

CHRONIC SPONTANEOUS URTICARIA

HISTOPATHOLOGIC CHARACTERISTICS

Shir Quinn

Mentor: Prof. Aviv Barzilai

Urticaria is a dermatological disorder characterized by the sudden appearance of itchy hives (wheals), angioedema or both¹



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

1. Central **swelling** of variable size, usually surrounded by a reflex erythema
2. Associated **itching** (pruritus), or sometimes a **burning** sensation
3. Usually resolves within a few hours and always by 24 hours

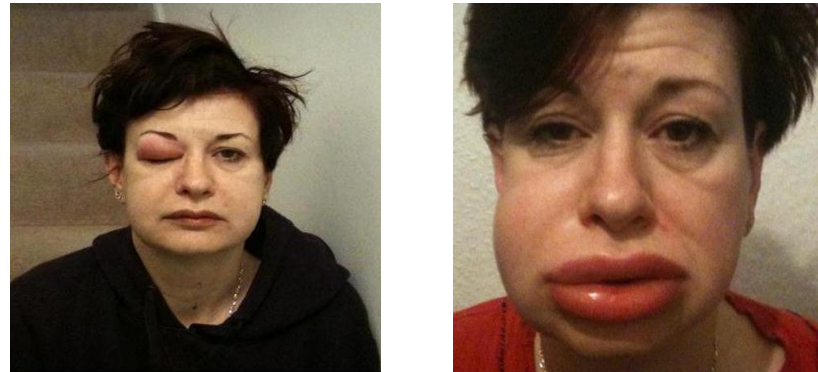
Hives: Superficial swellings with pale centres surrounded by a red flare

The terms 'itch/pruritus', and 'hive/wheel' are interchangeable. For the purpose of this training tool, itch and hive will be used to describe these key symptoms of urticaria

Urticaria is a dermatological disorder characterized by the sudden appearance of itchy hives (wheals), angioedema or both¹

Angioedema is typically characterized by:

1. Sudden, pronounced **swelling** of the lower dermis and subcutis
2. Sometimes **pain** rather than itching
3. Frequent involvement below mucous membranes
4. Up to 72 hours for resolution



Angioedema of the lips: Pronounced swelling of soft tissue in the mouth



Urticaria can be classified based on duration, frequency, and cause¹

Acute < 6 weeks

Chronic > 6 weeks

Spontaneous

No obvious
external
specific trigger

Known causes
(including
autoimmune,
infection)

