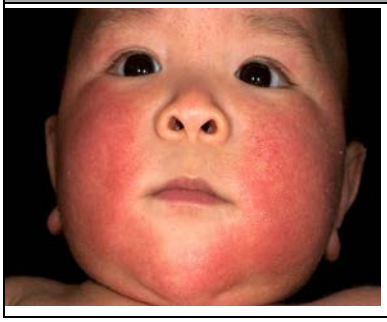
CASE THREE

Short case number: 3_20_3
Category: Children & Young People/ Respiratory & ENT Systems
Discipline: Paediatrics Medicine
Setting: General Practice
Topic: The atopic child.

Case



Christina Chang is a 9 month old girl who presents with her Father Eric. He is concerned that the rash on Christina's face [see picture] is getting worse and he thinks that it is itchy because she is often rubbing her face and eyes.
They have had to put cotton mittens on her hands because she often scratches herself.
He states that he has been told that her rash is because of allergy and asks you what she is allergic to.

Questions

1. Explain atopy and allergy to Christina's father.
2. In order to further explore the presence of atopic illness, what are the key components of your history and examination of Christina?
3. What are they key allergens that you would enquire about in your assessment of Christina?
4. Detail the key clinical features of atopic illness and describe the underlying pathophysiology.
5. Eric mentions that Christina's mother has recently purchased new bedding and a special vacuum cleaner to help stop dust mites, he asks you if you think this will help. What would you explain to him about these and other dust mite reduction methods?
6. Eric mentions that Christina often has a runny nose and mother has hay fever. He asks if they should use the nose spray like her mother does. Explain the use and mechanism of action of the nasal sprays used in the management of allergic rhinitis.
7. Outline the mechanism of action and side effects of the following medications used in the management of allergic illness, antihistamines, sympathomimetics, theophylline, cromolyn, corticosteroids and leukotriene agonists.

Suggested reading:

- South M, Isaacs D editors. Practical Paediatrics. 7th edition. Edinburgh: Churchill Livingstone; 2012.
- Australian Medicines Handbook Pty Ltd. Australian Medicines Handbook 2009. https://amhonline.amh.net.au/

ANSWERS

1. Explain atopy and allergy to Christina's father.

Atopy is defined as the ability of an individual to form specific IgE antibodies to one or more common inhaled aeroallergens such as animal dander, pollen, mould or house dust mite. The clinical expression associated with this immune dysregulation may be an atopic disease, which includes:

- atopic dermatitis
- asthma
- allergic rhinoconjunctivitis.

Although atopy is defined by an excessive production of IgE, this is only one of many immunological changes that characterize the condition, which is associated with a complex dysregulation of the humoral and cellular immune systems. For this to occur, both a genetic predisposition and early life environmental allergen exposure are important. Central to this understanding is that naive T helper lymphocytes respond in a particular way to an allergen by secreting specific cytokines that regulate the production of IgE. Continued allergen exposure initiates the allergy cascade, in which there is an early and late response. This occurs in cells located in the skin, respiratory tract, gastrointestinal tract and the vascular system; the end result in some individuals is an atopic disease.

2. In order to further explore the presence of atopic illness, what are the key components of your history and examination of Christina?

The history and examination should cover the following aspects:

- Specific symptoms - Nature, timing (seasonal, perennial, episodic), situational (specific site or circumstance)
- Severity of symptoms and degree of disability - Medication required to control symptoms, medical visits and hospitalisation, school absenteeism, interference with sleep, sport or play
- Use of medication - Current and past medications, efficacy, compliance, technique of use and side effects
- Environmental history - identification of triggers:
    - exposure to common allergens and non-allergen (e.g. cigarette smoke) triggers should be considered
    - a trigger may be easily identified if the onset of symptoms is acute and occurs soon after exposure, if symptoms occur in a specific geographic location, are seasonal, or occur repeatedly following similar exposures
    - a trigger may be difficult to identify when continuous exposure results in chronic symptoms
    - identification of possible triggers requires knowledge of the likely circumstances of allergen exposure.

