



L'ORTICARIA

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Ospedale Fatebenefratelli
Benevento**

|Position paper

EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria

Allergy 2009; 64: 1417–1426 2009

Definition

Urticaria is a heterogeneous group of diseases.
All types and subtypes of urticaria share a common distinctive skin reaction pattern, i.e. the development of urticarial skin lesions and/or angioedema.
Urticaria is characterized by the sudden appearance of wheals and/or angioedema



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A **wheal** consists of three typical features:

- 1) a central swelling of variable size almost invariably surrounded by a reflex erythema
- 2) associated itching or, sometimes, burning sensation
- 3) a fleeting nature, with the skin returning to its normal appearance, usually within 1–24 h



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Allergy 2009; 64: 1417–1426 2009

Angioedema is characterized by:

- 1) a sudden, pronounced swelling of the lower dermis and subcutis**
- 2) sometimes pain rather than itching**
- 3) frequent involvement below mucous membranes**
- 4) resolution that is slower than for wheals and can take up to 72 h**

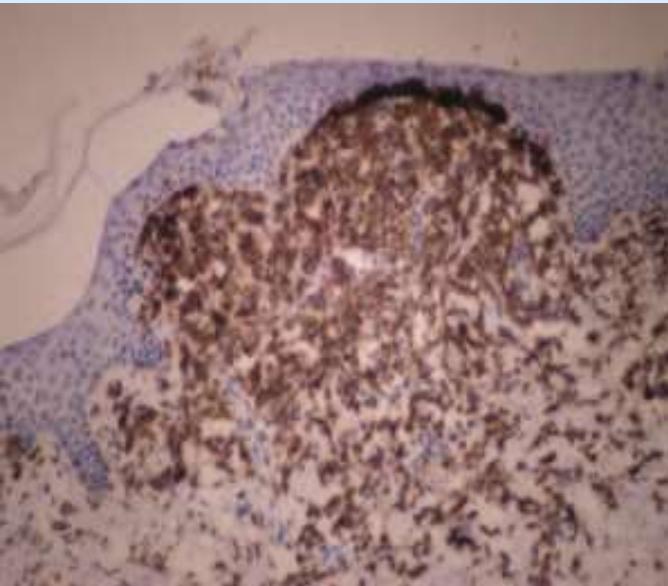


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Histological aspects



On histology, the classical fleeting wheal demonstrates edema of the upper and mid dermis, with dilatation of the postcapillary venules and lymphatic vessels of the upper dermis.

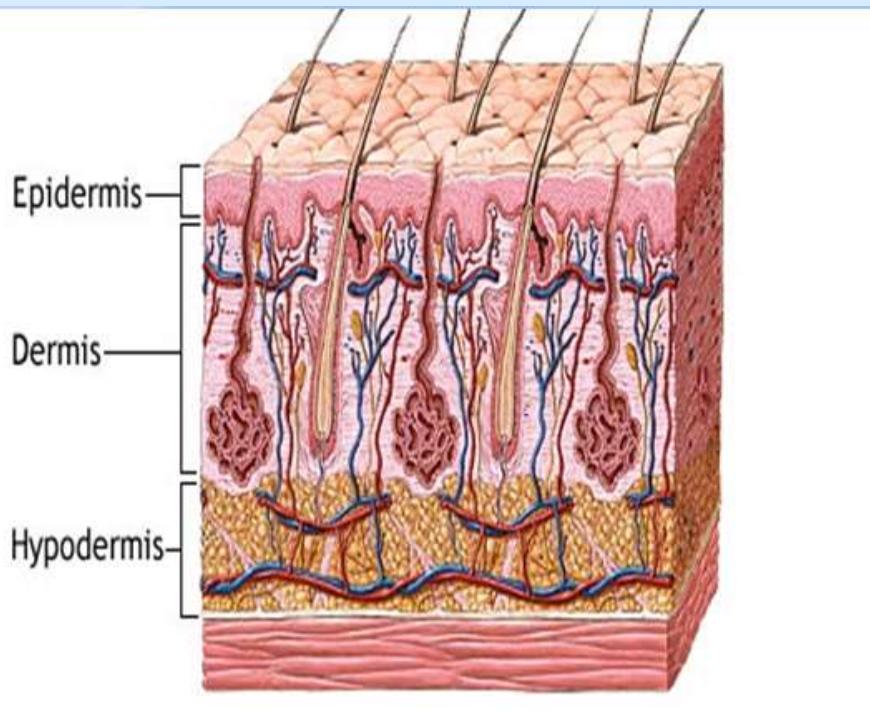
Skin affected by wheals virtually always exhibits up-regulation of endothelial adhesion molecules and a mixed inflammatory perivascular infiltrate of variable intensity, consisting of neutrophils and/or eosinophils, macrophages, and T-cells.

A mild to moderate increase of mast cell numbers has also been reported by some authors.

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Histological aspects

In angioedema, similar changes occur primarily in the lower dermis and the subcutis.

Position paper

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Classification of urticaria on the basis of its duration

Types	Subtypes	Definition
Spontaneous urticaria	Acute spontaneous urticaria Chronic spontaneous urticaria	 Spontaneous wheals and/or angioedema < 6 weeks Spontaneous wheals and/or angioedema > 6 weeks
Physical urticaria	Cold contact urticaria Delayed pressure urticaria Heat contact urticaria Solar urticaria Urticaria factitia/dermographic urticaria Vibratory urticaria/angioedema	Eliciting factor: cold objects/air/fluids/wind Eliciting factor: vertical pressure (wheals arising with a 3–12 h latency) Eliciting factor: localized heat Eliciting factor: UV and/or visible light Eliciting factor: mechanical shearing forces (wheals arising after 1–5 min) Eliciting factor: vibratory forces, e.g. pneumatic hammer
Other urticaria types	Aquagenic urticaria Cholinergic urticaria Contact urticaria Exercise induced anaphylaxis/urticaria	Eliciting factor: water Elicitation by increase of body core temperature due to physical exercises, spicy food Elicitation by contact with urticariogenic substance Eliciting factor: physical exercise

Position paper

EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria

Assessment of disease activity in urticaria patients

Score	Wheals	Pruritus
0	None	None
1	Mild (<20 wheals/24 h)	Mild (present but not annoying or troublesome)
2	Moderate(20-50 wheals/24 h)	Moderate (troublesome but does not interfere with normal daily activity or sleep)
3	Intense (>50 wheals/24 h or large confluent areas of wheals)	Intense (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep)

Sum of score: 0–6.

The EAACI/GA²LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update

CLINICAL PRACTICE GUIDELINE

Urticaria can occur in all age groups. Acute spontaneous urticaria is common in infants and young children, particularly in atopics. For example, it was experienced by 42% of the placebo-treated children in the 18-month EPAAC study.

EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria

Diagnosis of urticaria



Of all the diagnostic procedures, the most important is to obtain a thorough history including all possible eliciting factors and significant aspects of the nature of the urticaria.

History

Associated subjective symptoms of lesion, e.g. itch, pain

Relationship to the menstrual cycle

Family and personal history regarding urticaria, atopy

Associated angioedema

Previous or current allergies, infections, internal diseases, or other possible causes

Shape, size, and distribution of wheals

Psychosomatic and Psychiatric diseases

Diurnal variation

Gastric/intestinal problems (stool, flatulence)

Frequency and duration of wheals

Observed correlation to food

Previous therapy and response to therapy

Occurrence in relation to weekends, holidays, and foreign travel

Time of onset of disease



Induction by physical agents or exercise

Use of drugs (NSAIDs, injections, immunizations, hormones, laxatives, suppositories, ear and eye drops, and alternative remedies)

Smoking habits

Type of work

Hobbies

Stress (eustress and distress)

DIAGNOSI DI ORTICARIA

Second Step

Ricerca del DERMOGRAFISMO

Si applica uno stimolo puntorio
pressorio sulla cute del dorso
usando un oggetto a punta smussa
con pressione e velocità di media
entità o con apparecchi per la
produzione standard di uno stimolo
dermografico “dermographic
tester”

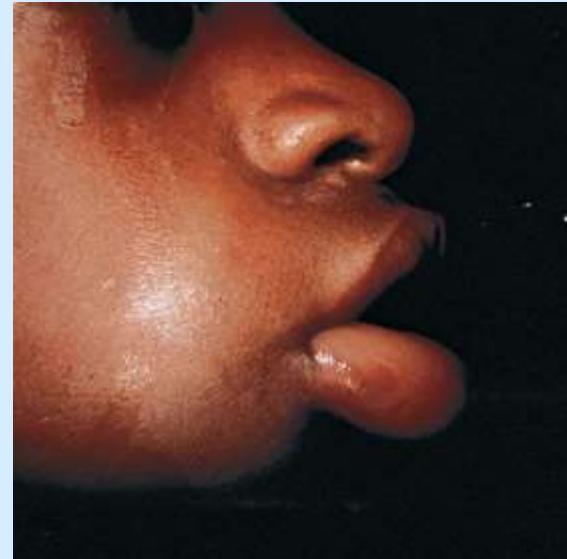
(gli antistaminici debbono essere
interrotti da almeno 2-3 giorni)



ANGIOEDEMA



Angioedema + Urticaria



Angioedema isolato

Non chiedere dosaggio C1-esterasi inibitore

Chiedere dosaggio C1-esterasi inibitore
C4 sierico (ridotto tra gli attacchi)

Allergy is not the main trigger of urticaria in children referred to the emergency room

G Ricci,* A Giannetti, T Belotti, A Dondi, B Bendandi, F Cipriani, M Masi

JEADV 2010, 24, 1347–1348

We included 814 children (aged 0–14 years, 50.4% males) out of 33917 children, consecutively referred to the emergency room between January 2006 and December 2007 (1.1 accesses/day) with a diagnosis of acute urticaria, isolated or associated with other clinical symptoms.

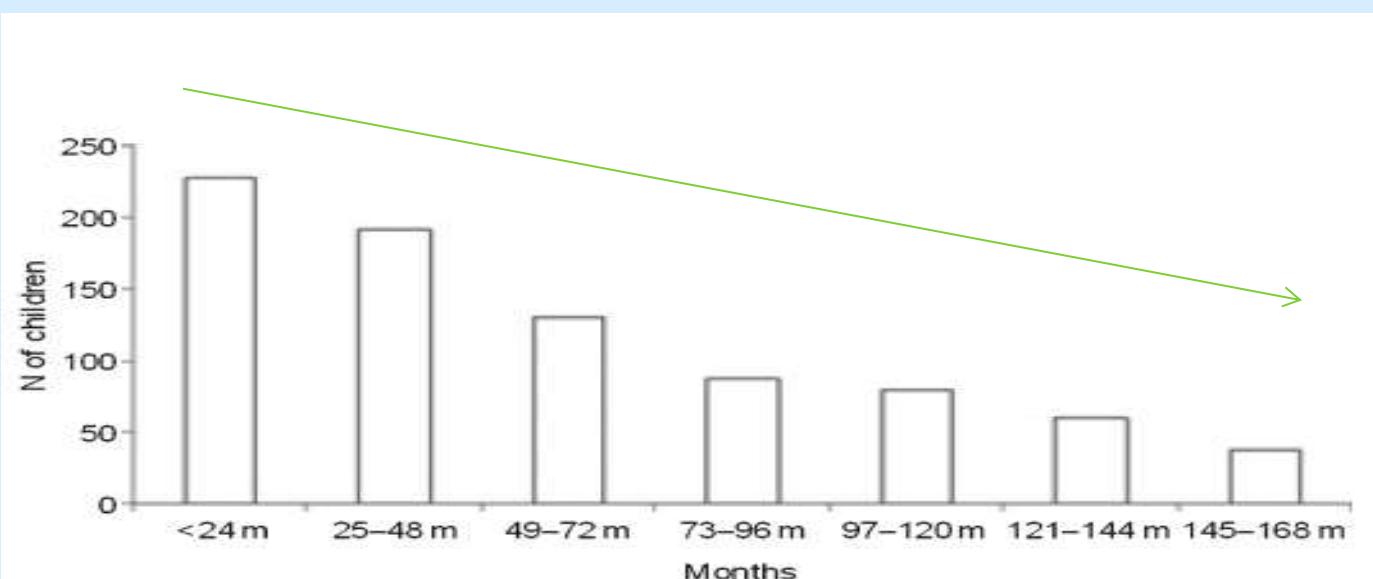


Figure 1 Number of children, divided by age, referred to the paediatric emergency room for acute urticaria.

Allergy is not the main trigger of urticaria in children referred to the emergency room

G Ricci,* A Giannetti, T Belotti, A Dondi, B Bendandi, F Cipriani, M Masi

JEADV 2010, 24, 1347–1348

In 88 patients (10.8%), an allergic mechanism could be clearly identified: foods (6.3%) and contact urticaria by inhalant allergens (4.5%).

