Angioedema

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KEYWORDS

• Urticaria • Angioedema • Histamine • Bradykinin • Hereditary angioedema
• Acquired angioedema • C1 esterase inhibitor • Factor XII gene mutations

KEY POINTS

- Wheals of urticaria and angioedema are due to short-lived edema in different layers of the skin, and differ in clinical and pathogenetic respects.
- The factors involved in the opening and closure of endothelial cell-cell adherens junctions, which are largely composed of vascular endothelial cadherin, are still unknown in urticaria and angioedema.
- In the spectrum urticaria/angioedema, 3 groups of diseases can be differentiated: diseases with urticaria and angioedema, diseases with angioedema alone, and diseases with urticarial lesions without angioedema.

INTRODUCTION

Urticaria and angioedema have several features in common, some of which are clinical. Both are based on a relatively short-lived edema in the skin and may be associated with edema episodes of other organs. Urticarial wheals and angioedema may be single or multiple. The individual lesion of either may persist for from a few hours to some days. Both belong to various disease entities (**Table 1**), and may occur in combination or in isolation. Local vasodilation and increased vascular permeability are the main changes in urticaria and angioedema.

PATHOPHYSIOLOGY

Common Pathophysiologic Features

Single urticaria and angioedema lesions have a localized fluid extravasation in common. The plasma passes through the vessel wall and, when extravascular, becomes interstitial fluid. The passage through the interstitial gaps of the endothelial cells has attracted more attention in recent years. Endothelial cells control the passage of plasma constituents from blood to underlying tissues. Endothelial permeability is mediated by transcellular and paracellular pathways (**Fig. 1**), which means that blood

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Table 1
Diseases with urticaria and/or angioedema

Diseases with Urticaria Combined with Angioedema	Diseases with Angioedema and Without Urticaria	Diseases with Urticaria and Without Angioedema
Acute urticaria	Hereditary angioedema due to C1-INH deficiency (HAE-C1-INH); types I and II	Cholinergic urticaria
Chronic spontaneous urticaria	Hereditary angioedema with normal C1-INH (HAE-nCI; HAE type III), subtypes HAE-FXII and HAE-unknown	Factitial urticaria
Cold urticaria	Acquired angioedema with C1-INH deficiency (AAE-C1-INH)	Delayed-pressure urticaria
Urticarial vasculitis	Angioedema due to ACE inhibitors (AE-ACEI)	Heat contact urticaria
Exercise-induced anaphylaxis/urticaria	Angioedema with unknown cause (AE-UC) responsive to antihistamines (AE-UC-h) or unresponsive to antihistamines (AE-UC-nh)	Solar urticaria
Episodic angioedema with eosinophilia		Aquagenic urticaria
Vibration-induced urticaria/angioedema		Contact urticaria

Abbreviations: ACE, angiotensin-converting enzyme; C1-INH, C1-inhibitor.

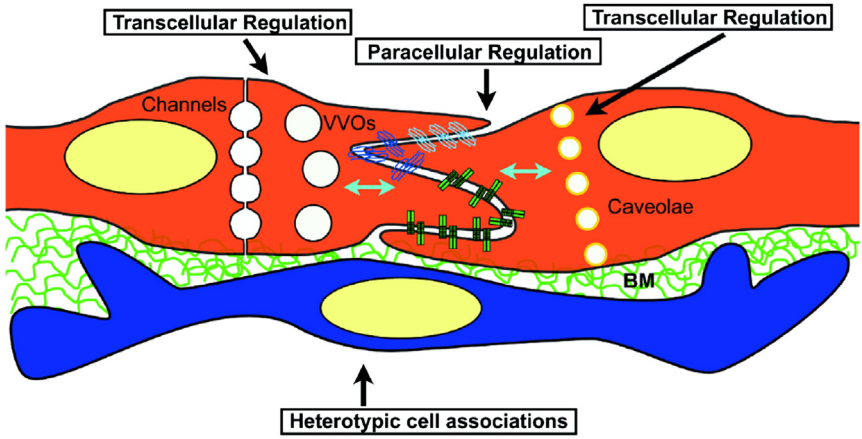

Fig. 1. Pathways that regulate barrier function in endothelial cells. The scheme shows 2 endothelial cells and the subendothelial space. Vascular permeability is regulated and maintained through 3 compartments: paracellular junctions (adherent and junctional complexes), transcellular pathways, and heterotopic cell interactions (usually pericytes). The details of this cross-talk remain largely unclear. BM, basement membrane; VVOs, vesiculovacuolar organelles. (*From* Goddard LM, Iruela-Arispe ML. Cellular and molecular regulation of vascular permeability. Thromb Haemost 2013;109:408; with permission.)