On examination atopic children may have atypical examination findings:

Growth	Weight
	Height
Facies	Facial pallor
	Allergic shiners - infraorbital dark circles due to venous congestion

	Dennie-Morgan lines - wrinkles under both eyes
	Mouth breathing
	Dental malocclusion - from long-standing upper airway obstruction
	Sinus tenderness
Skin	Atopic dermatitis
	White dermatographism - white discoloration of skin following physical pressure
	Xerosis - dry skin
	Urticaria and/or angio-oedema
Nose	Horizontal nasal crease
	Inferior nasal turbinates - pale and swollen
	Clear nasal discharge
Respiratory	Chest deformity - Harrison sulcus, increase in anteroposterior diameter
	Respiratory distress
	Wheeze and/or stridor
Eyes	Conjunctivitis
	Subcapsular cataracts associated with conjunctivitis
Ears	Tympanic membrane dull and retracted
Throat	Tonsillar enlargement
	Postpharyngeal secretions and cobblestoning of mucosa
Cardiovascular	Blood pressure

3. What are they key allergens that you would enquire about in your assessment of Christina?

Allergens that may trigger symptoms in atopic children

Inhaled allergens

- Animal dander - cat, dog, horse, rabbit
- Pollen - grass (rye, couch, timothy), weed (plantain), tree (olive, plane)
- Mould - *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium* spp.
- House dust mite - *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*
- Cockroach

Ingested allergens

- Food - cow's milk, egg, nuts, fish, shellfish, soy, wheat, fruit
- Medication - antibiotics (penicillin) and non-antibiotic medication

Miscellaneous

- Latex contained in balloons and surgical gloves

4. Detail the key clinical features of atopic illness and describe the underlying pathophysiology.

Atopic dermatitis

Atopic dermatitis is a chronic inflammatory skin disorder that is associated with filaggrin deficiency, overproduction of IgE and eosinophils due to a systemic Th2 cytokine response. Histamine, neuropeptides, proinflammatory cytokines, mast cells, eosinophils and antigen-presenting cells are all increased in skin affected by atopic dermatitis. The cardinal features of atopic dermatitis include:

- intense pruritus
- a relapsing course
- a typical distribution of skin rash
- a personal or family history of an atopic disease
- additional features that may be present:
    - dry skin (xerosis), skin infection, white dermatographism
    - other atopic diseases and atopic facies
    - food allergy and intolerance.

Asthma

Asthma is defined as a chronic inflammatory lung disorder that is usually associated with bronchial hyperactivity and presents as a symptom complex of cough, wheeze and shortness of breath.

Although the exact cause of asthma is not known, the two most significant risk factors are a family history and atopy. Specifically, between 60% and 80% of asthmatic children are atopic. Furthermore, sensitization to indoor allergens (house dust mite and cockroach) combined with exposure to high levels of these allergens is an important risk factor associated with symptomatic asthma. The implication is that exposure to indoor allergens may contribute to the development of asthma and that ongoing exposure or intermittent exposure may be a trigger factor for asthma.

Allergic Rhinoconjunctivitis

The primary functions of the nose are olfaction and air filtration and humidification. This is achieved by the nasal structure, which ensures that inhaled air is in contact with an extensive and highly vascular mucosal membrane. In sensitized individuals, mucosal contact with inhaled allergens in the nose and conjunctiva elicits IgE-mediated mast cell degranulation and a chronic inflammatory response.

The history should determine the specific symptoms, as the presentation is quite variable, with either rhinitis or conjunctival symptoms predominating:

- The symptoms of rhinitis are nasal obstruction, itch, sneezing and rhinorrhoea
- Conjunctival symptoms include itching and an increase in tear fluid.

The timing of symptoms provides important information concerning possible triggers. Symptoms may be seasonal, perennial, a combination of perennial and seasonal or episodic:

- Symptoms during spring, summer or autumn indicate seasonal allergic rhinoconjunctivitis, which may be triggered by pollen (grass, weed or tree) or mould
- Perennial symptoms may be due to indoor allergens (house dust mite, animal dander, cockroach)

- Episodic symptoms are most often due to exposure to animal dander but may occur in response to other allergens.

Examination of the nose and eyes is important:

- Nose: The inferior nasal turbinates being pale and swollen. When severe, the swollen nasal turbinates may extend to the nasal septum and may be mistaken for nasal polyps, which are uncommon in children. Typical findings may not be present.
- If nasal obstruction is the main symptom, it is important to exclude an anatomical cause

- Eyes: Conjunctival injection and oedema affect both the bulbar and tarsal conjunctiva and appear as redness and swelling.

5. Eric mentions that Christina's mother has recently purchased new bedding and a special vacuum cleaner to help stop dust mites, he asks you if you think this will help. What would you explain to him about these and other dust mite reduction methods?

