This study day has been organised by
The British Society for Allergy and Clinical Immunology (BSACI).

The BSACI is the national, professional and academic society which represents the specialty of allergy at all levels.

Its aim is to improve the management of allergies and related diseases of the immune system in the United Kingdom, through education, training and research.

The study day has been funded by an educational grant from Mylan.
RHINITIS IS STILL...

• IGNORED

• UNDERDIAGNOSED

• MISDIAGNOSED

• & MISTREATED
WHY TREAT RHINITIS?

- PREVALENCE
- CO-MORBIDITIES
- COMPLICATIONS
- QUALITY OF LIFE
- COSTS
How common is allergic rhinitis?

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>28.5% (24.5% - 32.5%)</td>
</tr>
<tr>
<td>France</td>
<td>24.5% (21.0% - 28.0%)</td>
</tr>
<tr>
<td>Germany</td>
<td>20.6% (16.5% - 24.6%)</td>
</tr>
<tr>
<td>Italy</td>
<td>16.9% (12.9% - 20.9%)</td>
</tr>
<tr>
<td>Spain</td>
<td>21.5% (18.5% - 24.4%)</td>
</tr>
<tr>
<td>UK</td>
<td>26.0% (20.3% - 31.7%)</td>
</tr>
<tr>
<td>All countries</td>
<td>22.7% (21.1% - 24.2%)</td>
</tr>
</tbody>
</table>

Prevalence of clinically confirmable allergic rhinitis in Europe

Bauchau V, Durham SR. Eur Respir J 2004; 24: 758-764
Patient 1

Patrick

• aged 14
• every summer he gets a “cold”
• which comes and goes.
• His nose blocks, runs and he sneezes
• He sleeps badly
• making it hard to get up for school
• And reducing his exam results
Question 1

- Does Patrick have rhinitis?
  - YES
RHINITIS DEFINITION

- Rhinitis means nasal inflammation, but is defined clinically as two or more of:
  - Running
  - Blocking
  - Sneezing/Itching
  - >1 hour per day
- Rhinoconjunctivitis in 50-70%
- Allergic when IgE mediated
Patient 2

Shona

Aged 8

Chronically blocked nose

Asthma

Worse in winter, also gets otitis media with effusion (glue ear)
Question 2

• Does Shona have rhinitis?

• POSSIBLY – in particular ask about post nasal secretions
RECOGNIZING RHINITIS IN CHILDHOOD

Classic symptoms and signs:

- **Rhinorrhoea** – clear or discoloured discharge, sniffing

- **Pruritus/sneezing** - nose rubbing, the “allergic salute”, “allergic crease”, “paroxysmal sneeze”, may be associated with complaints of an itchy mouth or throat in older children

- **Congestion** - mouth breathing, snoring, sleep apnoea, allergic shinners

- **Eustachian tube dysfunction** - ear pain on pressure changes (e.g. flying), reduced hearing, chronic otitis media with effusion
Recognising Rhinitis in Childhood

- Potential atypical presentations:
  - **Cough** – often mislabelled as asthma
  - **Poorly controlled asthma** – may co-exist with asthma
  - **Sleep problems** - tired, poor school performance, irritability
  - **Prolonged and frequent respiratory tract infections**

- **Rhinosinusitis** - catarrh, headache, facial pain, halitosis, cough, hyposmia

- **Pollen-food syndrome** in pollen driven allergic rhinitis
AR & Allergic Asthma: Immunology

Immediate symptoms
- Wheeze, Itch, sneeze
- Bronchospasm
- Watery discharge
- Congestion

Chronic symptoms
- Airway reduction
- Sticky Mucus
- Loss of smell
- “Hyper-reactivity’ Co-morbidities
Co-morbidities

Diagram showing the relationship between the nose, paranasal sinus, middle ear, lung, and airway smooth muscle.
Co-morbidities of rhinitis

• **Other atopic disease:** asthma, eczema, food allergy (particularly pollen-food syndrome), anaphylaxis, eosinophilic oesophagitis

• **Anatomical:** rhinosinusitis, chronic otitis media, laryngitis, cough, adenoidal hypertrophy

• **Sleep disturbance**
Impact of allergic rhinitis on patients’ daily life

**SLEEP & TIREDNESS**
- 46% of patients feel tired
- 77% of patients had trouble falling asleep

**DAILY ACTIVITIES IMPAIRED**

**WORK & SCHOOL PRODUCTIVITY**
- ≤90% effectiveness at work
- ≤93% impaired classroom performance

**LEARNING & COGNITIVE FUNCTIONS DISTURBED**

**EMBARRASSMENT**
- Adolescents embarrassed to use inhalers

1. Scadding G et al. XXVI EAACI, 2007; Abs 1408
Grass pollen counts 2003 and GCSEs

Summary

• Symptomatic hay fever in adolescents:
  
  • a 43% increase in the odds of dropping an exam grade between summer and winter
  
  • In those taking *sedating* antihistamines the risk increase was 71%.
  
