Immunology Update

Dr Lisa Devlin
Consultant Immunologist

Medical Staff

- **Consultants**
- Dr Lisa Devlin
- Dr Tanya Coulter
- Dr Cathal Steel (locum)







- **Junior medical staff**
- Dr Jayne McGuckan (ST7)
- Dr Vyanka Redenbaugh (ST5)
- Dr Inas Maki (ST4)
- Dr Michael Zhang (SAS)



Access to service

Royal College of Physicians | Quality in Primary Immunodeficiency Services

- Immunology
- Urgent
  - 27 patients
  - 6-8 weeks
- Routine
  - 88 patients
  - 39 weeks

Royal College of Physicians | Improving Quality in Allergy Services

- Allergy
- Urgent
  - 699 patients
  - 86 weeks
- Routine
  - 2359 patients
  - 390 weeks

Allergy Statistics

- **Food allergy affects about 8% of children in the Western countries** *Pediatr Allergy Immunol. 2021 May; 32(4): 647–657*
- **Food allergy may affect 7 to 11 percent of college-age individuals** *JAMA Netw Open 2019; 2:e185630.*
- **In a cross-sectional survey of over 40,000 adults in the United States conducted between 2015 and 2016, the estimate of convincing food allergy was significantly higher, at 10.8 percent, with a self-reported prevalence of twice that** *JAMA Netw Open 2019; 2:e185630.*
- **Allergic rhinitis affects 10–15% of children and 26% of adults in the UK** *Clin Exp Allergy. 2017;47:856–889*
- **Chronic urticaria affects 2–3% of individuals (lifetime prevalence)** *Clinical & Experimental Allergy, 45, 547–565*
- **Urticaria affects up to 20% of the population at some point in their lives.** *Kaplan AP. Urticaria and angioedema. In: Middleton's Allergy: Principles and practice, 7th, Adkinson NF, Bochner BS, Busse WW, Holgate ST, Lemanske RF, Simons FER (Eds), Mosby, St Louis, MO 2009. Vol 2, p.1063.*

Consequences of lengthy waiting times

- Patients with food allergy having no access to a formal diagnosis/management advice
- Patients with CSU having frequent attendances to A&E/GP practice
- Limited treatment options for patients with multiple drug allergy labels
- Patients with an episode of spontaneous urticaria waiting to be tested for the ‘hidden allergen’

Immunology referral triage

- Standard advice letter
- Specific advice referrer +/- patient
- Telephone call
- OP consultation
  - Immunology
  - Allergy
    - General allergy routine/urgent
    - Chronic spontaneous urticaria clinic
    - Venom clinic
    - Pollen desensitisation clinic
    - Drug allergy clinic
    - Local anesthetic clinic

Long waiters 1:

- 24 year old male
- 2 week history of relapsing/remitting pattern of urticaria 2015
- No recurrence
- Expecting ‘allergy test’
- Advice given re causes of urticaria, not suggestive of IgE mediated allergy
- Discharged

Long waiters 2:

- 64 year old male
- recurrent episodes of angioedema of lips/tongue
- adrenalin used multiple times
- ICU admission; intubation for airway involvement
- 5 years later at consult;
  - On Ramipril
  - Ramipril discontinued; no further episodes

Long waiters 3:

- 29 year old female
- Recurrent episodes urticaria, lip tingling
- Feels airway/oropharynx getting ‘tight’
- Can’t work out what she’s allergic to
- Avoiding nuts, seeds, seafood, crisps, Chinese takeaways, bread
- Significant food anxiety
- Multiple attendances to A&E

Detailed triage of referrals with the aim of:

- Providing a management plan for patients with well defined clinical conditions
  - CSU/A
  - Allergic rhinitis (AR)
  - Some drug allergies (e.g. clear reaction to NSAID)
- Interpretation of ‘immunology tests’
  - High IgM
  - Specific IgA deficiency

Detailed triage of referrals with the aim of:

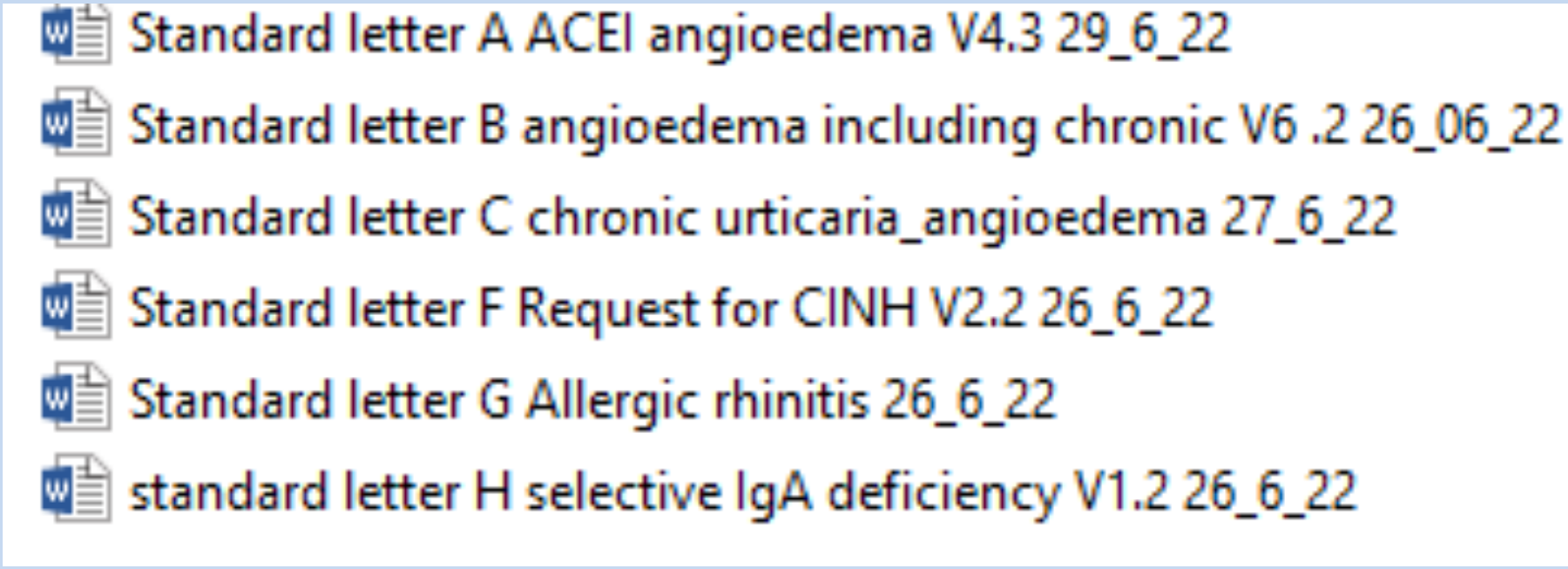
- Ensuring patients referred to the correct service
- Not offering an appointment when the immunology service is unlikely to add anything to the management of the patient
  - Chronic fatigue syndrome/ME
  - GI upset with bloating
  - ‘Allergy screen’ for patients with non-IgE mediated type symptoms

Detailed triage of referrals with the aim of:

- Streamlining patients to specific clinics
  - CSU/A
  - AR desensitisation
  - Venom
  - Drug allergy
  - Local anaesthetic allergy

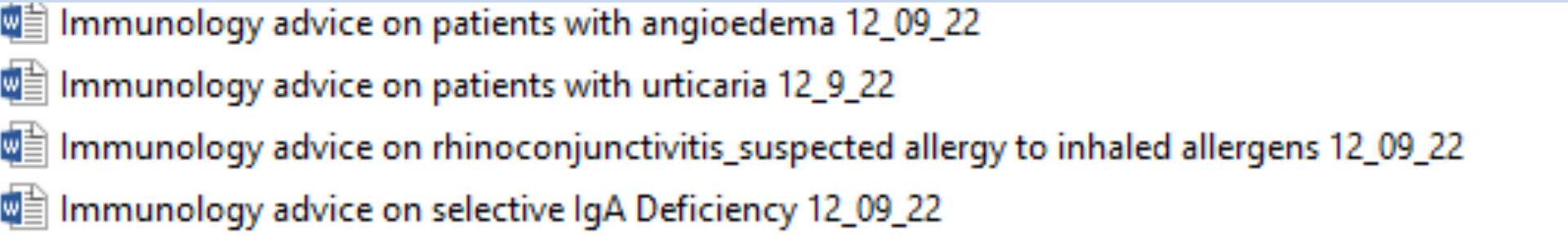
Referral triage outcomes

- Work in partnership with GP colleagues/other referrer to achieve a timely effective service


Standard letter A ACEI angioedema V4.3 29_6_22
Standard letter B angioedema including chronic V6 .2 26_06_22
Standard letter C chronic urticaria_angioedema 27_6_22
Standard letter F Request for CINH V2.2 26_6_22
Standard letter G Allergic rhinitis 26_6_22
standard letter H selective IgA deficiency V1.2 26_6_22

