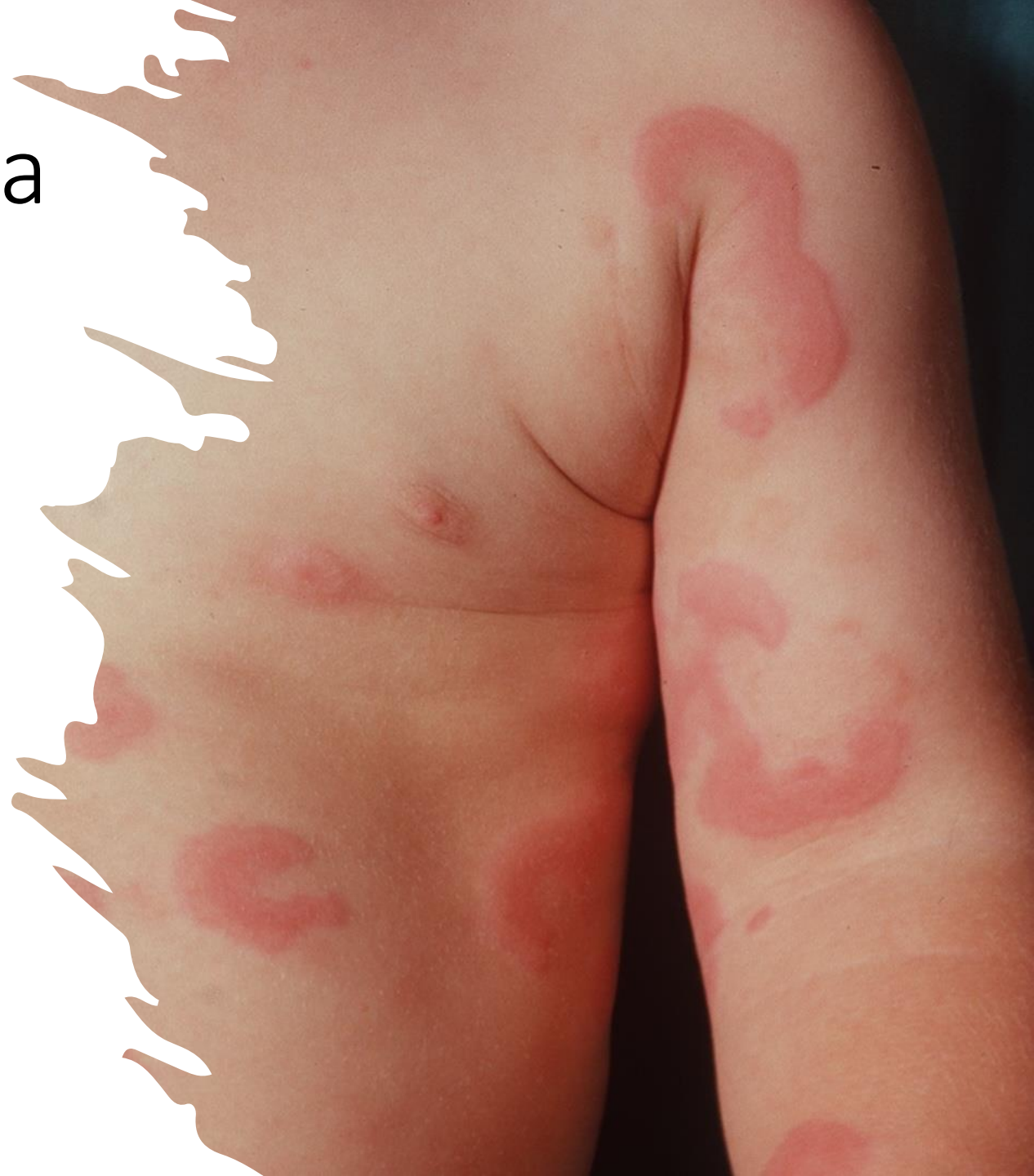
Understanding Urticaria



Dr Dermot Ryan FRCGP
Retd GP (34 years)
University of Edinburgh

THE PRIMARY CARE SHOW
14th - 15th May 2025 • The NEC, Birmingham

Learning Needs Analysis (LNA)

Allergy
EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY
EAACI

Results of an allergy educational needs questionnaire for primary care

D. Ryan, E. Angier, M. Gomez, D. Church, M. Batsiou, K. Nekam, N. Lomidze, R. Gawlik

N=670	Self Perceived **Knowledge**	Self Perceived **Learning need**
Asthma	82.2	48.1
Allergic rhinitis	71.2	52.8
Eczema/atopic dermatitis	55.8	65
Anaphylaxis	50.7	62.4
Contact dermatitis	40	69.6
Drug reaction/ allergy	38.5	74
Urticaria/ angioedema	**35.2**	**74.9**

There is a poor knowledge of CSU in primary care / ED

<u>All</u> patients initially treated for allergies or skin infections

- Many initial referrals through allergy service

<u>All</u> patients were initially prescribed steroids (9 by their GP)

GPs were reluctant to escalate antihistamine doses

Multiple missed opportunities for diagnosis

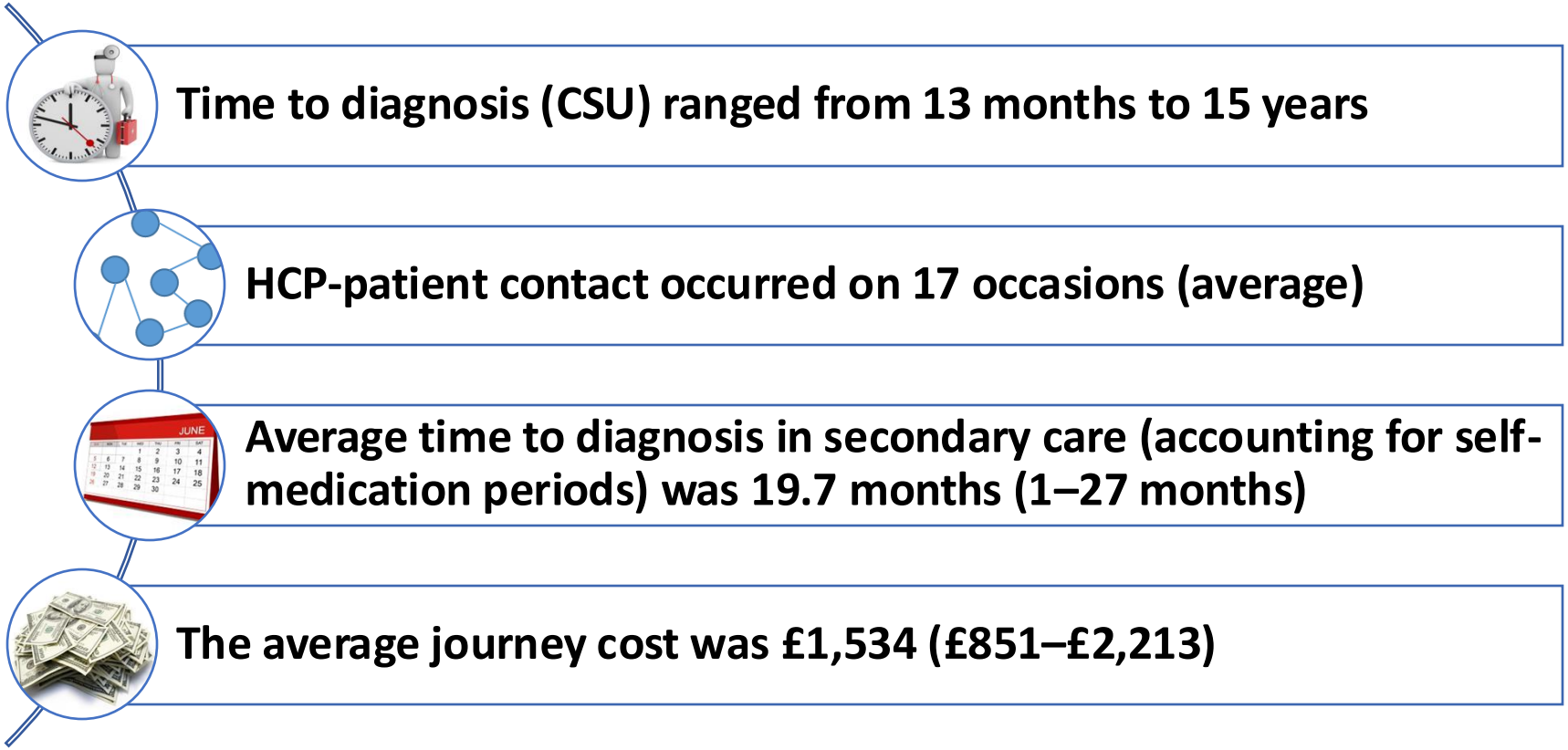
- CSU not recognised during skin testing in allergy services
- A&E patients treated for non-life threatening allergies

Mistry A, et al. Chronic Spontaneous Urticaria: impact of the diagnostic delay on healthcare resources. P.18. Poster presented at BSACI conference, 4–6 September, 2015.

JSL. CSU patient mapping report, version 3. Novartis. January 2015.

with thanks to Dr Susan Marinho

Patients are lost in the system



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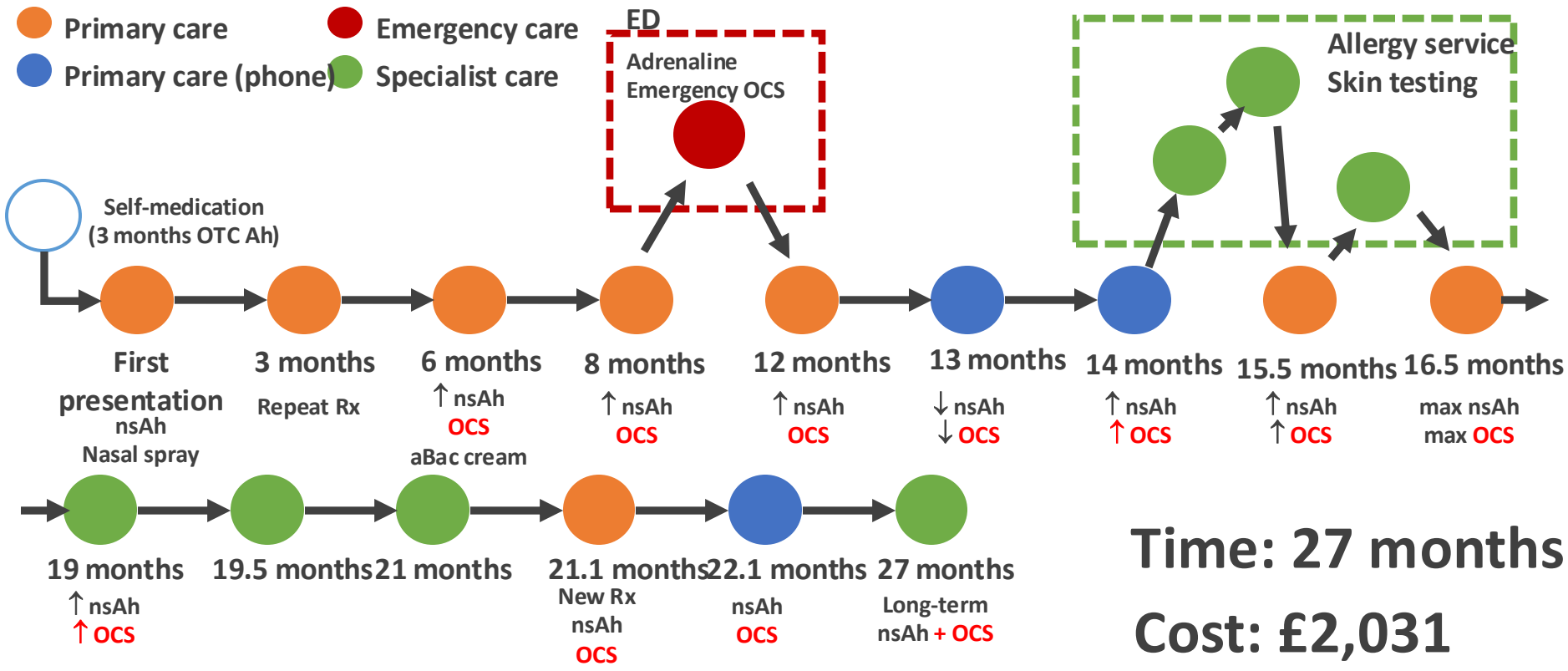
with thanks to Dr Susan Marinho

