Allergy testing

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Learning outcome

- How to diagnose food allergy
- When is allergy testing required
- When to refer to allergy service

26 years old lady attended A&E

- Shortness of breath
- Throat and tongue angioedema
- Urticarial rash
- Diagnosed with HAE when she was 10 years old.
- Treated in hospital with prednisolone 25 mg + fexofenadine 180 mg for 2 weeks
- Referred by GP to Allergy clinic to control her HAE.

In the clinic

- Recurrent urticarial rash + angioedema involving lip and tongue.
- Since she was 10 years old.
- Early in morning.
- Not related to any specific food.
- Fexofenadine improve symptoms
- Occasionally needs steroids to control her symptoms
- Diagnosed when she was 10 years old with HAE after developing urticarial rash and swellings
- No family history - No emergency plan

Cont. history

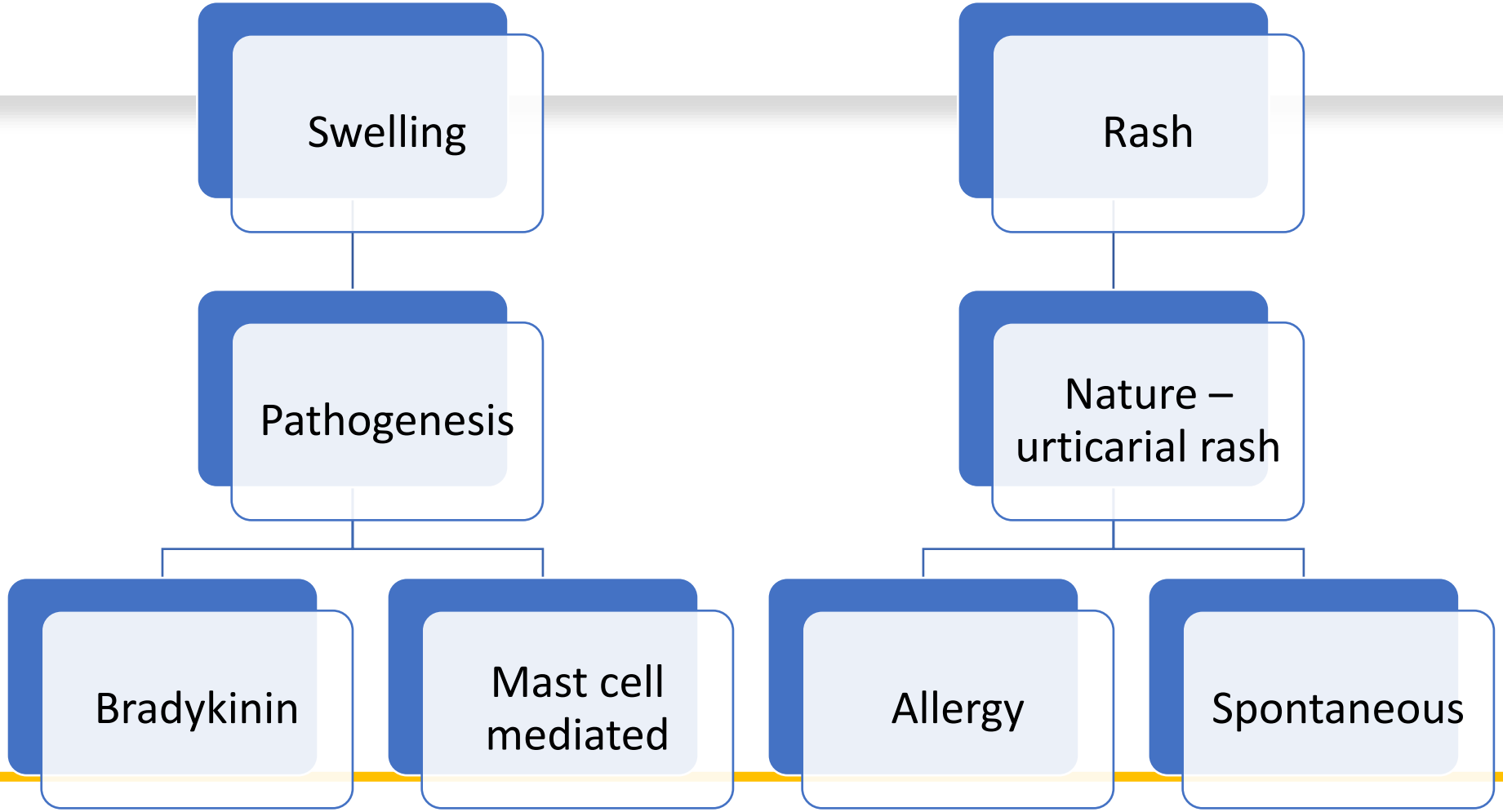
- Past Medical history
- Medications: No regular medications
  - ACE inhibitors
  - Oestrogen containing medications
  - Mast cell stimulators: NSIAD, opiates.
- Social: stress
- Family history
- Photos →


Is this
urticarial
rash ??