Unknown causes

Urticaria is more common than previously thought¹

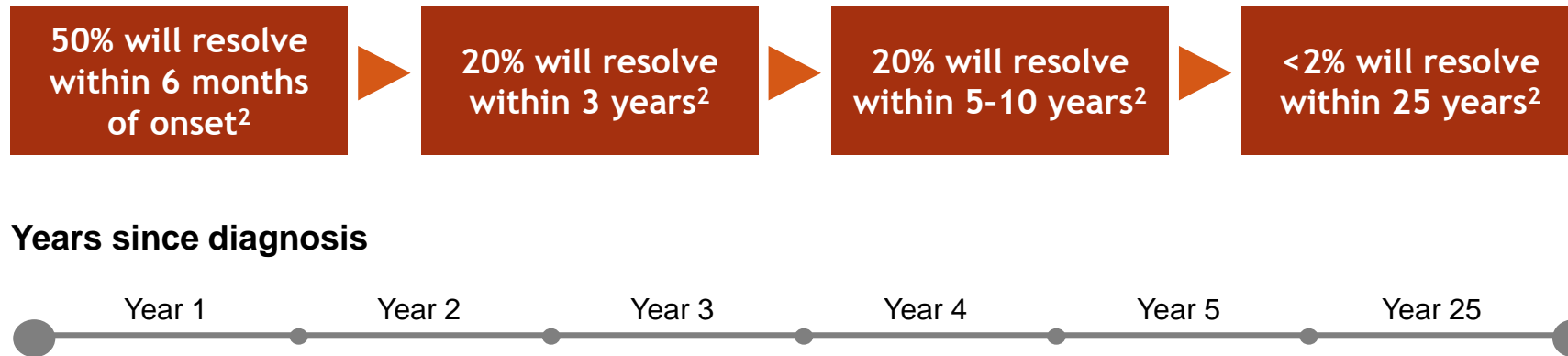


- ▶ CSU affects up to 1% of the population at any given time, accounting for approximately two-thirds of cases of CU¹⁻³
- ▶ Female:male ratio is 2:1¹
- ▶ All age groups can be affected, but peak incidence is between 20-40 years of age¹

1. Maurer M, et al. Allergy 2011;66:317-30;
2. Kozel MM, et al. Arch Dermatol 1998;134:1575-80;
3. Saini SS. Curr Allergy Asthma Rep 2009;9:286-90;

CSU is a chronic disease whose duration is estimated to be 1-5 years in most cases^{1,2}

Of the diagnosed CSU patient population:

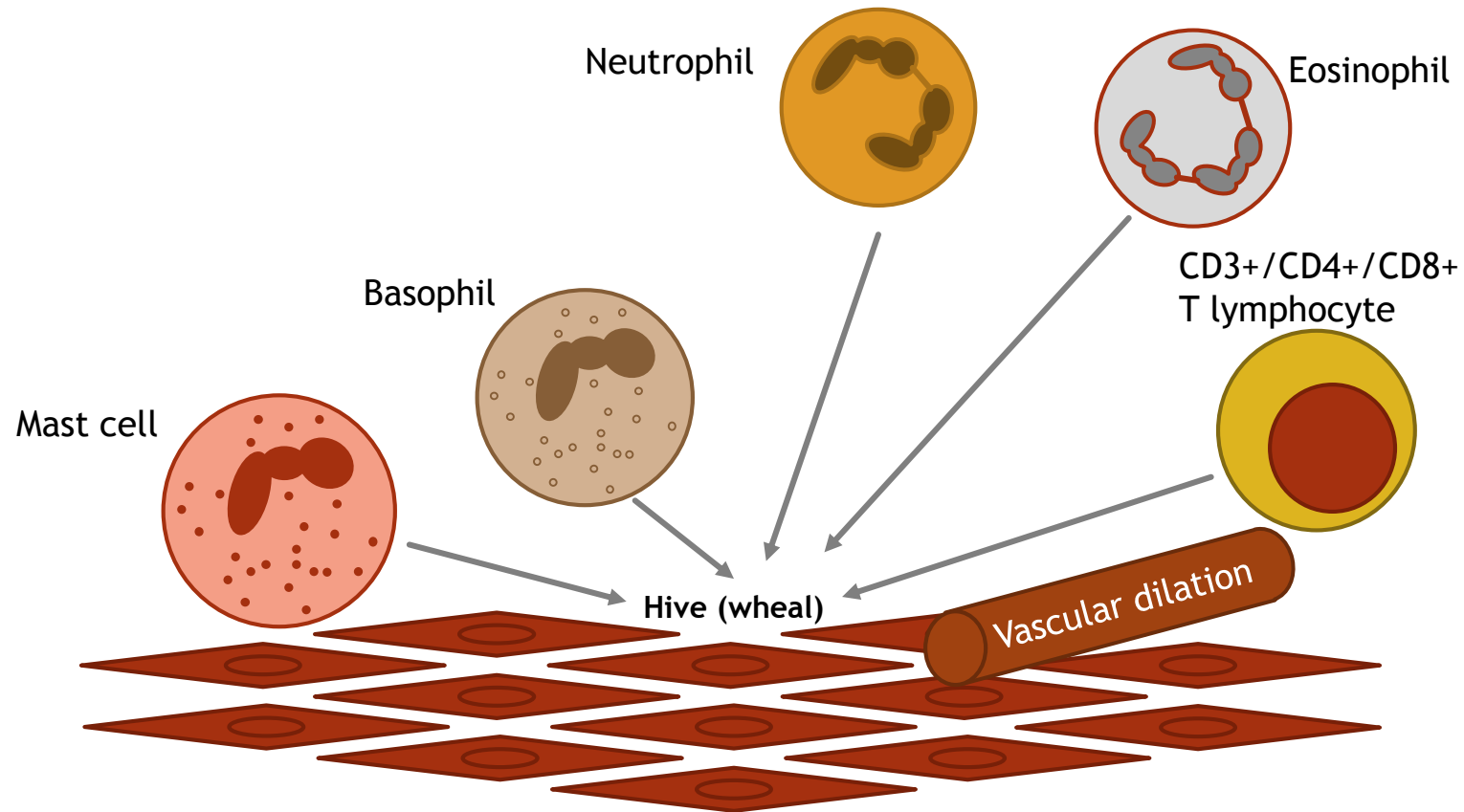


In very rare cases, CSU can persist for up to 50 years

1. Maurer M, et al. Allergy 2011;66:317-30;

2. Adapted from: Beltrani VS. Clin Rev Allergy Immunol 2002;23:147-69.

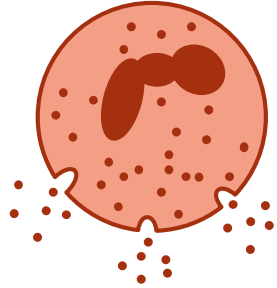
CSU skin lesions show recruitment of mast cells and also basophils, neutrophils, eosinophils and T lymphocytes¹⁻⁵



1. Elias J, et al. J Allergy Clin Immunol 1986;78:914-8; 2. Natbony S, et al. J Allergy Clin Immunol 1983;71:177-83;
3. Sabroe RA, et al. J Allergy Clin Immunol 1999;103:484-93; 4. Ying S, et al. J Allergy Clin Immunol 2002;109:694-700;
5. Zuberbier T, et al. Allergy 2009;64:1417-26; 6. Ito Y et al. Allergy 2011;66:1107-13.

EAACI/GA²LEN/EDF/WAO guidelines¹ state that urticaria is a mast cell-driven disease