  • **AVOID 1st GENERATION ANTI-HISTAMINES!**
Rhinitis is a predictor of onset of asthma in adults: data from European Respiratory Health Survey

Adjusted relative risk of developing asthma in those with allergic rhinitis at baseline: 3.53 (2.11 – 5.91)

Shabaan et al Lancet 2008
Rhinitis is dangerous!
Asthma and rhinitis

- Up to **80%** of asthmatics have rhinitis

Impact of Rhinitis on Asthma: one airway

- Rhinitis is a risk factor for asthma: OR>3, >7 farmers, >40 HDM

- Rhinitis reduces asthma control ≡ smoking, > poor Rx compliance

- Most asthma exacerbations start in the nose with a viral URTI.

- Rhinitis increases viral URTI effects

- Rhinitis treatment reduces need for emergency treatment and hospitalization for asthma

Scadding G, Walker S. Poor asthma control?--then look up the nose. The importance of co-morbid rhinitis in patients with asthma. Prim Care Respir J. 2012 Jun;21(2):222-8.
ARIA Classification of AR

Intermittent symptoms
- < 4 days per week
- OR < 4 weeks

Persistent symptoms
- > 4 days per week
- AND > 4 weeks

Mild
- Normal sleep
- Normal daily activities
- Normal work and school
- No troublesome symptoms

Moderate-severe
One or more items
- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Problems caused at school or work
- Troublesome symptoms
In Sweden, the cost of rhinitis is €2.7 billion/yr in terms of lost productivity

Impact of seasonal allergic rhinitis on work productivity

- Work is negatively impacted in over 90% of patients when symptomatic

Impact on work productivity

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
</tr>
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<tbody>
<tr>
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<td>40%</td>
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<td>50%</td>
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<td>60%</td>
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<td>80%</td>
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<tr>
<td>90%</td>
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</tbody>
</table>

Unable to...
The allergic rhinitis landscape

Most patients have ‘moderate/severe’ Allergic Rhinitis

European Survey
- 67.2% = moderate or severe
- 42.5% = persistent disease

Many patients have mixed forms of Allergic Rhinitis

Many patients are poly-sensitized

Evolution of treatment-resistant phenotypes
- Severe Chronic Upper Airway Disease (SCUAD)

SCUAD
- approx. 20% of AR patients

Canonica et al. Allergy 2007; Settipane, Allergy Asthma Proc 2001; Mösges et al. Allergy 2007; Bousquet et al. JACI 2009

Pie chart: data refers to non-infectious rhinitis; AR: Allergic Rhinitis
The allergic rhinitis landscape: Patients remain symptomatic on treatment

- 990 patients recruited by 161 GPs in France
- 72.5% were currently taking allergic rhinitis medication

The vast majority of treated patients remain symptomatic

- **89%** Rhinorrhea
- **82%** Sneezing
- **82%** Congestion
- **68%** Itching
- **68%** Ocular symptoms

Global discomfort caused by their AR during the previous week (VAS)

- De Novo: 61.2
- Treated: 60.8

There is a clear need for a new and more effective therapy

Bousquet et al. Int Arch Allergy Immunol 2013

VAS: visual analog scale; AR: allergic rhinitis
What do allergic rhinitis patients want and how do they treat their symptoms?

Results from a health survey including 1,000 patients

- 1,000 Allergic Rhinitis patients completed the survey
  - 254 mild
  - 746 moderate/severe patients (total nasal symptom score [TNSS]) \( \geq 8/12 \), (incl. congestion score \( \geq 2 \))
  - Recruited through a patient panel

- The survey included questions on respondents’
  - Treatment
  - Episode duration
  - Impact of symptoms on productivity
  - Other questions
Results from a health utilisation survey including 1,000 patients

Most patients use multiple therapies to control their symptoms

• Two thirds of all patients included in the survey reported using ≥ 2 AR medications
  – 70.5% of moderate to severe
  – 56.1% of mild patients

• The need for faster and more effective treatment was the primary reason for co-medicating
  – True for both moderate/severe and mild patients

Faster and more effective reduction of nasal and ocular symptoms are the treatment targets of drug development

Pitman et al, 2012; AR: Allergic Rhinitis
Patient 3

• 28 year-old woman,

• 1 year ‘hay fever’:
  - blocked nose
  - runny nose
  - sneezing

• ‘allergic’ to perfumes, dusts, pollution, spicy foods

• Moved into new flat 18 months ago
Patient 3

- What questions might you ask?
- Investigations?
Patient 3

- Perennial symptoms
- No childhood or family history of atopy
- No pets
- No changes in work environment
- No regular medications
- Reasonable sense of smell
- Takes ibuprofen for headaches
Patient 3

• Skin tests:
  HDM 0
  mixed grass 0
  Timothy grass 0
  Silver birch 0
  mugwort 0
  cat 0
  dog 0
  Alternaria 0
  Aspergillus 0
  +ve control 5
  -ve control 0

Specific IgE:
  HDM <0.35
  Mixed grass pollen < 0.35
  Cat dander < 0.35

Peak flow 450 L/min (110%)
  FEV1 3.5 L/s (108%)
  FVC 4.6 L/s (105%)

