Treatment of CIU

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DEFINITION OF CHRONIC URTICARIA

- Urticaria which persists for longer than 6 weeks in adults or 12 weeks in children
- 40 to 50% Chronic Autoimmune Urticaria (CAU)
- 50 to 60% Chronic Idiopathic Urticaria (CIU)
- A minority of cases can be characterized as physical urticarias: (heat, solar, light, cold, delayed pressure, dermatographism, vibratory, aquagenic or cholinergic)

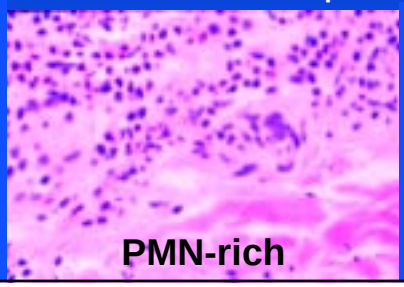
EPIDEMIOLOGY OF URTICARIA

- 20% of the population will be affected
- identified in 0.1% of routine physicals
- female / male = 2 / 1
- all ages
- 40% of pts with > 6 mos of CIU will still have urticaria 10 years later
- Association with autoimmune thyroid diseases (12 to 29% vs 6% for "normal" population) [Leznoff 1983; Zauli 2001]

ROUTINE HISTOLOGY

Nondiagnostic:

- Edema
- Nonspecific mild perivascular infiltrate
  - 4 - fold increase in mononuclear cells (mostly CD4+ cells)
  - 10 - fold increase in mast cells
  - Th1 and Th2 mediated [Ying, 2002]
  - Increase in basophils



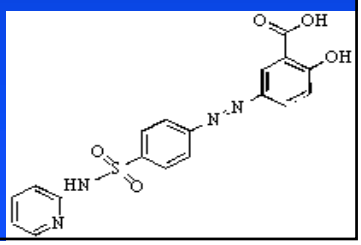
TREATMENT OF CIU/CAU

- **Antihistamines are the gold standard:** non-sedating and sedating H1 antagonists.
- **Second line therapy:** Leukotriene antagonists, H2 antagonists, corticosteroids, cyclosporine *(Gioacchino, 2003)*
  - Methotrexate *(Gach 2001)*
  - Hydroxychloroquin *(Reeves 2004)*
  - Dapsone *(Fox 1988)*
  - Cyclophosphamide *(Bernstein 2002)*
  - Plasmapheresis *(Grattan, 1992)*
  - Sulfasalazine (*Fisher, 1989)*
  - Anti-IgE (Zolair)
  - Anti-CD20 (Rituxan)

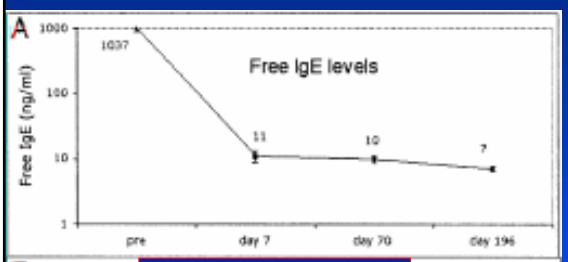
Asthma & Allergy

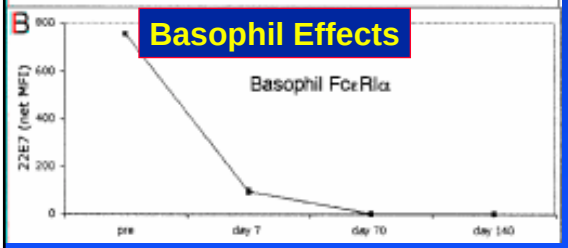
SULFASALAZINE

- Sulfapyridine covalently linked to 5-aminosalicylic acid.
  - Sulfa moiety: antimicrobial properties
  - Salicylate: anti-inflammatory agent
- Used to treat RA, JRA, UC
- Side effects: 33% headache, diarrhea, oligospermia (reversible). >10% gastric distress, photosensitivity, <3% Interstitial nephritis, hepatotoxicity, agranulocytosis.
- Retrospective Study (JHAAC; 1 to 4gm/day)
  - 19 adult pts (mean age = 39 y)
  - Most on antihistamines and LTA
    - 2/19 on CyA and 9/19 on systemic steroids
  - Responses:
    - 14/19 (74%) reported significant improvement
    - 4/19 (21%) reported minimal improvement
    - 1/19 (5%) reported worsening
    - 4/19 (5%)off all other medications
    - 9/9 had no need for steroids or significantly reduced (1 previously steroid naïve required burst after CIU initiation)



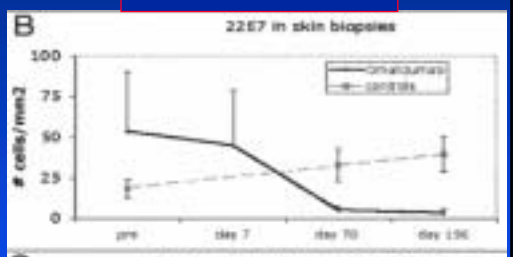
ZOLAIR Rx FOR CHRONIC URTICARIA?