Direct referral to sub-destinations

- Chronic spontaneous urticaria/angioedema clinic
- Allergic rhinitis desensitisation clinic
- Venom allergy clinic
- Immunology clinic
- Allergy clinic



Clinical vignettes

Reason for Referral/ History of Presenting Complaint

Description: immunology

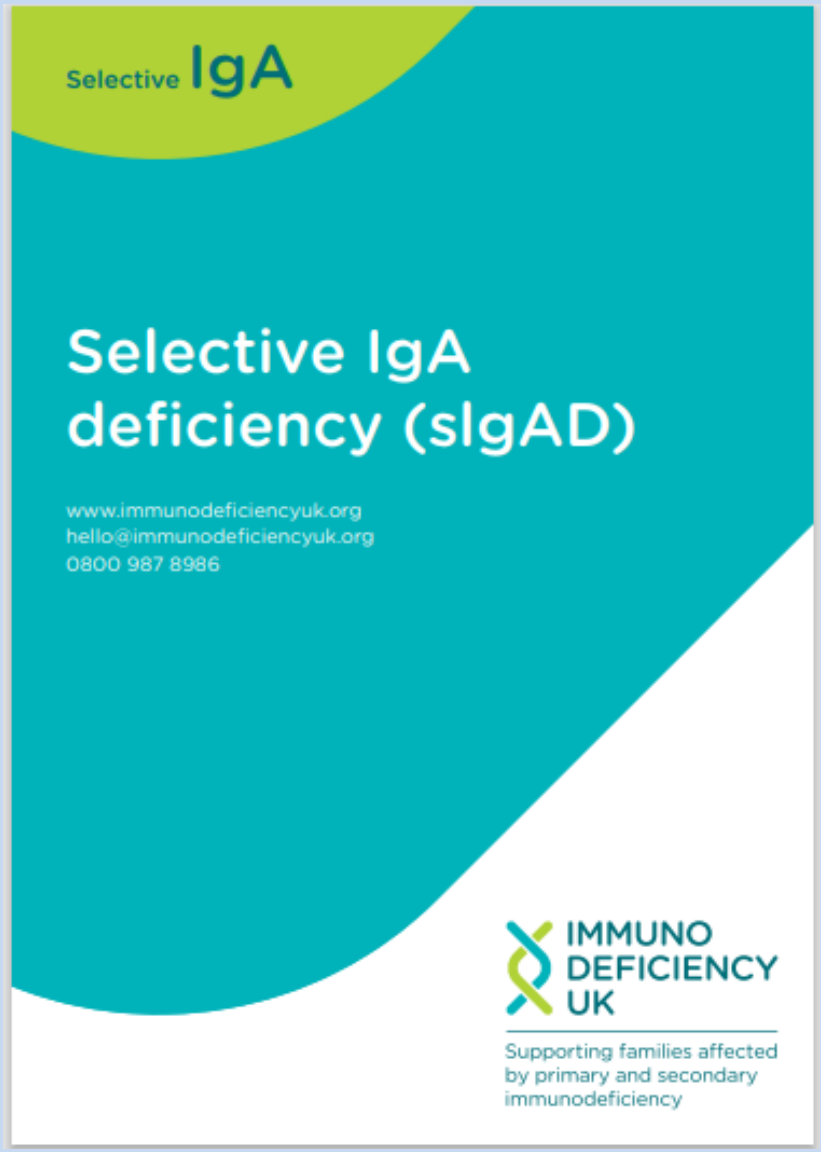
Comment: Dear Dr
Thanks for seeing this woman with very nonspecific symptoms.She describes alternating constipation /diarrhoea No weight loss energy poor had bloods Uss here 2016 and USA fatty liver and was told had autoimmune disease ? coeliac was suggested jejenal biopsy but had already stopped gluten and was so symptomatic when recommenced Also gets low energy occ prb no imb IgA was lower than normal range Could you advise re further management.

Results:

Test	Result	Ref. Range (Units)	Abnormality	Status
T Protein	69	60-80 (g/L)	Normal	Final
IgG	12.41	6.0-16.0 (g/L)	Normal	Final
IgA	* **<0.05**	0.80-2.80 (g/L)	**Below low normal**	Final
IgM	1.68	0.50-2.00 (g/L)	Normal	Final
SPE	No Paraprotein Detected			Final

Specific IgA Deficiency (sIgAD)

- IgA; protects against infections of the mucous membranes of the GI Tract and airways
- sIgAD Common 1/700 in Northern Ireland
- **Many patients are asymptomatic**
- Can be associated with:
  - Infections
  - autoimmune or allergic disease



HSC Belfast Health and Social Care Trust

caring supporting improving together

Advice on Selective IgA deficiency

Thank you for your referral for this patient with absent IgA.

Selective IgA Deficiency (sIgAD) is a common primary immunodeficiency.
It has a prevalence of approximately1 in 600 in the UK.

The majority of people with sIgAD are asymptomatic and the condition is often picked up incidentally on testing based around IgA autoantibodies (e.g. coeliac screen).

Patients usually fall into one of three categories:

- **Asymptomatic** (majority). No specific treatment is required.
- **Increased incidence of allergic and autoimmune disease**. No deviation from standard management of these conditions is required.
- **Recurrent infections**. In this case, sIgAD may be associated with another immune defect and requires investigation in an immunology clinic.

At this stage we will not be organising an outpatient appointment. However if your patient suffers from recurrent, severe, unusual or persistent infections – please send a follow up referral.

Further information and a patient information leaflet on selective IgA deficiency can be found at:
immunodeficiencyuk.org
in the section on resources for patients, carers and professionals.

Should you wish to discuss this further, please contact the Regional Immunology Services at 028961 50088.

Yours sincerely

Description: Low Ig

Comment: Many thanks for seeing this 77 year old patient with low IgM

Bloods done to investigate numbness in fingers
Awaits Rheumatology input

Low IgM - on several blood tests - latest results 0.37
No paraprotein detected
Normal bloods otherwise
Urine for Bence Jones protein negative

Feeling well, weight steady, no other concerns
No recurring infections

Given ongoing IgM, many thanks for seeing and assessing ? need for further investigations

2	3	Ref. Range (Units)
05-Feb 2018 14:37	13-Nov 2020 09:39	
[2] BHSCT	[3] BHSCT	
6.87	6.29	6.0-16.0 (g/L)
1.24	1.29	0.80-4.00 (g/L)
* **0.39**	* **0.39**	0.50-2.00 (g/L)

- Common finding with increasing age
- Reference ranges are calculated on 95% CI
  - 2.5% will be below normal reference range
- ?Evolving immune paresis
  - Primary antibody deficiency
  - Immunosuppression
  - Lymphoproliferative disease

Raised IgM- ? significance

Comment: Dear Dr,

I would be grateful for your advice on a raised IgM level. This has been checked in the context of feeling unwell. IgM initially was 5.15 g/L, Subsequent IgM check was 4.84g/L. Plasma protein electrophoresis and free light chain ratio are normal. I am wondering how significant a raised IgM is and how much monitoring is required/ if any? T[redacted]

	Number	1	Ref. Range (Units)
☐	Collected	05-Aug 2020 11:30	
	Signed		
	Source	[1] NHSCT	
☐	**IgA**	2.78	0.8-4.0 (g/L)
☐	**IgG**	10.97	6-16 (g/L)
☐	**IgM**	* **5.16**	0.5-2.0 (g/L)

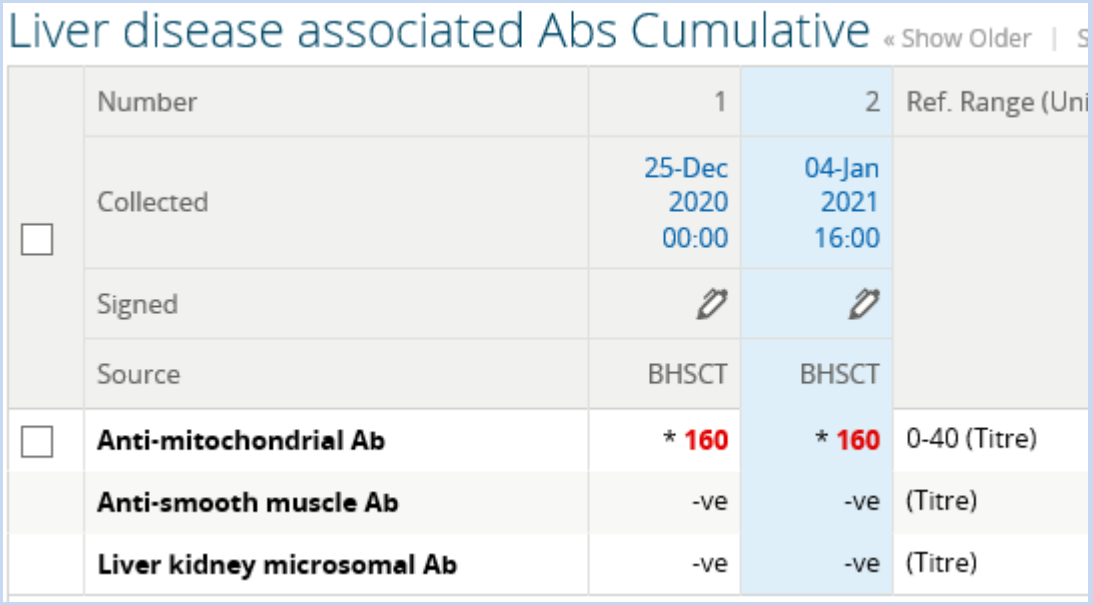
Graph No tests selected

	Number	1	Ref. Range (Units)
☐	Collected	27-Aug 2020 11:36	
	Signed		
	Source	BHSCT	
☐	**Free Kappa (Old)**	16.5	3.3-19.4 (mg/L)
☐	**Free Lambda (Old)**	12.2	5.7-26.3 (mg/L)
☐	**Kappa / Lambda ratio(Old)**	[a] 1.35	0.26-1.65 (Ratio)

Bence Jones Protein Cumulative « Show Older | Show Newer »

	Number	1	Ref. Range (Units)
☐	Collected	05-Aug 2020 11:30	
	Signed		
	Source	[1] NHSCT	
	Urine: Bence Jones' protein	Not Dete...	