Nasal examination:
  Rhinitic mucosa – mild turbinate hypertrophy, mild rhinorrhoea
Patient 3

- Diagnosis:
  Non-allergic rhinitis (idiopathic, NARES, other?)
Patient 4

- 32 year old man

- Blocked nose last 2 years, episodes of nose running and sneezing

- Diagnosed with asthma last year following acute attack of breathlessness day after a friend’s party

- Allergic to wine, lemon-lime cordial

- Seretide 250 2 puffs bd, salbutamol 4x/day, uniphyllin bd, 3 courses of oral prednisolone in the last year

- What questions might you ask?
Patient 4

- No history atopic disease
- Absent sense of smell and taste
- Took 2 ibuprofen the morning after party for a headache
- What do you expect to find on endoscopy?
Patient 4

Peak flow 300 (60% predicted)
FEV1 2.5 (60% predicted)
FVC 4.3 (85% predicted)

Skin tests:
All negative
Rhinosinusitis

- Facial pain / pressure
- Reduction / loss of smell
- Anterior / posterior rhinorrea
- Blockage / obstruction / congestion

web: www.ep3os.com
Chronic rhinosinusitis +/- nasal polyps
Rhinitis Diagnosis

**Rhinitis definition**
- Nasal discharge
- Blockage
- Sneeze/itch

2 or more symptoms for > 1 hour on most days

- History
- Examination
- Skin-prick tests/Specific IgE

**Allergy** (seasonal, perennial, or occupational)

**Infection** (acute or chronic)

**Structural** (polyps, septum, turbinates, etc)

**Other** (idiopathic, NARES, hormonal, etc)
Rhinitis Diagnosis

Rhinitis definition

- Nasal discharge
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2 or more symptoms for > 1 hour on most days

History
Examination
Skin-prick tests/Specific IgE

Allergy
(seasonal, perennial, or occupational)

Infection
(acute or chronic)

Structural
(polyps, septum, turbinates, etc)

Other
(idiopathic, NARES, hormonal, etc)
Causes of rhinitis/rhinosinusitis

Infectious
Viral
Bacterial
Other infective agents

Allergic
Intermittent
Persistent

Occupational (allergic/non-allergic)
Intermittent
Persistent

Drug-induced
Aspirin
Other medications

Hormonal

Other Causes
Non-allergic rhinitis with eosinophilia syndrome
Churg Strauss syndrome
Irritants
Food
Emotional
Atrophic
Gastro-oesophageal reflux
Idiopathic

HISTORY

- Worst symptoms - in order
- When?
- Where?
- What increases them?
- What decreases them?
- Treatment?

- Past history
- Family history
- Social history - housing
- Associated symptoms?
- School/ work, hobbies, food, medication and reactions, smoking, etc.
Symptoms typical of allergic rhinitis

• Dominant itch/sneezing
• Watery anterior discharge
• Associated eye symptoms
• Symptoms on exposure to the relevant allergen

NB: chronic, persistent exposure – e.g. HDM, cat dander – blockage may predominate
Symptoms not typical of allergic rhinitis

- Unilateral symptoms
- Nasal obstruction without other symptoms
- Absent sense of smell
- Facial pain
- Recurrent epistaxis
- Nasal crusting
- Unpleasant smell
- Predominant posterior, mucopurulent discharge
- Ear symptoms (adults)

Warrant referral to specialist clinic
Nasal sarcoidosis
Rare

- Granulomatous (sarcoid, Wegener’s)
- Atrophic (primary, secondary)
- Neoplasms (benign, malignant)
- CSF leak
Diagnosis: examination

Use an otoscope with largest attachment

Watery, boggy, swollen nasal mucosa

Large turbinates, ‘blue’

 Conjunctivitis – itch, redness, watering

Transverse nasal crease

Allergic salute
**EXAMINATION**

*Nose Seen From Below*

- **Inferior turbinate**
  - Sensitive
  - Pink
  - Attached laterally

- **Nasal polyp**
  - Insensitive
  - Greyish
  - Not attached laterally
SKIN TESTS FOR RHINITIS – basic panel

- Negative control (saline)
- House dust mite
- Grass pollen
- Positive control (histamine)
- Cat
- Tree pollen
OTHER SPTs

• HISTORY
  • Animal contact
  • Baker
  • Damp housing, asthma
  • Late summer exacerbation
  • Small child

• SPT
  • Relevant allergen
  • Wheat, amylase
  • Moulds
  • Moulds
  • Milk, egg etc
Patrick’s skin prick tests

Need to interpret IgE tests in the light of the history
Shona’s results

• Skin prick test negative

Non-atopic?
False negative results?
Causes of False Negative SPTs

- Anti-histamines
- Topical corticosteroid
- High dose oral corticosteroid
- Early in disease- local sensitization in nose
Shona’s blood test

- IgE present to
- Grass pollen - grade 2
- Birch pollen - grade 2
- Cat – grade 4
- House dust mite – grade 6
PRACTICAL SESSION
and coffee