Example patient pathway
Primary Care Snapshot Survey (pre covid)



OTC Ah: over the counter anti-histamines, nsAh: non-sedating anti-histamines, OCS: oral corticosteroids, Ste: steroids, aBac: antibacterial

Mistry A, et al. Chronic Spontaneous Urticaria: impact of the diagnostic delay on healthcare resources. P.18. Poster presented at BSACI conference, 4–6 September, 2015.

with thanks to Dr Susan Marinho

Negative impact of oral corticosteroids

One course OCS (1w)

of 1.54m, 327,000 (21%) received 1 course OCS over a three year period:

within 30 days:

- 5 fold increase in sepsis
- 3 fold incidence DVT
- 2 fold incidence of #

≥4 OCS (1w)(F/U 7 y)

increases lifetime risk

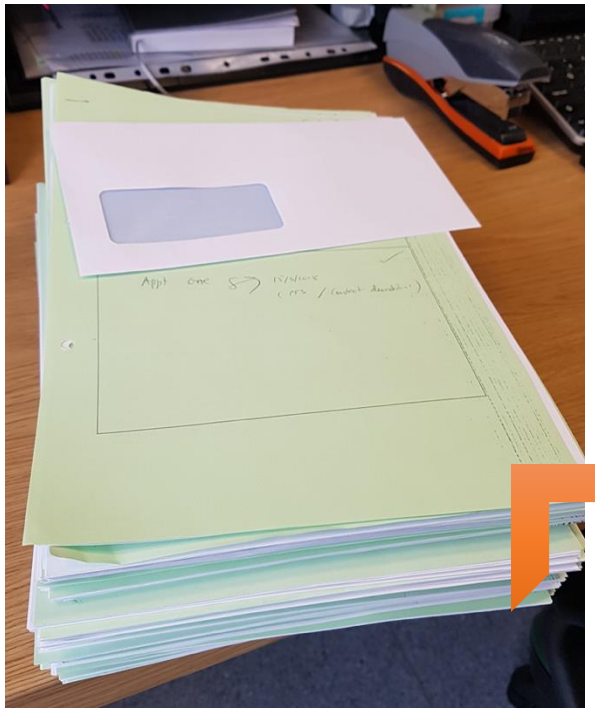
- 3 fold # (osteoporosis)
- 2.6 fold pneumonia
- 1.53 fold CVD
- 1.5 fold cataract
- 1.4 fold OSA
- 1.2 fold diabetes

This patient had 11 courses

BMJ 2017; 357 doi: https://doi.org/10.1136/bmj.j1415

Journal of asthma and allergy. 2018 Aug 29:193-204.

Secondary care referrals for CSU



Allergy Centre

Wythenshawe Hospital

~40-60%

urticaria referrals

per month

with thanks to Dr Susan Marinho

Inappropriate suspicion and investigations for food (and other) allergy

Please can you see my patient who is suffering with an itchy rash and is obviously allergic to something…

Please can you do allergy tests for my patient, who is clearly having allergic episodes with hives, presumably to something he is eating, but has been unable to pinpoint what he is allergic to…

Please see this patient who has allergic symptoms with a nettle-like rash, lip and tongue selling after eating certain foods. We have done RAST testing to milk, nuts, wheat, shellfish and fish but they have all come back negative…

… her IgE returned positive to wheat and the patient has been careful strictly avoiding this, but her symptoms have not resolved…

with thanks to Dr Susan Marinho

Inappropriate treatment

My patient has been having almost daily episodes of hives. These responded to a months' course of fexofenadine but recur as soon as he stops this treatment…

…we have tried cetirizine, 1 tablet per day, but rash persisted so I have added daily chlorphenamine*…

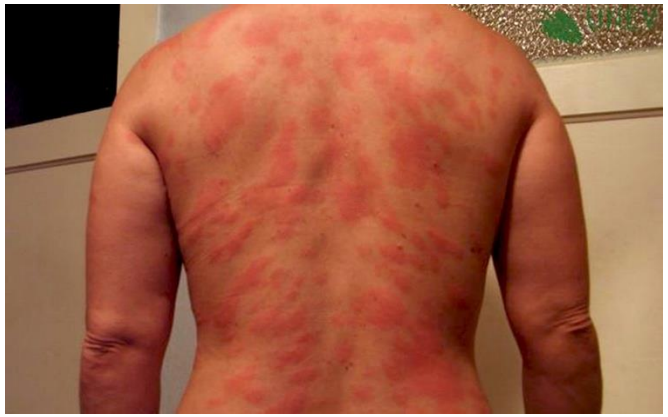
This patient is at her wits' end with a very itchy, allergic-type rash. We have tried several different antihistamines with no response. I have now given her regular prednisolone*, which appears to be the only treatment controlling her rash…

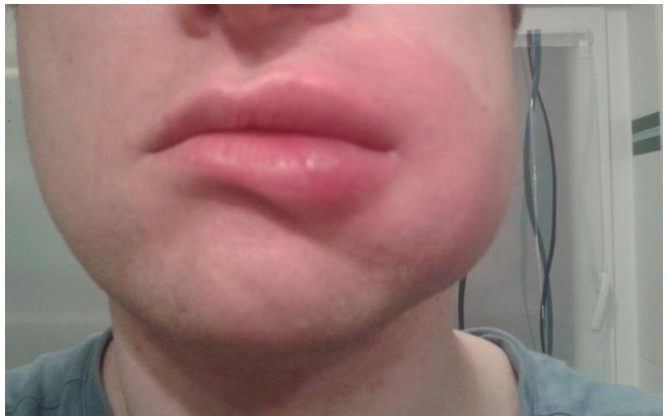
*Only standard dose H1-antihistamines and Xolair (omalizumab) are licensed for treatment in CSU

with thanks to Dr Susan Marinho

What is it?

- Urticaria (also known as hives, weals, or nettle rash) is a superficial swelling of the skin (epidermis and mucous membranes) that results in a red (initially with a pale centre), raised, and intensely itchy rash.
- It may be accompanied by angioedema, loosely, swelling under the skin rather than on the surface

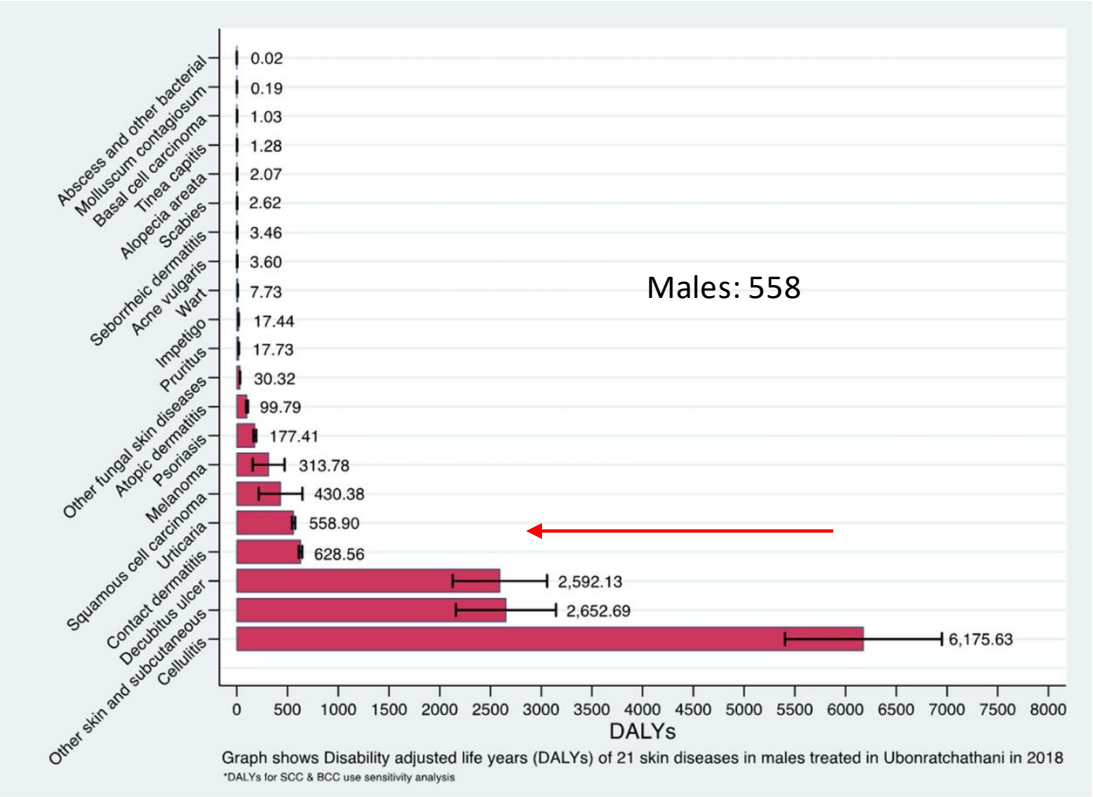


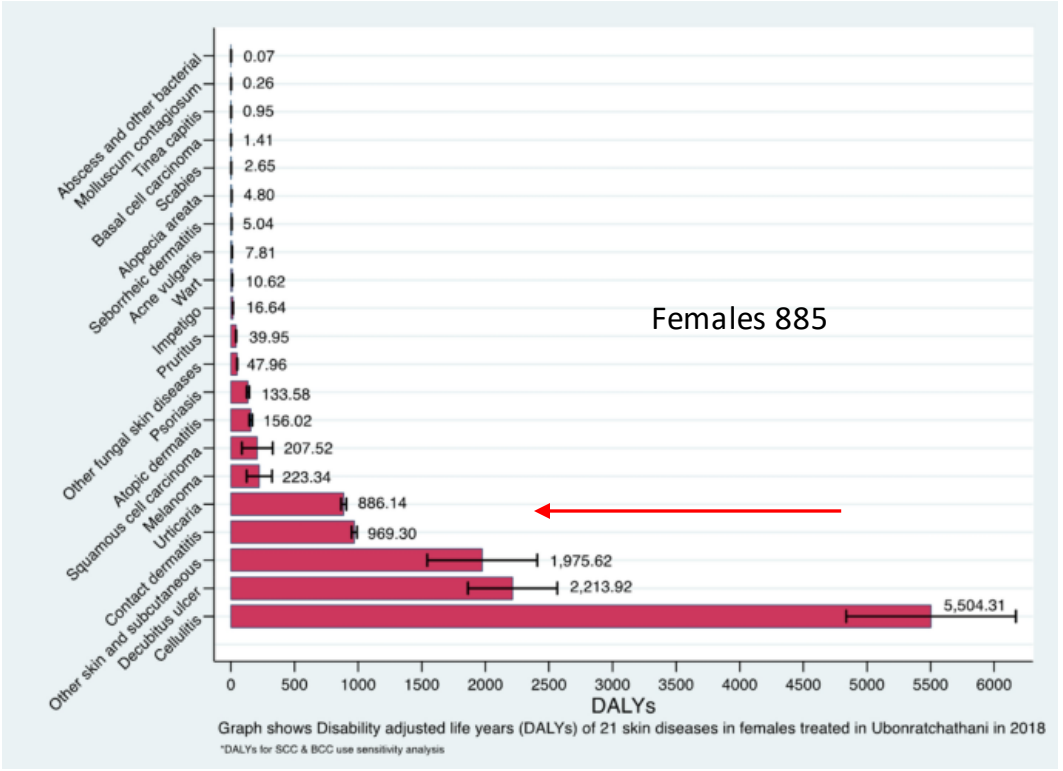


https://urtikaria.net/en/

Burden of disease

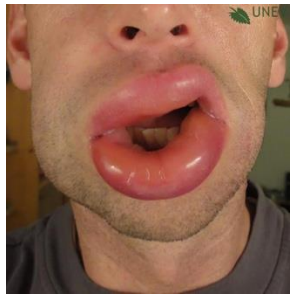
DALYs due to different skin diseases (N=1.5m of whom 110,000 had skin disease (7%) with 26,125 DALY's lost