Primary Biliary Cirrhosis



Liver disease associated Abs Cumulative « Show Older | S

	Number	1	2	Ref. Range (Uni
☐	Collected	25-Dec 2020 00:00	04-Jan 2021 16:00	
	Signed			
	Source	BHSCT	BHSCT	
☐	**Anti-mitochondrial Ab**	* 160	* 160	0-40 (Titre)
	Anti-smooth muscle Ab	-ve	-ve	(Titre)
	Liver kidney microsomal Ab	-ve	-ve	(Titre)

Autoimmune hepatitis

	Collected	27-Mar 2018 10:06	09-May 2018 00:00	04-Jun 2019 10:29	25-Feb 2020 10:29	05-Jan 2021 11:33	
	Signed						
	Source	[6] BHSCT	[7] BHSCT	[8] BHSCT	[9] BHSCT	[10] BHSCT	
	IgG	* **19.78**	* **18.77**	* **18.16**	* **18.26**	* **20.88**	6.0-16.0 (g/L)
	IgA	3.60	3.15	3.22	3.27	3.44	0.80-4.00 (g/L)
	IgM	1.38	1.31	1.11	1.24	1.66	0.50-2.00 (g/L)

Anti-mitochondrial Ab	-ve	-ve
Anti-smooth muscle Ab	* **160**	* **160**
Liver kidney microsomal Ab	-ve	-ve

Collected	04-Feb 2020 09:45	25-Feb 2020 10:29	26-Mar 2020 10:47	27-Apr 2020 10:15	05-Jan 2021 11:33	
Signed						
Source	[20] BHSCT	BHSCT	[21] BHSCT	[22] BHSCT	BHSCT	
T.Bilirubin	20	18	19	12	14	§
ALP	* **491**	* **420**	* **489**	* **339**	* **505**	§
AST	* **95**	* **83**	* **89**	* **85**	* **86**	§
GGT	* **538**	* **496**	* **510**	* **413**	* **514**	§
ALT	* **137**	* **99**	* **111**	* **79**	* **97**	§
Albumin	41	44	43	42	39	§

Reason for Referral/ History of Presenting Complaint

Description: Raised IgA

Comment: Raised IgA of 4.21. IgM and IgG normal. Recurrent infections in the form of throat infection and thrush. No UTI. ESR has been high at 32 but now improved to 17 CRP is normal. FBP and Bence Jones normal. Has been overweight and had some intentional weight loss.

OE HS NAD. HR 72, reg. RR 16. Glands NAD. Axilla NAD. Breasts normal. Chest clear.

Many thanks for your further assessment

	Number	1	2	Ref. Range (Units)
☐	Collected	06-May 2022 08:44	28-Jul 2022 08:44	
	Signed			
	Source	[1] NHSCT	[2] NHSCT	
☐	**IgA**	* **4.16**	* **4.21**	0.8-2.8 (g/L)
☐	**IgG**	**11.57**	**11.73**	6-16 (g/L)
☐	**IgM**	**1.01**	**1.12**	0.5-1.9 (g/L)

Appendix 7:

Immunoglobulin Reference Ranges

Age	IgA (g/L)	IgG (g/L)	IgM (g/L)
Cord	<0.02	5.2 - 18.0	0.02 – 0.20
0 - 2 weeks	0.01 - 0.08	5.0 - 17.0	0.05 - 0.20
2 - 6 weeks	0.02 - 0.15	3.9 - 13.0	0.08 - 0.40
6 - 12 weeks	0.05 - 0.40	2.1 - 7.7	0.15 - 0.70
3 - 6 months	0.10 - 0.50	2.4 - 8.8	0.20 - 1.00
6 - 9 months	0.15 - 0.70	3.0 - 9.0	0.40 - 1.60
9 - 12 months	0.20 - 0.70	3.0 - 10.9	0.60 - 2.10
1 - 2 years	0.30 - 1.20	3.1 - 13.8	0.50 - 2.20
2 - 3 years	0.30 - 1.30	3.7 - 15.8	0.50 - 2.20
3 - 6 years	0.40 - 2.00	4.9 - 16.1	0.50 - 2.00
6 - 9 years	0.50 - 2.40	5.4 - 16.1	0.50 - 1.80
9 - 12 years	0.70 - 2.50	5.4 - 16.1	0.50 - 1.80
12 - 15 years	0.80 - 2.80	5.4 - 16.1	0.50 - 1.90
15 - 45 years	0.80 - 2.80	6.0 - 16.0	0.50 - 1.90
Over 45 years	0.80 - 4.00	6.0 - 16.0	0.50 - 2.00

Source: PRU Handbook of clinical immunochemistry 9th edition.

Recurrent shingles

Reason for Referral/ History of Presenting Complaint

Description: recurrent shingles

Comment: please see
42 year old female
states 3 year hx of recurrent episodes of shingles
approx. 4 episodes per year
all classic of shingles presentation
right buttock and lower back area affected

bloods thus far normal
no underlying immunosuppression known

increasing frequency and severity of same
impacting upon work as SW

I would be most grateful for any input or advice for this lady
?shingles vaccination ?immunoglobulins required ?further investigations

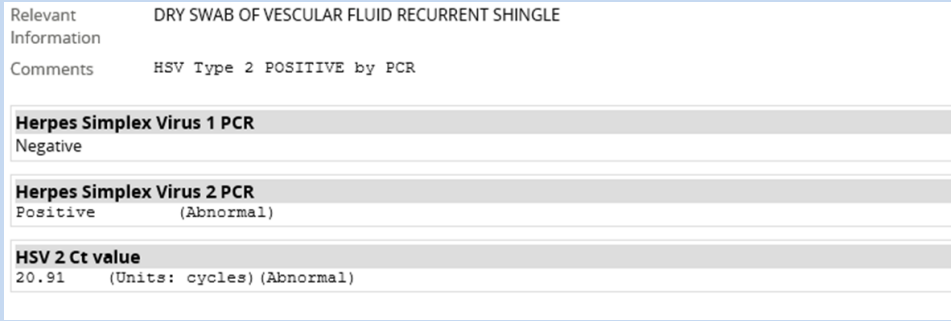






PCR for virology

- For recurrent ‘shingles’



Relevant Information	DRY SWAB OF VESCULAR FLUID RECURRENT SHINGLE
Comments	HSV Type 2 POSITIVE by PCR

Herpes Simplex Virus 1 PCR
Negative

Herpes Simplex Virus 2 PCR
Positive (Abnormal)

HSV 2 Ct value
20.91 (Units: cycles) (Abnormal)