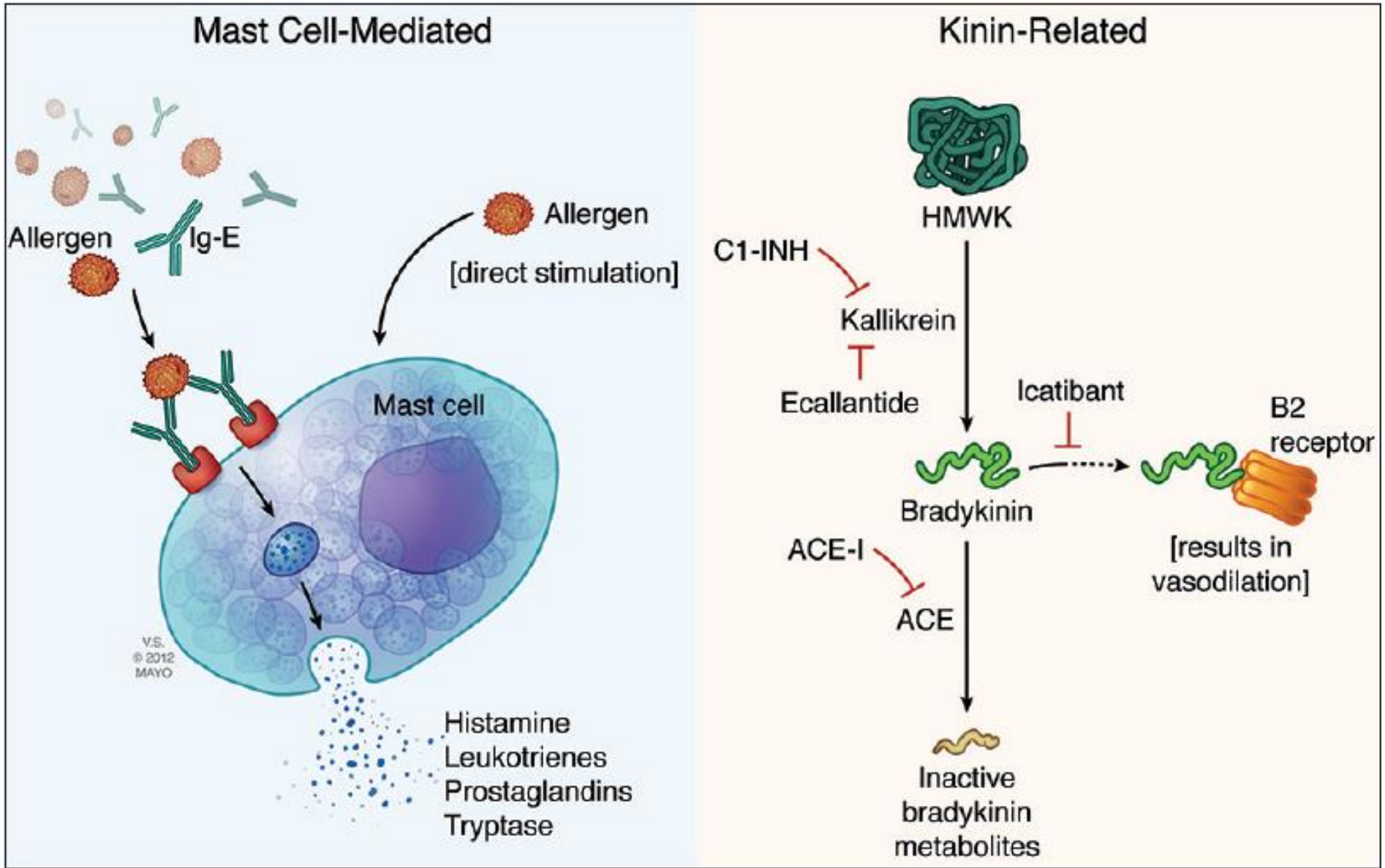
What is urticarial rash ??

- Red (initially with a pale centre), raised rash
- Itchy rash
- Individual lesions last less than 24 h
- Resolve completely – no evidence of residual petechial haemorrhage, purpura or bruising

How to diagnose this case?



Pathogenesis of angioedema

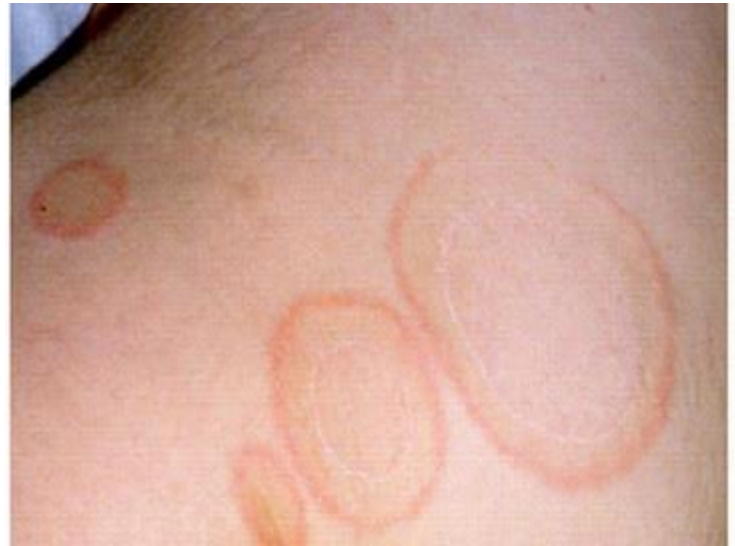


Bradykinin mediated angioedema

- Not associated with itching or urticarial rash
- Does not respond to antihistamines – takes longer to resolve
- D.D
  - HAE → type I, II → C4, C1 esterase inhibitor level and function
  - HAE type III → female, family history
  - Acquired angioedema → hematological malignancy and CT disease → C4, C1 esterase inhibitor level and function
  - ACE inhibitor induced → not related to when medication was started – C/W for 3 months after stopping.
  - Idiopathic angioedema.