Food allergy showed two peaks of age prevalence: the first in children under 2 years (cow's milk or egg) and the second in those older than 5 years (nuts). In eight patients (1.0%), urticaria was a result of food anaphylaxis (cow's milk allergy in four patients, nuts allergy in three and kiwi allergy in one).

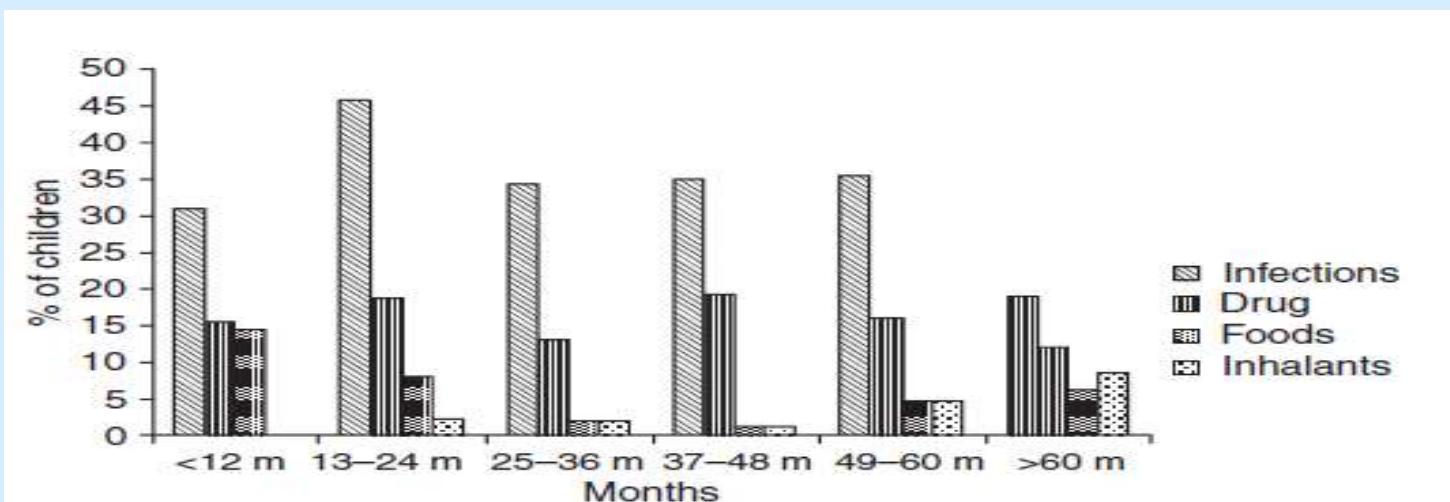
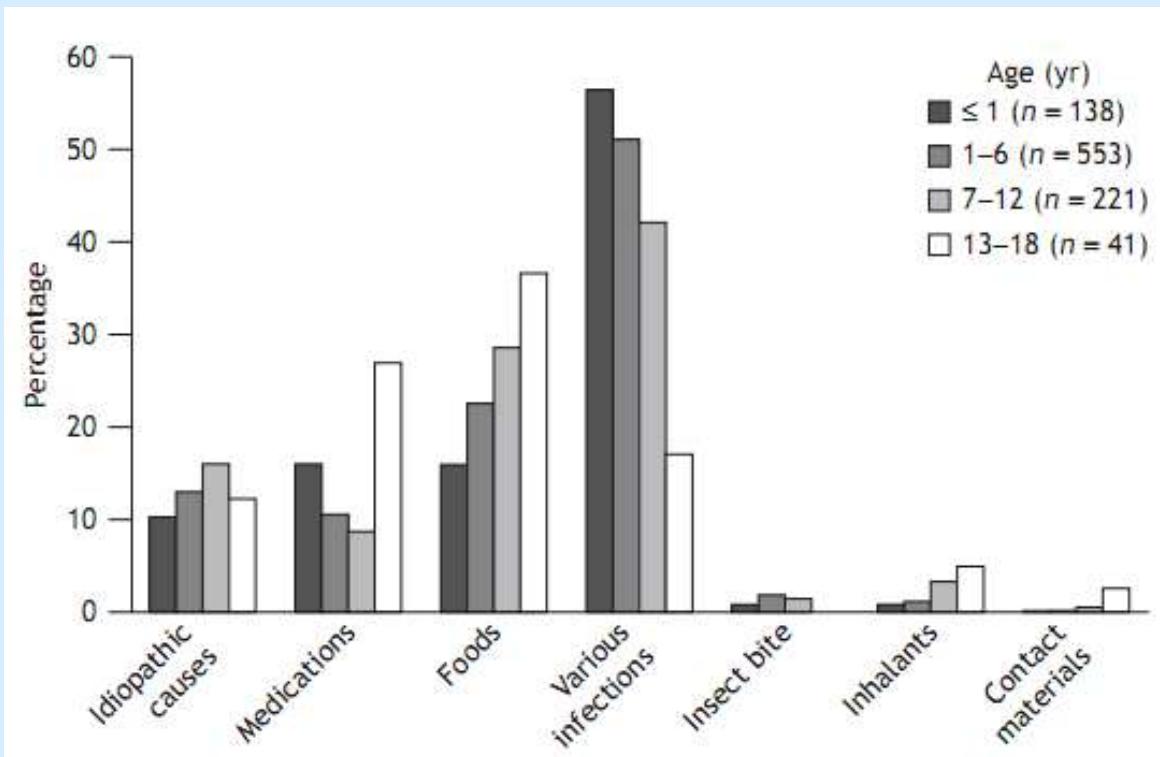


Figure 2 Possible factors related to acute urticaria in 814 children referred to the paediatric emergency room.

First Attack of Acute Urticaria in Pediatric Emergency Department

Studio retrospettivo, 953 bb in ED (Taiwan)



Infezioni:
rinofaringiti

Alimenti:
gamberi

Farmaci:
FANS (ibuprofene)

Acute urticaria in infancy and early childhood: a prospective study

- 57 bb (1-36 m) ospedalizzati, affetti da orticaria acuta
- Le infezioni, da sole o associate a farmaci, in causa nello 81% dei casi, gli alimenti nell'11%
- Storia di atopia, personale o familiare, nel 58%

Round table: urticaria in relation to infections

- 44 bb (1-12 a) affetti da orticaria acuta associata a malattia febbrale
- **Isolati virus** (*adenovirus; enterovirus; RSV; virus parainfluenzali 1, 2 e 3; influenza A e B; CMV; parvovirus B19; herpesvirus; EBV*) e **batteri** (*mycoplasma*)

Pediatr Dermatol, 2004 Mar-Apr;21(2):102-8.

The etiology of different forms of urticaria in childhood.

Sackesen C¹, Sekerel BE, Orhan F, Kocabas CN, Tuncer A, Adalioğlu G.

54 bb, 68,5% Urticaria Acuta, 48,6% si documentava una infezione

- Infezioni vie urinarie asintomatiche (E. coli)
 - Infezioni croniche, latenti o ricorrenti da Chlamidia pneumoniae
 - Streptococco beta-emolitico gruppo A
 - Helicobacter pylori
 - Meno frequente: cytomegalovirus, Epstein-Barr
 - Epatite raramente
 - Infezioni + farmaci
-
- **Indicati esame urine con urinocoltura e tampone faringeo**

ORTICARIA ACUTA

Unless allergen strongly suggested by history

Come, quando, quante volte, in che circostanze, rapporto con alimenti, punture di insetto, farmaci, altro



ORTICARIA ALLERGICA

- Quando possiamo, ragionevolmente sospettare che l'orticaria sia dovuta ad una allergia IgE-mediata?

3 REGOLE DI MASSIMA:
**SUBITO
SEMPRE
ALLERGENI NASCOSTI**



ORTICARIA ALLERGICA

SUBITO

**Compare da pochi minuti
a massimo due ore**



ORTICARIA ALLERGICA DA ALIMENTI

Mario, di anni 10, è allergico alla frutta secca (noci, nocciole, arachidi ecc)

Mangia, in ristorante, un solo boccone di pasta con il “pesto” (è senza i genitori e non immagina che il pasto contenga noci)

Dopo circa mezz'ora, giunge in PS con questo risultato



ORTICARIA ALLERGICA

SEMPRE

ma con molte eccezioni



ORTICARIA ALLERGICA DA ALIMENTI

Eccezioni alla regola del “sempre” **TOLLERANZA PARZIALE**

Edoardo, di anni 8, ha sempre assunto arachidi, in piccole quantità senza alcun problema. Una sera, ad una festa in casa di amici, ne ha mangiato un intero pacchetto.
Dopo circa mezz'ora, il risultato era questo:



ORTICARIA ALLERGICA DA ALIMENTI

Eccezioni alla regola del “sempre”



Uno sforzo fisico che segua di due o tre ore l'ingestione di un alimento cui si è sensibilizzati può smascherare una allergia verso alimenti abitualmente consumati

ORTICARIA ALLERGICA

ALLERGENI NASCOSTI



Alimenti contaminati dal latte



Alimenti contaminati dal latte

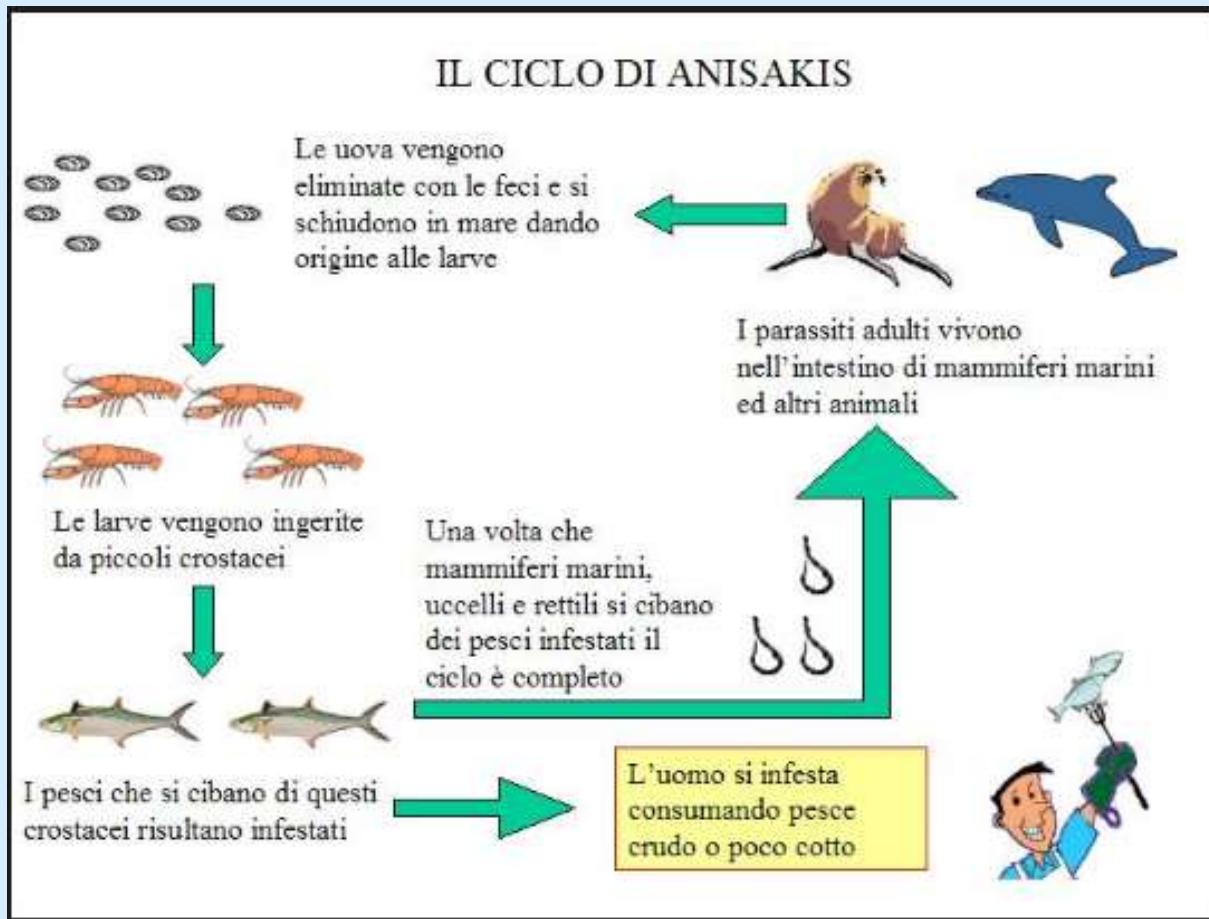


CLINICAL REPORT

Acute Allergic Reactions to *Anisakis simplex* After Ingestion of Anchovies

CATERINA FOTI¹, EUSTACHIO NETTIS², NICOLETTA CASSANO³, IRIS DI MUNDO¹ and GINO A. VENA¹

Department of Internal Medicine, Immunology and Infectious Diseases, ¹Unit of Dermatology and ³Unit of Allergology and Clinical Immunology, University of Bari, and ²Istituto Dermopatico dell'Immacolata, IDI, I.R.C.C.S., Rome, Italy



ORTICARIA ALLERGICA DA VELENO DI IMENOTTERI



ORTICARIA ALLERGICA DA VELENO DI IMENOTTERI



- Riconosce un meccanismo immunologico di tipo IgE-mediato
- Il quadro clinico varia dalla reazione locale estesa, all'orticaria-angioedema generalizzato fino alla anafilassi
- Di regola si verifica entro trenta minuti dalla puntura

ORTICARIA DA FARMACI

Tab. II. Classificazione di Gell & Coombs (da Pichler, 2003¹⁰, mod.).