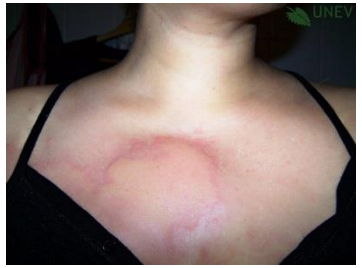


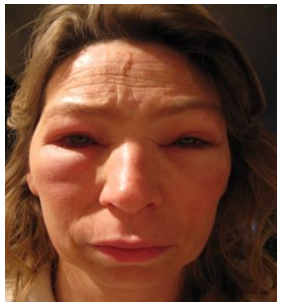


Prevalence and DALYs of skin diseases in Ubonratchathani based on real-world national healthcare service data. *Sci Rep* **12**, 16931 (2022). https://doi.org/10.1038/s41598-022-20237-0

Impact of (chronic) urticaria

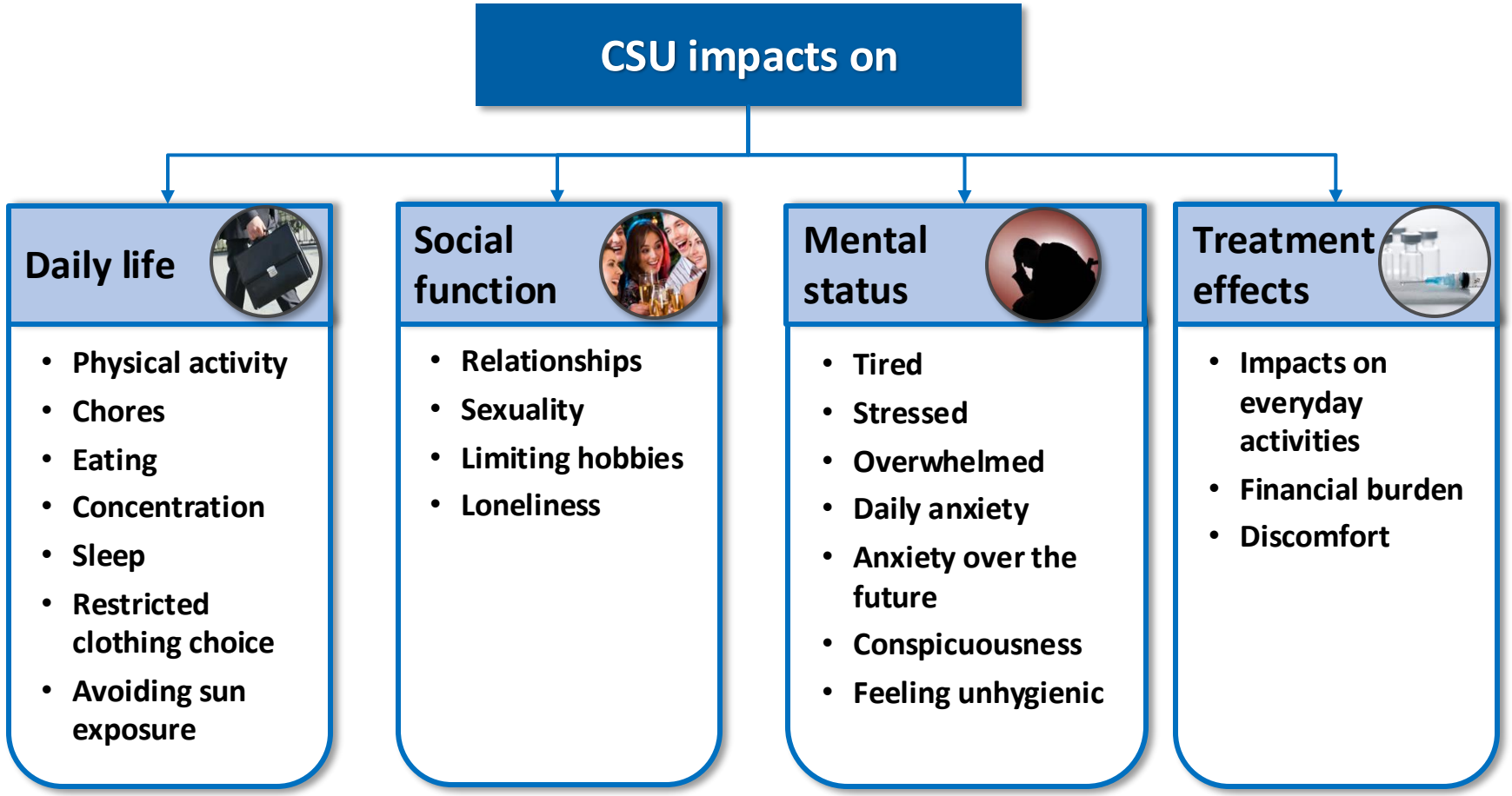






https://urtikaria.net/en/

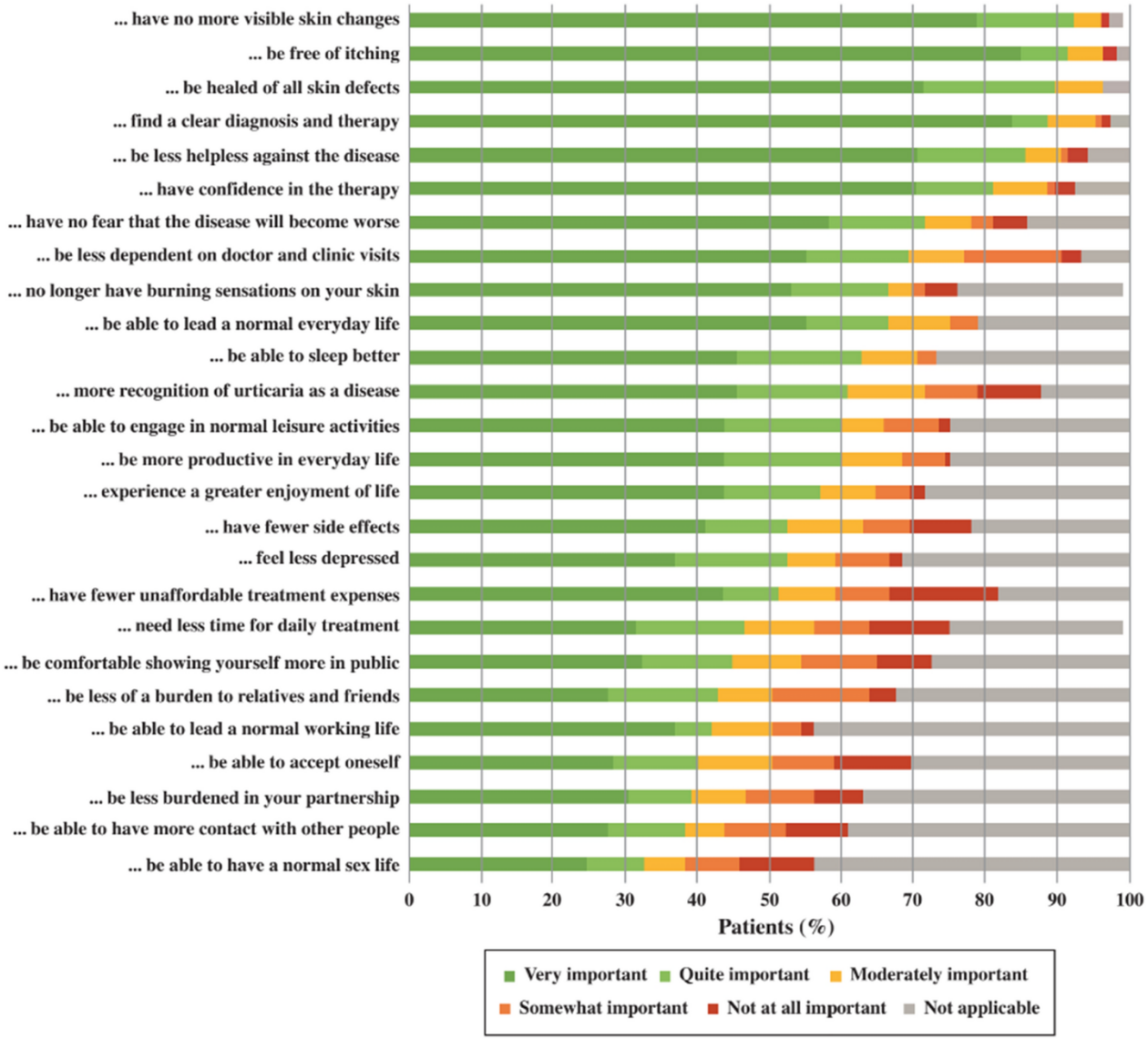
The impact of CSU is often underestimated



Kang MJ *et al. Ann Dermatol* 2009;21: 226–9.
Silvares MRC *et al. Rev Assoc Med Bras* 2011;57: 577–82.

with thanks to Dr Susan Marinho

What do patients want?

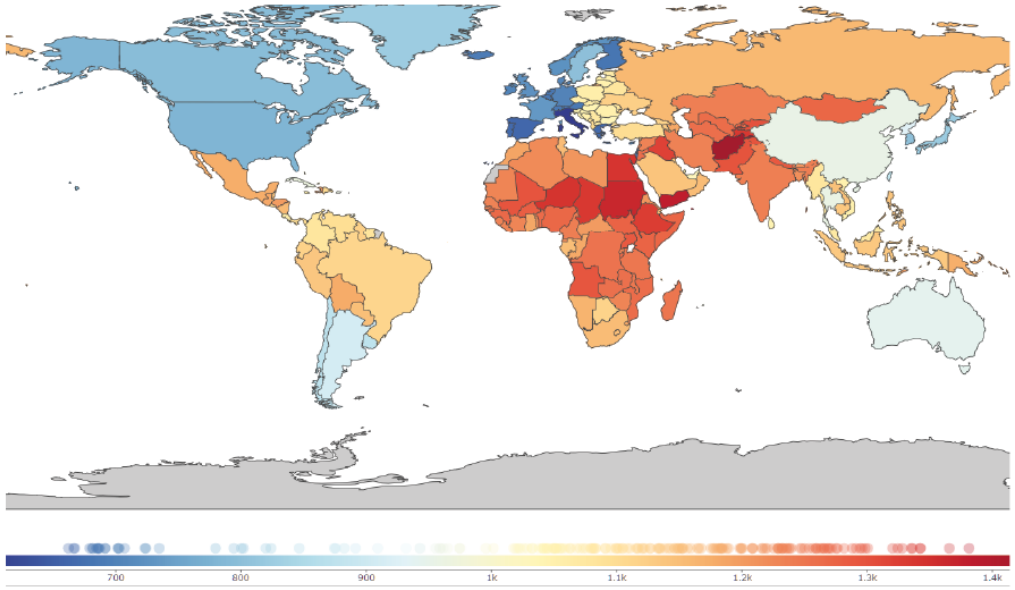


Normal skin
No itch
A diagnosis
Effective treatment
Normal life
Less depressed
Not burdening others
Normal working life
Normal social life
Normal sex life

A Patient Charter for Chronic Urticaria. Advances in Therapy. 2023 Nov 22:1-20.