Is that HAE attack ??

- HAE is NOT associated with urticarial rash or itching
- Prodromal symptoms: Erythema marginatum (a map-like rash on the skin
- Family history
- C4, C1 esterase inhibitor level and function
- Note HAE type III – Female, normal component profile.
- Alerts / letters
- Emergency management plan:
  - C1 esterase inhibitor / icatibant
  - Do not response to antihistamines or epipen



Mast cell mediated angioedema

- Associated with itching and usually urticarial rash
- Responds to antihistamine
- D.D
  - Allergy
  - Spontaneous urticaria and angioedema → 10% present with angioedema only

Is it histamine or Bradykinin mediated ??

Histamine mediated

1. Associated with urticarial rash
2. Responds to antihistamines

Urticarial rash

Food allergy

Spotaneous


Food allergies

Food allergy

- Occurs within 1 or 2 hours of eating a particular food
- Occurs each time this food is consumed
- Usually associated with other symptoms → chest, GIT, dizziness,….etc.
- Few exceptions
  - Meat (alpha gal), WDEIA and crustaceans (such as prawn) → 6 hrs
  - LTP

LTP allergy (PR14)

- Lipid transfer protein - stable to heat and digestion proteolytic stability
- Common in Mediterranean countries.
- Challenges:
  - Widespread distribution of LTP in plant kingdom – fruits, vegetables and nuts.
  - Clinical expression is extremely variable: tolerate / react with co-factors/ severe allergic reactions. Why ? due to differences in LTP epitope and differences in threshold
  - Link to co-factors making it difficult to predict whether a reaction to a particular food might occur

Is it due to food allergy??

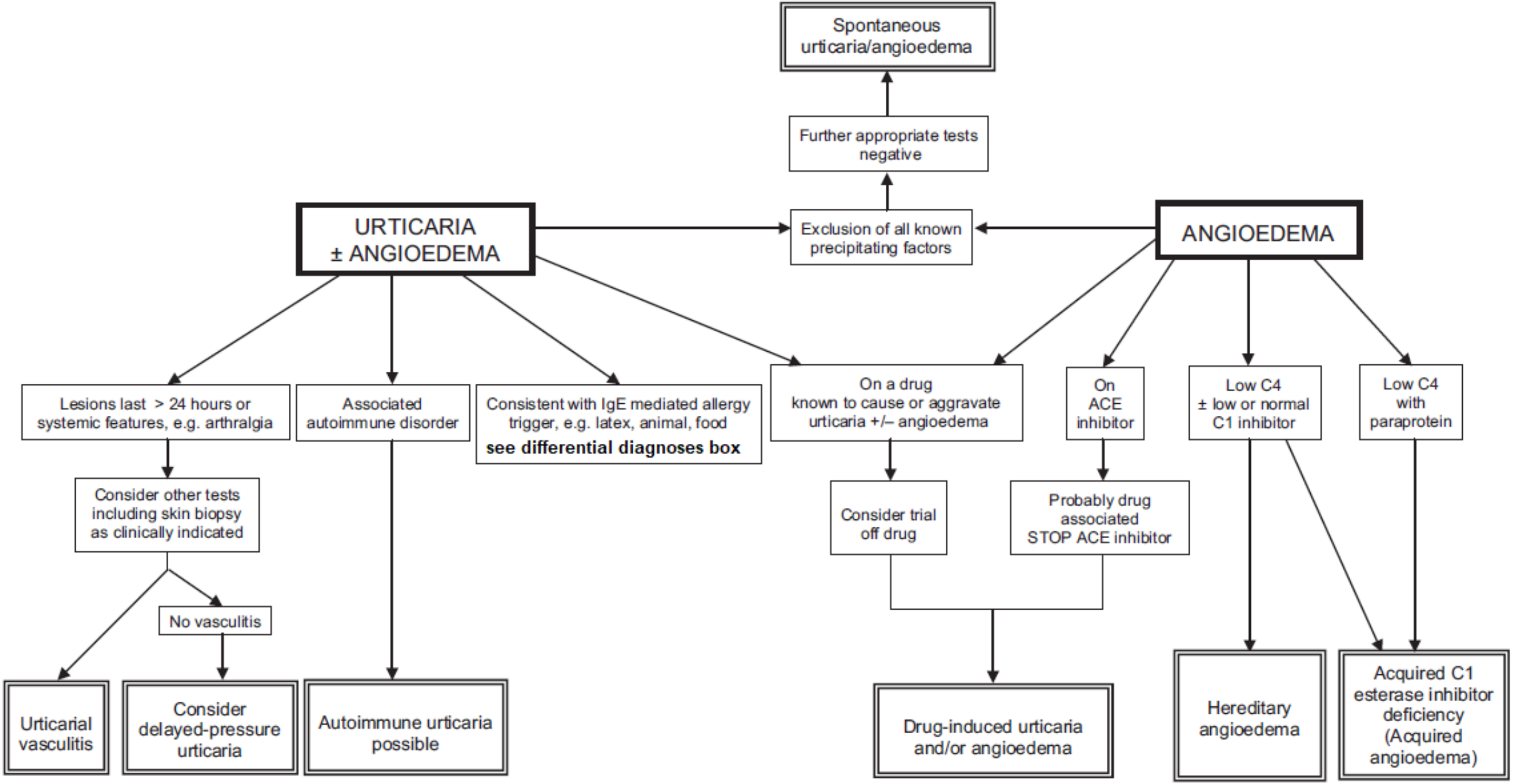
No

1. Occur early in the morning
2. No specific food trigger.

What is the diagnosis ??