- Skin prick tests
- Nasal examination
- How to use a nasal spray
Allergic Rhinitis - Treatment

- Allergen Avoidance
- Pharmacotherapy
- Immunotherapy
- RARELY Surgery
- Education, Education, Education

www.whiar.org
www.bsaci.org
www.eaaci.org
Managing Allergic Rhinitis

1. Diagnosis
2. Allergen avoidance
3. Choice of pharmacotherapy
4. Adherence and correct use of medication
5. Allergen Immunotherapy
(+ Diagnosis of concurrent asthma)
Scadding GK et al, CEA, 2017

Symptoms despite allergen avoidance and saline douching

Mild
AH

Moderate/Severe
INS

Rx failure

Check use, concordance, dose

Combination Rx with INS and INAH

Rx failure

Check use, concordance, dose

Watery rhinorrhea
Add ipratropium

Itch/sneeze/ extra nasal itch/ rash switch to non-sedating oral anti-H1

Catarrh
Add LTRA if asthmatic

Blockage, Add (briefly) IN decongestant

Rx failure

?Infection/structural problem, Surgical referral

Inflammatory rhinitis, Course of OC, continue local Rx

Consider immunotherapy if Sx predominantly due to one allergen

Key:
IN = intranasal
OC = oral corticosteroids
AH = antihistamine
LTRA = leukotriene receptor antagonist

www.bsaci.org
Managing Allergic Rhinitis

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Allergen avoidance

• Works - no hay fever in January

• Occupational rhinitis - important to remove patient from trigger before asthma develops

• Difficult - travel away or avoid high pollen days

• Evening - close windows, washing in, hair wash

• Put something in nose - Vaseline, cellulose, Hay Balm, filters
Pollens

Avoidance

• Holiday abroad
• Avoid grassy areas
• Stay indoors pm
• Fit a pollen filter to the car
• Keep windows tight shut
• Vaseline up the nose
• Wash hair
Pollens

- Holiday abroad
- Avoid grassy areas
- Stay indoors pm
- Fit a pollen filter to the car
- Keep windows tight shut
- Vaseline up the nose
- Wash hair

Avoidance

- ?
- ?
- ?
- ?
- ?
- ?
- ?
Allergen avoidance can work!

See: Peroni et al, AJRCCM 1994; 149:1442-6
<table>
<thead>
<tr>
<th></th>
<th>April</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>August</th>
<th>September</th>
<th>October</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grass pollens</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Timothy, rye, cocksfoot, meadow, dogstail, fescue, etc</td>
<td></td>
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</tr>
<tr>
<td>Tree pollens</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Birch, plane</td>
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<tr>
<td>Weed pollens</td>
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<td></td>
<td></td>
<td>Ash, pine</td>
<td>Nettle, dock</td>
<td></td>
</tr>
<tr>
<td>Fungal spores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cladosporium alternaria</td>
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</tr>
</tbody>
</table>
Allergen avoidance
Nasal air filters

Prevention of nasal inflammation

O’Meara et al., Allergy 2005
Scadding GK et al, CEA, 2017

Symptoms despite allergen avoidance and saline douching

- Mild
  - AH

- Moderate/Severe
  - INS

Rx failure

- Check use, concordance, dose

Combination Rx with INS and INAH

Rx failure

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Watery rhinorrhea
  - Add ipratropium

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www.bsaci.org
Managing Allergic Rhinitis

1. Diagnosis
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3. Choice of pharmacotherapy
4. Adherence and correct use of medication
5. Allergen Immunotherapy
(+ Diagnosis of concurrent asthma)
Question

• Which 2 forms of treatment for rhinitis have the lowest NNT?

• A) antihistamines and nasal steroids
• B) nasal steroids and antileukotrienes
• C) nasal steroids and immunotherapy
• D) antihistamines and antileukotrienes
**Benefit and harm in treatments for allergic rhinitis - Portnoy et al, 2004.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Benefit</th>
<th>NNT</th>
<th>Harm</th>
<th>NNH</th>
<th>Rx threshold,%</th>
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<tbody>
<tr>
<td><strong>Antihistamine</strong></td>
<td></td>
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<tr>
<td>Class mean</td>
<td>0.066</td>
<td>15.2</td>
<td>0.02</td>
<td>51</td>
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<tr>
<td><strong>Nasal sprays</strong></td>
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<td>Class mean</td>
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<td><strong>4.4</strong></td>
<td>0.021</td>
<td>48</td>
<td>8</td>
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<td><strong>Nasal antihistamines</strong></td>
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<tr>
<td>Azelastine (daily)</td>
<td>0.16</td>
<td>6.3</td>
<td>0.031</td>
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<tr>
<td>Azelastine (twice daily)</td>
<td>0.2</td>
<td>5</td>
<td>0.046</td>
<td>22</td>
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<td><strong>Other</strong></td>
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<td>Montelukast</td>
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<td>Immunotherapy</td>
<td>0.218</td>
<td><strong>4.6</strong></td>
<td>0.072</td>
<td>14</td>
<td>25</td>
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Evidence-based Recommendations in Allergic Rhinitis