Prevalence

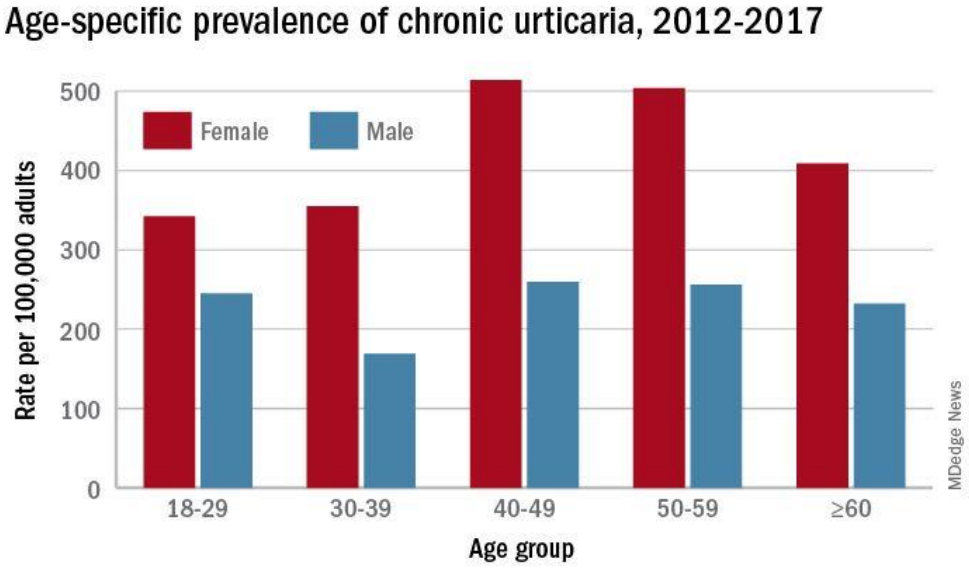
- Acute Urticaria
- lifetime prevalence 8-10%



700/10,000 1,400/100,100

Global distribution of urticaria.
Prevalence of urticaria per 100,000 population in 2017. *Source:* Global Burden of Disease, Institute of Health Metrics and Evaluation (IHME), University of Washington. https://vizhub.healthdata.org/gbd-compare/.

- Chronic urticaria
- lifetime prevalence 0.5-2%

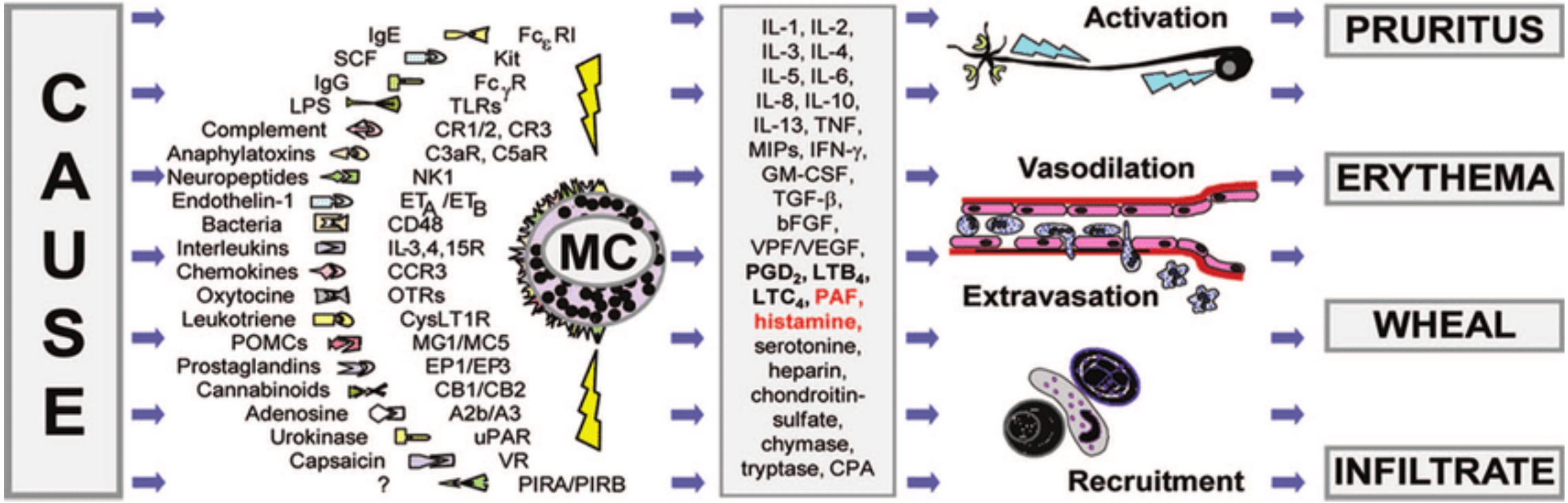


Note: The cross-sectional analysis used an IBM database encompassing 27 participating integrated health care organizations with over 55 million individuals.

Source: J Am Acad Dermatol. 2019. doi: 10.1016/j.jaad.2019.02.064

Urticaria – Pathogenesis

Mast cells are the key effector cells in the induction of urticaria symptoms



The World Allergy Organization Journal. 2010 Apr; 3(Suppl 1):S1.

Categorisation

Acute urticaria

Criteria:
Mostly resolves in 24-48 hours
Last 6 weeks or less

Chronic urticaria

Criterion:
Last 6 weeks or longer

Chronic spontaneous urticaria

Inducible urticaria

Acute urticaria

Causes/associations:

Idiopathic

Viral (respiratory)

Bacterial (strep B)

Drugs (NSAID)

- **It is self limiting (usually 24-28 hours)**
- **Never longer than six weeks**
- **Requires NO investigations**
- **Reassurance is very important**
- **Anti-histamines are used for symptomatic treatment**

NB: If systemic symptoms

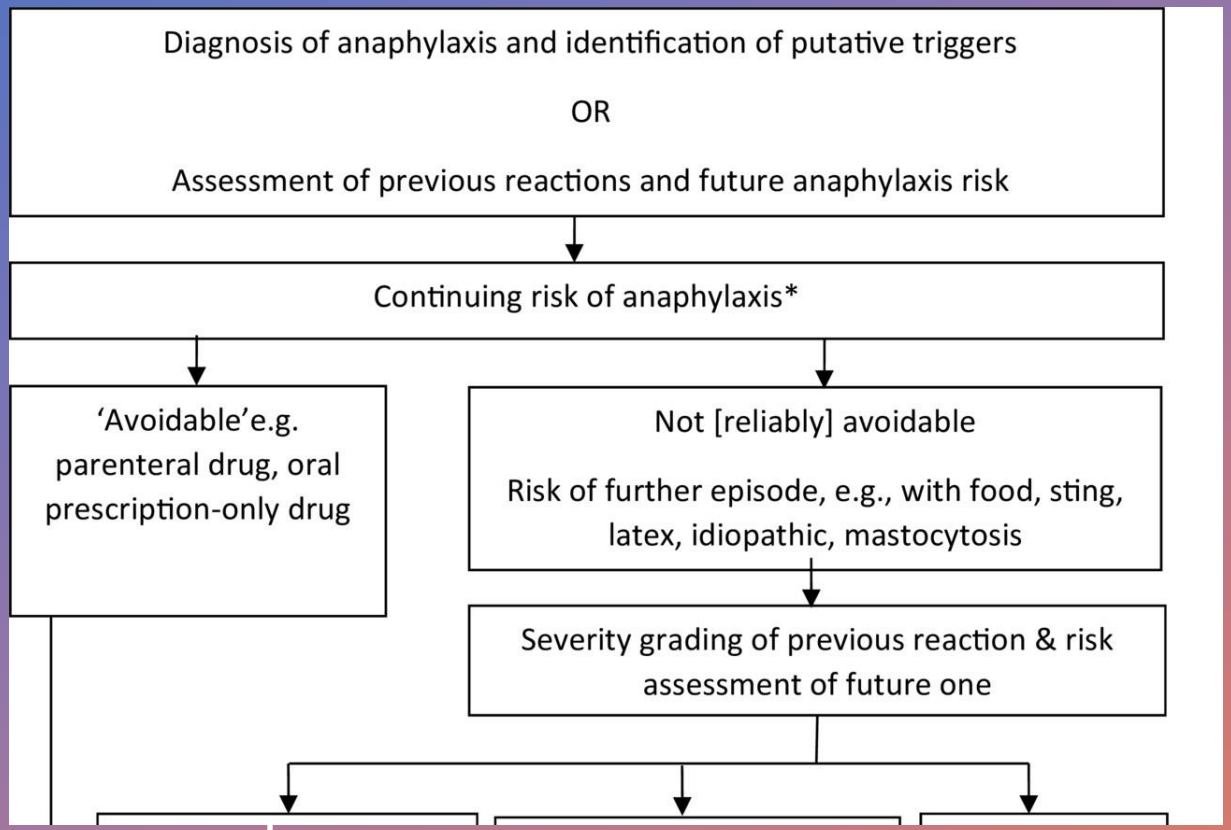
- **wheezing (respiratory compromise)**
- **fainting (reduced BP, Shock)**
- **acute diarrhea or vomiting**

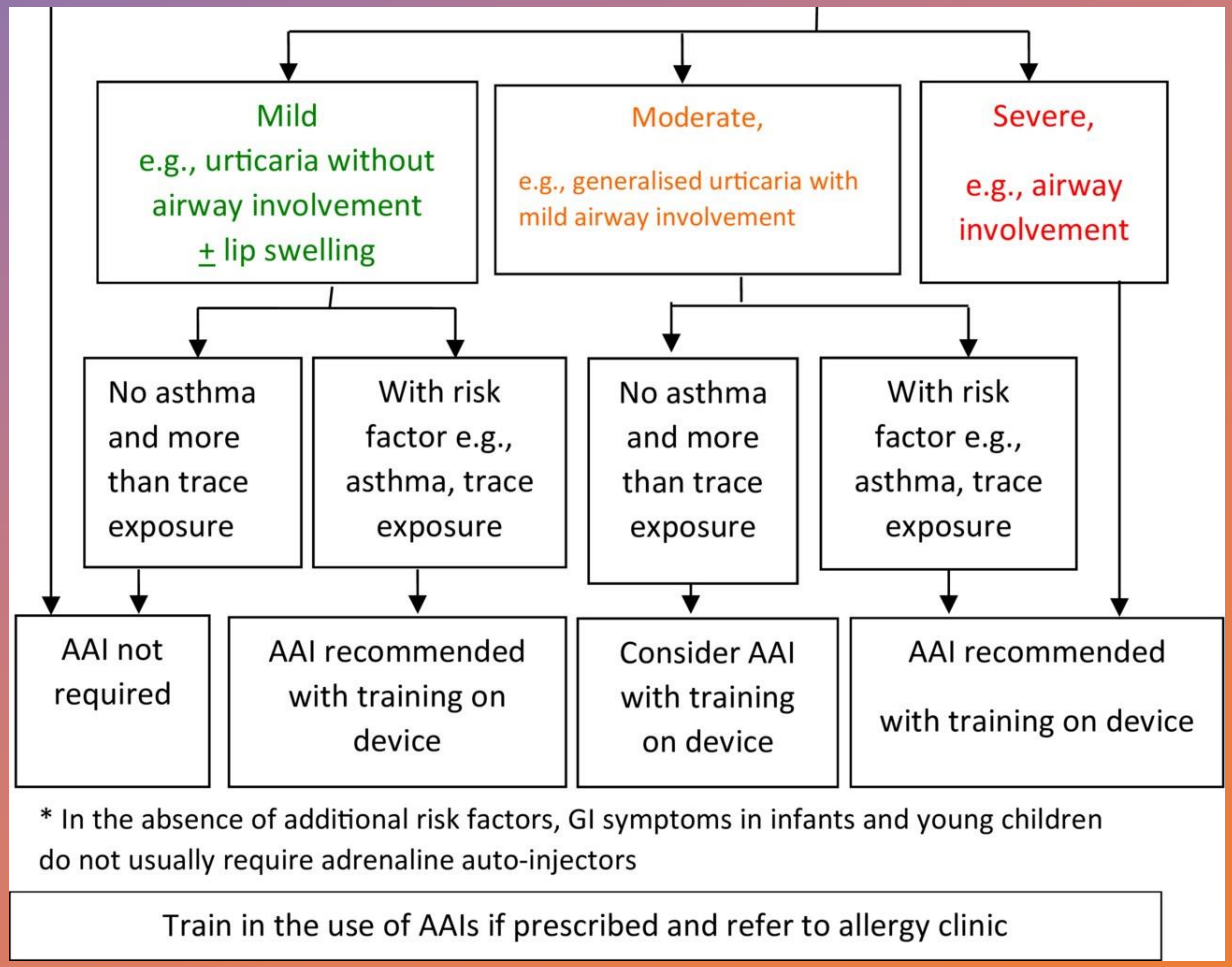
It is more likely to be anaphylaxis

Treat with adrenaline

Anaphylaxis safety netting

Adrenaline auto-injector prescription for patients at risk of anaphylaxis: BSACI guidance for primary care





https://onlinelibrary.wiley.com/doi/10.1111/cea.14325

Intra-muscular adrenalin is extremely safe to use

Acute Urticaria

(generally, <24 hours, always < 6 weeks)

Definition: Urticaria is a condition characterized by the development of wheals (hives) angioedema or both.