Chronic spontaneous Urticaria and Angioedema

Urticaria and Angioedema treatment pathway for GPs


Spontaneous urticaria/angioedema
Further appropriate tests negative
Exclusion of all known precipitating factors
URTICARIA ± ANGIOEDEMA
ANGIOEDEMA
Lesions last > 24 hours or systemic features, e.g. arthralgia
Associated autoimmune disorder
Consistent with IgE mediated allergy trigger, e.g. latex, animal, food
see differential diagnoses box
On a drug known to cause or aggravate urticaria +/– angioedema
On ACE inhibitor
Low C4 ± low or normal C1 inhibitor
Low C4 with paraprotein
Consider other tests including skin biopsy as clinically indicated
No vasculitis
Consider trial off drug
Probably drug associated STOP ACE inhibitor
Urticarial vasculitis
Consider delayed-pressure urticaria
Autoimmune urticaria possible
Drug-induced urticaria and/or angioedema
Hereditary angioedema
Acquired C1 esterase inhibitor deficiency (Acquired angioedema)

Acute and chronic CSU&A non-specialist treatment pathway

Symptoms and signs suggestive of CSU&A

Avoidance

- ACEI should be stopped.
- NSAIDS are not absolutely contraindicated but can exacerbate CSU&A
- Hence use NSAIDs with caution

Regular treatment

- Start long acting non-sedating antihistamines
- Good safety data to use higher unlicensed doses e.g. up to QDS (recommended by BSACI), which is what CIAU routinely uses
- Try this for at least 1 month
- Single agent e.g. Cetirizine 10mg up to QDS to achieve symptom control
- Updosing with a single antihistamine is preferable to mixing different antihistamines
- If ineffective, change agent, e.g. Fexofenadine 180mg BD or Loratadine 10mg up to QDS

Improved

Short history of symptoms:
- Treatment on PRN basis

Long history of symptoms:
- Daily treatment for 3–6 months
- Consider 6-12 months if protracted symptoms
- Gradual withdrawal over a period of weeks.

Poor response

If still symptomatic, add Montelukast 10mg nocte

Improved

- Daily treatment for 3–6 months
- Consider 6-12 months if protracted symptoms
- Gradual withdrawal over a period of weeks.

Poor response

Refer to CIAU

Angioedema

If angioedema is main symptom, start Tranexamic acid 0.5g up to 1g QDS if no contraindication (thrombosis)

Improved

- Daily treatment for 3–6 months
- Consider 6-12 months if protracted symptoms
- Gradual withdrawal over a period of weeks.

Poor response

Refer to CIAU

Anti-histamines in females of child-bearing age

- Higher unlicensed doses of antihistamines are safe to use in females of child bearing age but should be stopped in pregnancy.
- Please refer pregnant females to CIAU.

As required treatment

- Emergency prednisolone course (30mg for 5 days OD) for severe episodes.
- Injectable adrenaline is not routinely used (only if evidence of airway obstruction, in which case refer to CIAU).

Improved

No further steroids

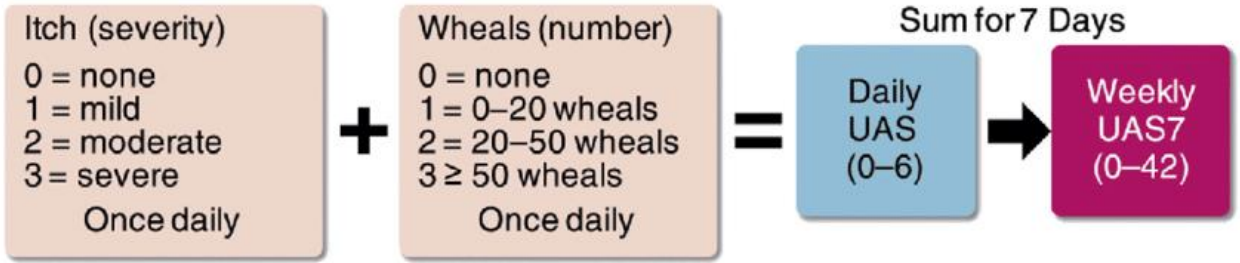
Poor response (>2 courses in 3 months)

Refer to CIAU

What will we do to these patients?