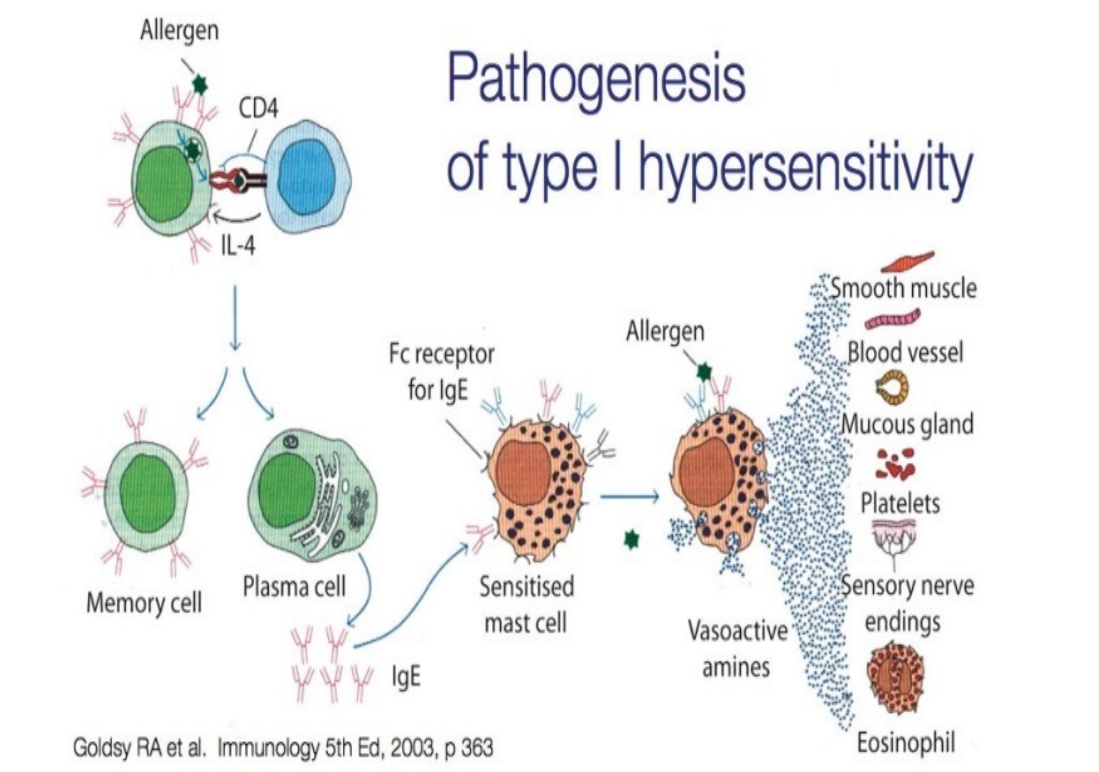
‘ALLERGIES’

Urticaria/angioedema

- Causes are numerous

- **urticaria/angioedema and allergy are not synonymous**

Allergic disease: IgE mediated reactions



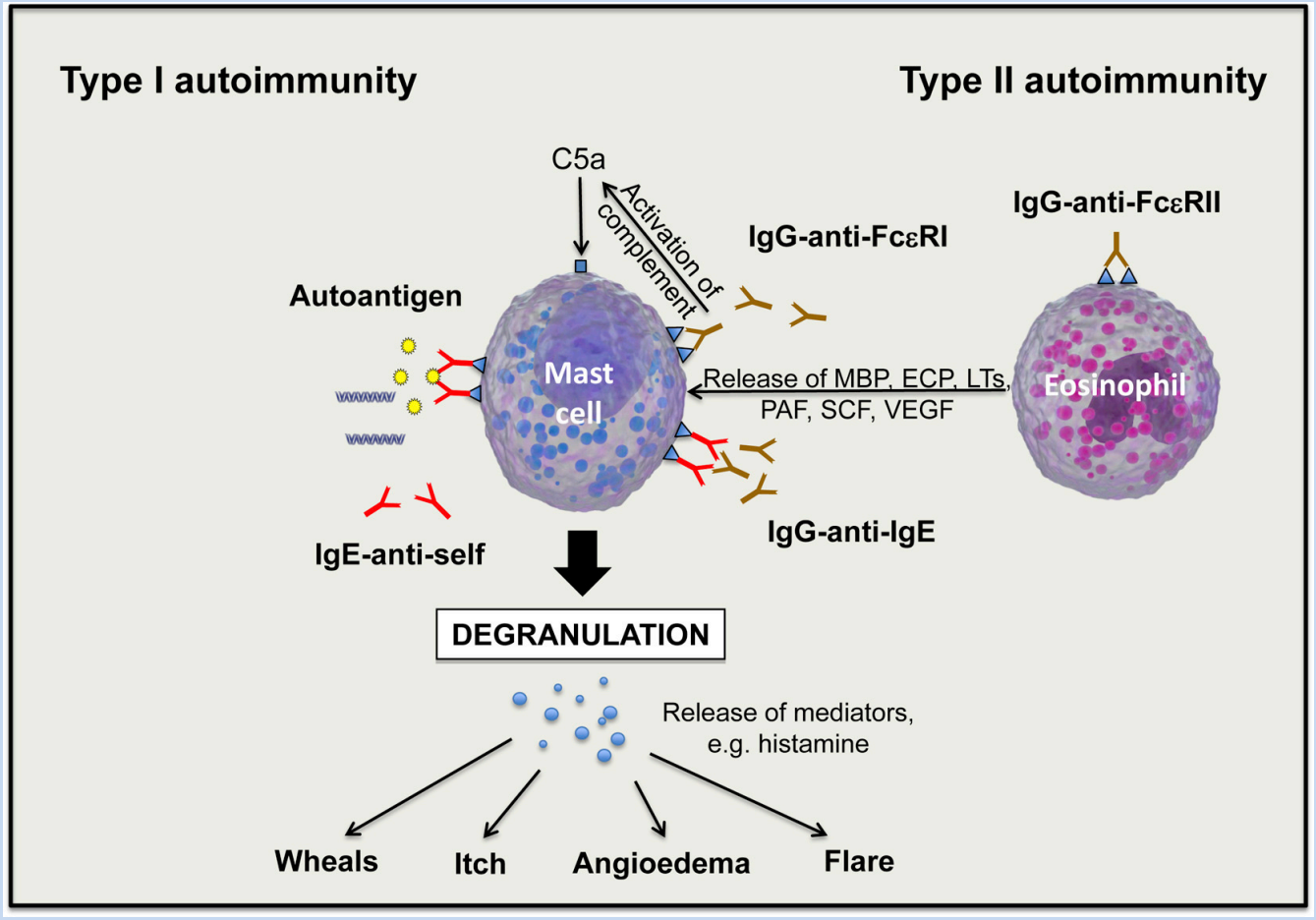
- Urticaria/angioedema/Itching of oropharynx
- Gastrointestinal upset; vomiting, diarrhoea
- Respiratory difficulty
- Cardiovascular collapse

Causes of urticaria:

mast cell degranulation can occur via non IgE mediated pathways

- Allergy; food, drug
- Infection
- Spontaneous; Chronic spontaneous urticaria/angioedema (CSU)
- Medication
- Physical
  - Dermographism
  - Cold
  - Cholinergic; exercise, heat, emotion
  - Pressure
  - solar
  - Aquagenic

- Urticaria Pigmentosa
- Urticarial Vasculitis
- Cryopyrin Associated Periodic Syndrome (CAPS)



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Reason for Referral/ History of Presenting Complaint

Description: Allergic Reaction

anaphylaxis anaphylaxis

anaphylaxis

Comment: in a&e on 8/3/22 following anaphylactic reaction.
unsure what allergic to; was eating turkey burger in bap- had seeds on it- unsure what type;
reports eats peanut butter all the time without issue;
see a&e note on ecr "Anaphylaxis - Site:Suspected Comments:Anaphylaxis, turkey burger unaware of possible allergen. 3 doses of Adrenaline IV Chlorphenamine + Hydrocortisone. Intended to observe for 6 hours howver patient CTMA after 3. Educated on epipens, given 2. Leaflet advice to reinforce. Safety netted "

patient says given epipens and educated on use- knows to carry on person at all times.
agreed come in for bloods inc RAST sesame seeds;

Urticarial reactions

Comment: Many thanks for seeing this 25yo with a recurrent significant urticarial reaction.
When this comes on she has extensive urticaria across her upper arms, ant/post torso, upper thighs, back of neck. Intensely itchy.
Has been coming and going spontaneously over the last number of weeks without warning or obvious trigger. Never associated with angioedema/respiratory symptoms.
Pt and parents have been trying to exclude causes- have ruled out kiwi/pineapple/laundry detergent/bedding.
Pt has required various anti-histamines and oral steroids to settle reactions.
Grateful for your assessment ?testing for possible allergens ?onward management.

urtacaria - progressing to angioedema requiring ED treatment.

Comment: 32 year old lady referred by a colleague in June 2019 as routine for idiopathic urticaria. recent episode angioedema affecting tongue and mouth, observe and treasted in ED with steroids and antihistamines for prolonged period. has epipens issued by GP in June 2019. takes piriton regularly, I've trialed fexofenadine. please can you upgrade her referral to urgent as her allergic reactions are progressing in severity and frequency. triggers not known.

Description: facial swelling twice

Comment: Please can you see this 42 year old gentleman- patient woke this morning with swollen cheeks, tongue a bit swollen too, urticarial rash on arms. Similar thing happened in August (3 months ago), no unusual foods etc. not sure what he could be allergic to. Has taken a piriton and things are starting to settle. As it has happened twice will refer allergy clinic for further advice- please can you see for further assessment?

Comment: Please see at clinic.

Please see this man who appears to be having recurrent allergic reactions to unknown triggers.

possible allergic reaction ? IgE type to certain foods

Comment: dear dr,

many thanks for assessing this lady.

11/03/2022 Telephone encounter pt- had covid in dec since then having episodes of what sounds like IgE mediated reactn facial burning, tingling lips/ tongue after eating certain foods- 2 bad reactions one 2w ago- when attended hosp- whole face/ neck/ down the body went very red, tingling of lips/ tongue, some urticarial spots l side of lip- no swallow/ breathing diff-after eating a bowl of pasta bolognaise- hosp adv ref to immunology
felt dairy may be the trigger factor so had avoided eating dairy altogether until got a take away - chicken goujons and chips- at the w/e which triggered off a similar reaction. has excluded gluten as well but feels can eat it ok without any reaction. not sure what other foods trigger reaction. presenytly quite cautious and apprehensive in eating any foods- can eat meat- white/ red ok, hasn't eaten any fish not sure if will react- ref immunology meanwhile have adv re antihistamines- chlorphenamine/ non sedating ones.