Allergen identification and avoidance remains an important component of management. Avoidance measures may involve considerable parental education, effort and expense. Note that:

- with ingested allergens identification and avoidance are particularly important when atopic disease is associated with a food allergy, as this is the only means of therapy
- with inhalant allergens, methods have been evaluated to reduce exposure to indoor allergens, most importantly the house dust mite. A number of studies in sensitized individuals have demonstrated improvements in atopic dermatitis and allergic rhinitis following house dust mite reduction measures. The benefit of house dust mite avoidance in asthma is much more controversial
- other indoor allergens (cat, cockroach, mould) and outdoor allergens are less easily avoided and alternative forms of therapy may be required.

Methods to reduce house dust mite exposure

Definitely useful
• Encase bedding in impermeable covers (dust mite covers): most important measure, since the bed is the major source • Hot water washing of bedding and clothes (>56°C): will destroy house dust mite and remove allergens
Probably useful
• Replacement of fitted carpets with smooth flooring • Hard-surface cleaning with a damp cloth, at least once a week
Possibly useful • Air filtration, ionizers and air conditioning
Unlikely to be useful • Acaricides (dust mite sprays) for the carpet and mattress

6. Eric mentions that Christina often has a runny nose and mother has hay fever. He asks if they should use the nose spray like her mother does. Explain the use and mechanism of action of the nasal sprays used in the management of allergic rhinitis.

Topical nasal corticosteroids are most effective for nasal obstructive symptoms but also reduce rhinorrhoea, sneezing and conjunctival symptoms. Steroids may take up to a week to work and may require prior use of a decongestant to allow adequate nasal delivery. In general, nasal steroids have been shown to be safe in children but epistaxis may be a problem in some children. This can be reduced by directing the nasal spray away from the nasal septum

Australian Medicines Handbook:
Corticosteroids (intranasal)
Beclomethasone
Budesonide
Fluticasone
Mometasone
Triamcinolone

Mode of action: Produce local anti-inflammatory effects, decrease capillary permeability and mucus production, and produce vasoconstriction in the nasal mucosa.

Indications**:** Allergic rhinitis, Rhinosinusitis, Nasal polyps

Precautions: *Severe nasal infection* (contraindicated), *bleeding disorders* (intranasal corticosteroids may cause nose bleeding), *recent nasal surgery or trauma* (intranasal corticosteroids may delay healing)

Adverse effects: Systemic adverse effects are rare with nasal products used at recommended doses.

Common: nasal stinging, itching, sneezing, sore throat, dry mouth, cough

Infrequent: nose bleed

Rare: nasal septal perforation, glaucoma, cataract, allergic reactions (urticaria, angioedema, bronchospasm, rash)

Practice points: all intranasal corticosteroids have similar efficacy. Onset of action within 3–7 hours; effective on an as-needed basis; optimum effect after several days of regular use. Patients transferred from oral to intranasal corticosteroids may have impaired adrenal function; intranasal corticosteroids have little systemic effect.

7. Outline the mechanism of action and side effects of the following medications used in the management of allergic illness, antihistamines, sympathomimetics, theophylline, cromolyn, corticosteroids and leukotriene agonists.

Medication	Examples	Mechanism of action	Side effects
Antihistamines (sedating)	Cyclizine Cyproheptadine Dexchlorpheniramine Dimenhydrinate Diphenhydramine Doxylamine Pheniramine Promethazine hydrochloride	Antagonise the action of histamine at H_1 receptors, reducing histamine-related vasodilation and increased capillary permeability. They also have	**Common** sedation, dizziness, tinnitus, blurred vision, euphoria, incoordination, anxiety, insomnia, tremor, nausea, vomiting, constipation, diarrhoea, epigastric discomfort, dry mouth, cough **Infrequent**