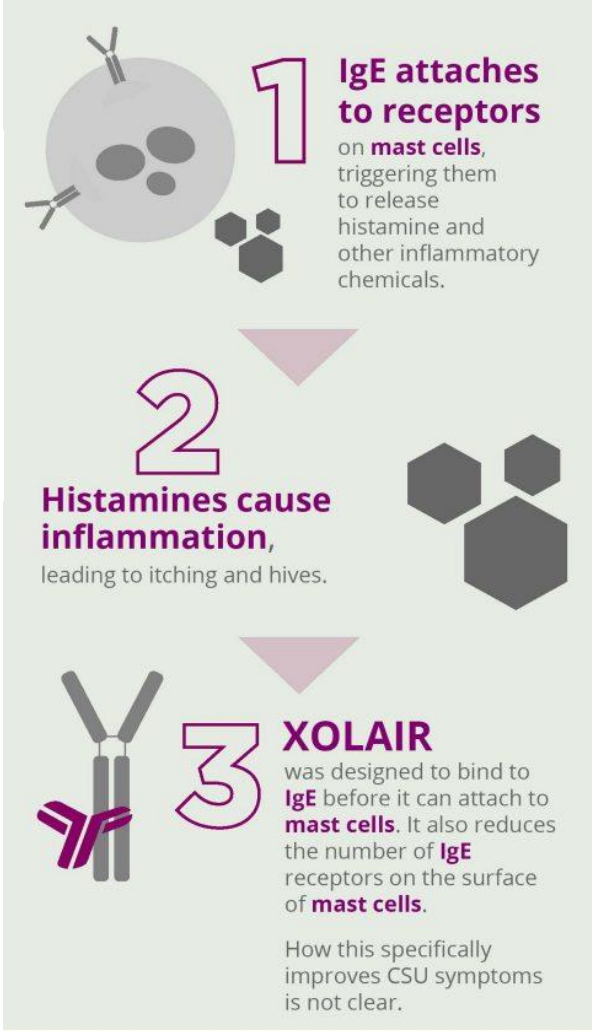
- Patient in MMT – high dose antihistamines and montelukast
- Look at photos
- Routine blood test – TSH
- UAS 7 scores

Score	Wheals	Itch
0 None	None	None
1 Mild	<20 wheals/24 h	Mild (present, but not annoying or troublesome)
2 Moderate	20–50 wheals/24 h	Moderate (troublesome, but does not interfere with normal daily activity or sleep)
3 Intense	>50 wheals/24 h or large confluent areas of wheals	Intense (severe itching, which is sufficiently troublesome to interfere with normal daily activity or sleep)



Omalizumab

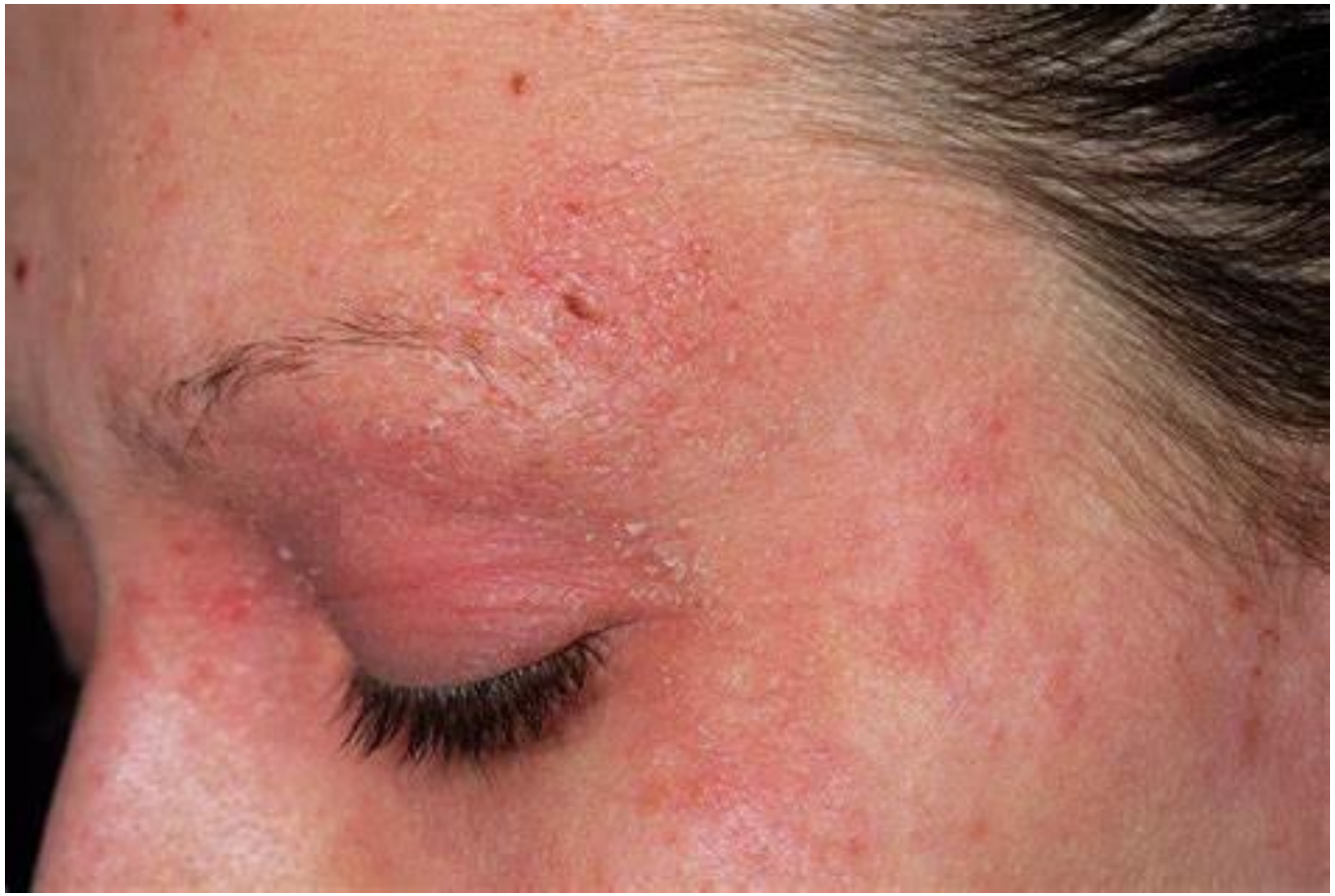
- Add-on therapy for treating severe chronic spontaneous urticaria only if:
- The severity is assessed objectively → UAS7 scores:
  - ≥ 28 or more
  - Despite high dose antihistamines and leukotriene receptor antagonists



Are these cases for Allergy Clinic?