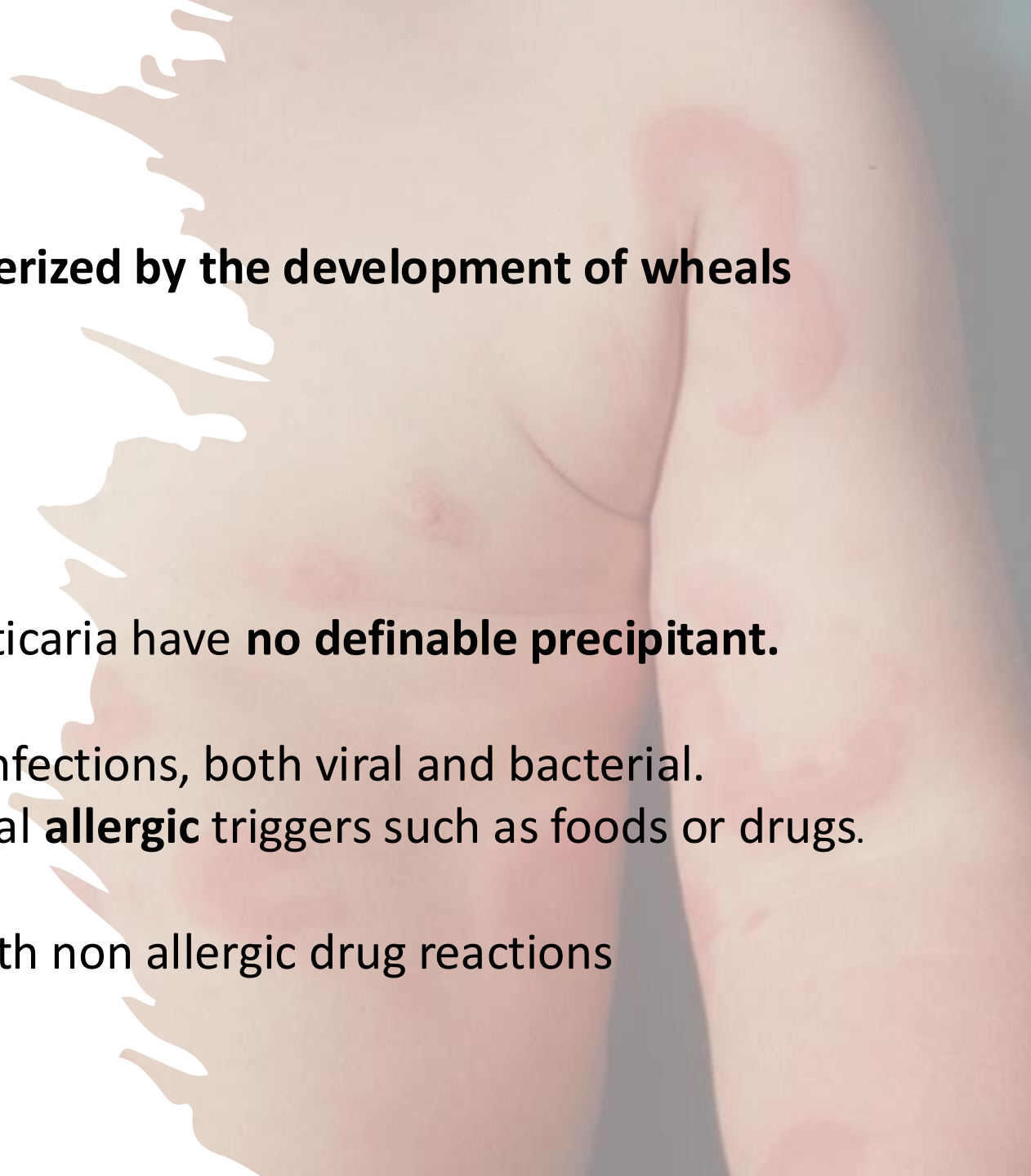
Prevalence : lifetime prevalence of 20%

Aetiology of Acute Urticaria

The vast majority of patients with acute urticaria have **no definable precipitant.**

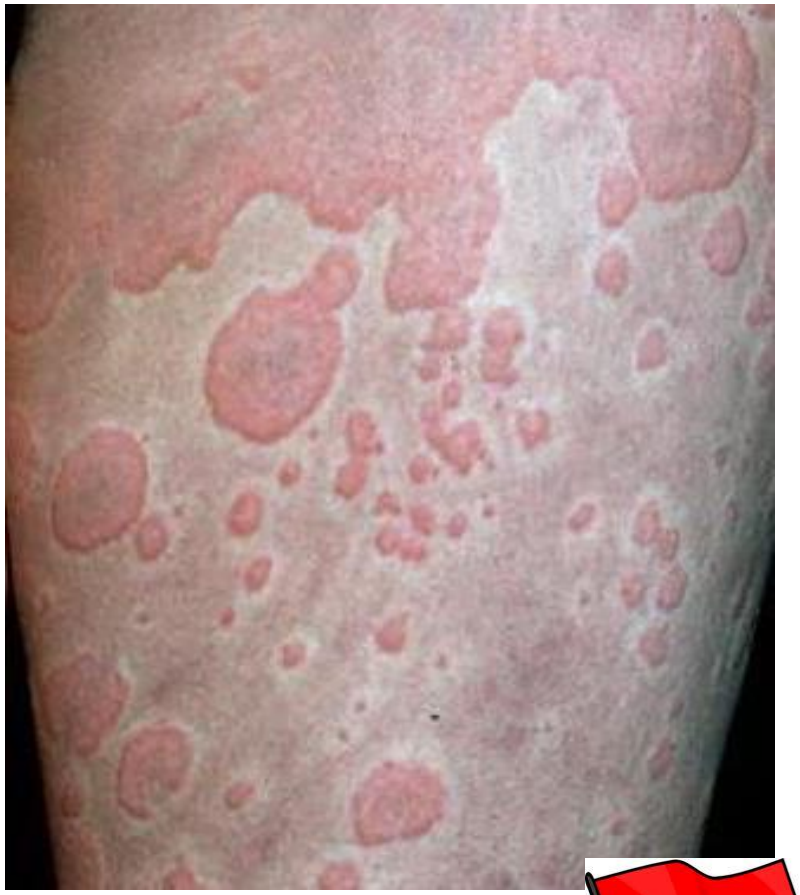
There is a clear association however with infections, both viral and bacterial.
It is important however to identify potential **allergic** triggers such as foods or drugs.

NSAIDs, in particular, may be associated with non allergic drug reactions

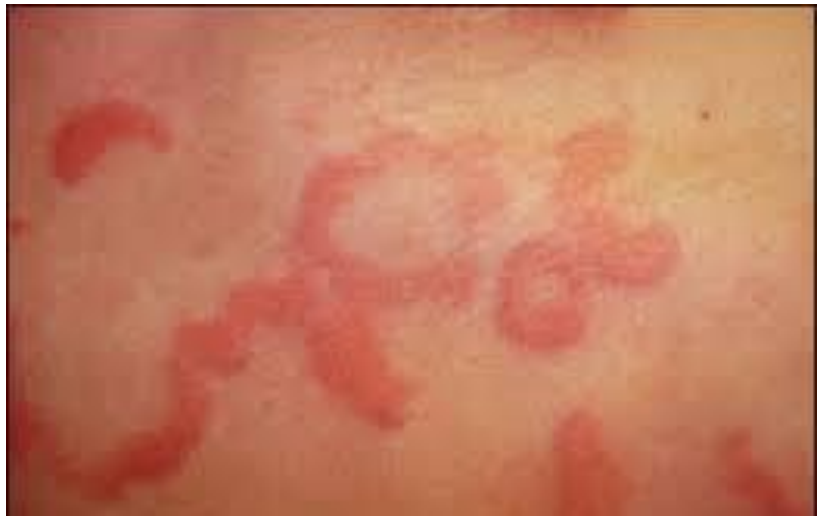


Consider urticarial vasculitis if:

- Individual weals last longer than 24 hours, bruise or are tender to touch – particularly if patient is systemically unwell
- **Refer for urgent dermatological review – may represent systemic vasculitis**

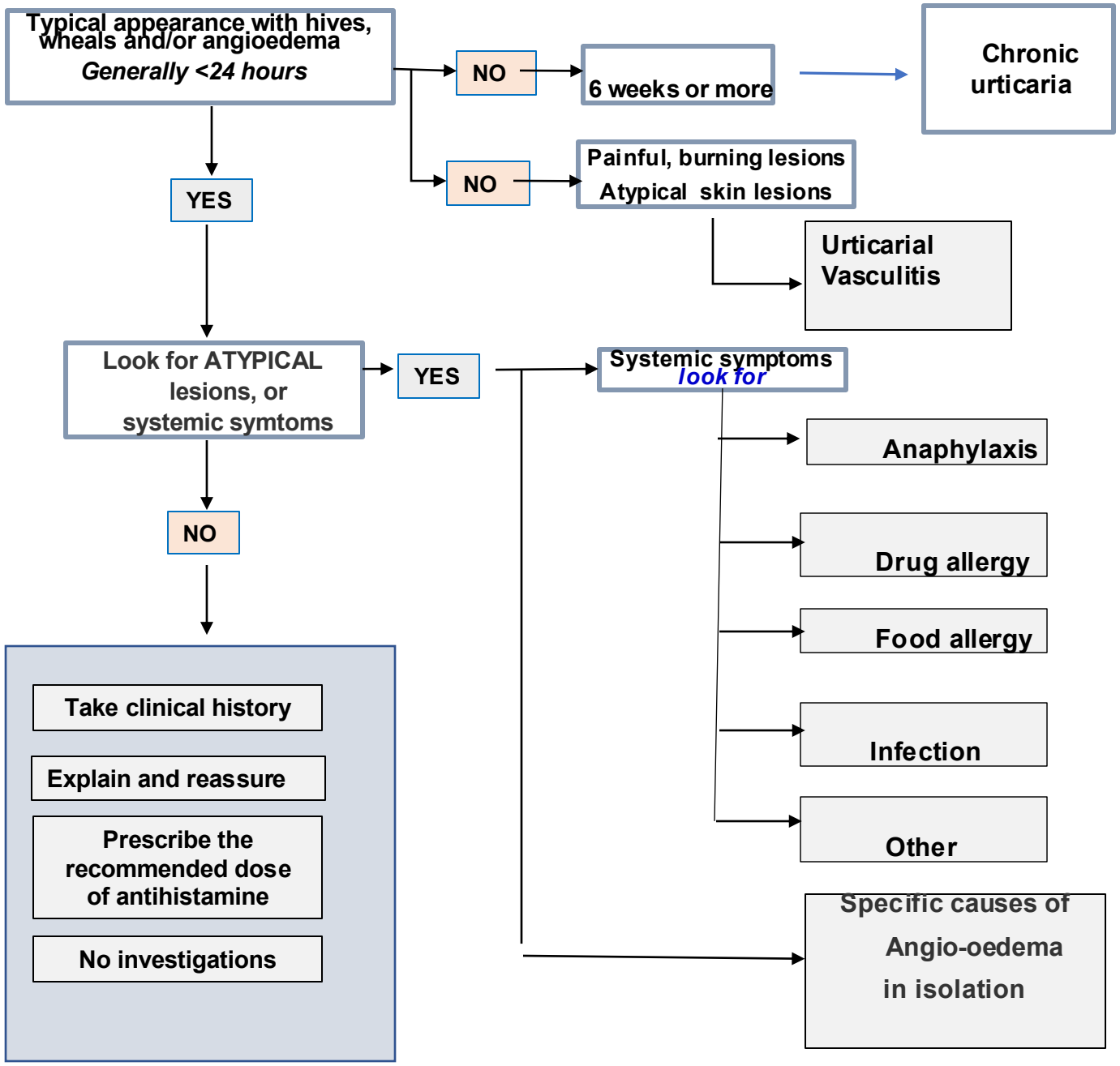


Approach to acute urticaria



Clinical review: the suggested management pathway for urticaria in primary care.