Classificazione di Gell e Coombs adattata	Tipo di risposta immunitaria	Caratteristiche fisiopatologiche	Segni clinici	Intervallo normale di comparsa dei sintomi
Tipo I	Ig E	Attivazione di mastociti e basofili	Shock anafilattico, angioedema orticaria, broncospasmo	Da qualche minuto a 1 ora dall'ultima assunzione (necessaria una sensibilizzazione)
Tipo II	IgG e FcR	Citotossicità dipendente della FcR	Citopenia	Da 5 a 15 giorni
Tipo III	IgG o IgM e complemento o FcR	Deposito di immunocomplessi	Malattia sierica, orticaria, vasculite lupus-indotta	7-8 gg per la m.sierica 7-21 gg per le vasculiti
Tipo IV a	Th1 (IFN- γ)	Attivazione di monociti	Eczema	*5-21 giorni
Tipo IV b	Th2 (IL-4 e IL-5)	Infiammazione eosinofilica	Esantema maculo-papuloso e boloso	*2-6 settimane per le sindromi di ipersensibilità (DRESS)
Tipo IV c	Linfociti T citotossici (perforine, granzima B, FasL)	Lisi dei cheratinociti mediata dai linfociti T CD4- o CD8-	Esantema maculo-papuloso e boloso e pustoloso	*Meno di 2 gg per l'EPF 7-21 gg per le sindromi di Stevens-Johnson e di Lyell
Tipo IV d	Linfociti T (IL-8/ CXCL8)	Reclutamento e attivazione dei neutrofili	Pustolosi esantematica acuta generalizzata (PEAG)	*Meno di 2 giorni

ORTICARIA DA FARMACI

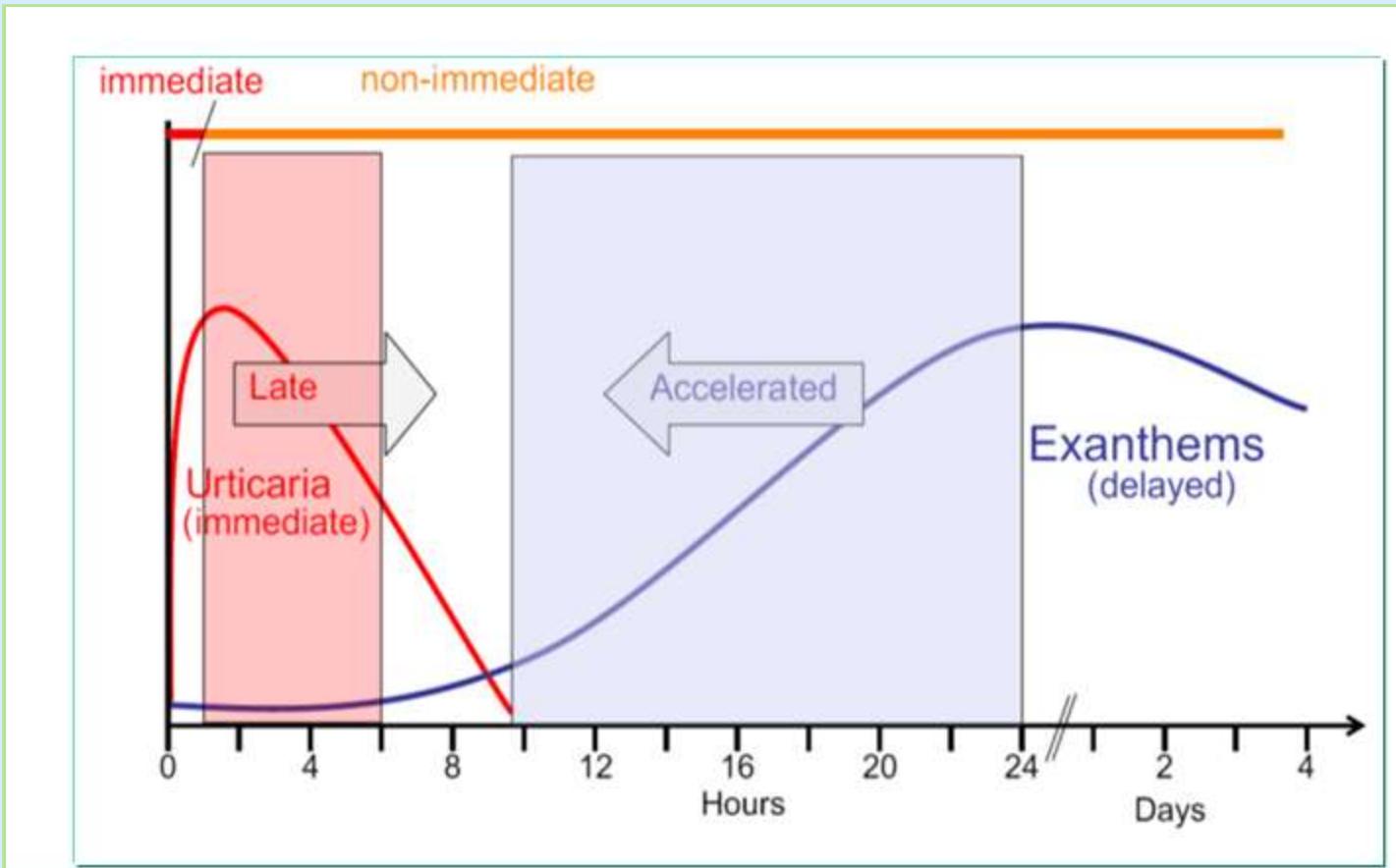
Farmaci responsabili di Reazioni IgE-mediate:

- Antibiotici, soprattutto Beta-lattamici
- ACE-inibitori
- ACTH
- Furosemide
- Insulina
- miorilassanti.

I quadri clinici compaiono entro pochi minuti, un'ora massimo dalla somministrazione del farmaco e vanno dall'orticaria generalizzata fino alla anafilassi

CLASSIFICAZIONE IN BASE AL TEMPO DI COMPARSA DEI SINTOMI

- Immediate < 1 ora
- Non immediate > 1 ora



REAZIONI IMMEDIATE

Le reazioni immediate possono essere IgE
mediate o determinate dall'azione diretta
del farmaco sui mastociti.

REAZIONI IgE-MEDIATE

Nel caso di reazioni IgE-mediated è richiesto un periodo di sensibilizzazione e, pertanto, tali reazioni non si verificano alla prima dose a meno che non vi sia stata una precedente sensibilizzazione

REAZIONI IgE-MEDIATE

Non sempre è comunque agevole identificare con certezza quando è avvenuta la assunzione della prima dose: la sensibilizzazione a penicilline, infatti, può avvenire molto precocemente, perfino in epoca neonatale (ad esempio tramite il latte materno) e a volte si verifica in forma occulta, ad esempio per ingestione di alimenti contenenti tracce di BL, come carni o surgelati.

REAZIONI IMMEDIATE non IgE-MEDIATE

Sono determinate dall'azione diretta del farmaco sui mastociti e, pertanto, possono insorgere anche all'assunzione della prima dose

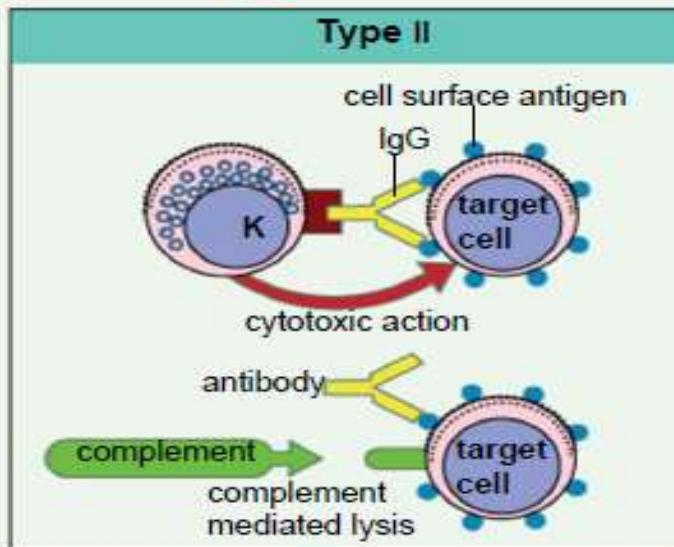
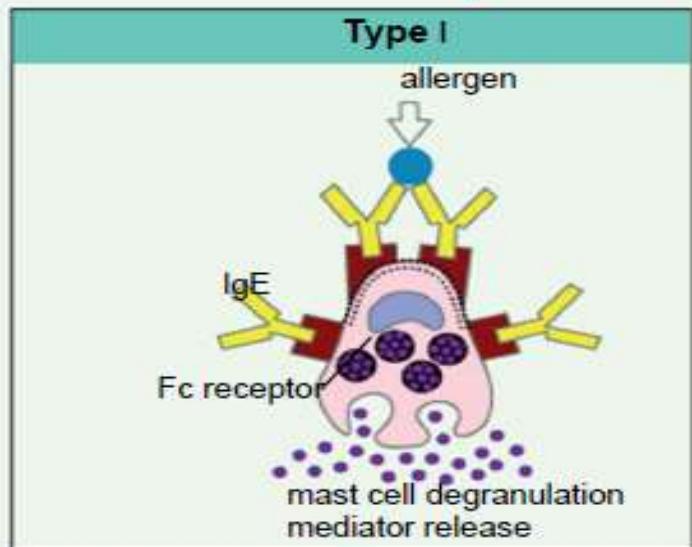
REAZIONI IMMEDIATE: QUADRI CLINICI

Classificazione di Gell e Coombs adattata	Tipo di risposta immunitaria	Caratteristiche fisiopatologiche	Segni clinici	Intervallo normale di comparsa dei sintomi
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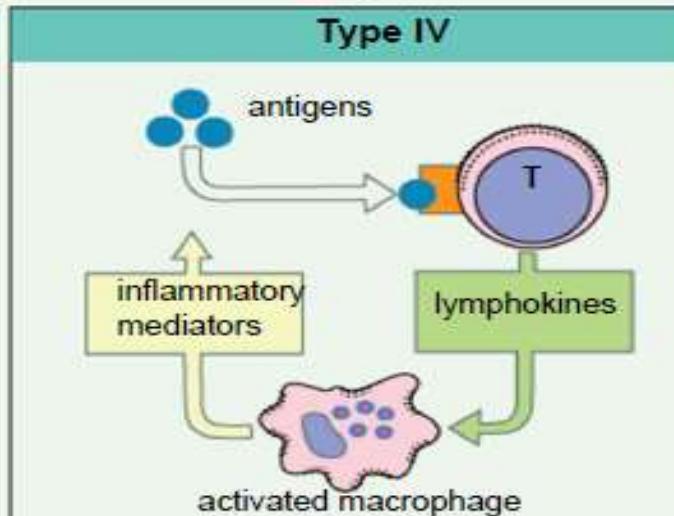
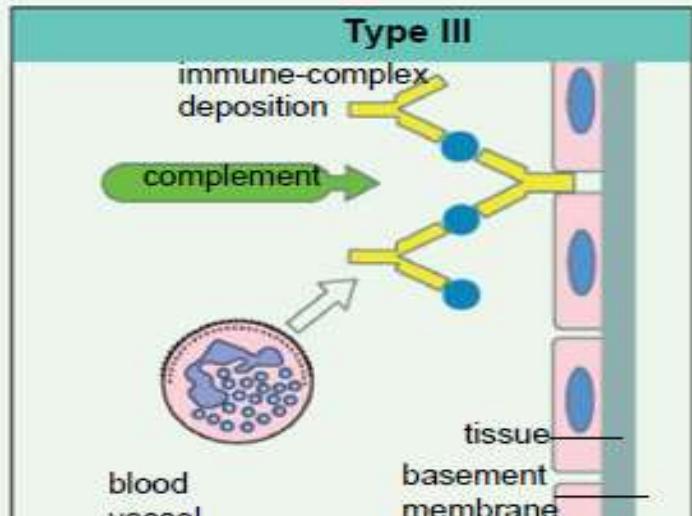


REAZIONI DI IPERSENSIBILITÀ AI FANS

1) Immunologic reactions



IV a	IV b
IFN γ , TNF α (TH ₁ cells)	IL-5, IL-4/IL13 (TH ₂ cells)
Maculo papular exanthema	DRESS



IV c	IV d
Perforin/ Granzyme B (CD8)	CXCL-8 GM-CSF (T cells- PMN)
S. Steven J TEN	AGEP

ORTICARIA DA FARMACI

PEDIATRIC ANNALS 39:10 | OCTOBER 2010

URTICARIAL DRUG ERUPTIONS

- solitary or multiple lesions
- size from a few millimeters to several centimeters
 - from small, pink macules and papules to large, red edematous wheals.
 - annular, pseudoannular (partial rings), or polycyclic (resembling a group of conjoined rings).