Test me for everything?

- Recurrent urticarial rash. Not able to identify allergen. Referred for allergy test



Patient treated in A&E with adrenaline ??

Rash last 2 weeks
Skin dryness and scales

Food intolerance – not allergy

- Isolated GIT symptoms – reflux, vomiting, diarrhea, abdominal pain, bloating,…etc
- No allergy test is useful – SPT, PPT, S.IgE, ALEX, ISAC, oral challenge.
- We do not interpret or accept private tests
- Need GIT and/or dietician
- D.D:-
  - IBS
  - Coeliac
  - Lactose intolerance
  - Eosinophilic oesophagitis → dysphagia

Allergy testing available

- S.IgE
  - Extract – all proteins
  - Components
    - Storage protein → anaphylaxis
    - Plant based cross reactant proteins → PR10, profilin, LTP
    - Albumin – meat and milk → unlikely to be significant
    - CCD → not clinically significant
    - Sea food cross reactant proteins → tropomyosin, arginine kinase, parvalbumin
- Panels – ALEX, ISAC - secondary care only
- SPT
- PPT
- Challenge

Food mixes

- Sea food mix → Cod, Shrimp, Blue mussel, Tuna, Salmon

Cod, Tuna, salmon → fish **Mussel → molluscs** **Shrimp → crustaceans**	**Parvalbumin** **Tropomyosin** **Arginine kinase**

- Any plant based mixes → nuts, fruits, vegetables,…etc
  - Different groups – legumes, tree nuts, groups of fruits and vegetables.
  - Storage proteins
  - PR10
  - Profilin
  - LTP
  - CCD

Outcome of allergy testing to foods

Positive	Negative
Extract versus component – PR10	Does not exclude allergy – low sensitivity
Sensitisation versus true allergy	Result depends on duration after the reaction – 4 weeks
False positive in atopic patients – T. IgE and PR10	

Need for allergy review +/- allergy dietician input

What to do with suspected food allergy

- Take history
  - Onset of symptoms after eating culprit food
  - What is the culprit food
  - Does it happen every time food is consumed
  - Co-factors – stress, alcohol, infections, NSAIDs
  - What symptoms appear
  - What type of rash – urticarial rash – photos
  - Does patient ever wake up with symptoms
- Still expecting food allergy → submit info via A&G

Total IgE

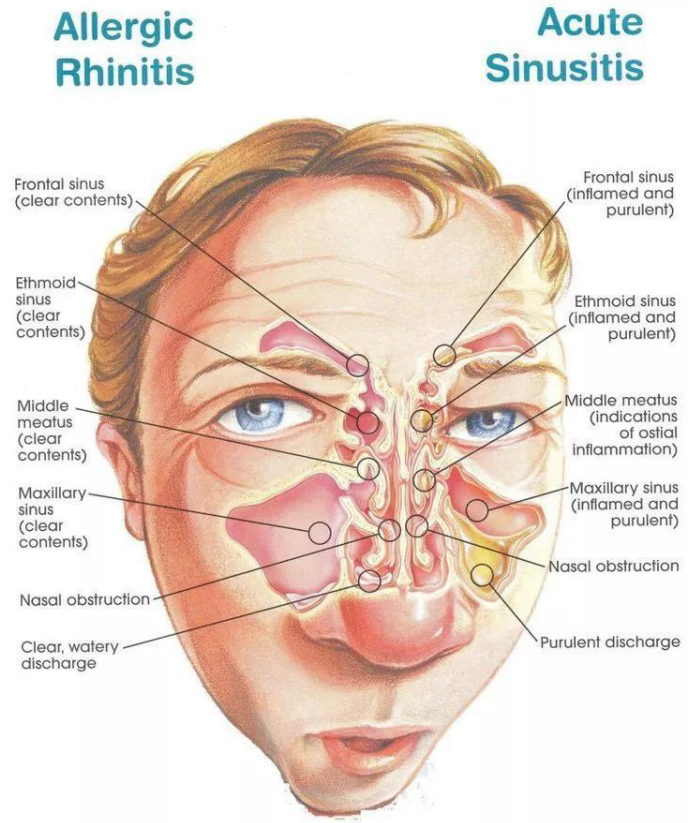
- Not specific
- Low → does not exclude allergy
- High →
  - Common in atopic patients – eczema (not allergy)
  - Other causes – bronchopulmonary aspergillosis, parasitic infections, ID
  - In isolation this is not an indication for allergy testing or review
    - Is it indicated??

Allergic Rhinoconjuntivitis

Diagnosis – History

- Rhino-conjunctivitis versus sinusitis

Rhino-conjunctivitis	Sinusitis
Sneezing Runny nose – clear Nasal itching Throat/palate itching Eyes – itching, redness, tearing +/- asthma symptoms	Sinus pain Nasal blockage Headache Posterior nasal discharge



