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## Core Messages

- Basic principles in the management of patients with urticaria include the identification and elimination of the underlying causes as causal treatment.
- Induction of tolerance can be tried in patients with CINDU where trigger avoidance is not practical.
- Symptomatic pharmacological treatment comprises a step-wise approach of different agents and should be regularly reassessed.

Management of patients with urticaria should follow some basic principles and should be based on a Shared-Decision-Making concept including the patient's participation and encouraging self-management.

Since to date there is no causal treatment option available in urticaria, the treatment aims at complete symptom alleviation.

This goal may be achieved using different approaches, including the identification and subsequent elimination of the underlying cause, avoidance of eliciting and aggravating factors, induction of tolerance and pharmacological interventions inhibiting mast cell mediator release and/or effect of these mediators. Not all approaches are feasible in each patient and should be evaluated based on clinical presentation, history and diagnostic results.

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## 10.1 Identification and Elimination of Underlying Causes

Acute as well as chronic urticaria may be attributed to or associated with distinct causes. Linking urticaria to a cause is not easily achievable since factors, e.g. infections, have been described as causative as well as aggravating factors, but can also be entirely unrelated to the urticarial symptoms. Additionally, spontaneous remission of urticaria can occur any time and the elimination of a factor suspected to be causative or aggravating can be coincidental.

Conducting a detailed medical history and a careful examination are the basic approach. It is not only prerequisite for accurate diagnosis but also essential for the detection of comorbidities such as infections, allergic conditions, autoimmune disorders or malignancy which may be associated as eliciting or aggravating factor but should certainly also be treated independent of the presence of urticaria.

In the management of urticaria, the following factors should be taken into consideration as being of possible causative or aggravating nature:

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## 10.2 Drugs

If pharmacological agents are suspected they should be omitted completely or substituted by agents of another pharmacological class. Frequent suspects are NSAIDs although case reports linking urticaria to many different substance categories have been published.

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## 10.3 Infection

If suggested by medical history or examination results, the diagnosis of bacterial, viral or fungal infection should be treated and/or followed-up.

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## 10.4 Food Intolerance

Although extremely rare as cause of urticaria, IgE-mediated food allergy and non-IgE-mediated food hypersensitivity should be considered if strongly indicated by patient's history.

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## 10.5 Physical Stimuli

Primarily in CIndU exposure to the respective stimulus should be investigated and patients should be trained to recognize and control the exposure, e.g. broadening the handle of heavy bags in delayed pressure urticaria or soft suspension for bikes in vibratory angioedema.

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## 10.6 Lifestyle Adjustments

Regardless of the search for an underlying cause the patient's social and occupational situation should be investigated. Not only can urticaria impair the patient's quality of life, but can also interfere with the ability to work. Patients with physical urticaria may not be able to avoid the respective trigger in their work environment and the disease may cause psychological stress. On the other hand, psychological as well as physical stress has been described to induce exacerbations and stress-reducing lifestyle adjustments can be helpful in the management of urticaria.

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## 10.7 Inducing Tolerance

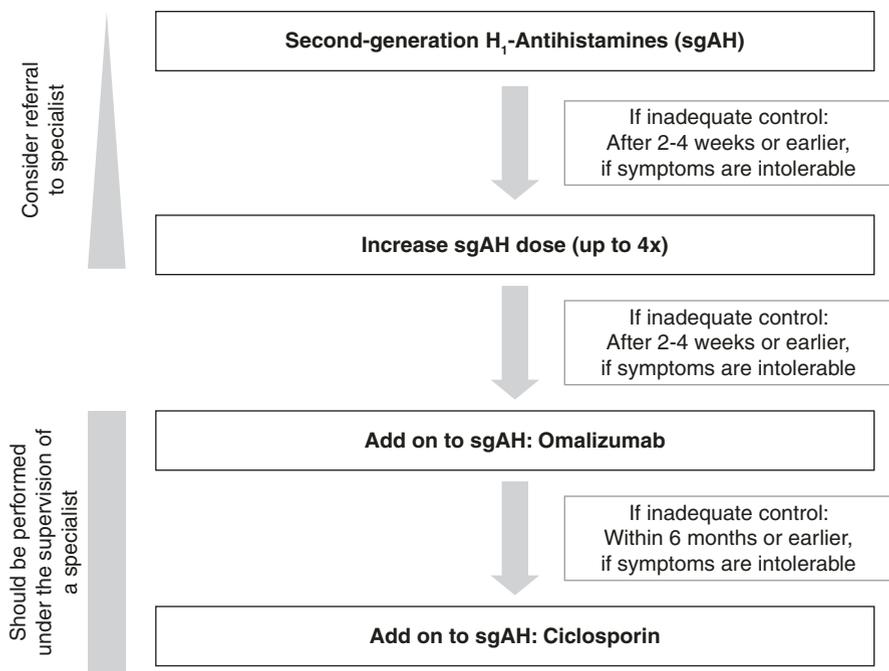
Tolerance induction protocols are available for some forms of inducible urticarias and normally consist of an induction phase where tolerance is obtained and the maintenance phase in which the patient needs to expose him- or herself regularly to the trigger at the obtained threshold. For example in solar urticaria therapy with UV-A has been proven to induce tolerance in 3 days, but constant exposure to UV light is necessary afterwards. As this can be difficult at times in most climates, specialized lamps may become necessary. Similar protocols for cold urticaria require the patient to take cold baths or showers on a daily basis and frequently encounter adherence problems.

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## 10.8 Pharmacological Treatment

Pharmacotherapy should comply with the principle to use as much as needed but as little as possible. The adequacy of pharmacological treatment should be evaluated regularly, extent and selection of medication may vary in the course of the disease.

According to the current guideline evidence-based pharmacological therapy should include second-generation antihistamines as first-line-therapy and their up dosing as second-line-therapy. As third-line treatment option the add-on of monoclonal anti-IgE-antibody omalizumab is recommended, fourth-line treatment includes ciclosporin A instead of omalizumab (Fig. 10.1). Other treatment options where evidence of efficacy is inconclusive are available and are discussed further in this chapter.



**Fig. 10.1** Treatment algorithm according to the International Guideline for the Definition, Classification, Diagnosis, and Management of Urticaria (REF)



Martin K. Church

## Core Messages

This chapter traces the development of H<sub>1</sub>-antihistamines from first generation drugs with marked sedative and other unwanted effects, through second generation drugs with minimal sedation, to the most recent drugs which do not penetrate the brain.

## 11.1 Introduction

To understand the strengths and weaknesses of H<sub>1</sub>-antihistamines, it is necessary to appreciate how they were developed in the 1930s. In his review about his own work [1] Daniel Bovet wrote ‘Three naturally occurring amines, acetylcholine, epinephrine, and histamine, may be grouped together because they have a similar chemical structure, are all present in the body fluids, and exert characteristically strong pharmacologic activities. There are alkaloids that interfere with the effects of acetylcholine. Similarly, there are sympatholytic poisons that neutralize or reverse the effects of epinephrine. It seemed possible to me, therefore, that some substance might exist which exerts a specific antagonism toward histamine’. It was against this background that Bovet, who was looking for antagonists of acetylcholine, asked his student, Anne-Marie Staub, to test some of these compounds against histamine. Anne-Marie Staub, who was preparing her doctorate thesis in his laboratory, used three types of laboratory methods for the evaluation of the degree of activity of the various compounds [1]. In the first test, they determined the action against the lethal

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