The varied appearance of the skin lesions is classic for an urticarial drug eruption (differentiating it from the monomorphic appearance of target lesions seen with erythema multiforme).



ORTICARIA DA FARMACI

Acute Urticaria Induced by Oral Methylprednisolone

Eun Jung Jang, Hyun Jung Jin, Young Hee Nam, Joo Hee Kim, Young-Min Ye, Hae-Sim Park*

Case Report

Allergy Asthma Immunol Res. 2011 October;3(4):277-279.

<http://dx.doi.org/10.4168/aair.2011.3.4.277>

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Le reazioni di ipersensibilità agli antibiotici beta-lattamici

RIAP 2012

a cura della Commissione Farmaci Lattice della SIAIP

L'esatta prevalenza delle reazioni allergiche a BL non è conosciuta: quella che emerge dai dati anamnestici dei pazienti risulta alta (10-20% dei casi), mentre minore è la prevalenza dopo un corretto iter diagnostico (0,7-1% dei casi); la prevalenza dell'anafilassi varia dal 0,015% al 0,004%.

L'amoxicillina, per il suo largo uso, costituisce l'antibiotico più spesso implicato nelle reazioni allergiche a farmaci.

Le reazioni di ipersensibilità agli antibiotici beta-lattamici

RIAP 2012

a cura della Commissione Farmaci Latici della SIAIP

Le ragioni di tali discrepanze sono attribuibili a diverse cause:

1) Mancanza della dimostrazione di allergia IgE e non IgE-mediata: molti bambini che presentano reazioni in seguito alla assunzione di farmaci vengono spesso identificati come allergici senza eseguire un adeguato “workup” allergologico.

Le reazioni di ipersensibilità agli antibiotici beta-lattamici

RIAP 2012

a cura della Commissione Farmaci Latice della SIAIP

Le ragioni di tali discrepanze sono attribuibili a diverse cause:

2) Errore diagnostico: molte manifestazioni cutanee che insorgono in corso di infezioni virali o batteriche (esempio rash cutanei, orticarie, esantemi) causate dall'agente eziologico possono facilmente essere confuse con reazioni allergiche a farmaci.

Tale errore è particolarmente frequente nei bambini, dove più spesso insorgono eruzioni cutanee in corso di infezioni.

Le reazioni di ipersensibilità agli antibiotici beta-lattamici

RIAP 2012

a cura della Commissione Farmaci Latice della SIAIP

Le ragioni di tali discrepanze sono attribuibili a diverse cause:

3) Perdita della sensibilizzazione allergica nel tempo: la risposta IgE ai BL è un fenomeno limitato nel tempo, in quanto dopo un iniziale “plateau” la produzione delle IgE specifiche decresce.

Tale fenomeno
si correla alla alta probabilità di negativizzazione
dei test allergologici qualora questi vengano eseguiti
dopo più di 6 mesi dalla reazione

Le reazioni di ipersensibilità agli antibiotici beta-lattamici

RIAP 2012

a cura della Commissione Farmaci Latice della SIAIP

Le ragioni di tali discrepanze sono attribuibili a diverse cause:

4) Interazione tra antibiotico e alcune malattie virali: ad es. infezione da virus di Epstein Barr ed aminopenicilline o infezione da HIV e cotrimossazolo (la frequenza degli esantemi maculopapulosi è 10-50 volte maggiore di quella presente nella popolazione generale)

Appare verosimile che il meccanismo immunologico che attiva la reazione cutanea al farmaco sia favorito dalla stessa infezione virale.



Fig. 1. Reazione cutanea in paziente affetto da mononucleosi infettiva in erronea terapia con amoxicillina + acido clavulanico.

Urticaria: “You’re Probably Just Allergic to Something”

Jordan Smallwood, MD

Pediatr Ann. 2016

Urticaria is a common symptom seen in pediatric patients, and it has multiple allergic and nonallergic causes. Unfortunately, it is far too common that when children present acutely for urticaria, they are told that it is an “allergy.” This statement often leads to increased anxiety while the patient waits to be evaluated by an allergist/immunologist.

Urticaria: “You’re Probably Just Allergic to Something”

Jordan Smallwood, MD

Pediatr. Ann 2016

Acute Urticaria

Acute urticaria will affect almost 20% of the population at some point in their life (Sabroe 2014). In a retrospective study performed by Liu et al. (2008), infections were the cause of acute urticaria in infants in more than 50% of cases. This prevalence decreased as patient age increased, with infection representing 42.1% and 17.1% of cases in school-aged children and adolescents, respectively.

Urticaria: “You’re Probably Just Allergic to Something”

Jordan Smallwood, MD

Pediatr. Ann 2016

Acute Urticaria

The infectious symptoms do not have to be concomitant with the appearance of the rash. In my clinic, patients have developed hives up to a few weeks after the appearance of infectious symptoms, most commonly an upper respiratory infection.

The remaining 50% of cases of acute urticaria are deemed idiopathic.

The diagnosis and management of acute and chronic urticaria: 2014 update

JACI

CLINICAL PRACTICE GUIDELINE

Although many cases of acute urticaria are caused by viral or other infectious illnesses, extensive evaluation for specific viral pathogens or antiviral therapy is not indicated unless suggested by the clinical history (AAAAI)

Orticaria acuta post-infettiva

MARIA PAOLA PILIA**, ROSANNA MENEGHETTI*, GIORGIO LONGO*

*UO di Allergologia, IRCCS "Burlo Garofolo", Trieste

**Dipartimento di Pediatria, Clinica Maciotta, Cagliari



Figura 1. Tipiche lesioni annulari alla coscia.



Figura 2. Lesioni confluenti policicliche (geografiche) agli arti e al tronco.

Spesso segue o accompagna infezioni comuni per lo più virali

Lesioni pomfoidi ,con scarso prurito, a insorgenza rapida, policliche/anulari

Pochi giorni o settimane, talora recidivanti con buona risposta all'antistaminico

La mancata diagnosi porta al sospetto di allergia a antipiretici o antibiotici

Orticaria acuta post-infettiva

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**Dipartimento di Pediatria, Clinica Maciotta, Cagliari

MECCANISMO PATOGENETICO

Degranulazione aspecifica dei mastociti durante una risposta
immune innata ?

Attivazione diretta del complemento con rilascio di C5a ?

Immuno-compleSSI antigene-anticorpo che attivano la via
classica del complemento ?

PEDIATRICS®

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"Urticaria Multiforme": A Case Series and Review of Acute Annular Urticular Hypersensitivity Syndromes in Children

Kara N. Shah, Paul J. Honig and Albert C. Yan

Pediatrics 2007;119:e1177-e1183

DOI: 10.1542/peds.2006-1553

This information is current as of May 3, 2007



A. Transient polycyclic and annular wheals.

B. Urticular lesions may sometimes appear dusky, resembling erythema multiforme, but there are no true target lesions and no blistering or necrosis.



"Urticaria Multiforme": A Case Series and Review of Acute Annular Urticular Hypersensitivity Syndromes in Children
Kara N. Shah, Paul J. Honig and Albert C. Yan
Pediatrics 2007;119:e1177-e1183
DOI: 10.1542/peds.2006-1553

- Acute urticaria related to infections is a benign manifestation in children, especially in infancy and early childhood.
- It typically happens at the same time or at the end of, or after, a viral infection.
- The eruption is self-limited, and episodes usually resolve within some days or few weeks;
- The presence of annular, polycyclic or geographic wheals are characteristic, and acral and facial angioedema and dermatographism are frequently observed.**



IMAGES IN CLINICAL MEDICINE. Urticaria Multiforme.

Kotlyar S¹.



- 3-year-old girl
- no history of exposure to medications or allergens
- a viral respiratory illness that had occurred 1 week earlier, with fever (38.8°C)

Association between urticaria and virus infections: A systematic review

Egidio Imbalzano, M.D.,¹ Marco Casciaro, M.D.,² Sebastiano Quartuccio, M.D.,¹ Paola L. Minciullo, M.D., Ph.D.,² Antonio Cascio, M.D., Ph.D.,³ Gioacchino Calapai, M.D.,^{1,4} and Sebastiano Gangemi, M.D., Ph.D.²

Allergy Asthma Proc 37:18 –22, 2016

- *Systematic review*
- *We searched for articles from January 1, 2008, through May 2015*
- *We reported cases of patients affected either by acute or chronic urticaria with a concurrent virus infection.*
- *Previous other causes of urticaria had to be excluded*
- *Due to the lack of case reports on this association, and to facilitate the finding of a possible etiologic agent by the reader, we decided to group the cases by virus family.*

Herpesviridae

Herpesvirus-Associated Acute Urticaria: An Age Matched Case-Control Study

Arianna Mareri¹, Stuart P. Adler², Giovanni Nigro^{1*}

- Mareri A et al. *tried* to find an association between herpesvirus infections and urticaria by analyzing the cases of 37 children affected by urticaria and by evaluating 37 healthy children.
- By performing a set of laboratory tests, they proved that the start of AU was associated with a herpesvirus infection.

Herpesvirus-Associated Acute Urticaria: An Age Matched Case-Control Study

Arianna Mareri¹, Stuart P. Adler², Giovanni Nigro^{1*}

Herpesviridae

- **RESULTS:** Specific infections were diagnosed in 26 of 37 cases and among 9 of 37 control children ($P=0.0002$). Single or concomitant herpesvirus infections occurred in 24 cases and in 4 controls (65% vs 11 %, $p=0.0003$). Cases had 10 HHV-6 infections, 8 CMV infections, 5 EBV infections, and 4 HSV-1 infections.
- **CONCLUSION:** Herpesvirus infections are associated with acute or recurrent acute urticaria.

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- Parvoviridae (Parvovirus B19)---→ descritto un caso di orticaria-angioedema in una donna di 47 anni (Soldo-Juresa 2010)
- Caliciviridae (Norovirus) --→ due casi in adulti (Leiste et al. 2008)
- Picornaviridae (Hepatitis A virus) --→ un caso in un'adulta (Griffin et al. 2012)
- Flaviviridae (hepatitis C virus) ---→ tre casi in adulti (Chiba et al. 2014, Pinto-Almeida et al. 2013, Foschi et al. 2010)
- Hepadnaviridae (hepatitis B virus) --→ un caso in adulta (Van Aalsburg et al. 2011)

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Multiple mechanisms were hypothesized as being involved in triggering urticaria. Sometimes more than one mechanism combined in augmenting vascular permeability:

- Cross reaction between viral IgM ed IgG with mast cell IgE → mast cell degranulation
- Circulating immune complexes, which stimulated basophils in producing vasoactive amines and activating complement → increasing vascular permeability
- Hyperbilirubinemia increases vascular permeability and, therefore, be a causal factor for urticaria
- A protein, largely secreted in the intestinal tract during hepatitis viral infections, induced the release of proinflammatory mediators (superantigen theory). This mediator secretion resulted in an augmentation of vascular permeability.

