Table 14. Urticaria and Angioedema (see also Anaphylaxis, Drug Allergy, Food Allergy)

Referral Guideline	Rationale	Evidence Type
Patients with acute urticaria or angiodema without an obvious or previously defined trigger	After a severe allergic reaction without a known cause, a trigger should be identified if at all possible[1]. An allergist/immunologist is the most appropriate medical professional to perform this evaluation[2], which may include a detailed history, physical examination, skin testing, in-vitro tests, and challenges when indicated. Future avoidance of the identified triggers should prevent subsequent anaphylactic episodes	Diagnostic Indirect outcome (avoidance)
Patients with acute urticaria or angioedema due to a presumed food or drug with need for diagnostic confirmation or assistance with avoidance procedures[3]	See Food Allergy and Drug Allergy sections	Diagnostic Indirect outcome (avoidance)
Patients with chronic urticaria or angioedema, i.e..those with lesions recurring persistently over a period of six weeks or more.	Allergists and dermatologists have more expertise in caring for patients with urticaria than other specialists.[4] Chronic urticaria often has an autoimmune pathogenesis.[5] Consultation with an allergist/immunologist would include: 1) reviewing possible etiologic factors (medications, supplements, dietary factors, animal exposures, physical factors), 2) possible skin testing 3) possible physical challenges 4) recommending changes in ingestants or contactants, and 5) optimal pharmacotherapy[1,2,4-9]. Allergy/immunology specialists are also knowledgeable of the minimal benefit of multiple laboratory tests in urticaria with an otherwise normal examination.[1,2,4,10]	Diagnostic Indirect outcome (avoidance, pharmacotherapy)

Referral Guideline	Rationale	Evidence Type
Patients who may have urticarial vasculitis or urticaria with systemic disease (vasculidities, connective tissue disease, rarely malignancies): a. Lesions last more than 24 hours, leave ecchymotic, purpuric or hyperpigmented residua on/under the skin, or are associated with pain or burning. b. Patients who have typical urticaria/angioedema but have signs and symptoms suggestive of systemic illness. c. Patients whose symptom control requires regular steroid use.	Allergist/immunologist training and expertise should allow appropriate differential diagnosis, determination of the need for biopsy, elimination of a specific inciting agent, and optimal pharmacotherapy.[2,6,10-13]	Diagnostic Indirect outcome (avoidance, pharmacotherapy)
Patients with chronically recurring angioedema without urticaria.	Such patients may have hereditary or acquired angioedema, paraproteinemia or B-cell malignancies. Allergist/immunologist expertise should allow optimal differential diagnosis, determination of the need for hematology/oncology evaluation, and pharmacologic therapy of hereditary or acquired angioedema due to C1 esterase inhibitor deficiency.[14-19]	Diagnostic Indirect outcome (pharmacotherapy)
Patients with suspected or proven cutaneous or systemic mastocytosis.	Allergist/immunologists are trained to diagnose and treat this disease[2,20-22].	Diagnostic Indirect outcome (pharmacotherapy)

References

1. Joint Task Force on Practice Parameters. The diagnosis and management of urticaria: a practice parameter Part I: Acute urticaria/angioedema Part II: chronic urticaria/angioedema. Ann Allergy Asthma Immunol. 2000;85(6 Pt 2):521-44. Evidence grade: IV

2. Allergy and Immunology Core Curriculum Outline 1996. Core Curriculum Subcommittee of the Training Program Directors. American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol. 1996;98(6pt1):1012-15, updated in 2002 (http://www.aaaai.org/professionals/careers/training_programs.stm. Evidence grade: IV

3. Powell RJ, Du Toit GL, Siddique N, et al. BSACI guidelines for the management of chronic urticaria and angio-edema. Clin Exp Allergy. 2007;37(5):631-50. Evidence grade: IV

4. Henderson RL Jr, Fleisher AB Jr, Feldman SR. Allergists and dermatologists have far more expertise in caring for patients with urticaria than other specialists. J Am Acad Dermatol. 2000;43(6):1084-91. Evidence grade: III