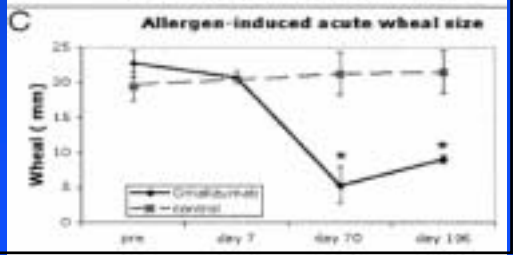




(Beck, 2004)

Mast Cell Effects





TREATMENTS OF URTICARIA

(Second generation antihistamines)

- Advise d/c of ASA, NSAIs and EtOH
- **Loratadine (Claritin):** 5 to 10 mg qD in AM
- **Desloratadine (Clarinex):** 5 to 10 mg qD in AM
- **Cetirizine (Zyrtec):** 5 to 20 mg qD or in divided doses
- **Fexofenadine (Allegra):** 180 mg qD or 60 mg b.i.d.

TREATMENTS OF URTICARIA
(First generation antihistamines)

- **Hydroxyzine HCL (Atarax or Vistaril):** 10 to 100 mg qD or 6 to 8hr PRN
- **Diphenhydramine (Benadryl):** 12.5 to 100 mg per dose q 4 to 6 hr PRN
- **Cyproheptadine (Periactin):** 4 to 8 mg q 6hr PRN

TREATMENTS OF URTICARIA
(H_2 blockers)

- **Zantac (Ranitidine):** 150 mg B.I.D. or 300 mg qD
- **Tagamet (Cimetidine):** 400 mg B.I.D. or 800 mg qD
- **Pepcid (Famotidine):** 20 mg B.I.D. or 40 mg qD
- **Doxepin (Sinequan):**
  - Adults: 25 to 100 mg qD up to max dose of 100 mg qD
  - Children: 1 to 3 mg/kg/day

TREATMENT OPTIONS FOR PTS THAT FAIL OR ARE INTOLERANT OF ANTIHISTAMINES

- **Dapsone:** 50 mg B.I.D.
- **Colchicine:** 0.6 mg qD to T.I.D.

NEUTROPHILIC CIU ONLY

LYMPHOCYTIC OR NEUTROPHILIC

- **Sulfasalazine:** 500 mg qD ⇒ 2 gms B.I.D.
- **Hydroxychloroquine:** 200mg B.I.D. (Adults)

TREATMENT OPTIONS FOR AUTO-IMMUNE URTICARIA

- **Cyclosporin A:** 3-5 mg/kg/day - only Rx for which there is a DBPC trial.
- **IVIG:** 0.4 mg/kg/day x 5 days
- **Thyroid replacement** if hypothyroid

British Journal of Dermatology 2000; 143: 365–372

Randomized double-blind study of cyclosporin in chronic 'idiopathic' urticaria

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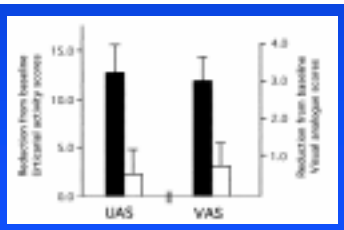
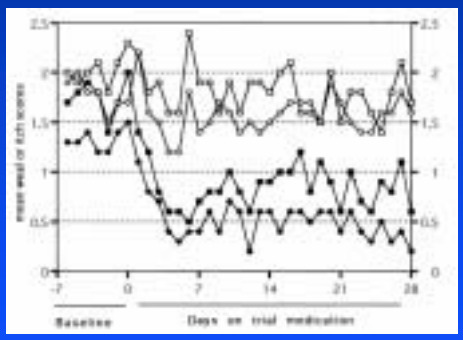
Table 1. Baseline clinical characteristics of patients randomized to cyclosporin or placebo. Results expressed as median (range)

	Active	Placebo
Number	20	10
Women	16 (80%)	8 (80%)
Age (years)	32·5 (19–72)	33·5 (23–60)
Duration (months)	12 (1–60)	8·5 (3–192)
Previous steroid use	14 (70%)	4 (40%)
Baseline urticarial activity score (max. 42)	20 (9–36)	28 (17–41)
Baseline visual analogue score (max. 10)	5·6 (2–10)	7·4 (5·4–8·7)





APPROACH TO STEROID DOSING IN PTS WITH SEVERE URTICARIA

1. **Start alternate day therapy**
   - e.g. 20 mg prednisone q.o.d.
2. **Daily steroids, taper to every other day**
   - e.g. 50, 50, 50, 45, 40, 35, 30, 25, 20, 15, 20, 10, 20, 5, 20, 0
3. **For uncommon severe angioedema**
   - 50 to 60 mg prednisone in single dose
   - 40 mg next day if swelling persists
   - Discontinue without tapering or return to prior every other day dosage

(from Kaplan A., Can. J. Allergy & Clin. Immunol. 1999)