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Allergy Asthma Proc 37:18 –22, 2016

CONCLUSIONS

- Data obtained seemed to indicate viral infections as potential triggers and sometimes as a main etiologic agent in causing AU and CU.
- Because herpesvirus is the most common probable etiopathologic agent, researchers should focus on identifying the most frequently associated symptoms during history collection

Urticaria and bacterial infections

Paola L. Minciullo, M.D., Ph.D.,¹ Antonio Cascio, M.D., Ph.D.,² Giuseppina Barberi, Ph.D.,² and Sebastiano Gangemi, M.D., Ph.D.^{1,3}

(Allergy Asthma Proc 35:295–302, 2014)

Table 2 Reported association between urticaria and bacterial infections

Bacterium	Type of Urticaria	Population	Urticaria/ Infection Association (rate)	Urticaria Remission/ Improvement after Infection Eradication (rate)	Rate of Urticaria Remission in Untreated Patients	First Author	Type of hymenoptera (no. of studies involved)	Reference No.
<i>Helicobacter pylori</i>	CU	Adults and children	Rate not stated	30.9%	21.7%	Federman DG	Review (10)	6
	CU	Adults	Rate not stated	84%	45%	Wedi B	Review (13)	4
	CU	Adults	Rate not stated	25%	27%	Wedi B	Review (9)	4
	Chronic spontaneous urticaria	Adults	Rate not stated	63.6%	Not stated	Chiu YC	Study	7
	Antihistamine-resistant CU	Adults	63%	28%	0%	Magen E	Retrospective study	8
<i>Streptococcus</i>	CU	Adults	30.5%	20% remission; 33% improvement	Not stated	Akashi R	Study	9
	CU/recurrent angioedema	Adults	68%	20%	10%	Kolacinska-Flont M	Study	10
	AU	Children	40.6%	100%	NA	Schuller DE	Study	13
	Acute recurrent urticaria/acute angioedema/CU	Adults	71.4%	71.42%	28.57	Calado G	Retrospective study	16
	Recurrent urticaria	Adult	Yes	Yes	NA	Edward A	Case report	17
<i>Staphylococcus</i>	AU	Adult	Yes	Yes	NA	Nousari HC	Case report	18
	Recurrent urticaria	Adults	88.8%	75% remission; 25% improvement	Not stated	Bonanni L	Study	20
	CU	Adults and children	53.2%	Not stated	Not stated	Ertam I	Study	21
<i>Mycoplasma pneumoniae</i>	CU	Adults	56.14%	28.12% remission; 12.5 improvement	Not stated	Sharma AD	Clinic-based study	22
	Antihistamine-resistant AU	Children	32%	100%	NA	Wu CC	Study	26
	AU	Child	Yes	Yes with antihistamine therapy	NA	Kano Y	Case report	28
<i>Salmonella</i>	Urticaria vasculitis	Adult	Yes	Yes with ibuprofen therapy	NA	Dua J	Case report	29
	Urticaria vasculitis	Adult	Yes	100%	NA	Jover F	Case report	30
	Non-episodic angioedema with eosinophilia	Adult	Yes	Partial	NA	Stockner I	Case report	32
	Recurrent urticaria	Adult	Yes	Yes	NA	Tachdjian R	Case report	34
	Urticaria	Child	Yes	Not stated	NA	Mittal S	Case report	35
<i>Brucella</i>	Urticaria-like papules and plaques	Adults and children	35.3%*	Not stated	Not stated	Metin A	Study	37
	Urticaria-like erythematous plaques	Adult	Yes	Yes	NA	Song Z	Case report	42
<i>Mycobacterium leprae</i>	Erythematous papules and plaques#	Adult	Yes	NA	NA	Booth AV	Case report	43
	Erythematous plaques#	Adult	Yes	NA	NA	Stafford SJ	Case report	44
	Multiple urticaria-like wheals#	Adult	Yes	NA	NA	Barman KD	Case report	45
<i>Borrelia</i>	CU	Not stated\$	33.3%	Not stated\$	Not stated\$	Svecova D	Study	48
	Urticaria-like	Children	25%	Not stated\$	Not stated\$	Passos SD	Cross-sectional study	49
sion.htm	Urticular vasculitis	Child	Yes	Not stated	NA	Olson JC	Case report	50
		Not stated\$	Yes	Yes	NA	Merkle T	Case report	51

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(Allergy Asthma Proc 35:295–302, 2014)

Table 2 Continued

Bacterium	Type of Urticaria	Population	Urticaria/ Infection Association (rate)	Urticaria Remission/ Improvement after Infection Eradication (rate)	Rate of Urticaria Remission in Untreated Patients	First Author	Type of hymenoptera (no. of studies involved)	Reference No.
<i>Chlamydia pneumoniae</i>	Acute and CU	Children	9.25%	Not stated	Not stated	Sackesen C	Prospective study	15
	Antihistamine- and corticosteroid-resistant angioedema	Child	Yes	Yes	NA	Uysal P	Case report	52
<i>Yersinia enterocolitica</i>	CU	Adults	4.65%	Not stated	Not stated	Wedi B	Study	53
	CU	Not stated	53.5%	Not stated	Not stated	Hellmig S	Controlled study	54



Urticaria and bacterial infections

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Many bacterial infections have been associated with urticaria manifestation, the pathogenesis remains generally unexplained.

In some cases the skin manifestations, described as urticaria, could be caused by the presence of the microorganism in the skin (*B. burgdorferi*, and *Mycobacterium leprae*), or for the action of their toxins (*Streptococcus* spp and *Staphylococcus* spp) or to the complement activation mediated by circulating immune complexes (*Streptococcus* spp).

Urticaria and bacterial infections

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and Sebastiano Gangemi, M.D., Ph.D.^{1,3}

CONCLUSIONS

Although only a weak association with urticaria of unclear pathogenesis exists, clinicians should consider these bacterial agents in the workup of the patients with urticaria.

The eradication of the infection could, in fact, lead to the resolution of urticaria.

Prospective studies and well-structured research are obviously needed to better clarify the real role of bacteria in the pathogenesis of urticaria and their relative prevalence

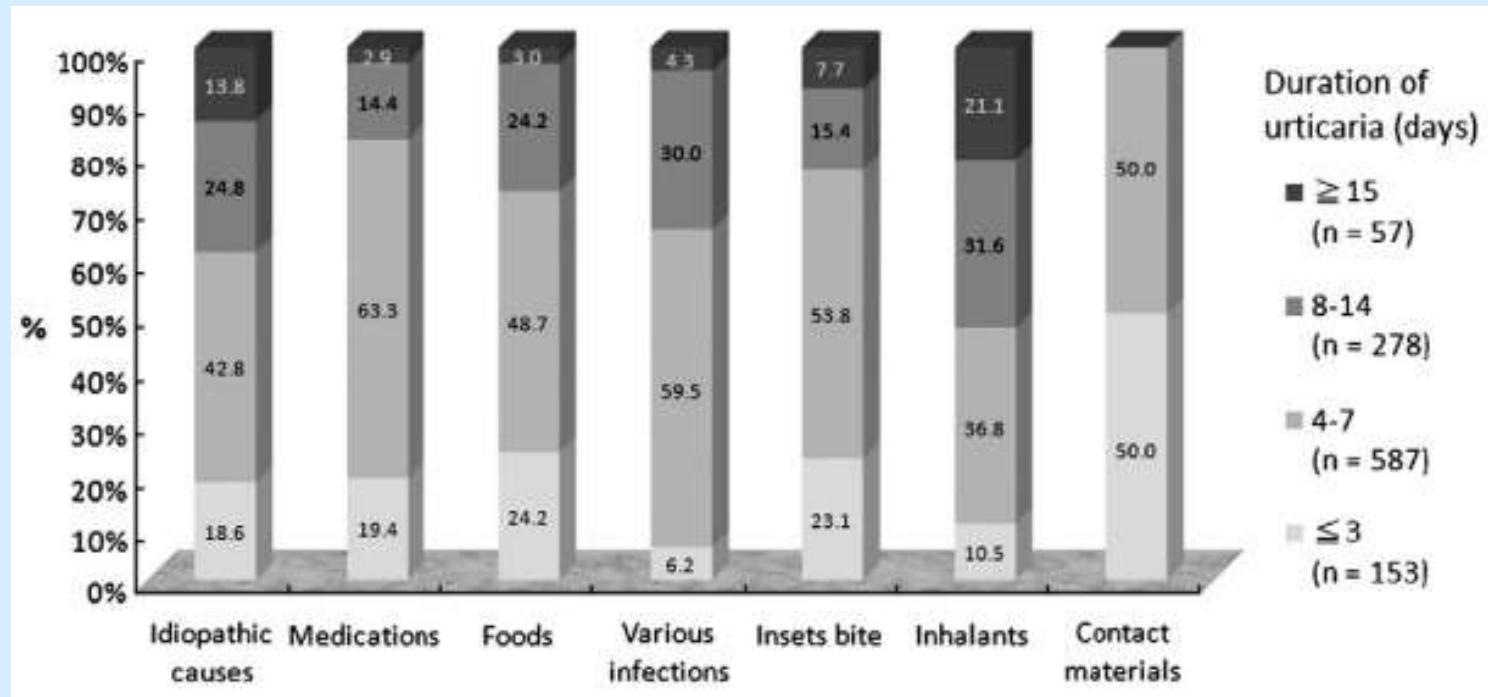
Predictive factors of the duration of a first-attack acute urticaria in children

- 1075 bb (≤ 18 aa) giunti al ED per primo attacco di orticaria
- Suddivisi in 4 gruppi:
 - ✓ 3 giorni o meno
 - ✓ 4-7 giorni
 - ✓ 8-14 giorni
 - ✓ 15 o più giorni
- Analisi delle caratteristiche cliniche e della storia personale e familiare

	First-attack acute urticaria of children (n = 1075)	
	No.	%
Sex		
Male	626	58.2
Female	449	41.8
Age, mean \pm SD, y	5.7 \pm 4.4	
Infant	174	16.2
Preschool age	570	53
School age	245	22.8
Adolescent	86	8
Personal allergic diseases		
Asthma history	98	9.1
Allergic rhinitis history	256	23.8
Atopic dermatitis history	47	4.4
Etiology of urticaria		
Medications	127	11.8
Foods	258	24
Various infections	486	45.2
Inhalants	22	2
Insects bite	16	1.5
Contact materials	2	0.2
Idiopathic causes	164	15.3

Lin Yan-Ren et al. American Journal of Emergency Medicine (2011) 29, 883–889

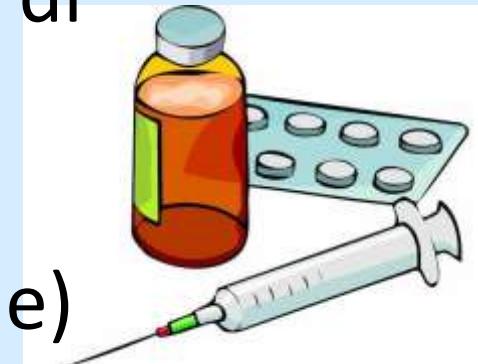
Predictive factors of the duration of a first-attack acute urticaria in children



1. Inalanti (8.7 ± 4.6 gg)
2. Cause idiopatiche (8.1 ± 5.7 gg)
3. Infezioni (7.0 ± 2.9 gg)
4. Punture d'insetto (6.6 ± 5.4 gg)
5. Alimenti (6.2 ± 4.4 gg)
6. Farmaci (5.5 ± 3.6 gg)
7. Da contatto (3.7 ± 0.9)

Predictive factors of the duration of a first-attack acute urticaria in children

- ✓ Urticaria + angioedema dura meno di urticaria da sola
- ✓ Urticaria senza febbre dura meno di urticaria con febbre
- ✓ Minor durata se trattamento associato (antistaminici + cortisone) in confronto al trattamento con solo antistaminico o solo steroide



REVIEW ARTICLE

Management of Childhood Urticaria: Current Knowledge and Practical Recommendations

TREATMENT

- Antihistamines are used to inhibit the effect of mast cell and basophil mediators on the target tissue and to induce symptom relief.
- The use of second-generation H1-antihistamines (2ndGAH) at a standard dose in spontaneous and cold urticaria is the only therapeutic option with a strong recommendation from current guidelines.

BSACI guideline for the management of chronic urticaria and angioedema

R. J. Powell¹, S. C. Leech², S. Till³, P. A. J. Huber⁴, S. M. Nasser⁵ and A. T. Clark⁶

¹Department of Clinical Immunology and Allergy, Nottingham University, Nottingham, UK, ²Department of Child Health, Kings College Hospital, London, UK,

³Division of Asthma, Allergy and Lung Biology, Kings College London, London, UK, ⁴BSACI, British Society for Allergy & Clinical Immunology, London, UK,

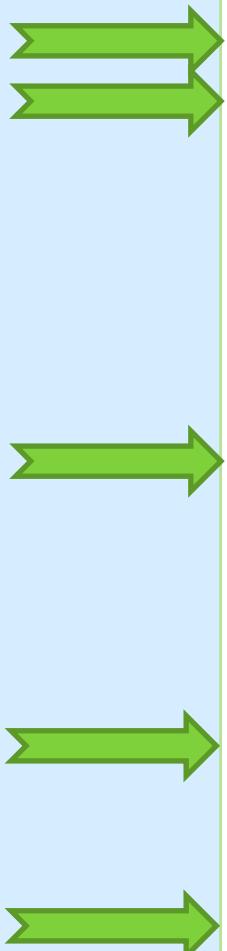
⁵Department of Allergy & Clinical Immunology, Addenbrooke's NHS Trust, Cambridge, UK and ⁶Department of Allergy, Addenbrookes NHS Trust, Cambridge, UK

DEFINIZIONE

Chronic urticaria/angioedema has traditionally been defined as **weals, angioedema or both** with daily or almost daily symptoms lasting for **more than 6 weeks.**

In these guidelines, we have also included patients with episodic acute intermittent urticaria/angioedema lasting for hours or days and recurring over months or years.