<table>
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<tr>
<th>Treatment</th>
<th>Seasonal allergic rhinitis (SAR)</th>
<th>Perennial allergic rhinitis (PAR)</th>
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<tbody>
<tr>
<td></td>
<td>Adults</td>
<td>Children</td>
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<tr>
<td>Oral anti-H1</td>
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<tr>
<td>Intranasal anti-H1</td>
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<td>A</td>
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<td>Intranasal CS</td>
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<td>A</td>
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<tr>
<td>Intranasal chromone</td>
<td>A</td>
<td>A</td>
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<td>Subcutaneous SIT</td>
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<td>A</td>
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<td>Sublingual/nasal SIT</td>
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<tr>
<td>Anti-leukotriene</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Allergen avoidance</td>
<td>A</td>
<td>D</td>
</tr>
</tbody>
</table>

**BSACI guidelines for the management of allergic and non-allergic rhinitis**

CS, corticosteroid; SIT, specific immunotherapy.

Scadding et al., Clin Exp Allergy. 2008 Jan;38:19-42
# Antihistamines licensed in UK for Allergy-related Indications

<table>
<thead>
<tr>
<th>First Generation</th>
<th>Proprietary forms</th>
<th>Manufacturer</th>
<th>Availability</th>
<th>Licensed indications (BNF)</th>
<th>Licensed dose (Adult)</th>
<th>Approx 1 month cost (BNF)</th>
<th>Time to Max plasma conc (hours)</th>
<th>Time to Onset (hrs)</th>
<th>Duration of Action (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpheniramine</td>
<td>Piriton</td>
<td>Non-proprietary</td>
<td>POM</td>
<td>Allergy such as hay fever, urticaria, anaphylactic reactions</td>
<td>4 mg, max 4 hrly</td>
<td>£0.69-£4.14</td>
<td>2.8</td>
<td>3</td>
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<td>Hydroxyzine</td>
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<td>Alliance</td>
<td>POM</td>
<td>Pruritis, anxiety</td>
<td>25 mg, max qds</td>
<td>£1.22-£4.88</td>
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<tr>
<td>Alimemazine</td>
<td>Vallergan</td>
<td>Sanofi-Aventis</td>
<td>POM</td>
<td>Pruritis, urticaria, premedication</td>
<td>10 mg bd-tds</td>
<td>£7.78-£1.67</td>
<td>N/A</td>
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<tr>
<td>Clemastine</td>
<td>Tavegil</td>
<td>Novartis</td>
<td>POM</td>
<td>Allergy such as hay fever, urticaria</td>
<td>1mg-6mg od</td>
<td>£1.18-£7.05</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Cypreheptadine</td>
<td>Periactin</td>
<td>MSD</td>
<td>POM</td>
<td>Allergy such as hay fever, urticaria, migraine</td>
<td>4-20mg daily</td>
<td>£0.86-£2.5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Promethazine</td>
<td>Phenergan</td>
<td>Sanofi-Aventis</td>
<td>POM</td>
<td>Hayfever, urticaria, anaphylaxis, sedation, motion sickness, premedication</td>
<td>25mg od or bd</td>
<td>£1.53 - £3.06</td>
<td>N/A</td>
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<tr>
<td>Doxepin</td>
<td>Sinepin</td>
<td>Marlborough</td>
<td>POM</td>
<td>Pruritis in eczema, depression</td>
<td>75-300mg daily</td>
<td>£11.31-£34.26</td>
<td>2.0</td>
<td>N/A</td>
<td></td>
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</tbody>
</table>

**Second Generation**

| Cetirizine       | Zirtek             | Non-proprietary | | Allergy such as hay fever, Chronic idiopathic urticaria | 10 mg od          | £0.50                    | 1.0                           | 1               |                        |
| Loratidine       | Claritin           | Non-proprietary | | Allergy such as hay fever, Chronic idiopathic urticaria | 10 mg od          | £0.99                    | 1.2                           | 2               |                        |
| Fexofenadine     | Telfast            | Aventis-Pharma | POM          | Seasonal allergic rhinitis, Chronic idiopathic urticaria | 120mg/180mg od    | £6.23-£7.89               | 2.6                           | 2               |                        |
| Mizolastine      | Mizollen           | Sanofi-Aventis | POM          | Allergy such as hay fever, urticaria | 10 mg od          | £5.77                    | 1.5                           | 1               |                        |

**Third Generation**

| Levocetirizine   | Xyzal              | UCB Pharma     | POM          | Allergy such as hay fever, urticaria | 5 mg od          | £5.20                    | 0.8                           | 1               |                        |
| Desloratidine    | Neoclarlyn         | Schering-Plough | POM          | Allergy such as hay fever, Chronic idiopathic urticaria | 5 mg od          | £7.04                    | 1 - 3                          | 2               |                        |


*Based on wheal and flare inhibition studies*
## Antihistamines licensed in UK for Allergy-related Indications

