Acute and Chronic Urticaria

Giovanni Cavagni, Gemma Trimarco

UOC di Allergologia

Dipartimento di Pediatria

Coordinatore: Alberto G. Ugazio

cavagni@opbg.net
URTICARIA IS NOT A DISEASE,
but a skin reaction generated by different stimuli, defined as recurrent, generalized, erythematous, pruritic lesions that have circumscribed border and blanch with pressure

Acute lesions show dilation of small vessels located in the superficial dermis with widening of the dermal papillae and swelling of collagen fibers

Urticaria can be associated with a swelling of the deeper skin layers, that often involves face, tongue, extremities or genitalia, defined ANGIOEDEMA
Urticaria affects 6% to 7% of preschool children. Among all age groups:

- most patients (50%) have both urticaria and angioedema
- 40 % have isolated urticaria
- 10% have angioedema alone.
Urticaria/angioedema: Time evaluation

- **ACUTE**: symptoms < 6 weeks’ duration (more common in young children)
- **CHRONIC**: symptoms for > 6 weeks
- **CHRONIC-INTERMITTENT**: recurrent episodes of chronic urticaria with a resolution of symptoms between the episodes of at least one week

*(Greaves MW, Allergy 2000; 55: 309-320)*
Pathogenesis

**IMMUNE-MEDIATED (25%):**

- Type I reactions (IgE mediated)
- Type II reactions (IgG mediated)
- Type III reactions (ICC)

**NON-IMMUNE MEDIATED (75%):**

- degranulation of mast cells
- excessive histamin absorption (PAR ???)
- complement –mediated (anaphylatoxins)
- impaired metabolism of arachidonic acid
Acute Urticaria: causes

- Infections (~80%)
- Drugs (~5%)
- Foods (<15%)

Common mediators:
- histamin, PGD2, LTC4, chinine
URTICARIA AND INFECTIONS

• The most common cause of acute urticaria is **infection**, especially in infants and children.

• In more than 60-70% of children < 3 years old, urticaria is normally present together with symptoms and signs from other organ systems, such as the respiratory (mortureux, 1998; Legrain 1993)

cavagni@opbg.net
Which infections?

Adenovirus  Mycoplasma
VRS        Streptococcus
Influenza A Campylobacter j.
Coxsakie    H. pylori
ECHO        Tricophyton
Rotavirus    Candida
H.S. tipo I  Giardia l.
EBV         Toenia spp.
VZV         Enterobius vermicularis
CMV         Ascaris l.
HBV         Toxocara canis
HCV
HIV

COMMON VIRAL INFECTIONS !!!
**Patella V et Al.** Endogenous superallergen protein Fv interacts with the VH3 region of IgE to induce cytokine secretion from human basophils. *Int Arch Allergy Immunol* 1999; 118: 197-9.

REACTIONS TO DRUGS

Many drugs implicated in childhood, especially antibiotics and NSAID

IgE mediated hypersensitivity: RARE in children.

Non-immune-mediated exanemas: more common. Sometimes there is no reaction after a second administration.

Serum disease: rare

cavagni@opbg.net
Polyvinylpyrrolidone
Dextran
Iodinated contrast media
Anesthetics

Heterologous proteins

IC

C3a C5a

histamine PGD2 LTC4 chinine

Cavagni@opbg.net
IgE -mediated food allergy

- Ingestion, contact (rarely by inhaling: fish).
- The incidence of acute food-dependent urticaria is about 1% - 2% in children
- < 2 aa: milk, egg
- > 2 aa: peanuts, fish, legumes, vegetables, fruits
- !! banana, chestnut, avocado, kiwi, mango: cross-reaction with latex)
Pharmacologic food reactions: Histamine-containing foods and Histamine-releasing foods

Seasoned cheese
fresh and not fresh fish, crustacean, mollusc susages
vine, beer, alcohol, coffee
game
canned food
Spinach, tomatoes, potatoes, cabbage, brussels sprouts
legumes
Sauces, baking-powder, chocolate
sauerkraut
Avocado, figs, grapes
strawberry, raspberry, pineapple, banana, kiwi
How much histamine can generate a skin reaction? 

