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CHAPTER 2

Pathogenesis of Rosacea

Mark V. Dahl, MD
Professor and Chairman, Department of Dermatology, Mayo Clinic Scottsdale, Scottsdale, Ariz

EDITOR'S COMMENT

Rosacea is a source of constant embarrassment and worry for our affected patients. Bright red cheeks, enlarged noses, and erythematous papules and pustules interfere with social and occupational interactions. Depression, anxiety, and inferences about alcoholism haunt sufferers of this fiery disease. To compound their misery, very few hard data exist regarding the etiopathogenesis of rosacea. Dr Mark Dahl, who has a long interest in helping alleviate the effects of this illness, shares his insights in this superbly written article. Mark separates rosacea into several subsets of specific findings. Explanations behind the appearance of each of them are reviewed. In the concluding section, a unifying concept is proposed to bring all of these contributing factors into focus and explain the totality of the signs and symptoms of this chronic and very public disease. Expanding this knowledge base and using our discoveries to improve therapy are goals we look forward to being realized.

William D. James, MD

Rosacea is a disease composed of many elements or subsets. Rosacea is more like a syndrome than a single disease. Although all patients with rosacea develop some erythema of their skin, not all patients develop all other stigmata. Some patients have centrofacial flushing and edema. Others are more troubled by papules and pustules. Still others are more troubled by burning and stinging sensations, or by rhinophyma. Subsets of rosacea are listed in Table 1.

The cause of the rosacea complex is unknown, and unifying hypotheses are speculative. Whatever the cause, facial skin is

TABLE 1.
Subsets of Rosacea

Erythema
Flushing
Edema
Papules and pustules
Telangiectasias
Stinging and burning sensations
Rosacea dermatitis
Rosacea cellulitis
Fibrosis/rhinophyma

predisposed. The disease affects only the facial skin and cornea. The tip of the nose is affected first, followed sequentially by the cheeks, forehead, and chin.

ERYTHEMA

Many people have ruddy complexions. Not all of these people have rosacea. The ruddy erythema of rosacea tends to persist (erythema congestivum) and usually waxes and wanes markedly in response to changes of body temperature, ingestion of certain foods, evoked emotions, or other factors. Sometimes the erythema involves the whole face, but more often it involves just the central face. Erythema is often striped by telangiectatic blood vessels.

A red complexion characterizes people of European extraction, particularly Celts. In addition to this obvious genetic element, erythema is more pronounced in some families than in others. The amount of blood in the facial skin and blood vessels is high. Total movement of red blood cells in flush areas of rosacea skin is 3 to 5 times higher than in controls.[1]

Finally, the erythema of rosacea seems aggravated by chronic sun exposure and photodamage. People without rosacea can develop poikiloderma of Civatte (erythromelanosis coli), and this same propensity toward erythema and telangiectasia seems to augment the baseline erythema among patients with rosacea and lightly pigmented skin. Solar damage is not a prerequisite for the development of rosacea.[2,3] Patients with rosacea are not more prone to sunburn.[4]

The blushlike redness that develops on rosacea faces during and after exposure to sunlight is more likely caused by heat from infrared radiation than by photons from ultraviolet radiation. The radiant heat–derived redness develops quickly during (rather than

after) exposure. Exposing facial skin to other sources of radiant heat, such as heat from a fireplace or stove, reproduces it.

Immunofluorescence staining of rosacea skin often finds immunoglobulins, especially IgG and IgM, at the dermal-epidermal junction of sun-damaged skin and facial skin of patients with rosacea. This can be an artifact produced by preserving specimens in Michel's transport media, which seems prone to increase nonspecific staining of dermis, dermal-epidermal junction, and blood vessels, especially in sun-damaged skin (unpublished observations). In other patients, the appearance of immunoglobulin deposits at the dermal-epidermal junction (especially in dermal papillae) is an artifact allegedly produced by compression of autofluorescing elastic tissue against the dermal-epidermal junction by edema and dilated papillary dermal blood vessels (Burnham's "fibrillar pseudoband").[5]

Perhaps in others, antibodies bind to sun-damaged connective tissue.[6-9] Circulating IgG and IgM antibodies to collagen, antinuclear antibodies, and anti-*Demodex* antibodies have been found in patients' sera. In addition, eluates from autologous circulating lymphocytes in peripheral blood of patients with rosacea have reacted with nuclei of "dermal cells," endothelial cells, and eccrine duct cells.[7]

FLUSHING

Both flush and erythema occur when blood vessels dilate and blood flow increases in superficial vessels of the skin. Whereas the erythema is chronic and persistent and varies subtly, the flushing can wax and wane quickly. Flushing usually involves the central face and is associated with a warming of surface skin.

Patients with mastocytosis and carcinoid syndrome can develop all the stigmata of rosacea, including ocular rosacea, facial telangiectasia, and connective tissue hypertrophy.[10-12] Flushing can be stimulated by various environmental trigger factors as listed in Table 2.

In hyperthermic, but not normothermic healthy human beings, cool venous blood from the face and scalp enters the dural venous sinus via vascular pathways or emissary veins. The cooler blood intermingling with the brain and meningeal blood vessels keeps the intracranial temperature cool. Brinnel et al[13] found that venous blood flow from the skin to the brain was suppressed in patients with rosacea, thus inhibiting selective brain cooling in hyperthermic conditions. Apparently, the facial skin acts like an automobile radiator to lose heat by radiation, convection, and conduction. In

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