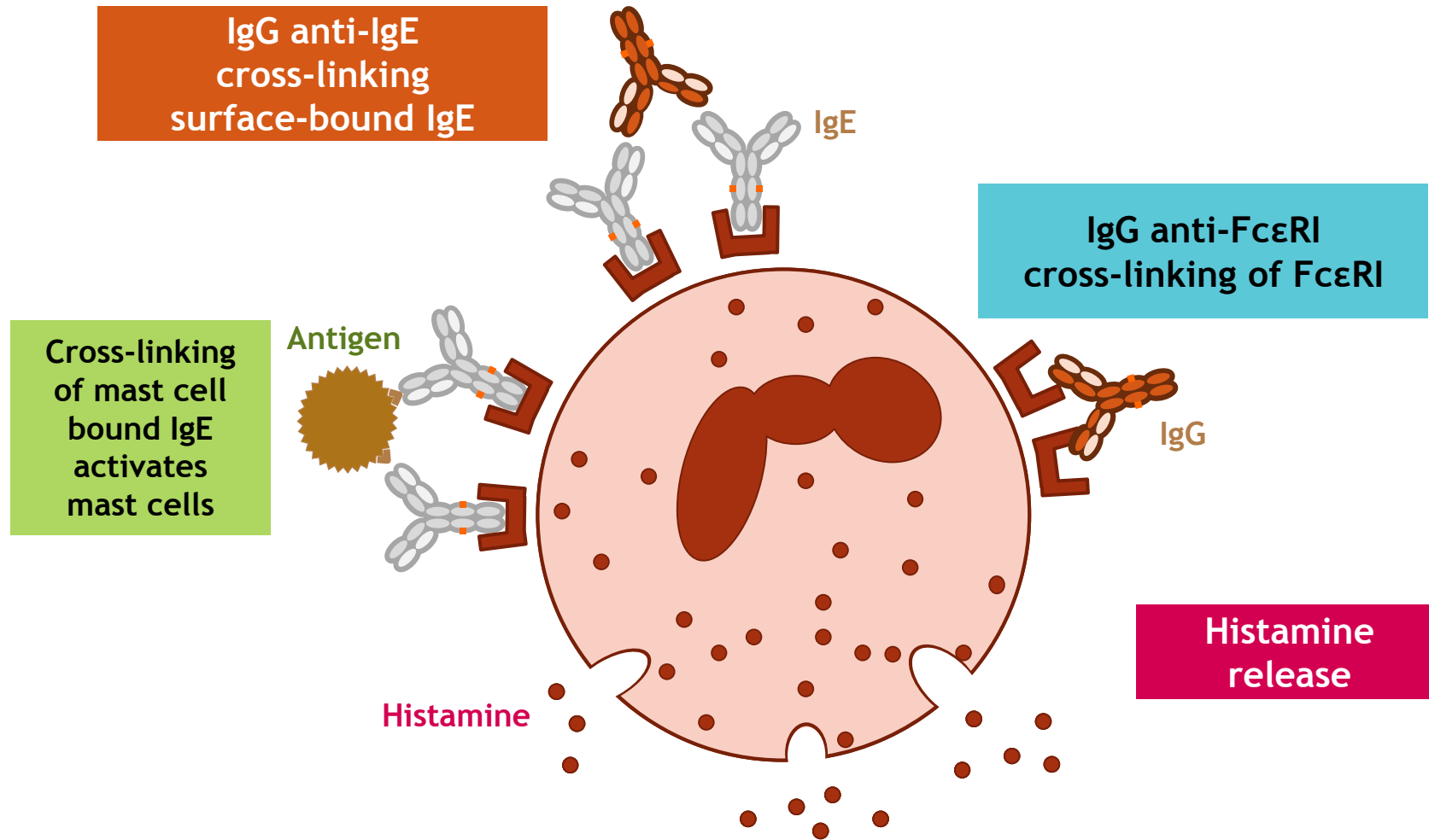
- ▶ Activated mast cells release histamine and other mediators



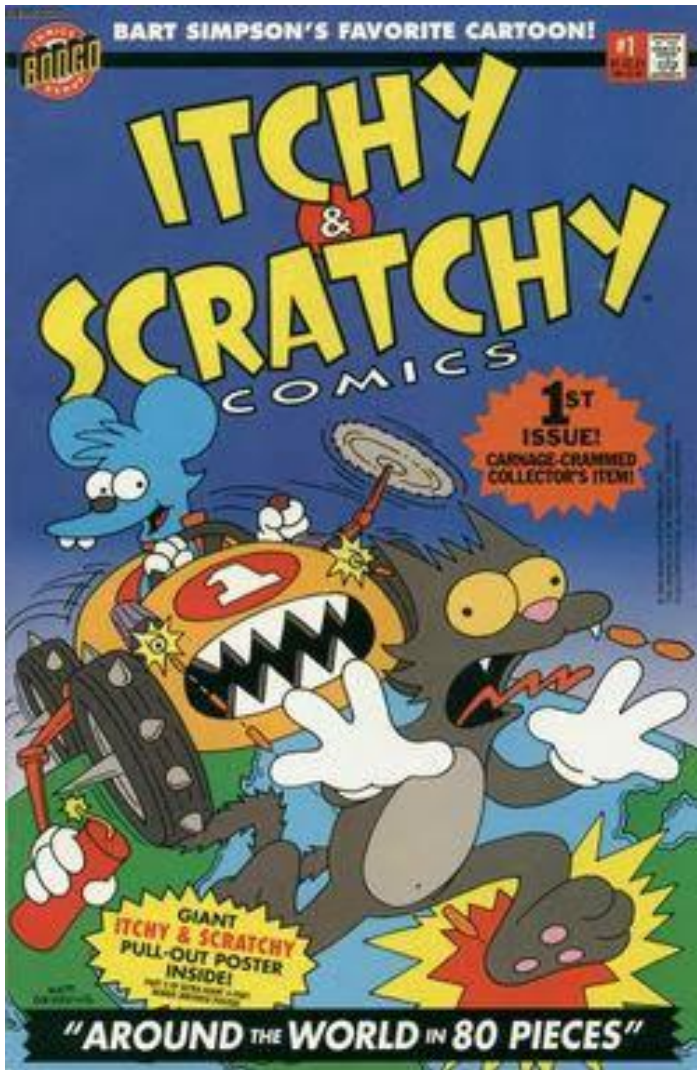
- ▶ These mediators activate sensory nerves
- ▶ Mast cell activating signals in urticaria are **ill-defined** and likely to be heterogeneous and diverse

