HPCSA.

The closing date for submission of this questionnaire is 31 March 2009.

ANAPHYLAXIS IN THE PAEDIATRIC ICU

1. **True or false:** Mortality from anaphylaxis in paediatrics is more common in young children.
   a) True
   b) False
2. **True or false:** Injectable adrenaline is the treatment of choice for severe upper airway obstruction as a result of anaphylaxis.
   a) True
   b) False
3. **Choose ONE correct answer:** The most common cause of anaphylaxis in young children is:
   a) penicillin
   b) bee stings
   c) food
   d) cephalosporins
4. **Choose ONE correct answer.** The link between sudden infant death syndrome (SIDS) and allergy is postulated to be:
   a) house-dust mites in the mattress
   b) prone sleeping
   c) gastro-oesophageal reflux
   d) anaphylaxis to inhaled regurgitated milk

ANAESTHETIC ASPECTS OF CUTANEOUS MASTOCYTOSIS

1. **True or false:** Cutaneous mastocytosis in a 6-month-old child may present as a reddish-brown macular rash on the trunk.
   a). True
   b) False
2. **True or false:** Pethidine and codeine are safe analgesics to use in patients with cutaneous mastocytosis.
   a) True
   b) False
3. **True or false:** Pre-operative administration of corticosteroids and COX2 inhibitors are the therapy of choice to reduce the risk of peri-operative anaphylaxis in cutaneous mastocytosis.
   a) True
   b) False
4. **Choose ONE correct answer:**
   a) During anaesthesia muscle relaxants with the least tendency to cause histamine release should be selected.
   b) An adrenaline infusion should be commenced before any potential triggering agents are administered.
   c) Intravenous access and full resuscitation measures are only necessary for patients with a severe form of the disease.
   d) NSAIDs are strictly avoided in patients with prostaglandin-induced flushing.

ANGELINA ANGIO-OEDEMA

1. **True or false:** A positive skin-prick test indicates an IgE-mediated allergic response to the allergen being tested.
   a) True
   b) False
2. **True or false:** The RAST (radioallergosorbent test) is a blood test that measures an IgE-mediated allergic response to a specific allergen.
   a) True
   b) False
3. **True or false:** The CAST (cellular antigen stimulation test) can be used to detect sensitivity to preservatives, drugs and additives.
   a) True
   b) False
4. **True or false:** Angio-oedema is characterised by swelling caused by oedema of the skin, mucous membranes and subcutaneous tissues.
   a) True
   b) False

WORK-RELATED ANAPHYLAXIS

1. **True or false:** Reduced blood pressure (BP) (>30% from the person's baseline or BP <90 mmHg) in response to a known occupational allergen is sufficient to diagnose occupational anaphylaxis.
   a) True
   b) False
2. **True or false:** Chemical substances, especially irritant gases, are the most common cause of occupational anaphylaxis.
   a) True
   b) False
3. **True or false:** Antihistamines administered in the initial management of anaphylaxis are strongly associated with a beneficial health outcome.
   a) True
   b) False

ALLERGIES IN THE WORKPLACE: CHOLINERGIC URTICARIA

1. **True or false:** Cholinergic urticaria is due to local increase of body temperature.
   a) True
   b) False
2. **True or false:** Cholinergic urticaria can present in young people who are in occupations requiring strenuous physical work.
   a) True
   b) False
3. **True or false:** A very small percentage of chronic urticaria is due to physical urticaria.
   a) True
   b) False

SKIN FOCUS - ACUTE URTICARIA IN INFANCY

1. **Choose ONE correct answer:** Urticaria in young children is commonly associated with:
   a) Vasculitis
   b) Viral infection
   c) TB drugs
   d) Allergy to latex
   e) Meningitis
2. **Choose ONE correct answer:** The best treatment for acute urticaria is:
   a) Skin-prick testing followed by topical steroids
   b) Oral steroids
   c) Adrenaline
   d) Avoidance of nuts, milk and eggs
   e) Non-sedating antihistamines

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