BURDEN OF CHRONIC SPONTANEOUS URTICARIA (CSU)

CSU is a serious, chronic and distressing skin condition that is difficult to diagnose and manage.

SYMPTOMS[1-4]

There is **no specific external trigger** for CSU, but the autoimmune system may play a role.

- SPONTANEOUSLY OCCUR
- CHRONIC (LASTING FOR AT LEAST SIX WEEKS)
- RED HIVES (WHEALS)
- ITCH
- DEEP TISSUE SWELLING (ANGIOEDEMA)

COMPLICATIONS[2]

- SLEEP DEPRIVATION
- LACK OF ENERGY
- DEPRESSION
- ANXIETY
- SOCIAL ISOLATION
- EMOTIONAL UPSET

PREVALENCE[1-2]

At any given time, **0.5-1% of the global population is affected by CSU.** Women are more likely than men to be diagnosed.



[5]

*Typical symptom presentation

DURATION[2]

People with CSU who experience deep tissue swelling (angioedema) may have a greater chance of **CSU lasting for >12 months or longer.**

The **disease generally lasts 1–5 years** but can last for decades.

TREATMENT[2]

Antihistamines are the current mainstay of treatment, but more than 50% of people with CSU on approved antihistamine doses do not achieve symptom relief.

4x

Symptoms remain uncontrolled even in many people with CSU receiving up to four times the approved antihistamine dose.

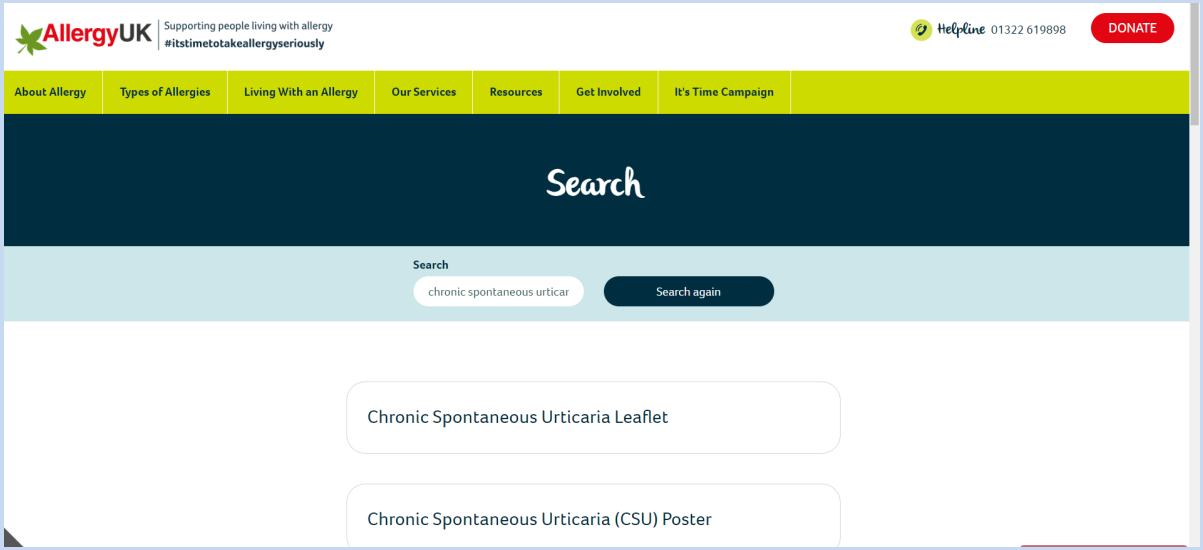
1. Primary Care Dermatology Society website. Available at http://www.pcds.org.uk/clinical-guidance/urticaria-spontaneous-syn.-chronic-ordinary-urticaria *[Last accessed August 2013]
2. Maurer M *et al.* Allergy. 2011;66:317–330.
3. Zuberbier T *et al.* Allergy. 2009;64:1417–1426.
4. Maurer M *et al.* Br J Dermatol. 2013 Feb;168(2):435–456.
5. Zuberbier T et al. Clinical and Experimental Dermatology. 2010;35:869–873.

XOL13-C082
September 2013

NOVARTIS

Chronic spontaneous urticaria/angioedema; treatment

- **Regular non sedating antihistamines**
- Leukotriene receptor antagonists
  - Short courses of rescue steroids may provide temporary control



CSU: omalizumab



Angioedema; Multiple causes?

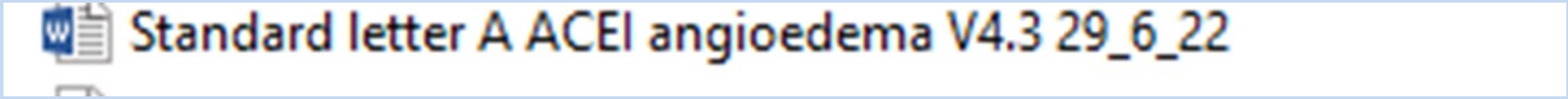
- Allergy
- Infection
- Spontaneous

- Drugs; ACEI
- C1 inhibitor deficiency

allergyic reaction

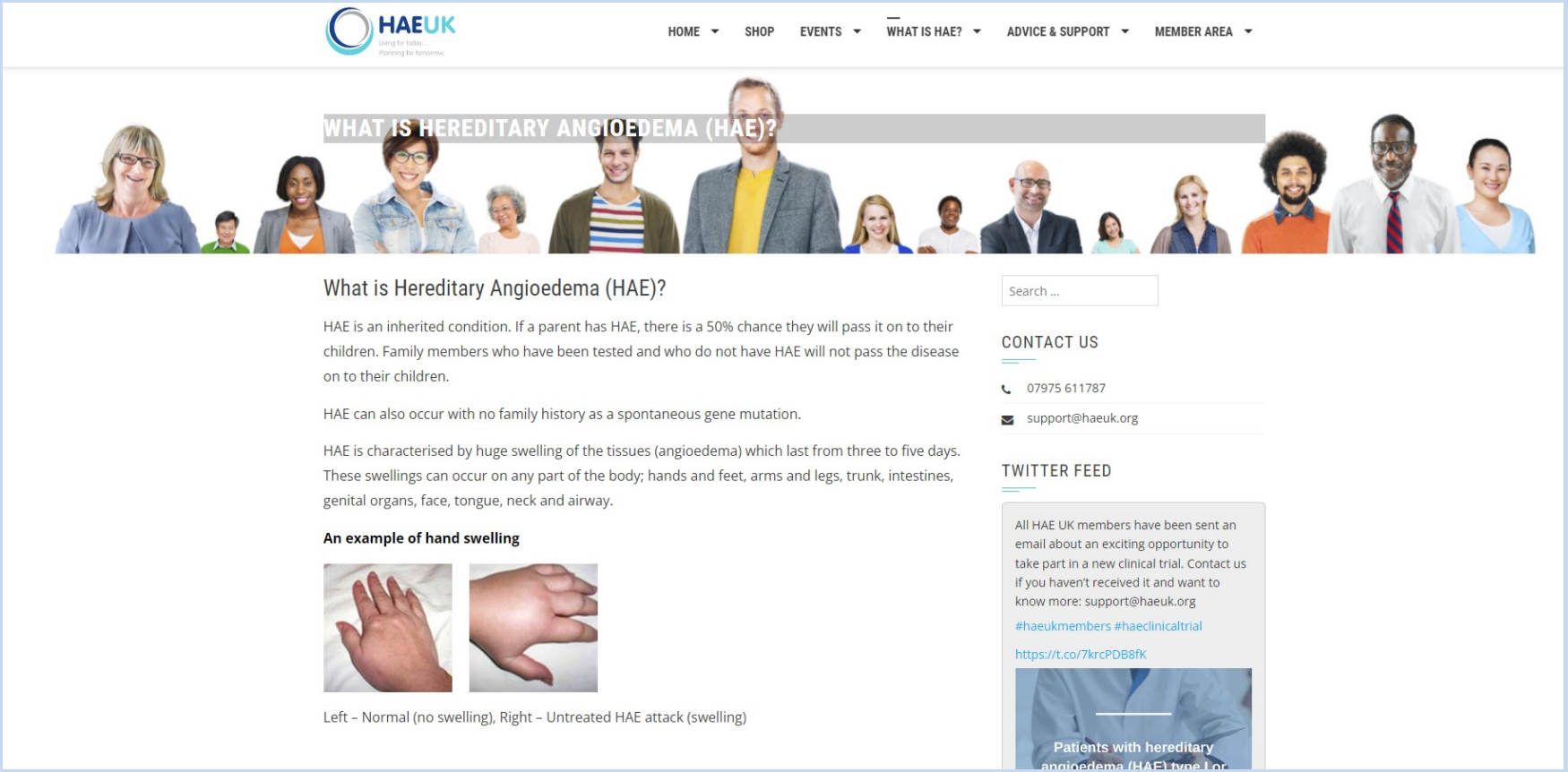
Comment: Thank you for seeing the above named patient who presents with recurrent allergic reaction. The first episode occurred in 2008 and more recently last week with signifiicant swelling of tongue. Seen in a+e both times and been issued with an epipen. A+E suggested onward referral to your department for fuller consideration. Thank you for your assessment

Cardioplen XL 2.5mg tablets (Chiesi Ltd)	11506711000001103	-	1 TAB MANE	-	25-Sep-2017	-
Ramipril 10mg capsules	318906001	-	TAKE ONE DAILY	-	03-Jan-2017	



Severe facial swelling ? cause

Comment: Thank you for seeing this 14yr old girl who has had 3 episodes of quite severe facial swelling over the past 12 months -- most recent requiring a+e attendance and a course of oral steroids. ? precipitated by a new brand of make up -- but not consistent. Is currently taking cetirizine twice daily with some benefit. We would be grateful for your assessment and advise.