As IgE is key to the release of histamine and other pro-inflammatory mediators from mast cells and basophils following degranulation, it may play a role in CSU

Mast cell activation in CSU may either be via autoimmune, allergic or idiopathic mechanisms¹⁻³



1. Greaves M. J Allergy Clin Immunol 2000;105:664-72;
2. Kaplan AP, Greaves M. Clin Exp Allergy 2009;39:777-87;
3. Metz M, Maurer M. Curr Opin Allergy Clin Immunol 2012;12:406-11.



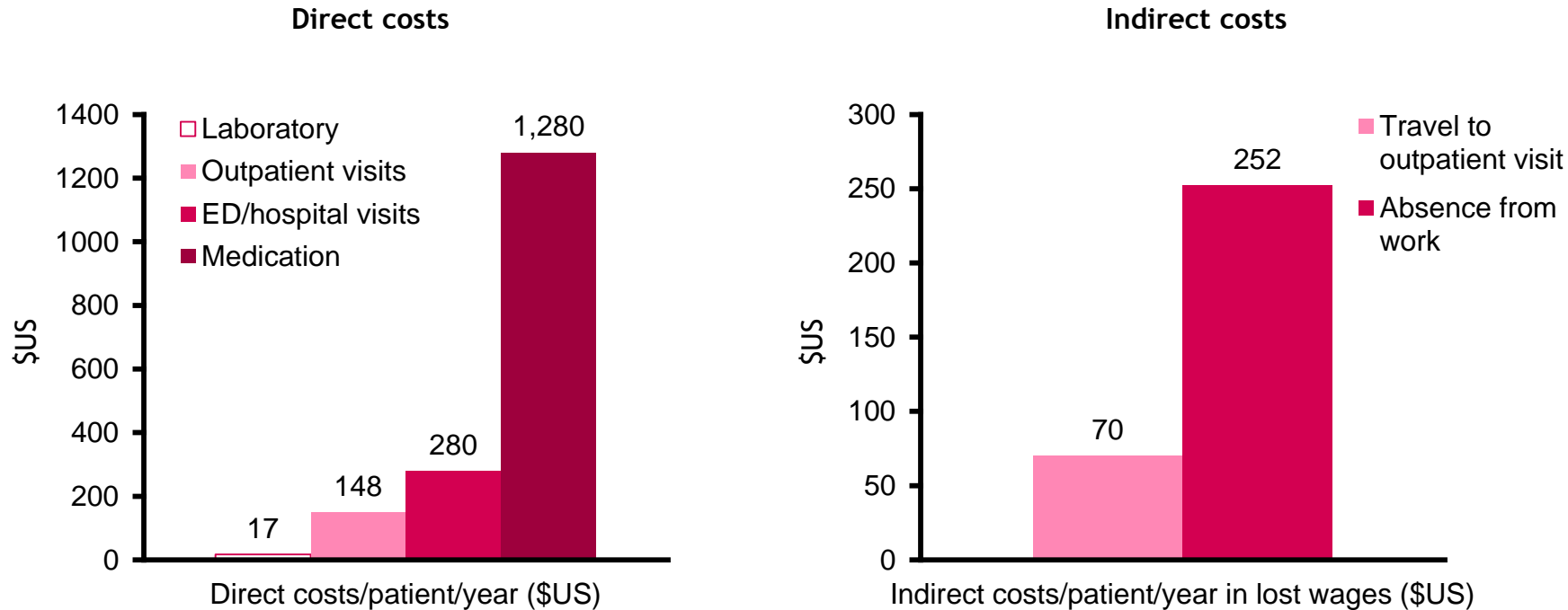
The extent of impaired QoL in patients with CSU