**Scombroid (histamine poisoning):**

Food is at risk when histamine’s concentration is > 50 mg/100 g 

*(Sanchez-Guerrero IM et Al. J Allergy Clin Immunol 1997; 100: 433-4)*
Canned fish

- Allice: 1.2 Kg
- Sardine: 3.3 Kg
- Tuna: 8.3 Kg
- Salmon: 7.1 Kg

Cavagni@opbg.net
Spinach 1.2 kg
Tomatoes 2 kg
Sauce 220 g
Pig’s liver

2 Kg

Sausages

312 g

Cheese (Cheddar, Gouda, Roquefort)
until 2,5 Kg

Fermented drinks
(vine, bieer)

2,5 l
Additive-induced urticaria

- The incidence of such reactions remains unknown, although it appears to be a relatively rare phenomenon
- **Danish:** 1-2 % of school children *(Fuglsang G Pediatr Allergy Immunol 1993; 4: 123-9)*
- **Food additive and acute u.:** unknown incidence
- **Food additive and chronic u.:**
  - Ehlers (Germania, 1998): 75%
  - Volonakis (Grecia, 1992): 2.6%

cavagni@opbg.net
FOOD ADDITIVES INTOLERANCE

SYNTHETIC COLORANTS (azo dyes):
- tartrazine
- sunset yellow
- Ponceau
- amaranth
- erythrosine
- annatto

FOOD DYES:
- Sodium benzoate
- parabens
- butylated-hydroxyanisole
- butylated-hydroxy toluene

SWEETNER:
- aspartame
CONTACT URTIC.

- foods
- Local application of a drug
- Cosmetics
- Animals (saliva, dander, venom)
- Plants
- Latex

INHALING U.

- Plumage
- Dander

PAPULAR URTICARIA (INSECTS)
CHRONIC URTICARIA:

less frequent in children

PHYSICAL URTICARIA:

Dermographism (u. factizia)
cholinergic u.
cold u.
solar u.
delayed pressure u.

VASCULITIC U.

AUTOIMMUNE U.

U.PIGMENTOSA (systemic mastocytosis)

PAPULAR U. (INSECTS)

CHRONIC IDIOPATHIC U.

(cavagni@opbg.net)

Physical Urticaria

Dermographism

Cold u. (2-8%)

Cholinergic u. (2 - 6%).

cavagni@opbg.net
Dermographism (urticaria factitia)
DERMOGRAPHISM

It can be diagnosed by observing the skin after stroking it with a tongue blade or fingernail

Or

With a special instrument (da 3200 a 4900 g/cm2):

Immediate reactions: within 5-10 minutes

Intermediate reactions: after 30 min - 2 h.

Delayed reactions: after 4 - 6 ore (dura 24 - 48 ore)
COLD URTICARIA: DIAGNOSIS

ICE CUBE TEST:
A simple test is to place an ice cube on the patient’s forearm for 10 - 20 minutes and observe the area for 10 minutes thereafter.

If the patient has cold urticaria, the area will become pruritic about 2 minutes after removing the ice cube, and by 10 minutes a large hive the shape of the ice cube will form.
Cholinergic urticaria: diagnosis

1. **Physical exercise** (running for 30’ or using a bicycle ergometer for 5-15’, etc.) to provoke an increase in core body temperature greater than 0.7 - 1 °C.

2. **Immersion in warmed water** (40-45°C) for 10 min

3. **Intradermal injection of 0.01 mg of methacholine**
Delayed pressure urticaria

- uncommon
- symptoms typically occur 4 to 6 hours after application of pressure to the skin
- long duration

**DIAGNOSIS:**

It can be diagnosed by hanging a 4.5 - 7 kg weight on the leg for 10 minutes.
**Solar urticaria**
- rare disorder
- brief exposure to light causes the development of urticaria within 1 to 3 minutes
- diagnosis: special fluorescent tubes

**Aquagenic urticaria**: direct application of a compress of tap water or distilled water to the skin (36°C) for 30 - 40 minutes.

**Vibratory urticaria**: lesions can be reproduced by gently stimulating the patient’s forearm with a laboratory vortex for 10 minutes.
Urticarial vasculitis

Extremely rare
Long duration
purpura
The response to H1-ant.may be disappointing

Collagen vascular diseases !!
Autoimmune Urticaria

25-50% of idiopathic forms

(Greaves, J Allergy Clin Immunol 2000; 105; 664-72)
Skin testing with autologous serum

POSITIVE:
Immediate wheal-and-flare response (mean wheal diameter at least 1.5 mm > than that induced by saline after 30’)

0.05 mL (= 50µL) i.d. + negative control (saline)
Chronic urticaria: other causes

**Thyroid disease:** as many as 12-14% of patients with chronic urticaria have circulating thyroid autoantibodies (antithyroglobulin and antithyroid peroxidase);

Hyperparathyroidism

Diabetes mellitus

Celiac disease

Parasitic infestations; chronic infections
Duration

- physic u.
- common u.
- vasculitic

Duration:
- 3 h
- 6 h
- 12 h
- 18 h
- 24 h
- >36 h
Chronic urticaria: infections

- Overestimated. Usually there is not a remission of symptoms after the treatment of the infection.

- Infections of the oral cavity, sinusitis, urinary tract infections; Hepatitis B – C; Helicobacter pylori

cavagni@opbg.net
Exams: which and when?