Ryan et al Clin Transl Allergy. 2022;12: e12195.

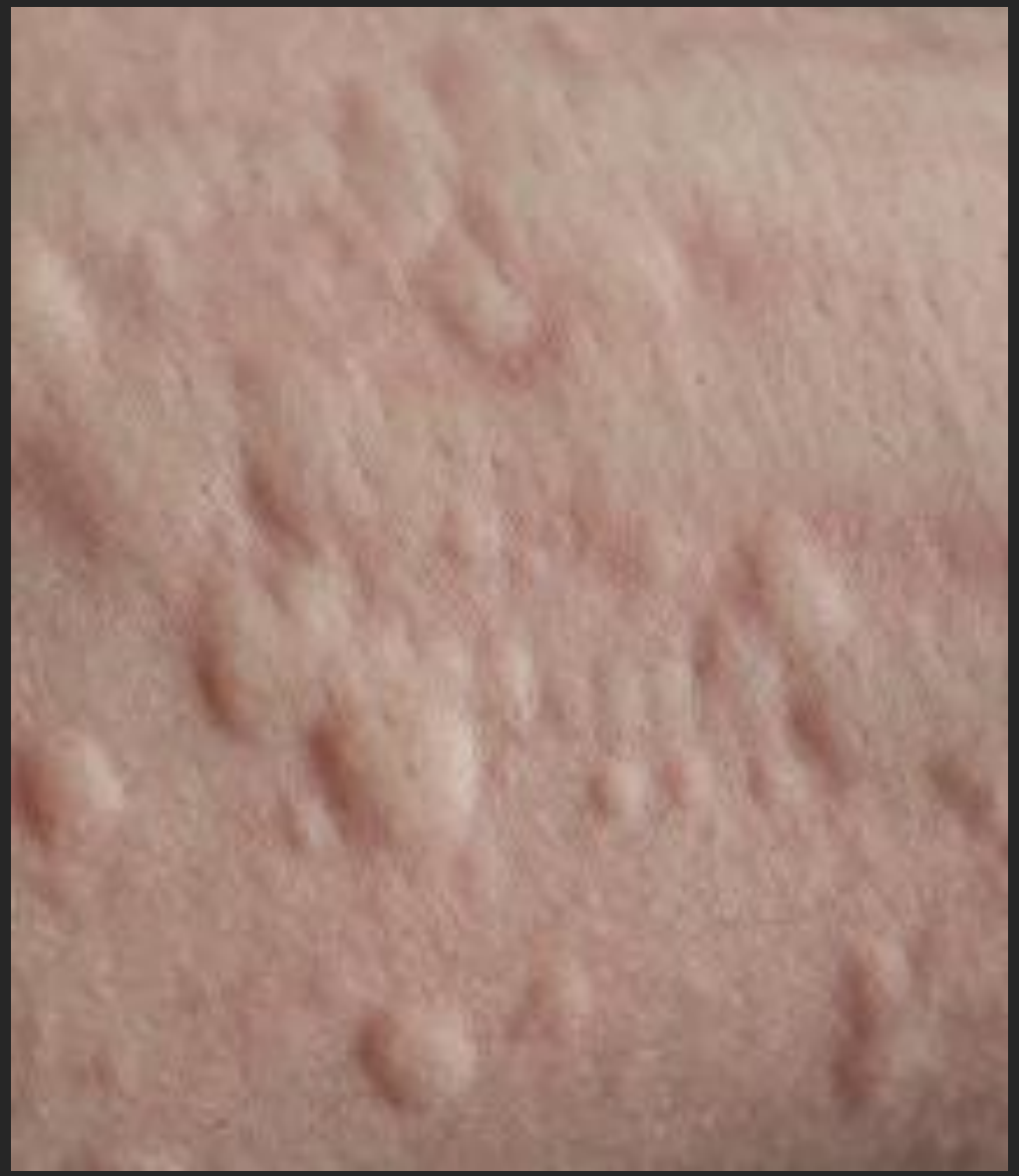


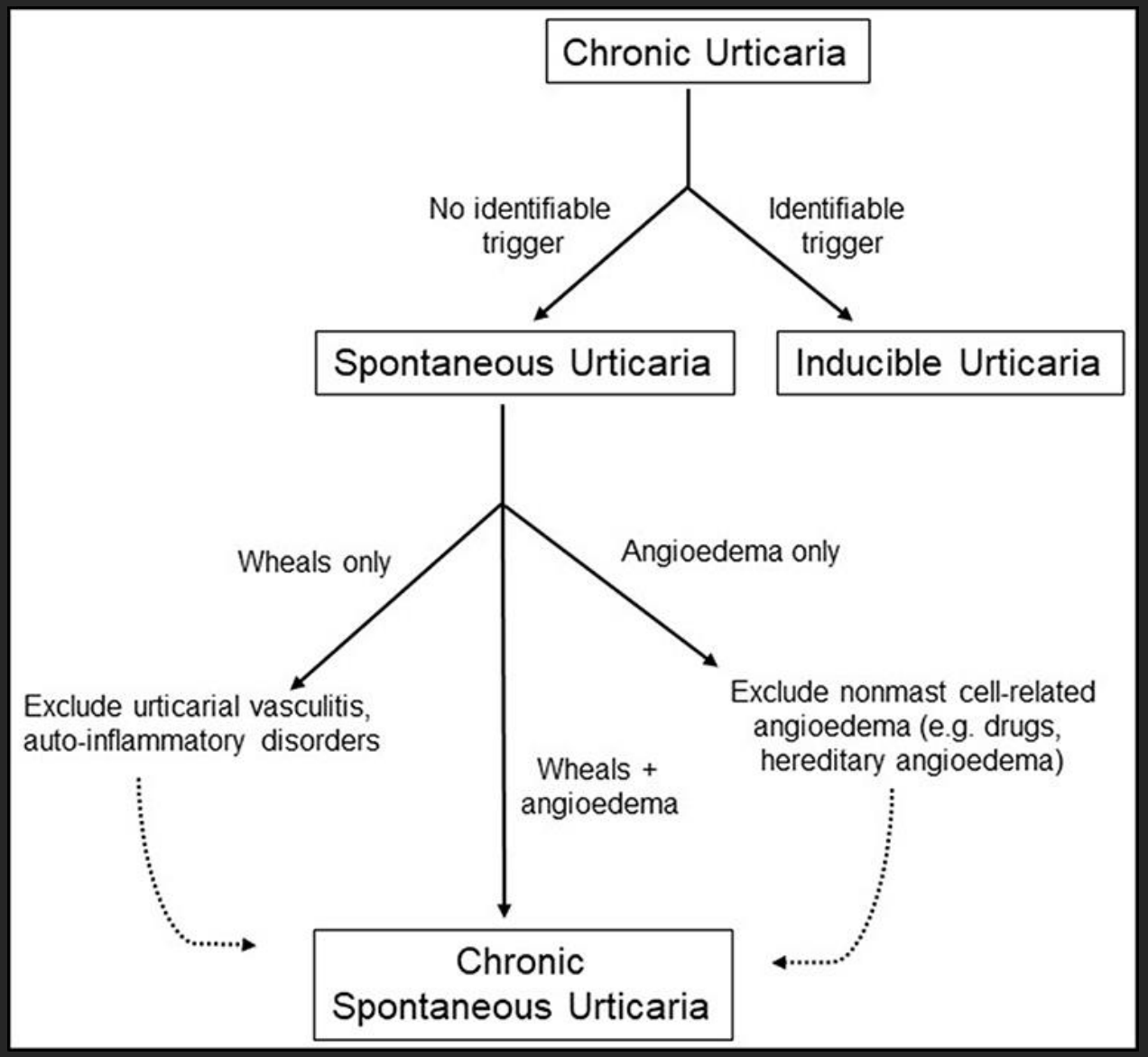
Management

Be:
- Clear
- Concise
- Confident

Reassurance:

- This is urticaria
- This is a very common problem – affects 6% population
- Trigger usually not identified
- Usually goes away by itself – sometimes in a matter of days, sometimes longer
- Not allergy (especially not food allergy) – so little value in looking for a trigger or doing tests
- Antihistamines won't cure the problem but should keep the symptoms under control; if you stop them and the symptoms recur - re-start them



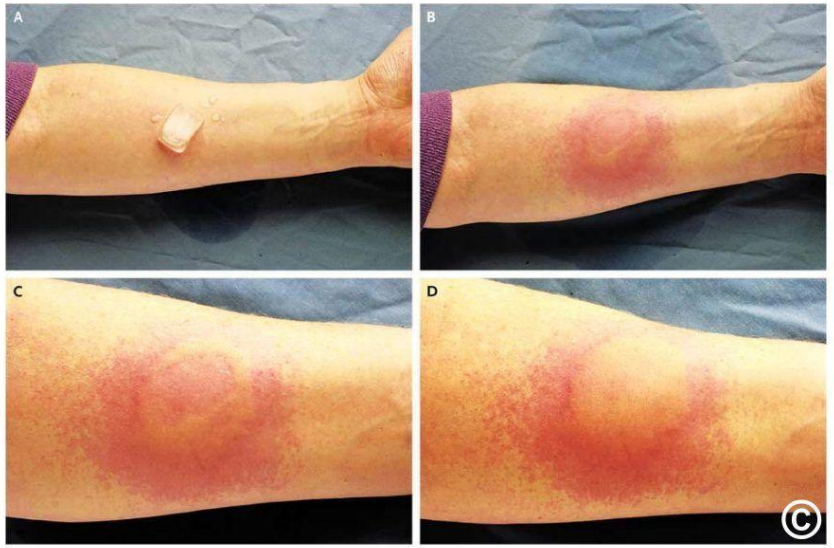

Chronic Urticaria
No identifiable trigger
Identifiable trigger
Spontaneous Urticaria
Inducible Urticaria
Wheals only
Angioedema only
Exclude urticarial vasculitis, auto-inflammatory disorders
Wheals + angioedema
Exclude nonmast cell-related angioedema (e.g. drugs, hereditary angioedema)
Chronic Spontaneous Urticaria

Inducible Urticarias

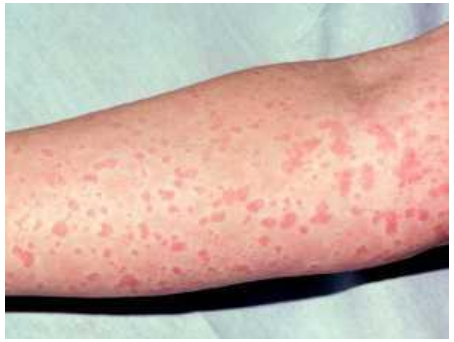
Dermatographism/
pressure

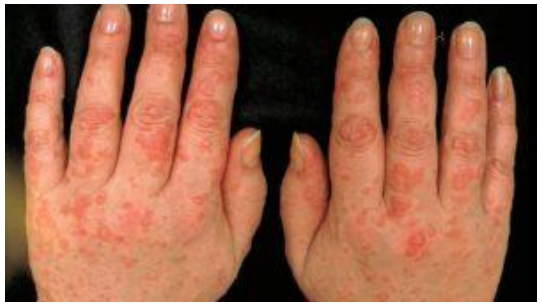
Very Rare:
Solar
Heat
Aquagenic
Vibratory
Contact