Standard letter F Request for CINH V2.2 26_6_22

When to prescribe an adrenaline autoinjector



NICE accredited

doi: 10.1111/cea.12788

Clinical & Experimental Allergy, 46, 1258–1280

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BSACI GUIDELINES

BSACI guideline: prescribing an adrenaline auto-injector

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Clinical & Experimental Allergy

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[*]Correction added on 13 October 2016, after first online publication: author's name corrected from "David Powell" to "Richard Powell".

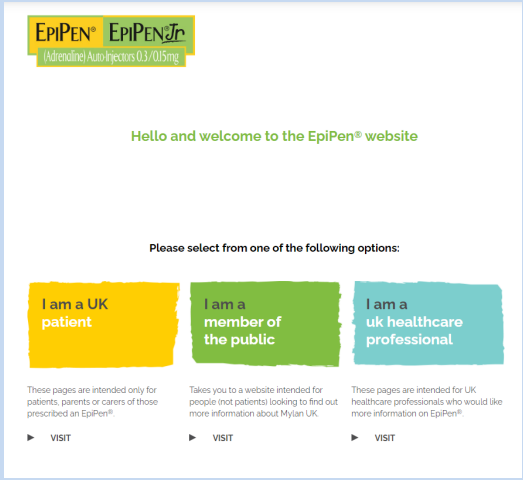
Summary

This guidance for the prescription of an adrenaline auto-injector has been prepared by the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI). There is insufficient quality evidence-based data in some areas, including the question of how often a second dose is required, and the optimal dose and absorption after subcutaneous vs. intramuscular injection. Thus, indications for adrenaline (which are partly opinion based) in guidelines from different countries vary slightly. The guideline is based on evidence as well as on expert opinion and is for use by both adult physicians and paediatricians practising allergy. During the development of these guidelines, all BSACI members were included in the consultation process using a web-based system. Their comments and suggestions were carefully considered by the SOCC. Evidence from randomized controlled trials is lacking in anaphylaxis for ethical reasons. Consensus was reached by the experts on the committee. Included in this guideline are aetiology, risk of recurrence and management of anaphylaxis (after treatment of the acute episode), including allergen avoidance and written treatment plans. There are sections on dose and absorption of adrenaline, and adrenaline auto-injectors, including indications for their prescription, risk assessment for the number required and training in their use. The guidelines are not intended to be prescriptive, and clinicians should use their clinical judgement. Finally, we have made recommendations for potential areas of future research.

Keywords adrenaline, anaphylaxis, auto-injector, British Society for Allergy and Clinical Immunology, epinephrine, guideline, Standards of Care Committee, tryptase
Submitted 30 June 2016; revised 28 July 2016; accepted 28 July 2016

Executive summary

- Adrenaline is the first-line treatment for anaphylaxis. It should be used in patients with significant airway involvement or hypotension, occurring as part of an anaphylactic (IgE- or non-IgE-mediated) reaction.
- An adrenaline auto-injector should be prescribed for those at risk of anaphylaxis.
- An auto-injector allows early administration of adrenaline as this improves outcome. It should be seen as a first-aid measure combined with calling for help (ambulance/emergency medical services).
- After acute anaphylaxis, an adrenaline auto-injector should be prescribed in the Emergency Department or primary care and an allergy referral immediately triggered (NICE guidance).
- Specialist allergy experience is required to make a risk assessment to determine the continuing need for an adrenaline auto-injector. This requires accurate diagnosis of the aetiology, assessment of severity and future risk, including consideration of the amount of allergen involved in previous reactions and the ease of avoiding the trigger. Certain co-factors increase the risk of anaphylaxis, for example asthma in the case of food allergy, raised baseline serum tryptase and the age of the patient.
- Patients at risk of anaphylaxis that should be considered for long-term provision of an adrenaline auto-injector include those
  - who have suffered a severe systemic reaction where the allergen cannot be easily avoided





Practical points for prescribing

- Supply 2 pens - advise patient to carry at all times
- Educate patient on use *only 1/3 - 1/2 patients demonstrate correct technique*
  - Practice pharmacist
  - Community pharmacist
  - Provide demonstration pens
- Train friends/relatives
- Device review and retrain
- Useful resources for patient
  - Epipen.co.uk
  - Anaphylaxis.org.uk

recalcitrant allergic rhinnits and asthma despite treatment

Comment: I would be grateful for your opinion on this young man who has ongoing problems with recalcitrant and persistent allergic rhinitis and also a background history of asthma. he has been seen locally by ent and no obstructive element to has nasal difficulties. his symptoms have been resistant to to treatment with numerous topical steroids/antihistamine and antileukotriene agents. I wonder whether further allergy related investigations would be indicated to assist in his further management. his symptoms trouble him on a daily basis and are impacting significantly on his life

The above named patient under your care has been referred with symptoms suggestive of rhino-conjunctivitis.

This letter includes treatment options for people with these symptoms based on the current guidelines.

Potential Allergens

Allergic rhino-conjunctivitis symptoms (sneezing, nasal congestion, itch +/- ocular symptoms) occur following exposure to a known causative allergen, such as:

- Tree pollens — symptoms occur from early to late spring.
- Grass pollens — symptoms occur from late spring to summer.
- Weed pollens — symptoms may occur from early spring to early autumn.
- House dust mites — symptoms often worse on waking and are present all year-round, but may maybe exacerbated by exposure to a dusty environment.
- Animal dander — symptoms follow exposure to animal dander, and may be all year-round if related to pet exposure.

Further Testing

Allergy testing in the form of Specific IgE to above allergens can be sent in a yellow bottle in brown immunology form to aid diagnosis in conjunction with history from the patient.

Treatment options

Most people with rhinitis symptoms will benefit from nasal irrigation with saline and allergen avoidance (where possible).

Mild symptoms

- Non-sedating oral antihistamine (such as cetirizine) as required, or regularly

Moderate symptoms

- Non-sedating oral antihistamine (such as cetirizine) as required, or regularly
- Regular intranasal corticosteroid spray
  - Advise that the onset of action occurs 6-8 hours after first dose and maximum effect may not be seen for up to two weeks.
  - Please ensure correct technique with nasal spray is being used and advice on this can be found at BSACI standard operating procedures section on the BSACI website (www.bsaci.org)
  - Intranasal corticosteroids can be taken regularly for perennial symptoms or seasonally (restarted two weeks prior to the suspected allergen season).

HSC Belfast Health and Social Care Trust
caring supporting improving together
Advice on allergic rhino-conjunctivitis

Severe / Refractory symptoms

- Check compliance with prescribed medications and nasal spray technique.
- Combination nasal spray such as azelastine hydrochloride and fluticasone propionate (*Dymista*).
- Non-sedating oral antihistamine (such as cetirizine) regularly. In some patients up to four times the recommended dose may be required; e.g. cetirizine 10 mg four times daily, or Fexofenadine 180 mg four times daily. Incremental up dosing of antihistamines is recommended depending on clinical response.
- Consider adding in leukotriene receptor antagonist such as montelukast particularly if there is a history of asthma.

Referral Options

- To immunology for severe / treatment refractory allergic rhino-conjunctivitis only. Sensitisation should be confirmed by specific IgE tests before referral.

  Desensitisation can be offered for grass pollen, tree pollen and house dust mite only.

- To ENT if persistent symptom/ structural component is suspected.