Clinical classification of chronic urticaria/angioedema

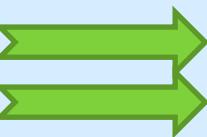


Description	Type	Examples of triggers
Spontaneous urticaria	Spontaneous	Stress, infection, drugs (e.g. NSAIDs)
Autoimmune urticaria	Autoimmune	None known
Inducible urticaria	Aquagenic Cholinergic Cold Delayed pressure Dermographism Exercise Heat Solar Vibratory	Contact with hot or cold water Exercise, emotion Swimming in cold water, cold wind Sitting, lying, tight clothing Minor trauma Physical exertion Hot bath/shower Sunshine Use of vibrating tools
Angioedema without weals	Spontaneous C1 inhibitor deficiency C1 inhibitor deficiency related to paraproteinaemia Drugs	Stress, infection, drugs (e.g. NSAIDs) Trauma, surgical procedures, stress, infection Trauma, surgical procedures, stress, infection ACE inhibitors, oestrogens, antipsychotic drugs, statins, NSAIDs
Vasculitis*	Urticular vasculitis	Infection, e.g. with hepatitis B/C or streptococcus; drugs, e.g. penicillins, allopurinol, quinolones or carbamazepine; autoimmune diseases; paraproteinaemia; malignancy
Rare syndromes*	Cryopyrin-associated periodic syndrome (CAPS) Schnitzler syndrome	Cold

*Vasculitis and rare syndromes are differential diagnoses of chronic urticaria and angioedema.

BSACI GUIDELINE 2015

Aetiological classification of chronic urticaria/angioedema



Aetiology	Mechanism	Examples	Investigations
Spontaneous (40–50% cases)	Unknown		Typically negative
Autoimmune	IgG auto-antibody to mast cell IgE receptor or to IgE bound to mast cells	Associated with autoimmune thyroiditis	ANA, thyroid auto-antibodies
Physical stimuli	Direct mast cell mediator release	Exercise, heat, cold, pressure, aquagenic, solar, delayed pressure, vibration, dermographism	Challenge testing with appropriate stimuli, e.g. ice cube, exercise. Cryoglobulins
Drug induced	Reduced kinin metabolism; elevated leukotriene levels	ACE inhibitors (angioedema alone) NSAIDs	Response to avoidance (may be delayed for weeks or months)
Infection	Complement activation due to immune complex formation	Parasites, EBV, hepatitis B and C, viral exanthems	Serology directed by clinical history
Allergic	IgE-mediated allergic contact urticaria	Latex, animals, grass, food	Skin tests, specific IgE to allergen
C1 inhibitor deficiency			
Genetic (i)	Enhanced kinin production	HAE Types I and II	C4, C1 inhibitor
Genetic (ii)	Activation of complement, fibrinolysis and coagulation systems	HAE Type III	C4, C1 inhibitor, Factor XII studies may be useful
Acquired	Binding of C1 inhibitor by paraprotein	Associated with paraproteinaemia	C4, C1 inhibitor, Paraprotein in both blood & urine
Non-IgE-mediated mast cell degranulation	Non-receptor-mediated	Opiates, Adrenocorticotrophic Hormones (ACTH)	Response to avoidance
Vasculitis	Small vessel vasculitis, deposition of immunoglobulin and complement	Urticarial vasculitis	FBC, ESR, renal function, urinalysis, LFT, ASOT, hepatitis B and C serology, immunoglobulin electrophoresis, autoimmune screen including ANA, ANCA, C3, skin biopsy
Food constituent (rare)	Unknown	Salicylates/benzoates	Response to exclusion and subsequent reintroduction

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Drug induced	Reduced kinin metabolism; elevated leukotriene levels	ACE inhibitors (angioedema alone) NSAIDs	Response to avoidance (may be delayed for weeks or months)
Infection	Complement activation due to immunocomplex formation	Parasites, EBV, hepatitis B and C, viral exanthems	Serology directed by clinical history
Allergic	IgE-mediated allergic contact urticaria	Latex, animals, grass, food	Skin tests, specific IgE to allergen
C1 inhibitor deficiency			
Genetic (i)	Enhanced kinin production	HAE Types I and II	C4, C1 inhibitor
Genetic (ii)	Activation of complement, fibrinolysis and coagulation systems	HAE Type III	C4, C1 inhibitor, Factor XII studies may be useful
Acquired	Binding of C1 inhibitor by paraprotein	Associated with paraproteinaemia	C4, C1 inhibitor, Paraprotein in both blood & urine
Non-IgE-mediated mast cell degranulation	Non-receptor-mediated	Opiates, Adrenocorticotrophic Hormones (ACTH)	Response to avoidance
Vasculitis	Small vessel vasculitis, deposition of immunoglobulin and complement	Urticular vasculitis	FBC, ESR, renal function, urinalysis, LFT, ASOT, hepatitis B and C serology, immunoglobulin electrophoresis, autoimmune screen including ANA, ANCA, C3, skin biopsy
Food constituent (rare)	Unknown	Salicylates/benzoates	Response to exclusion and subsequent reintroduction

BSACI GUIDELINE 2015

Aetiological classification of chronic urticaria/angioedema

Aetiology	Mechanism	Examples	Investigations
Spontaneous (40–50% cases)	Unknown		Typically negative
Autoimmune	IgG auto-antibody to mast cell IgE receptor or to IgE bound to mast cells	Associated with autoimmune thyroiditis	ANA, thyroid auto-antibodies
Physical stimuli	Direct mast cell mediator release	Exercise, heat, cold, pressure, aquagenic, solar, delayed pressure, vibration, dermographism	Challenge testing with appropriate stimuli, e.g. ice cube, exercise. Cryoglobulins
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Food constituent (rare)	Unknown	Salicylates/benzoates	Response to exclusion and subsequent reintroduction

Chronic urticaria



L'allergia alimentare è
raramente
la causa di una
urticaria cronica



Revisione delle cause associate all'orticaria cronica in gruppi di bambini

A cura della Commissione
“Allergia a farmaci, latico ed
orticaria” della SIAIP

Rivista di Immunologia e Allergologia Pediatrica •04/2009

Cause associate all' orticaria negli studi selezionati.

Cause	Harris '83 ⁶	Kauppinen '84 ⁷	Volonakis '92 ⁸	Brunetti '04 ⁹	Sackesen '04 ¹⁰	Du Toit '06 ¹¹
Idiopatica	79/94	19/55	171/226	27/93	8/17	-
Fisiche	8/10	16/55	14/226	25/93	9/17	-
Agglutinine a frigore	0/8	-	3/22	-	-	-
Infezioni	2/87	4/55	3/226	20/93	6/17	-
Parassiti	0/2	1/55	7/189	-	0/17	1/39
Allergie alimentari	2/48	5/55	9/21	5/93	2/17	0/80
Allergie inalanti	0/34	0/55	5/196		0/17	-
Additivi	-	12/55	6/23	-	0/17	-
Farmaci	-	0/55	4/226	-	3/17	-
Auto abtiroidei	0/5	-	-	0/93	0/17	-
T3,T4,TSH	0/5	-	0/16	0/93	-	-
Autoimmune						
Asst	-	-	-	22/49	-	18/44
Altri	-	-	-	21/52 (HR-test)	-	37/78 (FcεR1α)
RA	-	-	0/56	-	-	-
ANA	1/20	-	0/56	0/93	0/17	-
Ab anti-DNA	-	-	-	0/93	0/17	-
Complementemia	1/68	0/55	0/112	-	-	-

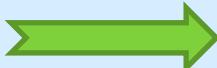
REVIEW ARTICLE

Aetiological Factors Associated with Chronic Urticaria in Children: A Systematic Review

Carlo CAFFARELLI¹, Barbara CUOMO², Fabio CARDINALE³, Salvatore BARBERI⁴, Carlotta POVESI DASCOLA¹, Fabio AGOSTINIS⁵, Fabrizio FRANCESCHINI⁶ and Roberto BERNARDINI⁷

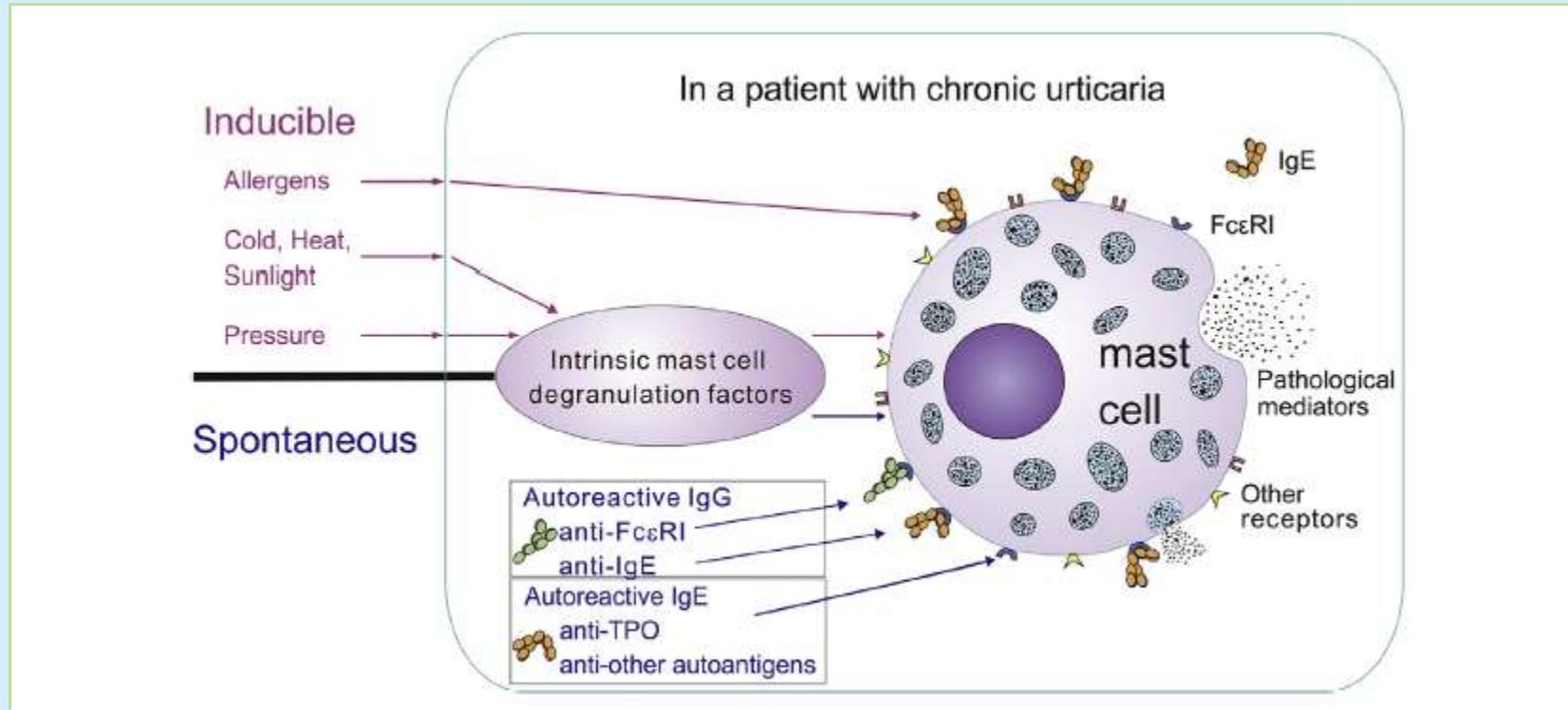
¹Clinica Pediatrica, Dipartimento di Medicina Clinica e Sperimentale, Università di Parma, Azienda Ospedaliera-Universitaria, Parma, ²UOC Pediatria, Ospedale di Viterbo, Viterbo, ³UOC Medicina Pediatrica e Pneumo-Allergoimmunologia, Azienda Ospedaliero-Universitaria "Policlinico-Giovanni XXIII", Bari, ⁴Ospedale S.Paolo, Clinica Pediatrica, Università di Milano, ⁵USC di Pediatria, OORR di Bergamo, Bergamo, ⁶U.O Pediatria, Ospedale G Salesi, Ancona, and ⁷UOC Pediatria, Nuovo Ospedale S.Giuseppe, Empoli, Italy