Cold induced: Caution



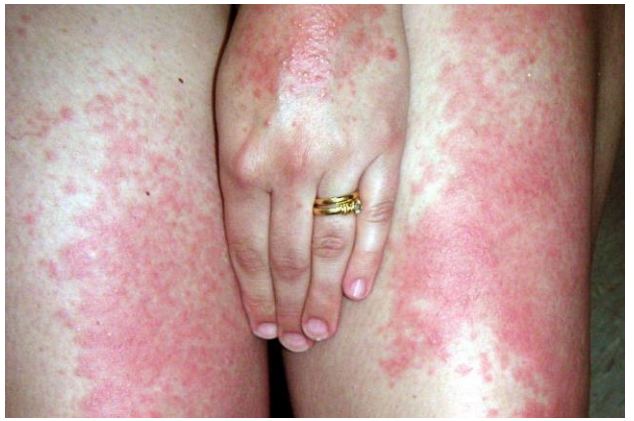
Cholinergic
Exercise, stress,
emotion, spices



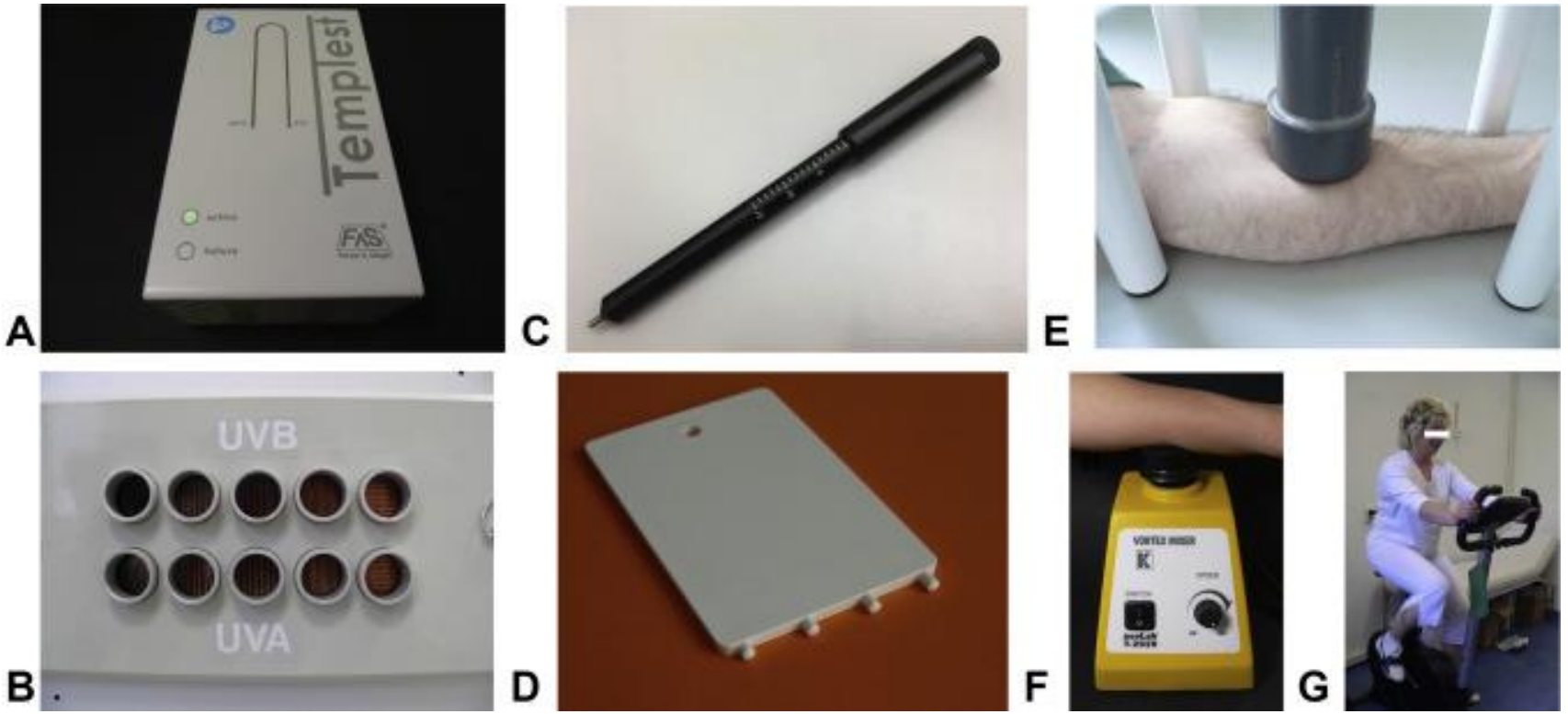


Aquagenic: Caution

Solar V Rare



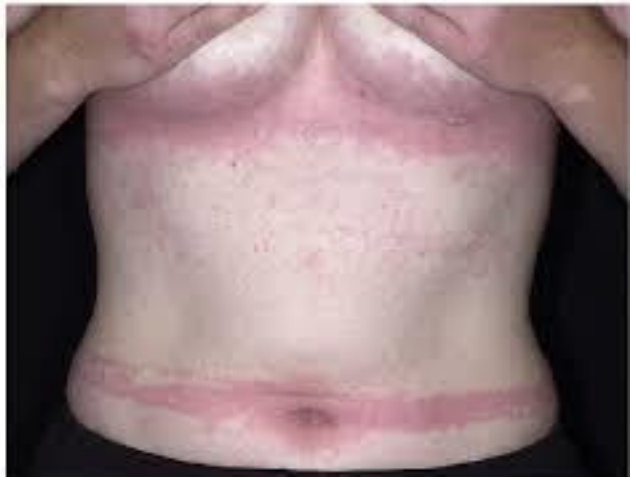
History is the key:
Provocation testing for CindU



A: TEMP TEST; COLD URTICARIA
B. UVA +B; SOLAR URTICARIA
C: HTZ DERMATOGRAPHER
D: FRIC TEST. PROVOCATION AND THRESHHOLD TESTING IN DG
E: FOR DELAYED PRESSURE URTICARIA
F:VORTEX DEVICE; VIBRATORY U
G: BICYCLE ERGOMETER; CHOLINERGIC U

JACI IN PRACTICE: 2018, Vol.6(4), p.1119-1130

Management of CindU



1, Avoidance of triggers

2. Induction of Tolerance (Heat, cold, cholinergic)

3. Pharmacological

1. **Second-generation H_1 antihistamines**

If inadequate control after 2–4 weeks or earlier if symptoms are intolerable

Consider referral to a specialist

2. **Increase antihistamine dose (up to 4 times)***

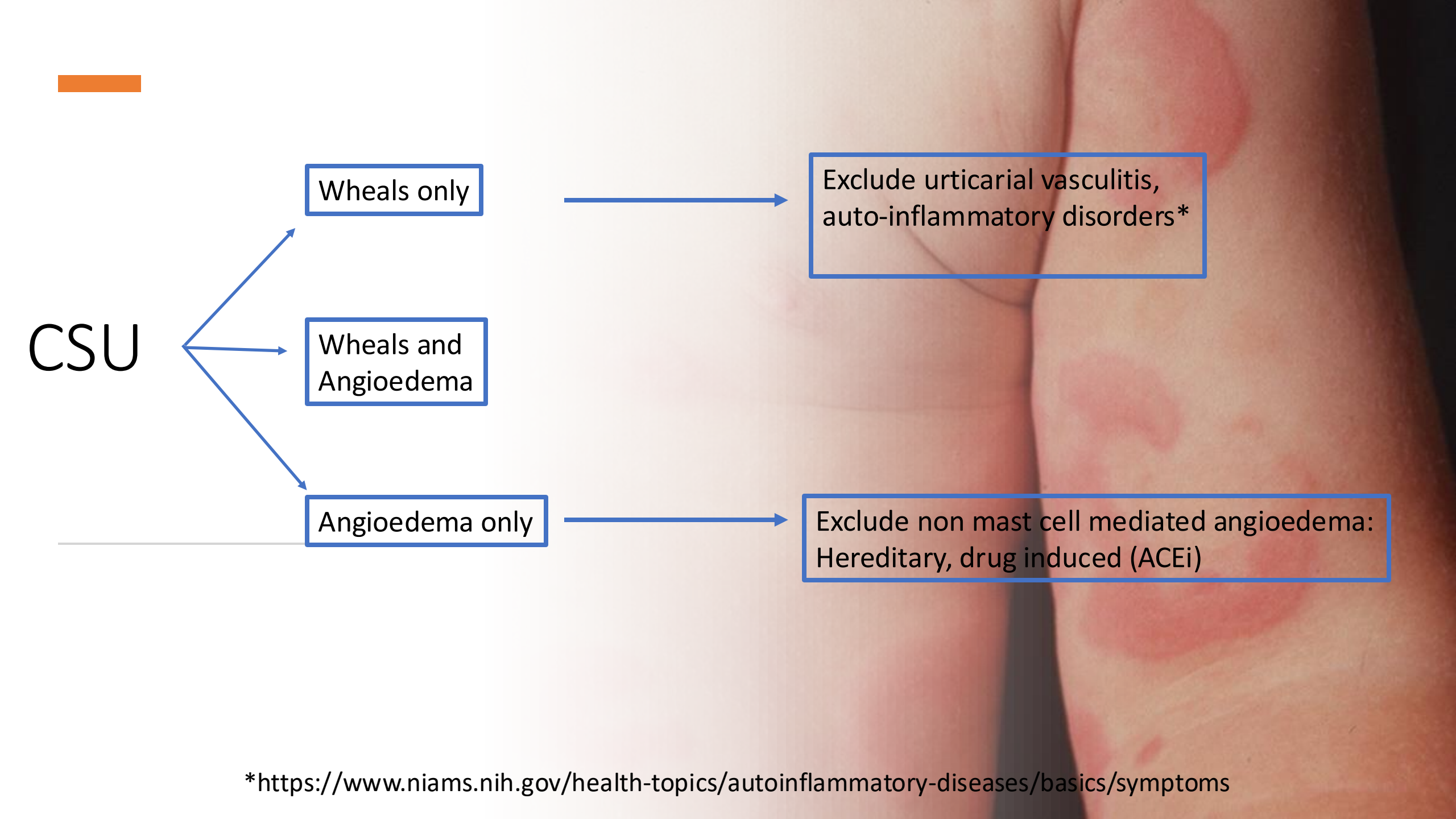
If inadequate control after 2–4 weeks or earlier if symptoms are intolerable

3. Add omalizumab†

Treatment under supervision of a specialist

If inadequate control within 6 months or earlier if symptoms are intolerable

4. Ciclosporin



*https://www.niams.nih.gov/health-topics/autoinflammatory-diseases/basics/symptoms

Chronic Spontaneous Urticaria Pathophysiology

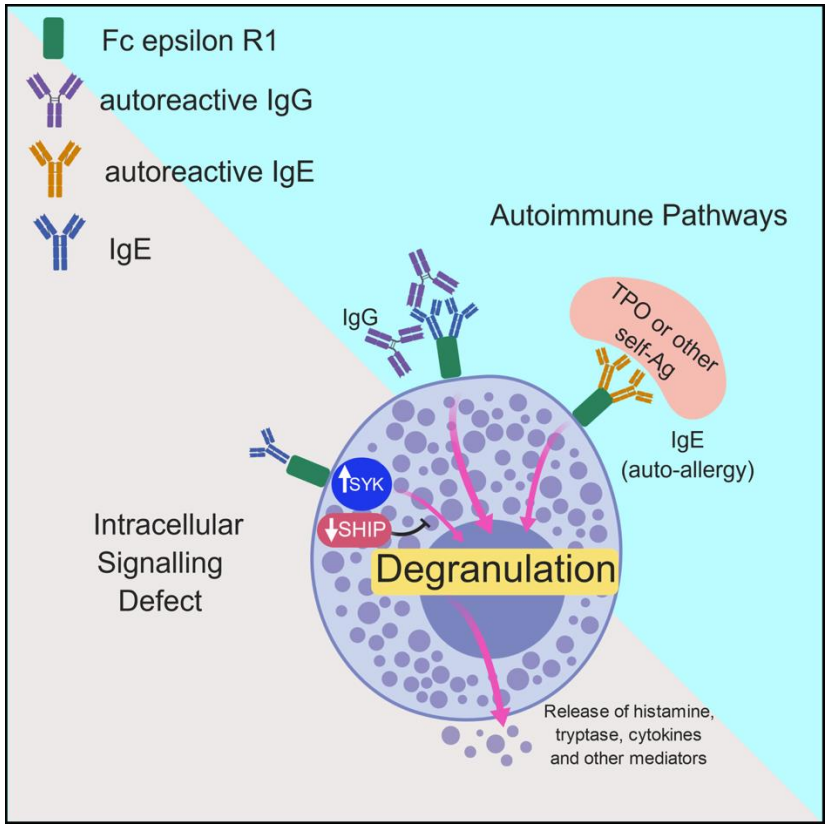
Pathologic activation of mast cells and basophils

Two theories

Intracellular signalling Pathway dysregulation

inappropriate activation of molecules such a spleen tyrosine kinase (SYK) or inhibition of negative regulators (SHIP)

Autoantibody development to FcεRIα *or IgE or IgG patients with autoallergy, crosslinking of Fc epsilon R1 (Fc+R1) via autoreactive IgE molecules directed against self-antigens such as thyroid peroxidase (TPO)*



Frontiers in immunology. 2019 Mar 29;10:627.