Medication	Examples	Mechanism of action	Side effects
	Trimeprazine	anticholinergic activity, some have alpha-blocking activity and some have antiserotonin activity, e.g. cyproheptadine	urinary retention, palpitations, hypotension, headache, hallucination, psychosis **Rare** leucopoenia, agranulocytosis, haemolytic anaemia, allergic reactions, arrhythmias, dyskinesia, paraesthesia, paralysis, hepatitis **Paradoxical stimulation** CNS stimulation (excitation, hallucinations, ataxia, seizures) may occur rarely, especially in children, rather than sedation.
LESS SEDATING ANTIHISTAMINES	Cetirizine Desloratadine Fexofenadine Levocetirizine Loratadine	Selectively antagonise the action of histamine at H_1 receptors. Histamine release causes vasodilation and increases capillary permeability.	**Common or infrequent** drowsiness, fatigue, headache, nausea, dry mouth **Infrequent** elevated liver enzymes, weight gain **Rare** rash, hypersensitivity (eg anaphylaxis, bronchospasm)
Sympathomimetics (for allergy)	Adrenaline	Nonselective adrenergic agonist. Positive inotrope and chronotrope (beta$_1$ receptors); vasodilator at low dose (beta$_2$ receptors); vasoconstrictor at high dose (alpha receptors). Bronchial smooth muscle relaxant (beta$_2$ receptors). Stabilises mast cells.	**Common** anxiety, headache, fear, palpitations, tachycardia, restlessness, tremor, dizziness, dyspnoea, weakness, sweating, pallor, hyperglycaemia **Infrequent** excessive increase in BP, ventricular arrhythmias, pulmonary oedema, angina, peripheral ischaemia and necrosis (at infusion site or in local anaesthesia of fingers, toes, ears, nose or genitalia) **Rare** allergic reaction (sodium metabisulfite in products)

Medication	Examples	Mechanism of action	Side effects
			Overdose or rapid IV administration arrhythmias (ventricular and supraventricular), severe hypertension, cerebral haemorrhage, pulmonary oedema
Theophylline	Theophylline	Not entirely understood. Possible effects include bronchial smooth muscle relaxation, anti-inflammatory effects, increase in diaphragm contractility and CNS stimulation.	Theophyllines have a narrow therapeutic range; toxicity is closely related to plasma theophylline concentration. **Common** nausea, vomiting, diarrhoea, gastro-oesophageal reflux, headache, insomnia, irritability, anxiety, tremor, palpitations **Rare** seizures, arrhythmias (at high concentrations), tachycardia
cromolyn	Cromoglycate Nedocromil	Act by inhibiting release of inflammatory mediators from mast cells.	**Common** cough, throat irritation, bitter taste, transient bronchospasm **Rare** allergic reaction including severe bronchospasm
Corticosteroids (intranasal)	Beclomethasone Budesonide Fluticasone Mometasone Triamcinolone	Produce local anti-inflammatory effects, decrease capillary permeability and mucus production, and produce vasoconstriction in the nasal mucosa.	Systemic adverse effects are rare with nasal products used at recommended doses. **Common** nasal stinging, itching, sneezing, sore throat, dry mouth, cough **Infrequent** nose bleed **Rare** nasal septal perforation, glaucoma, cataract, allergic reactions (urticaria, angioedema, bronchospasm, rash)
Corticosteroids (inhaled)	Beclomethasone Budesonide	Reduce airway inflammation and	**Common** dysphonia, oropharyngeal

Medication	Examples	Mechanism of action	Side effects
	Ciclesonide Fluticasone	bronchial hyper-reactivity.	candidiasis, bruising, facial skin irritation following nebulisation **Rare** allergic reactions, including bronchospasm, rash, urticaria and angioedema **Systemic adverse effects** Occurrence depends on systemic absorption which is: -influenced by dosage, duration of treatment and the delivery system -reduced by inhaling with MDI plus spacer, then rinsing mouth with water, gargling and spitting out. -*Adrenal suppression* can occur with high doses; when using high doses do not stop treatment suddenly and consider need for additional corticosteroids during periods of stress. -*Bone density loss*: clinical implications concerning risk of osteoporosis and fracture are still unknown. Consider screening adults on long term high dose inhaled corticosteroids for osteoporosis. -*Glaucoma, cataract*: risk may be increased. -*Skin thinning and bruising*: increased risk with higher doses particularly in older patients. -*Impaired growth*: inhaled corticosteroids may reduce growth velocity, mainly in the first year of treatment; limited data indicate no long term effects on eventual adult height. Effect on growth of other organs (eg brain and lung) is not well defined; poorly controlled asthma may also cause growth retardation.
leukotriene agonists	Montelukast Zafirlukast	Inhibit the cysteinyl leukotriene receptor; antagonise airway smooth muscle contraction and	**Common** headache, abdominal pain, diarrhoea **Rare**

Medication	Examples	Mechanism of action	Side effects
		inflammation caused by leukotrienes.	Churg–Strauss syndrome (below), allergic reaction including urticaria, angioedema and anaphylaxis **Churg–Strauss syndrome** Cases have been reported with both montelukast and zafirlukast; the syndrome may have predated leukotriene-receptor antagonist treatment, or been unmasked when corticosteroid treatment was reduced; however, a causal role cannot be totally excluded.