Table II. Diagnosis in children with chronic urticaria

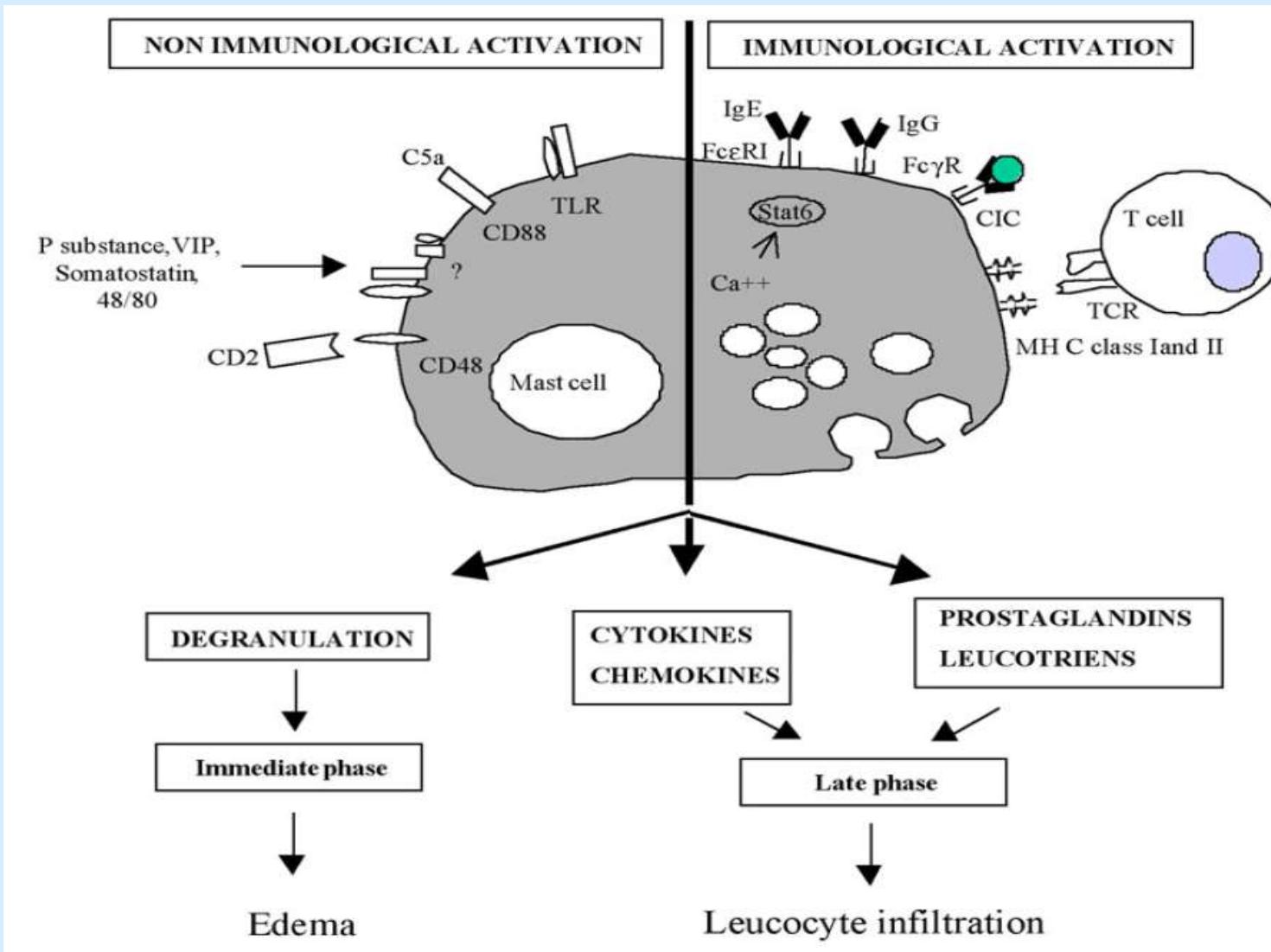


Diagnosis	n (%)
Idiopathic	316/565 (55.9)
Autoimmune (positive autologous serum skin test)	76/267 (28.4)
Physical triggers	59/391 (15)
Allergy/intolerance	52/565 (9)
Additives	18/95 (18.9)
Food allergy	22/565 (3.8)
Drugs	7/298 (2.3)
Inhalant allergy	5/268 (1.8)
Parasites	14/394 (3.5)
Infections	33/307 (1)
Thyroid disease	0/220
Collagen vascular disease	0/485

PATOGENESI



PATOGENESI



EPIDEMOIOLOGIA

- Mancano i dati sulla prevalenza dell'OC in età pediatrica
- Le linee guida BSACI stimano una prevalenza *lifetime* di 0,3-1% ma mancano i riferimenti bibliografici
- Per l'adulto uno studio cross-sectional condotto a Berlino su 13.300 abitanti stima in 8,8% la prevalenza dell'orticaria e in 1,8% quella dell'OC (*Zuberbier, Clin Exp Dermatol 2010*)

STORIA NATURALE

- Tendenza alla risoluzione spontanea
- Il 35% dei pazienti va incontro a remissione dopo 3 anni

Autoantibodies to the high-affinity IgE receptor in children with chronic urticaria (Du Toit et al, AAAI 2006;96:341)

- 80 bb con OC e 38 bb con AEDS
- CAP-RAST, dermografismo, ICE cube test, esame parassitologico, ASST, HR-Assay (IgG-FC ϵ RI- α)
- 47% bb con OC avevano Ab anti-FC ϵ RI vs 0% dei bb con AEDS
- Pochi avevano allergie (dieta inefficace)
- **Remissione nel 36% a 3 anni**

Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

Le conoscenze sull'eziopatogenesi della OC in pediatria sono limitate. Conseguentemente, una percentuale tra il 25 e l'85% dei casi a tutt'oggi rimane idiopatica

Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

Le cause fisiche sono tra i trigger più comuni nella OC e ricoprono da sole più del **25%** delle eziologie.

L'orticaria dermografica e quella colinergica rappresentano le forme più frequenti.

Physical urticaria

John P. Dice, MD

*Department of Allergy and Immunology, Wilford Hall Medical Center, Lackland Air Force Base,
2200 Bergquist Drive, Suite 1, San Antonio, TX 78236, USA*

- 20-25% dei casi di OC
- **Possibile coesistenza di 2 o più tipi di OF**
- Comparsa di pomfi pruriginosi immediatamente dopo applicazione di appropriato stimolo (eccetto o. da pressione ritardata) che persistono per pochi minuti o non più di 2 ore dopo rimozione dello stimolo (eccetto o. da pressione ritardata)
- Refrattarietà cutanea per poche ore → 1-2 giorni
- **Patogenesi non completamente chiarita (fattori sierici trasmissibili in alcune forme)**
- **Manifestazioni sistemiche rare (eccetto nell'O. colinergica e da freddo)**
- Trattamento: evitare i fattori trigger
antistaminici per profilassi
- Adrenalina auto-iniettabile nei pazienti a rischio

SYMPTOMATIC DERMOGRAPHISM

ORTICARIA FACTITIA

“dermographic tester”



CHOLINERGIC URTICARIA

Rara nei bambini piccoli, la più alta frequenza si ha negli adolescenti e giovani adulti. E' indotta dall'aumento della temperatura corporea legata ad esercizio fisico, sudorazione, stress emotivi, ingestione di cibi caldi ed iperpiressia.

Il quadro clinico è caratterizzato da piccoli pomfi, molto pruriginosi, circondati da eritema diffuso, ad insorgenza immediata e di breve durata.

Si può riprodurre con:

- Test da sforzo
- Immersione degli arti superiori in acqua a 45° per 15-20 minuti



COLD INDUCED URTICARIA

Si distinguono:

- Una forma familiare (autosomica dominante)
- Una forma acquisita, idiopatica o secondaria ad infezioni, criopatie ecc, talora associata ad angioedema o a sintomi sistemici



COLD INDUCED URTICARIA

- Si diagnostica con il “**Test del cubetto di ghiaccio**” mantenuto sulla faccia flessoria dell'avambraccio, per 10-20 minuti (si sviluppa un pomfo pruriginoso che mima la forma e le dimensioni del cubetto)



PRESSURE URTICARIA

Piuttosto rara nel bambino, insorge dopo circa 2-24 ore dalla applicazione di uno stimolo pressorio più o meno intenso

E' caratterizzata da manifestazioni eritemato-edematose, con aspetto a "peau d'orange", precedute da prurito, dolore, bruciore o sensazione puntoria

Si diagnostica applicando un peso di 2-10 Kg su un'area cutanea di 2-3 cm² (coscia o regione scapolare) per 10-30 minuti.



SOLAR URTICARIA

E' una FOTODERMATOSI IDIOPATICA, piuttosto rara, clinicamente caratterizzata dalla comparsa di una eruzione pomfoide immediata e di breve durata dopo esposizione al sole o a sorgenti artificiali (lunghezza d'onda compresa tra i 290 ed i 700 nm)



Si diagnostica mediante **Fototest** con diverse lunghezza d'onda irradiando aree cutanee, in genere del dorso, del diametro di circa 1 cm

AQUAGENIC URTICARIA

- Aquagenic urticaria is a very rare form of hives. The people who it does affect, however, are very unfortunate.
- When you have this type of hives, you will find that the hives are actually caused by the exposure to water.



Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

L'incidenza di **infezioni** nei bambini
con OC non è superiore
a quella della popolazione generale.
La conferma del ruolo eziologico
viene dalla risposta al
trattamento antinfettivo.

Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

E' possibile che determinati tipi di infezione o infestazione (ad esempio *Helicobacter Pylori*, parassitosi) abbiano un ruolo causale in alcuni pazienti

Effectiveness of *Helicobacter pylori* eradication in chronic urticaria: evidence-based analysis using the Grading of Recommendations Assessment, Development, and Evaluation system.

Shakouri A¹, Compalati E, Lang DM, Khan DA.

Revisione di **10 trials**
dimostranti gli effetti della
terapia eradicante per l'HP
nella OC adoperando
l'approccio GRADE

Evidenze a sostegno
dell'intervento di grado
MOLTO BASSO

The evidence that
HP eradication leads to improvement of CU
outcomes is
weak and conflicting...

Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

Sebbene in letteratura siano riportati singoli casi
l'allergia alimentare e l'**ipersensibilità ad additivi** o
a **farmaci** normalmente non sono implicati
nell'eziologia della OC

Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

L'OC del bambino
può associarsi alla tiroidite autoimmune
e alla celiachia

Orticaria cronica e autoimmunità tiroidea

- La prevalenza di autoimmunità tiroidea è superiore rispetto a quella nella popolazione generale: 4,3% (14-33% nell'adulto) (*Levy Y. ADC 2003;88:517*)
- La tiroidite autoimmune ha una prevalenza maggiore nei soggetti con orticaria cronica che nella popolazione generale (*Dreskin SC. COACI 2005;5:408*)

Orticaria cronica e celiachia

- Nell'orticaria cronica è utile verificare la presenza di malattia celiaca
 - *Levine A. Celiac disease associated with familial chronic urticaria and autoimmunity in a child. Pediatrics 1999;104(2):e25*
 - *Meneghetti R. Chronic urticaria and celiac disease. ADC 2004;89:293*
 - *Caminiti L. Chronic urticaria and associated celiac disease in children: a case-control study. PAI 205;16:428*

Orticaria cronica in età pediatrica.