Management of CSU

Investigations: (in primary care)

FBC
CRP

Treatment

- **Once daily second-generation antihistamine**
- **up to 4x standard dose (40%)**

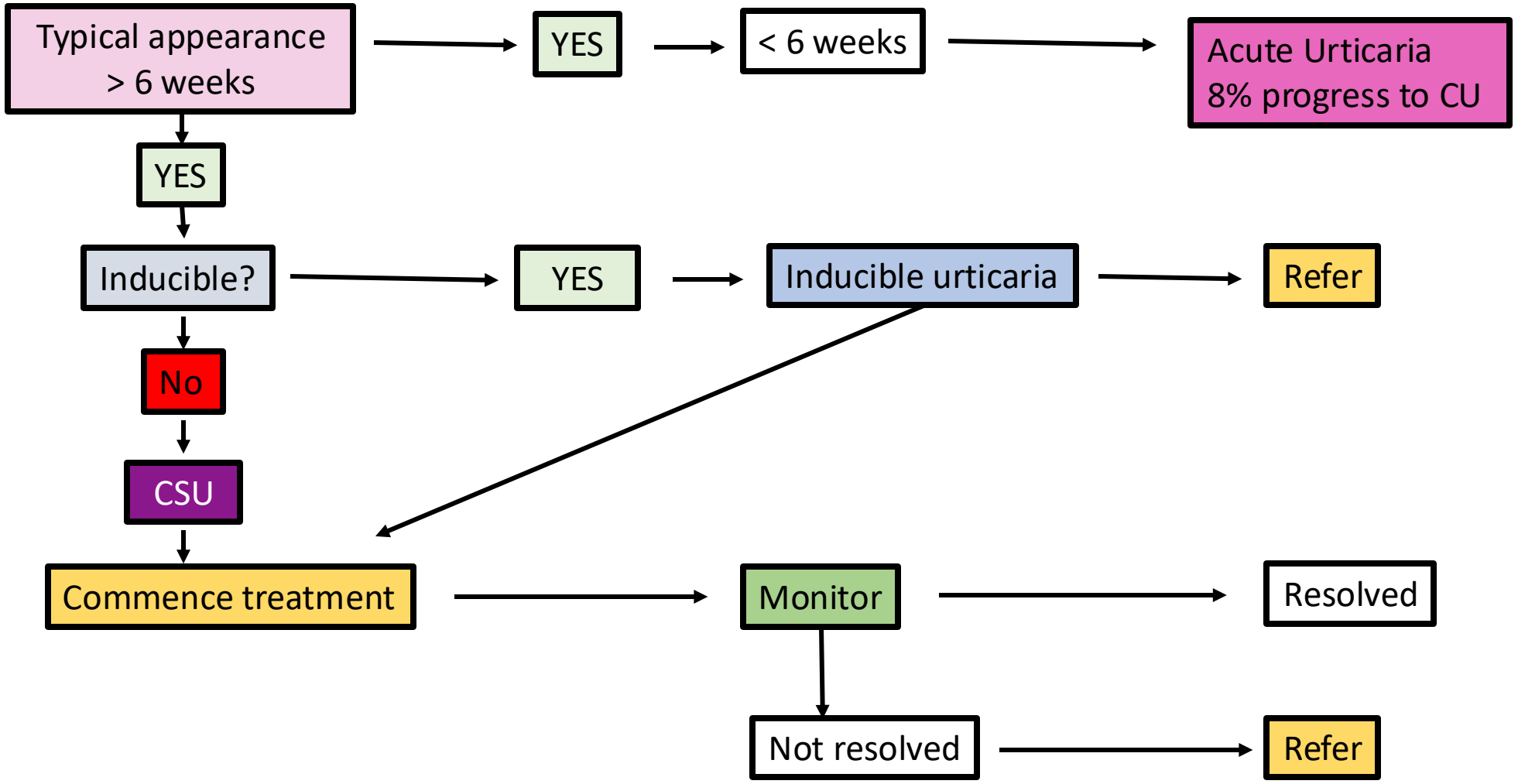
- **Resistant cases: Omalizumab (70%)**
- **and /or cyclosporin or other agents**

Monitoring

Clinical review: the suggested management pathway for urticaria in primary care. Ryan et alClin Transl Allergy. 2022;12: e12195.

UCARE
Urticaria Centers of Reference and Excellence
A GA²LEN NETWORK

CSU: Simplified flow chart



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Some general principles

Exacerbated by
Infections
Medications (NSAIDs)
Alcohol
Stress
Heat
Exercise
Rubbing

Spontaneous remission of CSU:

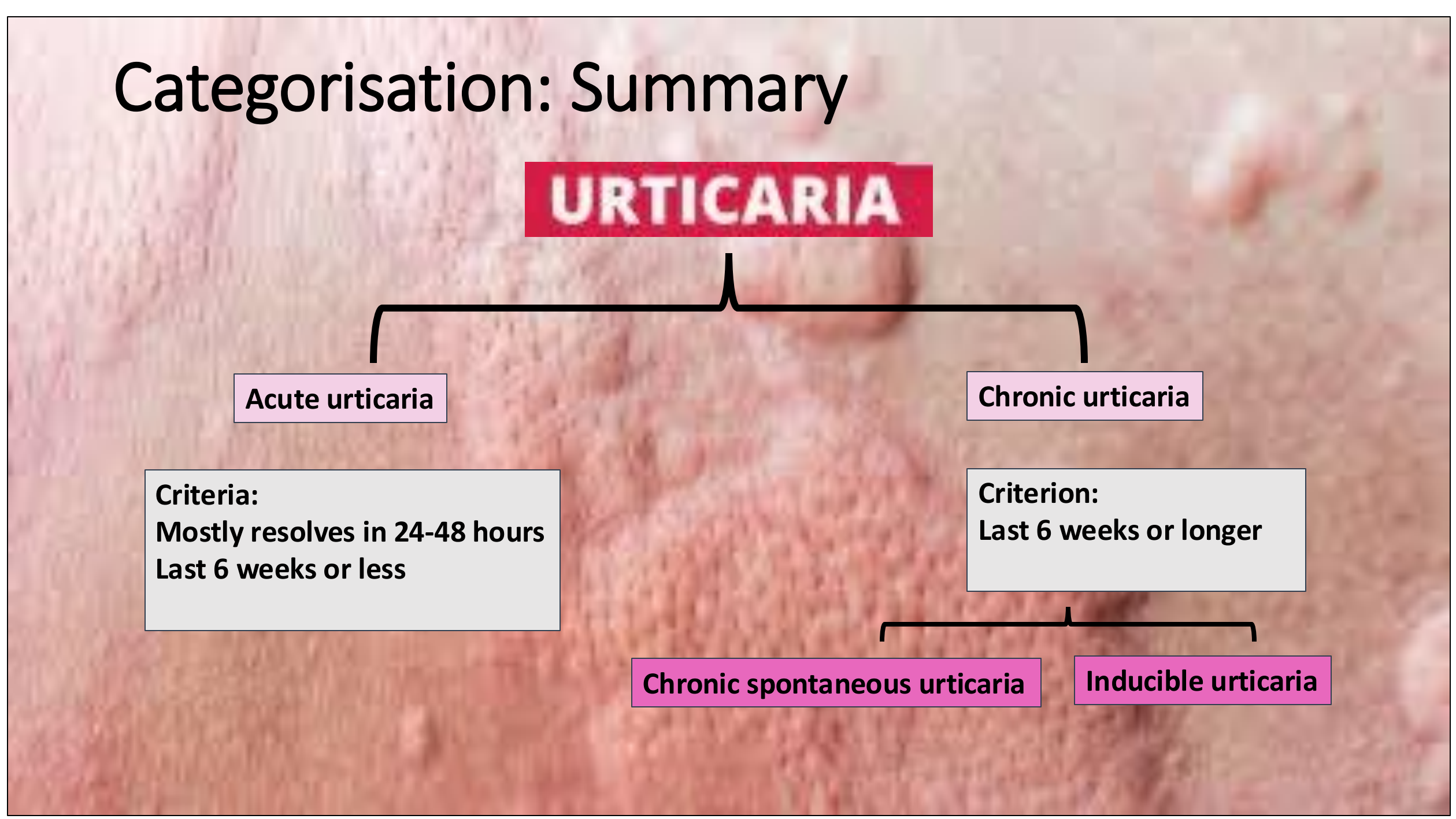
50% after 6 months
30% by 3 years
10% by 10 years
8% at 25 years

Self-monitoring
CRUSE
Symtrac Hives
Urticaria activity score

Patient Charter

Principle 1	• Patients should be able to expect an accurate and timely diagnosis without the burden of unnecessary diagnostic tests. Achieving these expectations will help in relieving a patient's frustration and anxiety induced by diagnostic delays.	
Principle 2	• Patients should have access to specialty care when needed to ensure appropriate and adequate treatment.	
Principle 3	• Patients should have access to innovative treatments to improve symptoms and reduce their burden of disease. The severity of disease should be monitored by patient-reported outcomes and available biomarkers and clinical characteristics may be used to tailor individualized treatment.	
Principle 4	• Patients with CU should be prescribed guideline-recommended treatments to avoid unnecessary side effects from first-generation antihistamines and long-term OCS use. The potential side effect burden of each CU treatment should be part of the shared decision-making conversations between healthcare providers and patients.	
Principle 5	• The goal of therapy for CU should be to address all components of life that are negatively affected by CU, not only to relieve symptoms. Shared decision-making conversations are an opportunity to discuss the patient's goals.	

Categorisation: Summary



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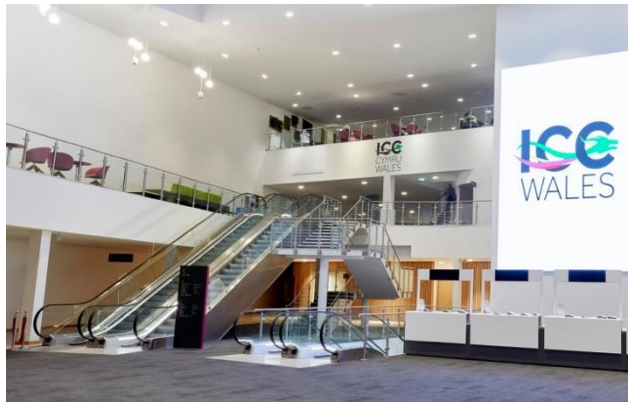

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