- Acute u. with a **specific suspect** (food; latex)
- Urticaria with **symptoms of anaphylaxis**
- Acute u. > 3 weeks and non-responsive to treatment
- Frequent or **chronic urticaria**
It is possible to detect a cause in the:

- 40-60% of acute u.
- 20-30% of chronic u.

Usually it is not easy to remove the cause

Symptomatic therapy
THERAPY

ACUTE URTICARIA

+ ANAPHYLAXIS

SIMPLE U.

cavagni@opbg.net
ANAPHYLAXIS THERAPY

1. **EPINEPHRINE** 1:1000 i.m. (s.c.)
   0.01 mg (ml) / Kg every 5 to 15’ as necessary

2. **CHLORPHENIRAMINE** 0.20 mg/Kg e.v.
   (slowly !! In 3’-5’) or i.m.

3. **HYDROCORTISONE** 10 mg/Kg or
   **METHYLPREDNISOLONE** 2 mg/Kg e.v or
   i.m.

4. **CRYSTALLOID** 10-20 ml/Kg e.v. in 30’

5. **DOPAMINE, SALBUTAMOLO, XANTINE**

cavagni@opbg.net
ACUTE URTICARIA: DRUGS

Sedating ANTIHISTAMINE H₁

Low sedating ANTIHISTAM. H₁

CORTICOSTEROIDS

DIET

cavagni@opbg.net
LOW SEDATING ANTIHISTAMINE vs SEDATING ANTIHIST.

- **Efficacy**: > placebo; > sedating antihistamine.
- They are highly effective in suppressing skin reactivity and they have a greater and more prolonged effect on wheal and flare suppression (late-phase)
- < penetration of CNS
- > selective
- Once daily

TOLERANCE
USE OF STEROIDS IN ACUTE URTICARIA

The use of steroids is based on “habits” more than on evidence based medicine (habits are hard to be given up!)

USE ONLY IN:

• severe acute forms (especially if extremely pruritic) with angioedema;

• recurrent urticaria

• severe serum disease
CORTICOSTEROIDS AND CHRONIC URTICARIA

• Corticosteroids are effective at reducing urticaria severity, although the lowest therapeutic dose is recommended.

• Acute episodes refractory to antihistamines may be treated with standard doses.

• They may be particularly effective in urticarial vasculitic or delayed pressure urticaria.
ELIMINATION DIET

- No after a single acute episode! It could be useful to avoid those foods with a high content of histamine.
- A 2-3 week trial elimination diet may be implemented if a specific food is suspected, followed by an oral food challenge, or in recurrent acute episodes of acute urticaria.
- Ordinarily elimination diets should last no longer than 2 or 3 weeks.
Chronic urticaria: Avoiding unspecific factors (I)

1. Woolen clothes.

2. Close-fitting garments and tight shoes.

3. Rubbing on the skin
Chronic urticaria: avoiding unspecific factors (II)

4. Excessively hot temperature.

5. Solar exposure

6. Long hot bath
Chronic urticaria: avoiding unspecific factors (III)

7. EXERCISE (with tight clothes)

8. STRESS

9. DRUGS (NSAIDs, Alcohol)

10. FEVER, VIRAL INFECTIONS
Acute U: the therapy does not provide relief?

- compliance

- Replacement of a 2° generation antihist.

- + sedating H₁ antihistamine at bedtime

- + corticosteroids for 3-5 days

- + 2-3 weeks elimination diet
Chronic U: the therapy does not provide relief?

- Compliance and aspecific factors (!!!)
- Replacement of a 2° generation antihist.
- Addition of a sedating $H_1$ antihistamine at bedtime
- Addition of an $H_2$ antihistamine (adults)
- Addition of a leukotriene receptor antagonists (adults)
- Addition of short cycle of oral corticosteroids
- Second line agents: cyclosporin A, IgG e.v., plasmapheresis, dapsone, PUVA

cavagni@opbg.net
Conclusions (I)

Acute urticaria, with lesions lasting less than 6 weeks, is more common in children, but all forms of urticaria may be observed during childhood.

In children, reports of success in identifying a cause range from 21% to 83%. Infection, not allergy, appears to be the most common cause of acute urticaria in children.

Acute urticaria does not require extensive laboratory evaluation or elimination diet, but only symptomatic therapy.
In chronic urticaria, findings from the history and physical examination should direct laboratory investigation.

In chronic urticaria, physical etiologies proved to be the most common causes (cold and cholinergic urticaria, dermographism), followed by autoimmune phenomena.
Conclusions (III)

The elimination diet should be proposed only in those patients with a strong suspicion for a specific food.

It could be useful to avoid for a short period the ingestion of histamine-containing foods and histamine-releasing foods.
Thanks for your attention
cavagni@opbg.net