- ▶ In addition to the classical symptoms associated with CSU, factors of major importance to patients that contribute to a reduced QoL include¹:
 - ▶ Unpredictability of attacks
 - ▶ Persistent lack of sleep
 - ▶ Fatigue
 - ▶ Disfigurement
- ▶ Patients with CSU may also have comorbidities such as depression and anxiety²⁻⁴

1. Maurer M, et al. Allergy 2011;66:317-30;
2. Engin B, et al. J Eur Acad Dermatol Venereol 2008;22:36-40;
3. Staubach P, et al. Br J Dermatol 2006;154:294-8;
4. Uguz F, et al. J Psychosom Res 2008;64:225-9.

CSU has a high socioeconomic burden

- ▶ The socioeconomic cost of CSU is high in terms of direct medical costs and indirect costs, such as lost wages because of absences from work^{1,2}



Based on a CSU prevalence of 0.04% among the US population, estimated mean total indirect and direct costs would be \$244 million per year

The aim of therapy for CSU is quick and complete symptom control¹

- ▶ Symptomatic treatment aims to reduce the effect of mast cell/basophil (effector cell) mediators, e.g. histamine, on target organs leading to the symptoms of urticaria^{2,3}

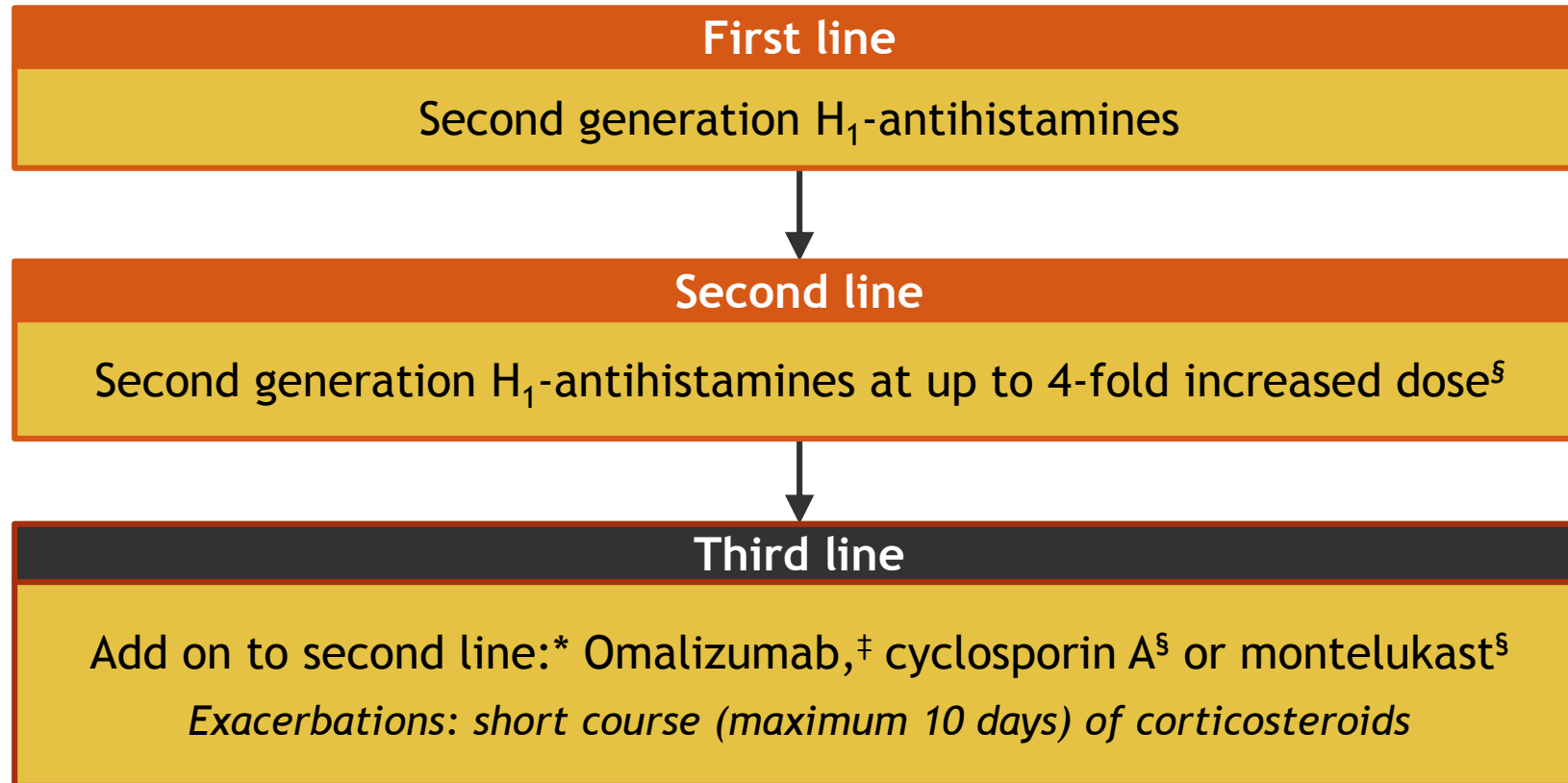


1. Maurer M, et al. Allergy 2011;66:317-30;

2. Zuberbier T, et al. Allergy 2014;69:868-87;;

3. Urticaria and angioedema. Zuberbier T, Grattan C, Maurer M editors. Berlin: Springer-Verlag, 2010.

Treatment algorithm for urticaria according to the 2013 EAACI/GA²LEN/EDF/WAO guidelines¹



A number of additional treatment options are mentioned in the EAACI/GA²LEN/EDF/WAO guidelines, but are not included in the recommended treatment algorithm due to limited supporting evidence; *the order of third-line treatments does not reflect preference; †Licensed in Europe and the US; ^sNot licensed. EAACI = European Academy of Allergy and Clinical Immunology; GA²LEN = Global Allergy and Asthma European Network; EDF = European Dermatology Forum; WAO = World Allergy Organization.



THE HISTOPATHOLOGY OF CHRONIC SPONTANEOUS URTICARIA -CLINICAL PATHOLOGICAL STUDY

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

Areas of further research in urticaria:

- ▶ Identification of new histological markers
- ▶ A search for more specific histological biomarkers for different subtypes of urticaria is desirable.



Background – The classic histopathological findings of urticaria include dermal edema and a sparse perivascular infiltrate of neutrophils, eosinophils, macrophages, and lymphocytes. However, this pattern is **inconsistently described**.