Yours sincerely

APPROVED BUT NOT SIGNED

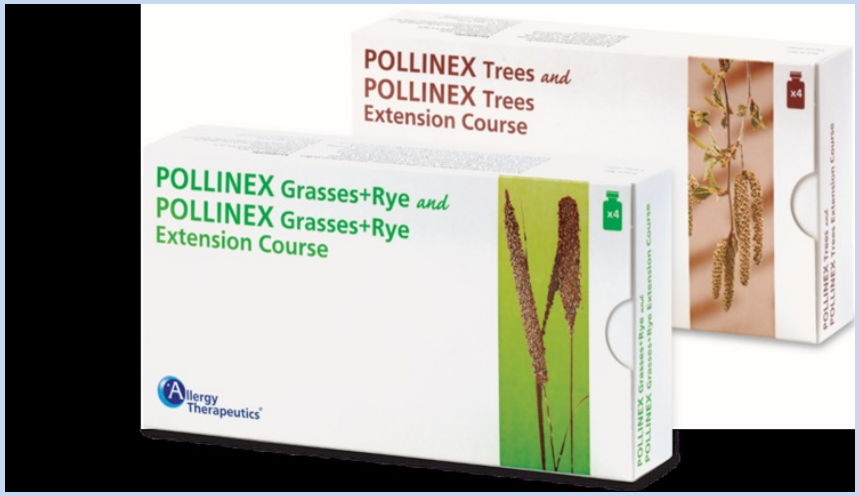
Dr Lisa Devlin/Dr Tanya Coulter
Consultant Immunologists

References

Scadding G, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). Clin Exp Allergy. 2017; 47: 856-889.

CC. patient


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Common queries

- Allergic to peanut
  - Rash occurred 3 days after eating peanut

Common queries

- Allergic to multiple foods:







- Chronic urticaria

Common queries

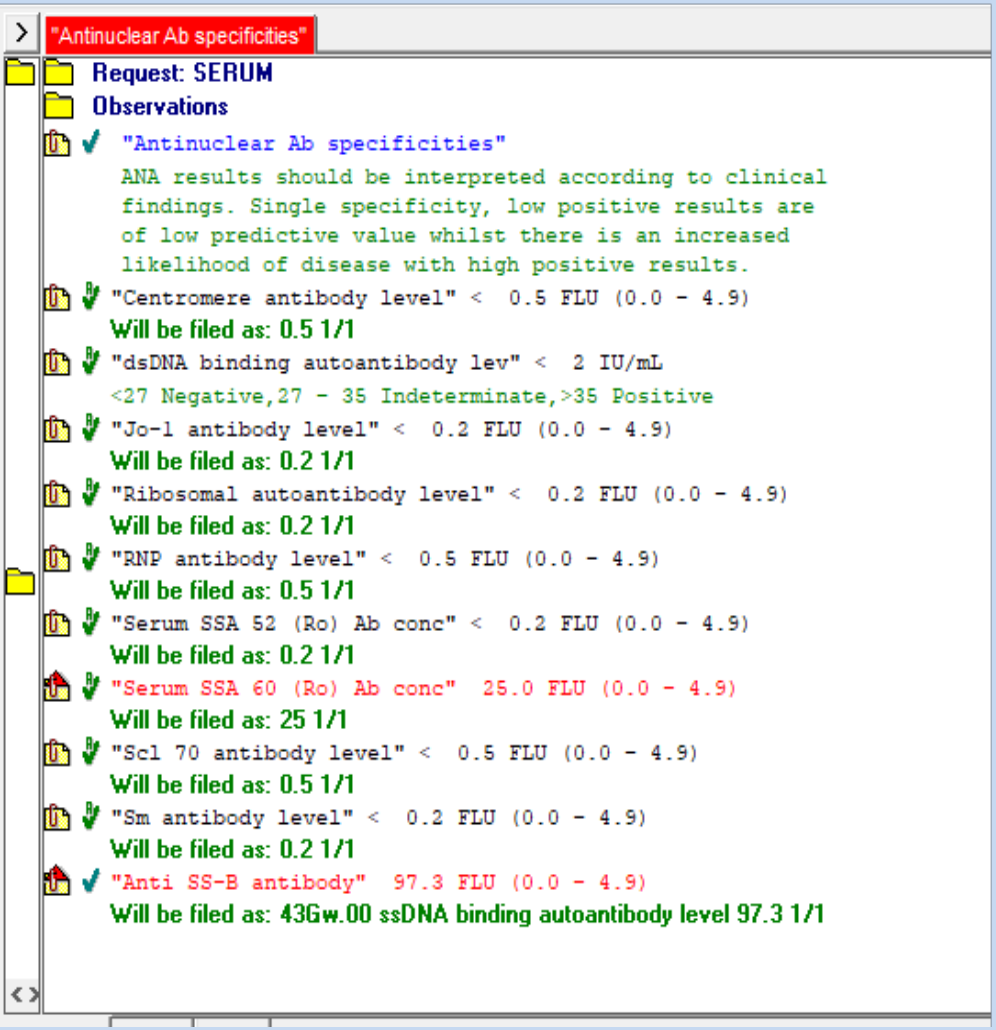
- Recurrent ‘allergy’; swelling of tongue
  - On ACEI
  - Always consider C1 inhibitor deficiency

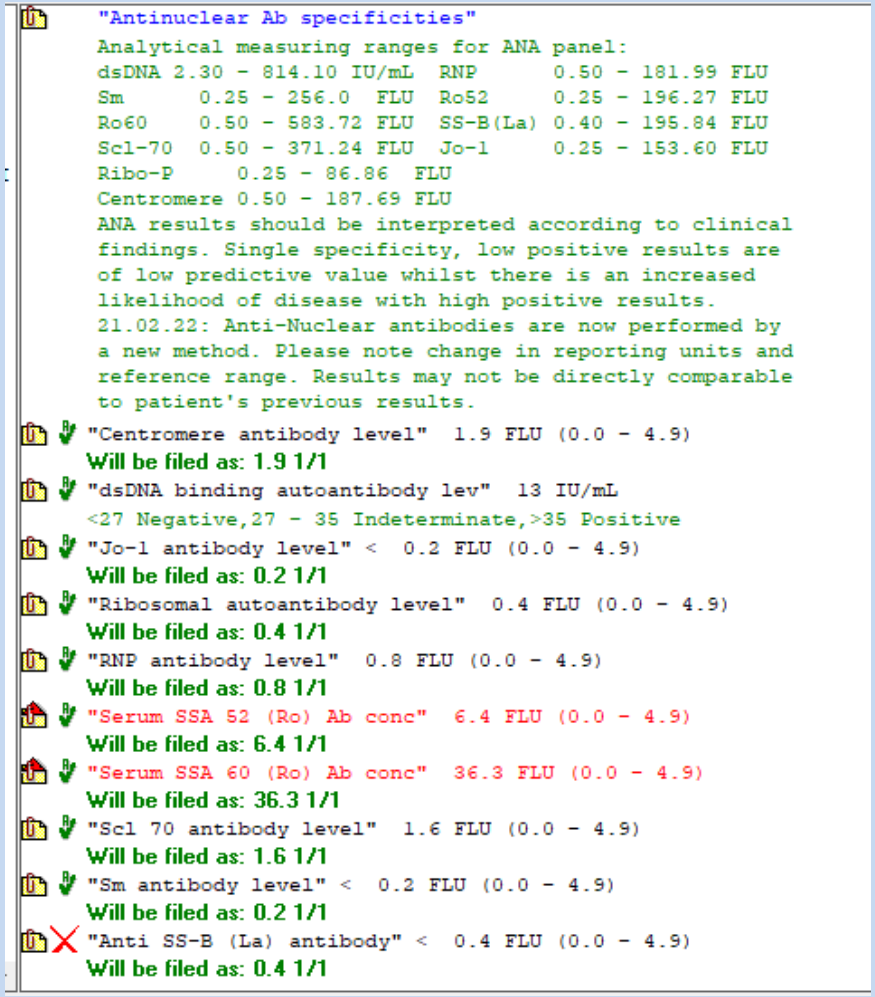
ANTI NUCLEAR ANTIBODY TESTING UPDATE

ANA specificity	BIOPLEX AMR & measuring units	APTIVA AMR & measuring units
Anti-dsDNA	1.0- 300.0 IU/mL	2.3 – 814.1 IU/mL
Anti-ribosomal P	0.2-8.0 AI	0.25-86.86 FLU
Anti-Ro52	0.2-8.0 AI	0.25-196.27 FLU
Anti-Ro60	0.2-8.0 AI	0.5-583.72 FLU
Anti-La	0.2-8.0 AI	0.4-195.84 FLU
Anti-Sm	0.2-8.0 AI	0.25-256 FLU
Anti-RNP	0.2-8.0 AI	0.5-181.99 FLU
Anti-Scl-70	0.2-8.0 AI	0.5-371.24 FLU
Anti-Jo-1	0.2-8.0 AI	0.25-153.6 FLU
Anti-Centromere B	0.2-8.0 AI	0.5-187.65 FLU

Concerns

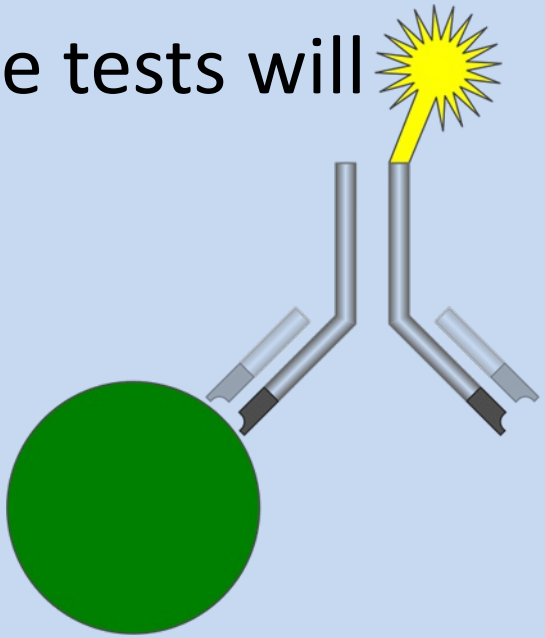
- Positive autoimmune serology in patients without clinical disease!