<table>
<thead>
<tr>
<th>Proprietary forms</th>
<th>Manufacturer</th>
<th>Availability</th>
<th>Licenced indications (BNF)</th>
<th>Licenced dose (Adult)</th>
<th>Approx 1 month cost (BNF)</th>
<th>Time to Max plasma conc (hours)</th>
<th>Time to Onset (hrs)</th>
<th>Duration of Action (hrs)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Generation</strong></td>
<td></td>
<td></td>
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<tr>
<td>Chlorpheniramine</td>
<td>Piriton</td>
<td>Non-proprietary</td>
<td>POM</td>
<td>Allergy such as hay fever, urticaria, anaphylactic reactions</td>
<td>4 mg, max 4 hrly</td>
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| **Second Generation** |
| Cetirizine        | Zirtek       | Non-proprietary | POM | Allergy such as hay fever, Chronic idiopathic urticaria | 10 mg od | £0.50 | 1.0 | 1 |       |
| Loratidine        | Clarlyn      | Non-proprietary | POM | Allergy such as hay fever, Chronic idiopathic urticaria | 10 mg od | £0.99 | 1.2 | 2 |       |
| Fexofenadine      | Telfast      | Aventis-Pharma | POM | Seasonal allergic rhinitis, Chronic idiopathic urticaria | 120mg/180mg od | £6.23/£7.89 | 2.6 | 2 |       |
| Mizolastine       | Mizollen     | Sanofi-Aventis | POM | Allergy such as hay fever, urticaria | 10 mg od | £5.77 | 1.5 | 1 |       |

| **Third Generation** |
| Levocetirizine    | Xyzal        | UCB Pharma    | POM | Allergy such as hay fever, urticaria | 5 mg od | £5.20 | 0.8 | 1 |       |
| Desloratidine     | Neoclarityn  | Schering-Plough | POM | Allergy such as hay fever, Chronic idiopathic urticaria | 5 mg od | £7.04 | 1-3 | 2 |       |


*Based on wheal and flare inhibition studies
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<td>Zirtek</td>
<td>Non-proprietary</td>
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<td>Clarityn</td>
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<td>Levocetirizine</td>
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<td>Desloratidine</td>
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<td>5 mg od</td>
<td>£7.04</td>
<td>1 - 3</td>
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*Based on wheal and flare inhibition studies
# Evidence-based Recommendations in Allergic Rhinitis

<table>
<thead>
<tr>
<th></th>
<th>Seasonal allergic rhinitis (SAR)</th>
<th>Perennial allergic rhinitis (PAR)</th>
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<tr>
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<td>Anti-leukotriene</td>
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<tr>
<td>Allergen avoidance</td>
<td>A</td>
<td>D</td>
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</tbody>
</table>

**BSACI guidelines for the management of allergic and non-allergic rhinitis**

CS, corticosteroid; SIT, specific immunotherapy.

Scadding et al., Clin Exp Allergy. 2008 Jan;38:19-42
Intranasal steroids v antihistamines: Total nasal symptoms

JM Weiner et al, BMJ 1998;317;1624-1629
Glucocorticoid efficacy (Rhinitis)

• Superior in meta-analyses to:
  - Oral antihistamine (Weiner et al., 1998)
  - Topical antihistamine (Yanez & Rodrigo, 2002)
  - LTRAs (Wilson et al., 2004)
  - Also superior to antihistamine + LTRA (Di Lorenzo et al., 2004)
INS and eye symptoms

Nasal symptoms

Eye symptoms

Kaiser HB, JACI 2007
Troublesome eye symptoms

• Sodium cromoglicate or nedocromil sodium first line

• Inadequate response: add in azelastine, olopatidine or other topical anti-histamine

• Ensure patient also taking an intranasal corticosteroid

• Still inadequate response or worrying signs: request ophthalmology opinion
Which nasal steroid?
<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade name</th>
<th>Efficacy</th>
<th>Safety</th>
<th>Once Daily</th>
<th>Eye Sx</th>
<th>No Odour</th>
<th>No BKC</th>
<th>Device</th>
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<tr>
<td>FP</td>
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<td>++</td>
<td>++</td>
<td>+</td>
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<td>MOM</td>
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<td>FLUNIS</td>
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<td>?</td>
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<tr>
<td>FF</td>
<td>Avamys</td>
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<td>++</td>
<td>++</td>
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<td>-</td>
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</tr>
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</table>
Systemic Bioavailability of Nasal Corticosteroids

Nasal absorption

80% Swallowed

G-I absorption

Hepatic metabolism

+- Metabolite activity
QUESTION

• The least bioavailable nasal steroids are:

• A) FF, FP and MF

• B) BDP, MF and Betnesol

• C) Triamcinolone, Syntaris, Budesonide?
Bioavailability of intranasal steroids

- Fluticasone furoate: 0.5%
- Mometasone furoate: <0.5%
- Fluticasone propionate: 0.5%
- Budesonide: 33%
- Beclometasone dipropionate: 44%
- Triamcinolone: 44%
- Flunisolide: 50%
- Betnesol: 100%