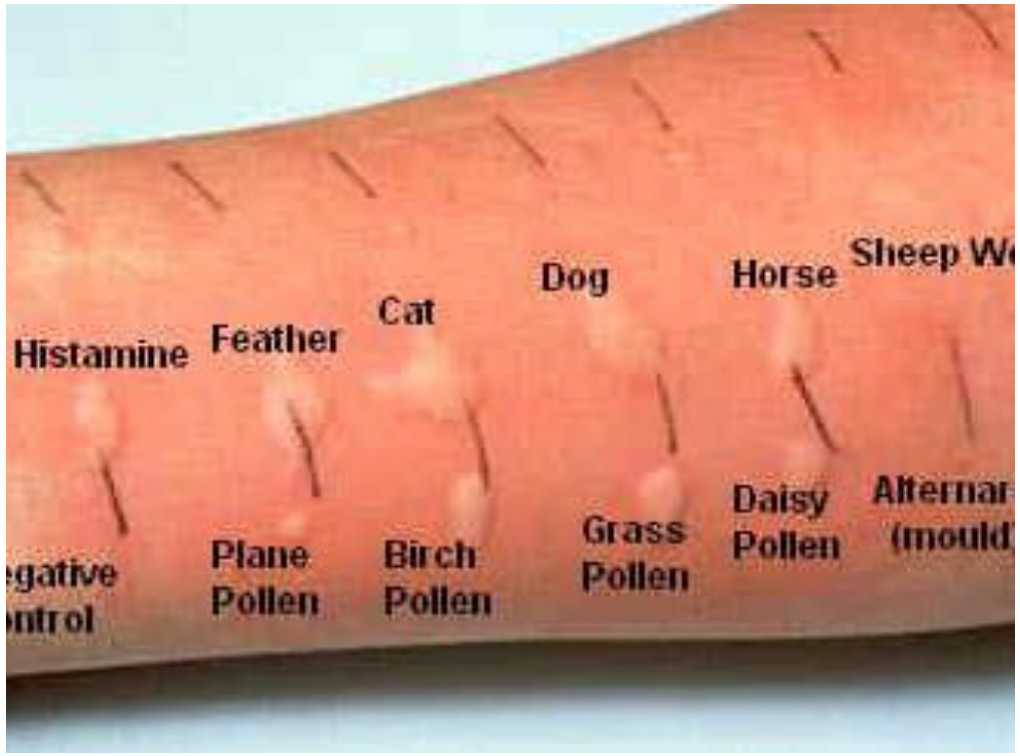
Diagnosis of Allergic rhinitis – History

- Rhino-conjunctivitis versus sinusitis
- If Rhino-conjunctivitis then ask

Seasonal	Perennial
Tree - spring. Grass - summer. Weed -early spring to early autumn.	House dust mites - worse on waking up - may peak in autumn. Animal dander - depending on exposure. Occupational - improve when away from work,

Diagnosis of Allergic rhinitis – Investigations

- SPT
- Blood test
  - S.IgE (aeroallergen panel)
  - ISAC/ALEX
- Challenge



Management of allergic rhinitis

1. Nasal Spray

- Right technique
- 2 weeks before season
  - Steroid nasal sprays e.g. Beconase
  - Antihistamine e.g. Azalastine
  - Combined - Dymista®
    - Combined azelastine and fluticasone proprionate)
    - Fast acting with relief of nasal congestion within 30 mins
    - significantly more effective in seasonal allergic rhinitis than fluticasone alone
  - Ryaltris →
    - Combined mometasone furoate/olopatadine

2. Oral antihistamines

- Cetirizine 10 mg BD
- Loratadine 10 mg BD
- Fexofenadine 180 mg BD

3. Montelukast

- Useful in patients with asthma and allergic rhinitis (multiple sensitisation)
- Not first line treatment
- Side effects: thirst, abdominal pain, headache, anxiety, tics, behavioural change, suicidal ideation