5. Kaplan AP. Chronic urticaria: pathogenesis and treatment. J Allergy Clin Immunol. 2004;114(3):465-74. Evidence grade: IV

6. Dibbern DA, Dreskin SC. Urticaria and angioedema: an overview. Immunol Allergy Clin North Am. 2004;24:141-62. Evidence grade: IV

7. Finn AF, Kaplan AP, Fretwell R, Qu R, Long J. A double-blind, placebo-controlled trial of fexofenadine HCI in the treatment of chronic idiopathic urticaria. J Allergy Clin Immunol. 1999;104:1071-78. Evidence grade: Ib

8. Kalivas J, Breneman D, Tharp M, Bruce S, Bigby M. Urticaria: clinical efficacy of cetirizine in comparison with hydroxyzine and placebo. J Allergy Clin Immunol. 1990;86:1014-18. Evidence grade: Ib

9. Greene SL, Reed CE, Schroeter AL. Double-blind crossover study comparing doxepin with diphenhydramine for the treatment of chronic urticaria. J Am Acad Dermatol. 1985;12:669-75. Evidence grade: Ib

10. Kaplan AP. What the first 10,000 patients with chronic urticaria taught me: A personal journey. J Allergy Clin Immunol. 2009;123:713-17. Evidence grade: IV

11. David MD, Brewer JD. Urticarial vasculitis and hypocomplementemic urticarial vasculitis. Immunol Allergy Clin North Am. 2004;24:183-213. Evidence grade: IV

12. Mehregan DR, Hall MJ, Gibson LE. Urticarial vasculitis: a histopahtologic and clinical review of 72 cases. J Am Acad Dermatol. 1992;26:441-48. Evidence grade: III

13. Sheikh J, Saini SS, Kulczycki Jr A, Dreskin SC. Urticaria and Angioedema Committee of the American Academy of Allergy, Asthma & Immunology. A survey of allergists regarding the association of thyroid autoimmunity with chronic urticaria. J Allergy Clin Immunol. 2009;123(5):1173-75. Evidence grade:

14. Cicardi M, Zingale LC, Pappalardo E, Folcione A, Agostoni A. Autobodies and lymphoproliferative diseases in acquired C1 inhibitor deficiencies. Medicine (Baltimore). 2003;82(4):274-81. Evidence grade: III

15. Agostoni A, Aygoren-Pursun E, Binkley K, et al. Hereditary and acquired angioedema: problems and progress. Proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. J Allergy Clin Immunol. 2004;114:s51-s131. Evidence grade: IV

16. Gelfand JA, Sherins RJ, Alling DW, Frank MM. Treatment of hereditary angioedema with danazol. Reversal of clinical and biochemical abnormalities. N Engl J Med. 1976;295:1444-48. Evidence grade: Ib

17. Prematta MJ, Prematta T, Craig TJ. Treatment of hereditary angioedema with plasma-derived C1 inhibitor. Ther Clin Risk Manag. 2004;4(5):975-82. Evidence grade:

18. Frank MM. Hereditary angioedema. J Allergy Clin Immunol. 2008;121(2 Suppl):s398-s401. Evidence grade:

19. Frank MM, Jiang H. New therapies for hereditary angioedema: disease outlook changes dramatically. J Allergy Clin Immunol. 2008;121(1):272-80. Evidence grade:

20. Brockow K. Urticaria igmentosa. Immunol Allergy Clin North Am. 2004;24:287-316. Evidence grade: IV

21. Akin C, Metcalfe DD. Systemic mastocytosis. Annual Review of Medicine. 2004;55:419-32. Evidence grade: IV

22. Valent P, Sperr WR, Schwartz LB, Horny HP. Diagnosis and classification of mast cell proliferative disorders: delineations from immunologic diseases and non-mast cell hematopoietic neoplasms. J Allergy Clin Immunol. 2004;114:3-11; quiz 12. Evidence grade: I