Linee Guida

Caffarelli C, Cardinale F, Paravati F. Area Pediatrica 2010; 6: 5-26

EZIOPATOGENESI

Una percentuale pari a quasi il 50%
delle forme di OC in età pediatrica
ha una patogenesi autoimmune,
da anticorpi anti-FcεRIa

ASST

- 1) Pz con OCI in fase acuta
- 2) Prelievo di sangue venoso a T° ambiente per 30 min
- 3) Centrifuga a 500 g per 15 min
- 4) Iniezione intradermica su superficie cutanea indenne di 50 µl di:
 - Siero autologo
 - Sol. Salina 0.9%
 - Istamina 10 µg/ml (SPT)
- 5) Distanza tra sedi d'iniezione: >3-5 cm
- 6) Lettura a 30 min



ASST+ se pombo rosso con siero autologo

1.5 mm > risp al pombo controllo neg

ASST

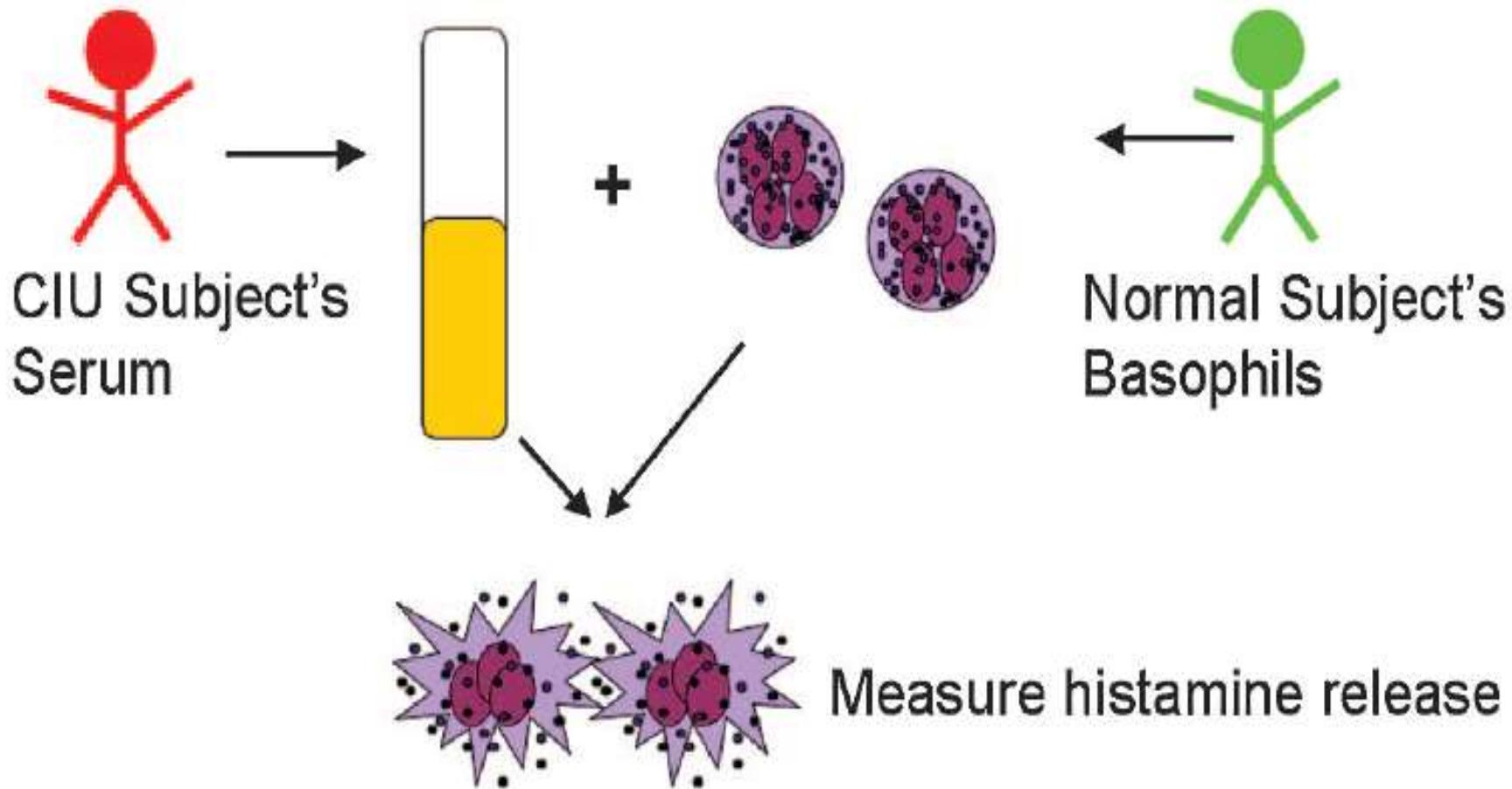
- Test di riferimento nella diagnosi di OC autoimmune nei comuni settings clinici
- Sensibilità 70%; specificità 80%
- Correlazione con titolo Ab anti-Fc ϵ R $\text{I}\alpha$
- Presenza anche in individui sani e affetti da altre patologie (autoimmuni e non)
- Indice di *Histamine-releasing factors* nel siero



*Greaves, JACI 2000;105:664
Kaplan, NEJM 2002;346:175
Kaplan, JACI 2004;114:465
Greaves, Clin Rev Allerg Immunol 2007;33:134*

...the GOLD STANDARD

Histamine releasing activity (HRA) assay



BSACI GUIDELINE

BSACI guideline for the management of chronic urticaria and angioedema

R. J. Powell¹, S. C. Leech², S. Till³, P. A. J. Huber⁴, S. M. Nasser⁵ and A. T. Clark⁶

¹Department of Clinical Immunology and Allergy, Nottingham University, Nottingham, UK, ²Department of Child Health, Kings College Hospital, London, UK,

UK, ³Division of Asthma, Allergy and Lung Biology, Kings College London, London, UK, ⁴BSACI, British Society for Allergy & Clinical Immunology, London, UK, ⁵Department of Allergy & Clinical Immunology, Addenbrooke's NHS Trust, Cambridge, UK and ⁶Department of Allergy, Addenbrookes NHS Trust, Cambridge, UK

Additional investigations if clinically indicated.

- Urinalysis
- Full blood count (FBC)
- Erythrocyte sedimentation rate (ESR)
- Liver function tests (add viral hepatitis screen if transaminases are abnormal)
- Elimination rechallenge diets: rarely, it may be necessary to undertake carefully planned and dietitian supervised elimination and rechallenge diets

BSACI GUIDELINE**BSACI guideline for the management of chronic urticaria and angioedema**

R. J. Powell¹, S. C. Leech², S. Till³, P. A. J. Huber⁴, S. M. Nasser⁵ and A. T. Clark⁶

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Additional investigations if clinically indicated.

- Antinuclear antibodies should only be measured if a connective-tissue disorder is clinically suspected
- A skin biopsy may be indicated if vasculitis is suspected
- C4 and C1 inhibitor quantitation to detect C1 inhibitor deficiency are only indicated for children, typically teenagers, presenting with angioedema without urticaria to define the presence or absence of C1 inhibitor deficiency
- Tests for current or past viral, bacterial or parasitic infections should be guided by the history, clinical findings and initial screening tests, e.g. eosinophilia

BSACI

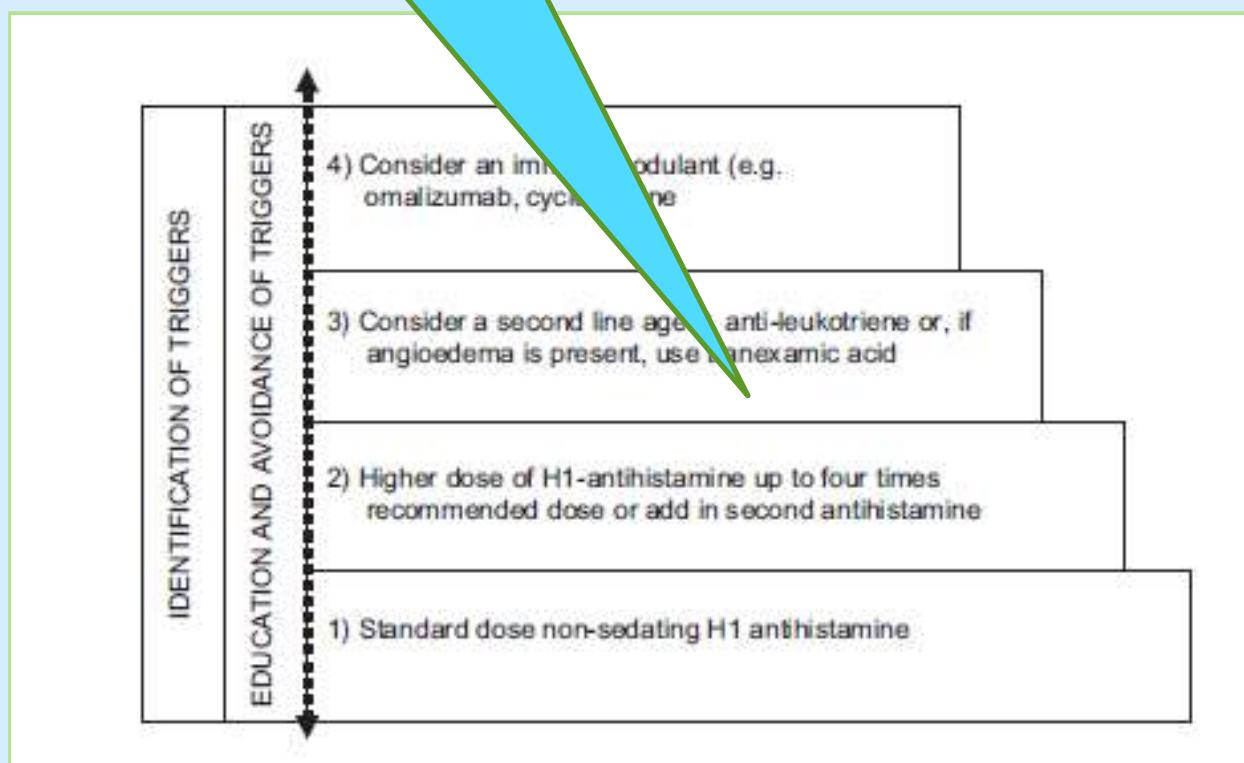
A lack of response to high-dose
antihistamine therapy should
raise the possibility
of an underlying diagnosis
such as vasculitis.

UK, ¹Department of
UK, ⁵Department of
Cambridge, UK

Management of chronic urticaria and angioedema

A. T. Clark⁶

¹Nottingham, UK, ²Department of Child Health, Kings College Hospital, London, UK, ³Department of Dermatology, King's College Hospital, London, UK, ⁴BSACI, British Society for Allergy & Clinical Immunology, London, UK, ⁵Cambridge University Hospitals NHS Trust, Cambridge, UK and ⁶Department of Allergy, Addenbrookes NHS Trust, Cambridge, UK



Leukotriene receptor antagonists for chronic urticaria: a systematic review

- A systematic review of randomised trials
- The heterogeneity of trials were high
- LTRA are not superior to placebo or antihistamine therapy
- **Combination therapy of LTRA and antihistamines** appear to be **more efficacious** compared to antihistamine alone
- The use of LTRA as monotherapy cannot be recommended

The potential pharmacologic mechanisms of omalizumab in patients with chronic spontaneous urticaria

TABLE I. The potential pharmacologic mechanisms of omalizumab in patients with CSU

Mechanisms	Effects
Binding of omalizumab to IgE	
Free IgE concentration in blood and interstitial space	↓
FcεRI on mast cells and basophils	↓
IgE-FcεRI engagement	↓
Potentiating of mast cells	↓
Secretion of cytokines (without degranulation)	↓
Mast cell pool	↓
Immune complexes of IgE-omalizumab	↑
Trapping of autologous antigens (eg, TPO)	↑
Trapping of IgE-specific IgG autoantibodies	↑
Binding of omalizumab to membrane-bound IgE on B lymphocytes	
Continual synthesis of IgE in extended periods	↓
IgE pool in the immune system	↓
Overall effects	
Release thresholds for mast cells for various degranulators	↑
Degranulation of mast cells	↓
Secretion of mediators, cytokines, and chemokines	↓
Recruitment of T cells, macrophages, and eosinophils	↓
Inflammatory manifestation in skin	↓
Vasopermeability, wheal, edema, itch, and erythema	↓

When IgE is bound by omalizumab, forming a complex, IgE cannot bind to FcεRI. This inhibits TPO-specific IgE autoantibody binding of FcεRI. Because IgE-specific IgG autoantibodies bind to IgE in accumulating IgE-omalizumab complexes, fewer of these autoantibodies can bind to IgE on FcεRI.



*Giunta Regionale della Campania
Direzione Generale per la Tutela della Salute ed il
Coordinamento del Sistema Sanitario Regionale
UOD 08 - Politica del Farmaco e Dispositivi*

Si comunica che sulla G.U. n. 193 del 21.08.2015 è stata pubblicata la Determinazione Aisa n.1060 del 31 luglio 2015 avente ad oggetto “Regime di rimborsabilità e prezzo a seguito di nuove indicazioni terapeutiche del medicinale XOLAIR (omalizumab)”: *trattamento dell'orticaria cronica spontanea (CSU) in pazienti adulti e adolescenti (età pari o superiore a dodici anni) con risposta inadeguata al trattamento con antistaminici H1*”.

Classe di rimborsabilità “A”. Medicinale soggetto a prescrizione medica limitativa, vendibile al pubblico su prescrizione di centri ospedalieri o di specialisti: *allergologo, pediatra, dermatologo (RRL)*.

A cura di Iride Dello Iacono e Carmen Verga



Provincia Religiosa di San Pietro
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Ospedale "Sacro Cuore di Gesù", Fatebenefratelli
UOC PEDIATRIA-NEONATOLOGIA-UTIN

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entro il 1/03/2017

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di linee guida comuni

Marzo
Dicembre **2017**

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