Scratching The Surface:
Approach to Chronic Urticaria in Children

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Disclosures

Consultant for:
Pfizer and Valeant (pediatric psoriasis).

Not relevant to this presentation.

I will discuss off-label use of drugs to treat chronic urticaria in children.
Focus Points

- Etiologies/Associations of CU in pediatric patients
- Individualized investigation of patients
- Key principles of management
Chronic Urticaria in Children

- ~50% have angioedema also
- Huge impact on quality of life
- Only 25% will remit within 3 years
  - 67% may remit within 5 years

Cause identified in ~25% of cases despite exhaustive investigations.

Remainder designated as chronic idiopathic (spontaneous) urticaria

Clinical and Experimental Allergy 2007;37:631–650

Immunologic and non-immunologic mast cell degranulation

Vasoactive & Inflammatory Mediators → Histamine, Bradykinin, Eicosanoids, Cytokines
Urticaria Classification System

Acute < 6 wks

Chronic > 6 wks

CSU: Chronic Spontaneous Urticaria (chronic idiopathic urticaria)

CSU: Chronic Inducible Urticaria (physical urticaria)

95% Drugs & Bugs: antibiotics, viral, bacterial

<5% Foods, Bites and Stings: nuts, eggs, shellfish, milk

CIU/CSU: Chronic Autoimmune Urticaria (30-50%) (histamine-releasing antibodies in serum)

Physical: 40%
Other: 10%
Idiopathic: 50%

Chronic Urticaria in Children
Most common precipitants

Zitelli and Cordoro
Pediatric Dermatol 2011
Chronic Urticaria in Children

Most common precipitants:
- Dermatographism
- Delayed Pressure
- Cholinergic
- Cold
- Solar
- Vibratory
- Aquagenic

Chronic Inducible Urticaria:

- Physical 40%
- Other 10%
- Idiopathic 50%

CIU/CSU: Chronic Autoimmune Urticaria (30-50%)
(histamine-releasing antibodies in serum)

Zitelli and Cordoro
Pediatric Dermatol 2011
Chronic Inducible Urticaria

Reliably reproduced by challenge testing

Often co-occurs with other causes of CU

Prolonged duration

More resistant to standard doses of AH

Chronic Urticaria in Children

Most common precipitants

- Infection, allergen exposure, drugs (ASA, NSAID: Cox1 -> AA -> ↑LT)
- Dietary pseudo-allergens/intolerances (dyes, preservatives -> salicylates)
- Auto-inflammatory/periodic fever syndromes (s/s of systemic inflammation)

Chronic Urticaria in Children
Most common precipitants
<table>
<thead>
<tr>
<th>Autoimmune Disease</th>
<th>Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid (most common)</td>
<td>H. Pylori</td>
</tr>
<tr>
<td>Others (rare):</td>
<td>Parasites</td>
</tr>
<tr>
<td>Celiac</td>
<td>(endemic regions; travel)</td>
</tr>
<tr>
<td>Systemic lupus</td>
<td>UTI</td>
</tr>
<tr>
<td>Juvenile arthritis</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
</tr>
</tbody>
</table>

Treating AI or infections may eliminate CU in a subset of patients.

Arch Dis Child 2003.
Sackesen C. Pediatr Dermatol. 2004


Almost Never

Malignancy

Occult Infection

Dental or sinus abscesses
GI or vaginal candidiasis
H&P Directed Stepwise Approach

Mild, antihistamine responsive disease, negative history
No investigations

History-directed investigations
Provocation testing for physical inducers
SPT/specific IgE to candidate allergens

1st Tier Screening
AH non-responders, +Hx, severe disease
CBC/diff
ESR/CRP
Urinalysis
Thyroid Function
Thyroid auto-Ab (microsomal/TPO, thyroglobulin)

2\textsuperscript{nd} Tier Screening
guided by the initial H&P and screening labs

Serum cryoproteins
(select cases of cold urticaria)

Celiac disease screen

Infectious disease screen
(viral, bacterial, parasitic)

LFT/viral hepatitis serologies

ANA / other specific antibodies

CU Index
(histamine releasing Ab in serum)

Skin biopsy: lymphs, neuts, r/o UV
Choosing Wisely Campaign, 2012 AAAAI
Statement on CU Investigations

Do not routinely do diagnostic testing in patients with chronic urticaria.

- In the overwhelming majority of CU pts, a definite etiology is not identified.
  - Targeted laboratory testing based on clinical suspicion is appropriate.
- Routine extensive testing is neither cost effective nor a/w improved outcomes.
- Allergy testing indicated only if a clear history implicates an allergen as causal.

http://www.choosingwisely.org/clinician-lists/american-academy-allergy-asthma-immunology-chronic-urticaria/
Treatment Summary

1st line: 2nd gen long acting non-sedating H1 antihistamines

Cetirizine, fexofenadine, desloratadine: 6 months and older

- Always dose on a schedule, never reactively (except prn breakthru)
- Escalate up to 4 times standard doses and in combination

1st gen sedating H1 AH (qHS) (diphenhydramine, hydroxyzine)

J All Clin Immunol 2014
Staubach P et al. JEADV 2016
Pediatr Allergy Immunol 2015
Treatment Summary

2nd line: Leukotriene antagonists (6 months and older)
   H2 blockers (1 month and older)

3rd line: severe cases: immunomodulators/immunosuppressants
   - Omalizumab (12+)
   - Cyclosporine
   - Dapsone, Plaquenil
   - Others (IVIG, Rituximab)

J All Clin Immunol 2014
Staubach P et al. JEADV 2016
Pediatr Allergy Immunol 2015
Take Home Points: CU in Kids

- Numerous studies document lack of diagnostic utility of lab investigations
- Systematic review of 29 studies involving > 6000 patients concluded:
  - history is most important, trigger diaries are helpful
  - routine lab tests are of little value; only useful if based on the history
- Individualized approach and management is key

Zitelli and Cordoro *Pediatric Dermatol* 2011
Clinical and Experimental Allergy, 2008.
The Dermatology Foundation has supported & advanced my career.