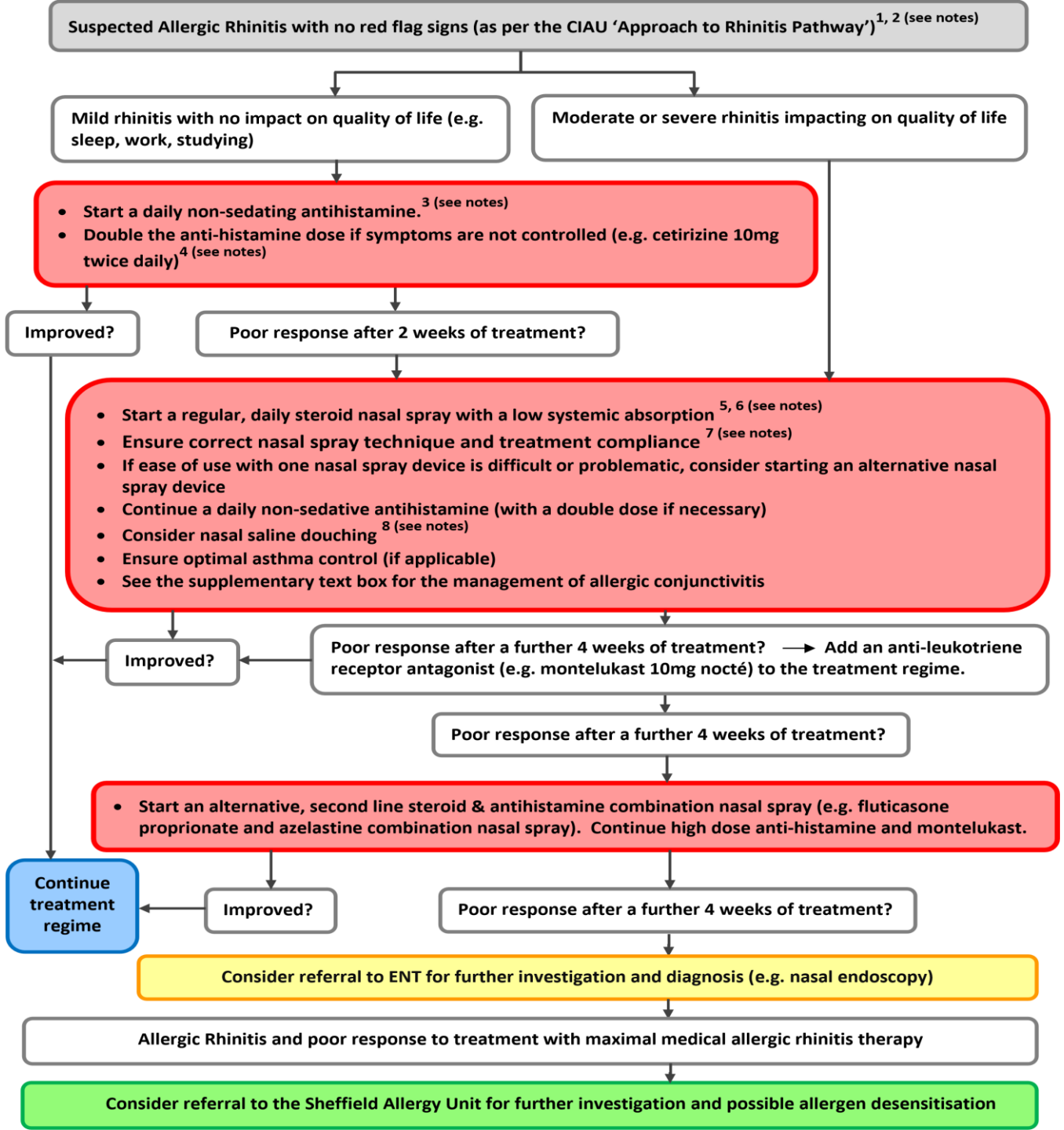
4. Eye drops

Topical anti-histamines (olopatidine, azelastine)

- Effective in treating conjunctivitis
- Side effects: eye irritation/discomfort, blurred vision, headache, dry nose, unpleasant taste in mouth

Sodium cromoglycate

- Very effective in treating conjunctivitis conjunctivitis
- Side effects: burning, stinging and blurred vision


Suspected Allergic Rhinitis with no red flag signs (as per the CIAU 'Approach to Rhinitis Pathway')[1, 2 (see notes)]
Mild rhinitis with no impact on quality of life (e.g. sleep, work, studying)
Moderate or severe rhinitis impacting on quality of life
Start a daily non-sedating antihistamine.[3 (see notes)]
Double the anti-histamine dose if symptoms are not controlled (e.g. cetirizine 10mg twice daily)[4 (see notes)]
Improved?
Poor response after 2 weeks of treatment?
Start a regular, daily steroid nasal spray with a low systemic absorption[5, 6 (see notes)]
Ensure correct nasal spray technique and treatment compliance[7 (see notes)]
If ease of use with one nasal spray device is difficult or problematic, consider starting an alternative nasal spray device
Continue a daily non-sedative antihistamine (with a double dose if necessary)
Consider nasal saline douching[8 (see notes)]
Ensure optimal asthma control (if applicable)
See the supplementary text box for the management of allergic conjunctivitis
Improved?
Poor response after a further 4 weeks of treatment? → Add an anti-leukotriene receptor antagonist (e.g. montelukast 10mg nocté) to the treatment regime.
Poor response after a further 4 weeks of treatment?
Start an alternative, second line steroid & antihistamine combination nasal spray (e.g. fluticasone proprionate and azelastine combination nasal spray). Continue high dose anti-histamine and montelukast.
Continue treatment regime
Improved?
Poor response after a further 4 weeks of treatment?
Consider referral to ENT for further investigation and diagnosis (e.g. nasal endoscopy)
Allergic Rhinitis and poor response to treatment with maximal medical allergic rhinitis therapy
Consider referral to the Sheffield Allergy Unit for further investigation and possible allergen desensitisation

Who to refer

- Severe seasonal/perennial allergic rhinitis who are still symptomatic and have a reduced quality of life despite:
  - Twice daily high dose second generation antihistamines taken regularly
  - Steroid and antihistamine combined nasal spray daily
  - Nasal douching
  - Trial of montelukast
- Pet allergy – history of occupational exposure

Eligibility criteria for desensitization

- Patient assessed in allergy clinic – allergy confirmed
- Severe seasonal/perennial allergic rhinitis
  - Maximum medical treatment
  - still symptomatic
  - Reduced quality of life
- Pet allergy – history of occupational exposure
- D/W Immunology MDT – SCIT and SLIT are both offered to patient

When is Allergy testing required for AR

- Confirm diagnosis before desensitisation
- Does not change initial management plan
- Would be useful if pet allergy needs to be excluded

Summary

- We do not recommend food mixes or isolated total IgE for investigating food allergy.
- Allergy testing should only be done when history is suggestive of allergy – not screening tool
- Take history if food allergy is suspected and discuss via A&G – form to be filled.
- AR
  - History is important
  - S.IgE aeroallergens help confirm allergen
  - Does not change the initial management.

Best Practice guidelines for Specific IgE testing in primary care

- Published on the RCPath website
- https://www.rcpath.org/static/a49f66cc-3c78-4ee7-97814c34a9d7d462/G194-BPR-Use-of-laboratory-allergy-testing-in-primary-care.pdf

Thank you

Any Questions ?