References:
- Kariyawasam H and Scadding GK. Journal of Asthma and Allergy 2011
- Scadding GK. Paediatric Drugs 2008
- Homer JJ, Gazis TJ. BMJ 1999
OUTCOMES

Fine on pre- and co- seasonal INS

SCUAD
Majority of patients with chronic upper airway diseases controlled during treatment (81.5%)

But many patients inadequately controlled despite adequate (i.e. effective, safe and acceptable) pharmacologic treatment (SCUAD) (18.5%)

SCUAD patients have impaired quality-of-life, social functioning, sleep, daily and work performances
Scadding GK et al, CEA, 2017

Symptoms despite allergen avoidance and saline douching

Mild
- AH

Moderate/Severe
- INS

Rx failure

Check use, concordance, dose

Combination Rx with INS and INAH

Rx failure

Check use, concordance, dose

Watery rhinorrhoea
Add ipratropium

Itch/sneeze/extra nasal itch/rash switch to non-sedating oral anti-H1

Catarrh
Add LTRA if asthmatic

Blockage, Add (briefly) IN decongestant

Rx failure

Inflammatory rhinitis,
Course of OC, continue local Rx

Consider immunotherapy if Sx predominantly due to one allergen

Key:
IN = intranasal
OC = oral corticosteroids
AH = antihistamine
LTRA = leukotriene receptor antagonist

www.bsaci.org
Efficacy of combined fluticasone propionate + azelastine nasal spray (Dymista)

Data presented as LS mean change from baseline delta placebo with 95% CI

† p<0.0031 vs FP + AZE; ‡ p=0.0001 vs FP +AZE

Hampel et al, 2010
FP + AZE (n=153) FP: fluticasone propionate (n=151); AZE: azelastine (n=152); rTNSS: reflective total nasal symptom score

Data presented as LS mean change from baseline delta placebo with 95% CI
Efficacy of combined fluticasone propionate + azelastine nasal spray - % of patients with a 50% + improvement

Responder rate = % of patients with a 50% or more reduction in Total Nasal Symptom Score

Bachert et al. 2011

AZE: Azelastine; FP: Fluticasone propionate; PLA: placebo; AR: allergic rhinitis
Approach to therapy for paediatric allergic rhinitis

1. Antihistamine, oral or nasal*
2. Nasal corticosteroid
3. Trial of addition of antihistamine ± leukotriene receptor antagonist to nasal corticosteroid

Specific immunotherapy

Step down therapy if well controlled

Step up therapy if poorly controlled**

Avoid triggers

Saline douching
Managing Allergic Rhinitis

1. Diagnosis
2. Allergen avoidance
3. Choice of pharmacotherapy
4. Adherence and correct use of medication
5. Allergen Immunotherapy
   (+ Diagnosis of concurrent asthma)
Scadding GK et al, CEA, 2017

IN=intranasal
OC=oral corticosteroids
AH=antihistamine
LTRA=leukotriene receptor antagonist

Symptoms despite allergen avoidance and saline douching

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if Sx predominantly due to one allergen

www.bsaci.org
Technique for nasal spray

- Head down and forward position
- 1 or 2 sprays each nostril
- Don’t sniff too hard

How long does a bottle last you?
How many bottles over the pollen season?

BSACI guidelines for the management of allergic and non-allergic rhinitis
Scadding et al., Clin Exp Allergy. 2008 Jan;38:19-42
Scadding GK et al, CEA, 2017

Symptoms despite allergen avoidance and saline douching

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Blockage, Add (briefly) IN decongestant

Rx failure

Inflammatory rhinitis,
Course of OC, continue local Rx

Consider immunotherapy if Sx predominantly due to one allergen

Key:
IN=intranasal
OC= oral corticosteroids
AH= antihistamine
LTRA= leukotriene receptor antagonist

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Symptoms despite allergen avoidance and saline douching

Mild

AH

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Check use, concordance, dose

Combination Rx with INS and INAH

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Scadding GK et al, CEA, 2017

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Managing Allergic Rhinitis

1. Diagnosis
2. Allergen avoidance
3. Choice of pharmacotherapy
4. Adherence and correct use of medication
5. Allergen Immunotherapy
(+ Diagnosis of concurrent asthma)
Allergen immunotherapy

• ‘Allergen-specific immunotherapy is the practice of administering (gradually increasing) quantities of an allergen product to an individual with IgE-mediated allergic disease in order to ameliorate the symptoms associated with subsequent exposure to the causative allergen.’ E. Alvarez-Cuesta et al. Standards for practical allergen-specific immunotherapy. Allergy 2006: 61 (Suppl. 82): 1–20
Allergen immunotherapy – indications

- Allergic rhinitis/conjunctivitis, (allergic asthma*) and systemic reactions to wasp/bee venom

- Effective in IgE-mediated disease with a limited spectrum (1 or 2) of allergies

- Should be combined with allergen avoidance, pharmacotherapy and patient education

*not currently in UK, except with allergic rhinitis
Allergen immunotherapy – contraindications

- Uncontrolled asthma or FEV1 < 70% predicted
- Beta-blockers
- Malignancy
- (Systemic) autoimmune/inflammatory disease
- Pregnancy at initiation of treatment
- (Acute) infection/illness
Allergen immunotherapy – allergic rhinitis

• IgE-mediated disease: IgE identified, symptoms on allergen exposure
• Troublesome symptoms
• Inadequate response to intranasal corticosteroids and anti-histamines
• Allergen avoidance impractical and/or ineffective
• Allergen (vaccine) product available
• Ability to comply with treatment (clinic visits/daily tablets)
• Absence of contraindications
• *Polysensitisation* ok, *polyallergy* less favourable
Allergen immunotherapy – how?

