

# Etiologies and management of cutaneous flushing



## Nonmalignant causes

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### Learning objectives

After completing this learning activity, the participant should be able to describe the recommended diagnostic workup for uncommon serious causes of cutaneous flushing and describe the best management practices for causes of flushing.

### Disclosures

#### Editors

The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

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The flushing phenomenon may represent a physiologic or a pathologic reaction. Although flushing is usually benign, it is prudent that the physician remains aware of potentially life-threatening conditions associated with cutaneous flushing. A thorough investigation should be performed if the flushing is atypical or not clearly associated with a benign underlying process. The diagnosis often relies on a pertinent history, review of systems, physical examination, and various laboratory and imaging modalities, all of which are discussed in the 2 articles in this continuing medical education series. This article reviews flushing associated with fever, hyperthermia, emotions, menopause, medications, alcohol, food, hypersensitivity reactions, rosacea, hyperthyroidism, dumping syndrome, superior vena cava syndrome, and neurologic etiologies. (J Am Acad Dermatol 2017;77:391-402.)

**Key words:** blushing; climacterium; dumping syndrome; emotional flushing; fever; flushing; hot flush; hypersensitivity reactions; hyperthermia; hyperthyroidism; menopause; rosacea; SVC syndrome.

## HISTORY

The concept of the flushing reaction dates back to 1839 when T. H. Burgess published a report on blushing. He proposed that blushing was a uniquely human trait designed by the creator in "order that the soul might have sovereign power of displaying in the cheeks the various internal emotions of the moral feelings."<sup>1-3</sup> Charles

Darwin further discussed blushing in the *Expression of the Emotions in Man and Animals* in 1872.<sup>1,2,4</sup> E. J. Tilt coined the term "flush" in 1882. In 1890, descriptive works were provided by Henry Campbell.<sup>1,5</sup> It was not until 1980 that research began unraveling the pathophysiology of the complex mechanisms of flushing.<sup>1</sup> This delay may be explained by the fact that flushing reactions

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were viewed primarily as emotionally rooted and cosmetic for some time. The association of flushing and specific chemical mediators of various disease processes sparked a renewed interest in the subject of flushing.<sup>2</sup>

### DEFINITION/DISTRIBUTION/ANATOMY

Flushing is defined as visible reddening of the skin accompanied by a sensation of warmth.<sup>2,6-8</sup> Synonyms of flushing include hot flashes, hot flushes, hot blooms,<sup>1</sup> and blushing.<sup>2</sup> Classic areas of flushing are the face, ears, neck, and upper aspect of the chest (Fig 1).<sup>1,2,6-9</sup> The greater visibility of flushing in these areas is caused by the superficial nature of the cutaneous vasculature and an increased vascular capacitance for dilation in these regions. Variations in the stratum corneum, a thin papillary dermis, flatter epidermal rete ridges, wider diameter of blood vessels, and subpapillary plexus closer to the skin surface contribute to increased visibility in these blush regions.<sup>8</sup>

Vasodilation of flushing is mediated by nerves or vasoactive substances acting on vascular smooth muscle. The transient nature of flushing is related to variances in the vascular response of the blush areas. There are 4 neurally mediated vascular responses in the face: (1) sympathetic vasoconstrictor fibers have a tonic constricting influence on the vessels of the ears, lips, and nose, while sparsely supplying other areas of the face; (2) sympathetic vasodilation of the face during heat, stress, and emotion; (3) parasympathetic vasodilation with reflexes in the facial and glossopharyngeal nerves increase blood flow to exocrine glands, the eyes, nose, and mouth during irritation of these tissues; and (4) axon reflexes release vasoactive peptides from sensory fibers that contribute to a local inflammatory response.<sup>10</sup>

### PHYSIOLOGIC FLUSHING

#### Key points

- Physiologic forms of flushing are classified as benign cutaneous flushing
- The most common forms are thermoregulatory, emotional, and extrinsic-mediated
- Extrinsic agents, or substances that have been topically applied, ingested, or systemically administered, are a frequently encountered cause of flushing, and in many cases, extrinsic mediators exacerbate flushing in patients who are predisposed

#### Thermoregulatory flushing

Thermoregulatory flushing is caused by fever and hyperthermia.<sup>6</sup> During febrile episodes, body heat



**Fig 1.** A 54-year-old woman with idiopathic flushing.

is dissipated using a mechanism of cutaneous vasodilation and perspiration. Some patients are exceptionally sensitive to this pathophysiologic mechanism.

Hyperthermia can be induced by exercise or exogenous heat, such as a warm environment or ingestion of hot substances.<sup>6</sup> Ingestion of hot food and beverages can increase the temperature of the oropharyngeal cavity and cause flushing by a countercurrent exchange model. Increased heat in the mouth dissipates to the tissues surrounding the oral cavity, including the internal jugular vein and common carotid artery. The increased temperature of the blood flowing through this vasculature is transferred to the internal carotid artery and base of the brain. The body's thermostat, the anterior hypothalamus, reacts to slight changes in temperature of the arterial supply. This triggers heat dissipation via autonomic reactions, such as flushing and sweating.<sup>11</sup> Thermoregulatory flushing also occurs in climacterium because of circadian cycling of core body temperature.<sup>1,6,7</sup>

Thermoregulatory flushing can be controlled by resetting the body's thermostat. This can be accomplished by applying cold compresses to the face or neck, drinking ice water, or holding ice chips in the back of the mouth. Any mechanism that cools the oropharyngeal cavity for periods of >30 min can lead to countercurrent-induced central cooling, which increases the hypothalamic tolerance to hyperthermia.<sup>6</sup>

#### Emotional flushing

Emotional flushing is temporally related to situations of emotional distress or embarrassment. Women are affected more than men.<sup>12</sup> Emotional flushing is typically resistant to medications.<sup>6,12</sup> Management with beta blockers has been attempted, but data on efficacy are lacking.<sup>6</sup> Treatment options include psychological modification in the form of biofeedback, paradoxical intention, and

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