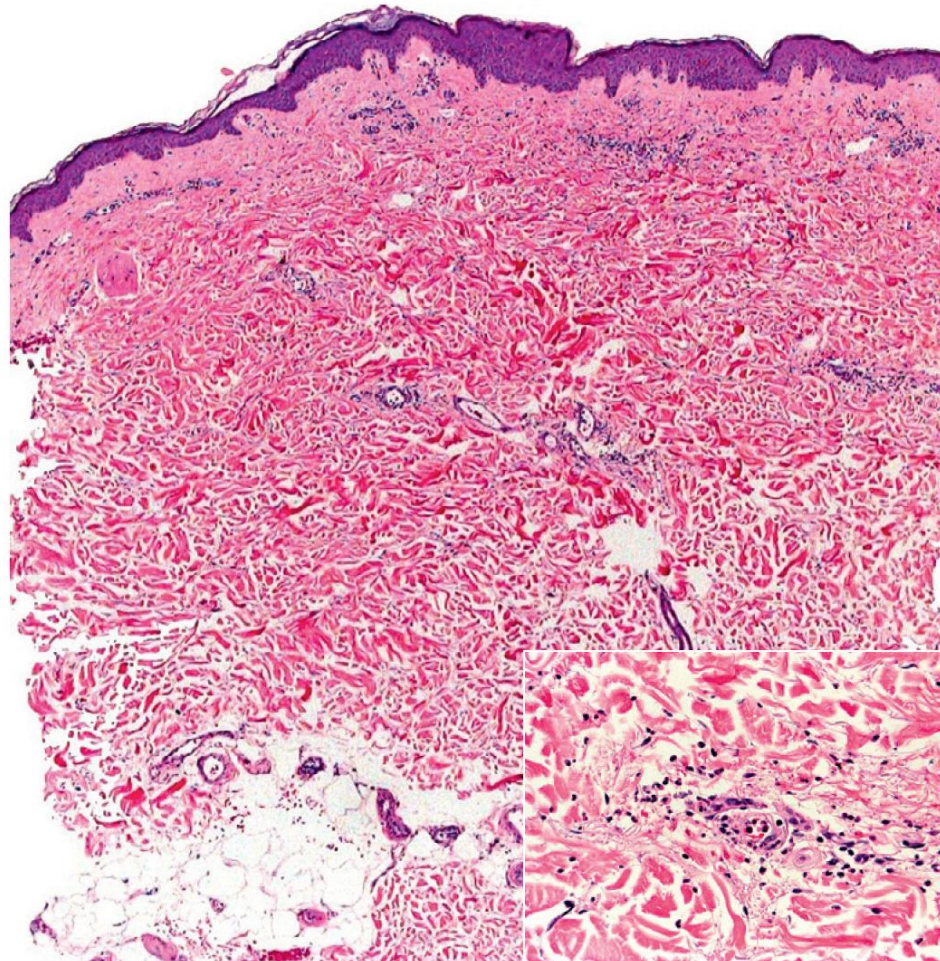


Fig. 18.14 Ordinary urticaria – histologic findings. A sparse, mainly perivascular inflammatory infiltrate and scant edema within the superficial and mid dermis. Note several neutrophils and a few eosinophils (insert).

Courtesy, Lorenzo Cerroni, MD.

The American Journal of Dermatopathology- THE HISTOPATHOLOGY OF URTICARIA REVISITED -CLINICAL PATHOLOGICAL STUDY, 2017

Author(s): Barzilai, Aviv; Sagi, Lior; Baum, Sharon; Trau, Henri; Schvimer, Michael

Two distinctive patterns of urticaria were recognized :

- Lymphocyte predominant characterized by a perivascular location.
- Neutrophil predominant associated with an interstitial location and a denser infiltrate.

Mast cells were relatively sparse, better demonstrated with special stains.

THE HISTOPATHOLOGY OF CHRONIC SPONTANEOUS URTICARIA -CLINICAL PATHOLOGICAL STUDY

Objectives:

1. Validating the previous research regarding two histopathological entities of urticaria – Lymphocyte predominant & Neutrophil predominant.
2. Look into the clinical - pathological correlations of those entities in search of unique characteristics and possibly therapeutic implications



Methods:

- A retrospective study in which the medical files and biopsy specimens of 88 patients with chronic spontaneous urticaria are reviewed.
- Pathological parameters will be quantified.
- A retrospective telephone questionnaire
 - Duration of illness
 - Frequency of attacks
 - Duration of single lesion
 - Pruritus intensity
 - Secondary symptoms (hyperpigmentation/ purple/ purpuric)
 - Treatments for CSU and effectiveness
 - UAS7 (Urticarial activity score)
 - UCT (Urticaria control test)





THANK YOU