Subcutaneous

Sublingual
Allergen immunotherapy – protocols

• **Subcutaneous immunotherapy:**

• Dose-escalation over 12-14 weeks, weekly injections – ‘up-dosing’ phase
  – May be slowed down/reduced if large local reactions occur
  – Dose-reduction (or abandonment) in the event of systemic reactions

• High dose injections every 4-6 weeks thereafter, for 3 years – ‘maintenance’ phase
  – E.g. for venom immunotherapy, dose equivalent to approximately two full stings
  – Grass pollen: approximately 20µg major allergen per month

• Suitable facilities – specialist unit, in hospital
• ‘Rush’ and ‘cluster’ protocols may be used
Sublingual immunotherapy:

- Tablets (or drops)
- Usually single dose (or short up-dosing)
- Once daily, applied beneath the tongue
- UK: first dose under observation, in a suitable facility
- Subsequent doses at home for 3 years
  - Grass pollen: approximately 15µg major allergen per day
- Seasonal treatment with some vaccines (rather than perennial)
Allergen immunotherapy – which allergens?

• Efficacy demonstrated in DBRPCTs for:
  – Grass pollen
  – Silver birch pollen
  – House dust mite
  – Cat dander
  – Ragweed

• Efficacy for venom immunotherapy demonstrated using sting challenges

• Treatment only as good as the quality of the vaccine

• Major allergen content previously been shown to differ considerably between commercial vaccines
SLIT vs SCIT: safety

• SCIT:
  - systemic reactions: 1 in 1,000 injections
  - Grade 4 systemic reactions: 1 in 1,000,000 injections
  - Deaths: 1 in 2-2,500,000 injections

• SLIT:
  - one SLIT-related serious adverse reaction per 384 treatment years
  - Twelve non-fatal systemic reactions published
  - Local side effects common

Grass pollen tablets - long-term efficacy with effect sustained 2 years after treatment

**Total daily rhinoconjunctivitis symptom score**\(^{1,2,3}\)

(median values)

![Graph showing symptom score reduction](chart.png)

SLIT Tablet in Children
Efficacy by sub-group of age

Median improvement vs placebo - ITT population

House dust mite sublingual immunotherapy

- Add on treatment to ins + oral anti-histamine + azelastine eye drops
- 22% reduction vs placebo (12 SQ dose)
# Immunotherapies: comparison

<table>
<thead>
<tr>
<th></th>
<th>Subcutaneous</th>
<th>Sublingual</th>
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</thead>
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<td><strong>Efficacy</strong></td>
<td>Proven(^1-5)</td>
<td>Proven(^7-9)</td>
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<td><strong>Prevention of asthma (children)</strong></td>
<td>Documented(^6)</td>
<td>Documented(^7)</td>
</tr>
</tbody>
</table>

2. Jacobsen L et al. *Allergy* 1997; 52: 914-20
Allergen immunotherapy: who?

- **Case 1:**
  - 26 year old man, sneezing, itching, red eyes, blocked nose
  - May-July for 10 years, poor response to pharmacotherapy, good compliance
  - Examination unremarkable
  - Skin test positive to grass only; sIgE mixed grass pollen 13.50

- **Case 2:**
  - 18 year old girl, 4 years nasal blockage, post nasal drip: perennial
  - itching, sneezing, irritable eyes: March-August
  - Dislikes nasal sprays; pet cat
  - skin test positive to HDM, birch, grass, cat, alternaria, cladosporium
  - examination: rhinitis

- **Case 3:**
  - 35 year old man, 2 years nasal blockage, running, absent sense of smell
  - poor response to anti-histamines and nasal sprays
  - skin test positive to dust mite only
  - previous operation for nasal polyps, 18 months ago

**YES**

**NO**

**NO!**
Allergy referral

- Uncontrolled symptoms (SCUAD)
- Investigation of allergens/ triggers
- Consideration of immunotherapy
- Occupational allergy
- Multisystem allergy
- Systemically unwell
- Recurrent nasal polyps
EDUCATION

• Nature of disease
• need for long term treatment
• how to use it
• possible side effects
• contact number
Scadding GK et al, CEA, 2017

Symptoms despite allergen avoidance and saline douching

Mild
- AH

Moderate/Severe
- INS

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BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis

By British Society for Allergy and Clinical Immunology | 1 August 2017
Treat the Whole Airway