"Antinuclear Ab specificities"
Request: SERUM
Observations
"Antinuclear Ab specificities"
ANA results should be interpreted according to clinical findings. Single specificity, low positive results are of low predictive value whilst there is an increased likelihood of disease with high positive results.
"Centromere antibody level" < 0.5 FLU (0.0 - 4.9)
Will be filed as: 0.5 1/1
"dsDNA binding autoantibody lev" < 2 IU/mL
<27 Negative,27 - 35 Indeterminate,>35 Positive
"Jo-1 antibody level" < 0.2 FLU (0.0 - 4.9)
Will be filed as: 0.2 1/1
"Ribosomal autoantibody level" < 0.2 FLU (0.0 - 4.9)
Will be filed as: 0.2 1/1
"RNP antibody level" < 0.5 FLU (0.0 - 4.9)
Will be filed as: 0.5 1/1
"Serum SSA 52 (Ro) Ab conc" < 0.2 FLU (0.0 - 4.9)
Will be filed as: 0.2 1/1
"Serum SSA 60 (Ro) Ab conc" 25.0 FLU (0.0 - 4.9)
Will be filed as: 25 1/1
"Scl 70 antibody level" < 0.5 FLU (0.0 - 4.9)
Will be filed as: 0.5 1/1
"Sm antibody level" < 0.2 FLU (0.0 - 4.9)
Will be filed as: 0.2 1/1
"Anti SS-B antibody" 97.3 FLU (0.0 - 4.9)
Will be filed as: 43Gw.00 ssDNA binding autoantibody level 97.3 1/1


"Antinuclear Ab specificities"
Analytical measuring ranges for ANA panel:
dsDNA 2.30 - 814.10 IU/mL RNP 0.50 - 181.99 FLU
Sm 0.25 - 256.0 FLU Ro52 0.25 - 196.27 FLU
Ro60 0.50 - 583.72 FLU SS-B(La) 0.40 - 195.84 FLU
Scl-70 0.50 - 371.24 FLU Jo-1 0.25 - 153.60 FLU
Ribo-P 0.25 - 86.86 FLU
Centromere 0.50 - 187.69 FLU
ANA results should be interpreted according to clinical findings. Single specificity, low positive results are of low predictive value whilst there is an increased likelihood of disease with high positive results.
21.02.22: Anti-Nuclear antibodies are now performed by a new method. Please note change in reporting units and reference range. Results may not be directly comparable to patient's previous results.
"Centromere antibody level" 1.9 FLU (0.0 - 4.9)
Will be filed as: 1.9 1/1
"dsDNA binding autoantibody lev" 13 IU/mL
<27 Negative,27 - 35 Indeterminate,>35 Positive
"Jo-1 antibody level" < 0.2 FLU (0.0 - 4.9)
Will be filed as: 0.2 1/1
"Ribosomal autoantibody level" 0.4 FLU (0.0 - 4.9)
Will be filed as: 0.4 1/1
"RNP antibody level" 0.8 FLU (0.0 - 4.9)
Will be filed as: 0.8 1/1
"Serum SSA 52 (Ro) Ab conc" 6.4 FLU (0.0 - 4.9)
Will be filed as: 6.4 1/1
"Serum SSA 60 (Ro) Ab conc" 36.3 FLU (0.0 - 4.9)
Will be filed as: 36.3 1/1
"Scl 70 antibody level" 1.6 FLU (0.0 - 4.9)
Will be filed as: 1.6 1/1
"Sm antibody level" < 0.2 FLU (0.0 - 4.9)
Will be filed as: 0.2 1/1
"Anti SS-B (La) antibody" < 0.4 FLU (0.0 - 4.9)
Will be filed as: 0.4 1/1

Autoimmune serology; Immunoassays

- Not ‘diagnostic’ tests
- Positive ANA found in 5% of ‘normal’ population (depending on screening dilution of sample)
- Sensitivity and specificity of these tests will vary between methods



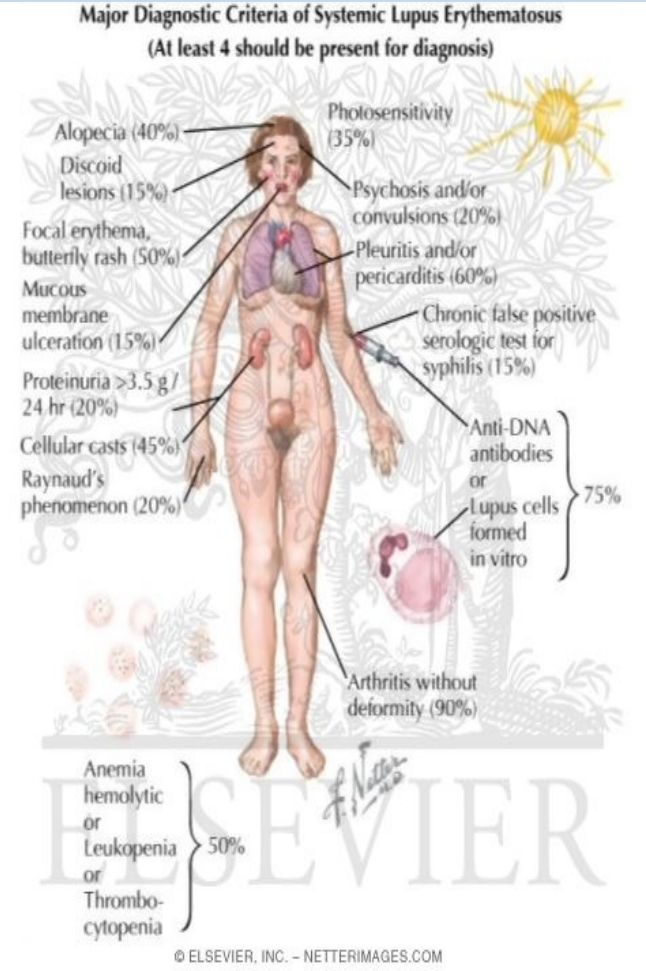


Table 4. Conditions Associated With Positive IF-ANA Test Results*

Disease	Frequency of Positive ANA Result, %
Diseases for which an ANA test is very useful for diagnosis	
SLE	95–100
Systemic sclerosis (scleroderma)	60–80
Diseases for which an ANA test is somewhat useful for diagnosis	
Sjögren syndrome	40–70
Idiopathic inflammatory myositis (dermatomyositis or polymyositis)	30–80
Diseases for which an ANA test is useful for monitoring or prognosis	
Juvenile chronic oligoarticular arthritis with uveitis	20–50
Raynaud phenomenon	20–60
Conditions in which a positive ANA test result is an intrinsic part of the diagnostic criteria	
Drug-induced SLE	~100
Autoimmune hepatic disease	~100
MCTD	~100
Diseases for which an ANA test is not useful in diagnosis	
Rheumatoid arthritis	30–50
Multiple sclerosis	25
Idiopathic thrombocytopenic purpura	10–30
Thyroid disease	30–50
Discoid lupus	5–25
Infectious diseases	Varies widely
Malignancies	Varies widely
Patients with silicone breast implants	15–25
Fibromyalgia	15–25
Relatives of patients with autoimmune diseases (SLE or scleroderma)	5–25
Normal persons†	
≥1:40	20–30
≥1:80	10–12
≥1:160	5
≥1:320	3

* IF indicates immunofluorescent; ANA, antinuclear antibody; SLE, systemic lupus erythematosus; and MCTD, mixed connective tissue disease.

† Values are titers. Prevalence of positive ANA test result varies with titer. Female sex and increasing age tend to be more commonly associated with positive ANA.

Kavanaugh et al.
Arch Pathol Lab med.
2000;124:71-81

- **Clinical limitations of ANA testing** – The higher the prior probability that a patient has a systemic autoimmune disease, the more likely the results of an ANA test will assist in establishing the diagnosis. As an example, if there is clinical evidence of systemic lupus erythematosus (SLE) (eg, photosensitivity, pleurisy), systemic sclerosis (eg, Raynaud phenomenon, skin changes), or Sjögren's syndrome (eg, unexplained dry eyes, dry mouth), the ANA results are likely to be helpful. By contrast, if the ANA test is ordered indiscriminately, the majority of positive results will be falsely positive and may potentially distract the clinician from the correct diagnosis. (See 'Clinical limitations of ANA testing' above.)

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