Rosacea: Considerations for a better understanding of the disease

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Rosacea is a common condition. While much has been written about it, several concepts are not well appreciated or are misunderstood. Because the diagnosis is made solely on the basis of clinical observations and patient history, unambiguous definitions are necessary.[1] To date there are key points that have not been enunciated. Additionally, several concepts promulgated by the American National Rosacea Society (NRS) are hinged on theories derived by extrapolating basic scientific results that do not coincide with the clinical findings.[2] Finally, understanding these concepts will lead to better education and treatment for patients.

Clinical diagnosis

Clinical definition #1

The key to diagnosis is prolonged central facial erythema. In a manuscript I co-authored soon after the first iteration of the NRS publication, we proposed this to be the one necessary finding for the diagnosis of rosacea.[1] It needs to be fixed in the centre of the face, being prominent on the convex surfaces of the skin (cheeks, chin, and forehead). But how long? We proposed that it should be present for at least three months.[1] This is much longer than typical systemic lupus central facial erythema or the kind caused by photosensitivity, allergic contact dermatitis (ACD), erysipelas, or other mimicks of rosacea. The addition of a time factor to the criteria would make the diagnosis more specific.

Clinical definition #2

There is periocular sparing. This is not emphasised in most references, including the NRS papers. However, it is clearly visible in typical photos depicting rosacea and in patients.[2,3] It should be emphasised in any definition of rosacea.

Clinical definition #3

Between the first NRS paper and the most recent update, two disorders were added to eliminate possible confusion between facial erythema caused by systemic lupus erythematosus and topically applied corticosteroids.[2,3] We suggested excluding these and other conditions such as polycythemia vera, dermatomyositis, carcinoid syndrome, mastocytosis, and mixed connective tissue disease from our 2004 publication.[1] All of these may have prolonged central facial redness but each have their specific laboratory abnormalities that help define them. But rosacea has no such defining blood test, emphasising the need for precision in its clinical definition.

Clinical definition #4

Many of the above diseases that need to be excluded have additional signs and symptoms that are not typical of rosacea. Symptoms like erythema are visible on other body parts in case of dermatomyositis, mixed connective tissue disease, photosensitivity, and allergic contact dermatitis. The presence of mastocytomas can be used to differentiate mast cell disease. The fixed central facial redness of rosacea is unique to the disease with rare exceptions like involvement of the scalp in balding men.

Clinical definition #5

Flushing is a transient erythema often seen in the non-phymatous expression of rosacea. However, it is not like the short-lived sudden redness associated with embarrassment, heat, spicy foods, or exercise. Rosacea patients tend to have redness that may start with the above triggers, yet it lasts usually for more than ten minutes, and at times over an hour. It may be accompanied by a burning sensation or an

How to cite this article: James WD. Rosacea: Considerations for a better understanding of the disease. Indian J Dermatol Venereol Leprol. doi: 10.25259/IJDVL_1789_2024

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Received: November, 2024 **Accepted:** January, 2025 **Epub Ahead of Print:** March, 2025

DOI: 10.25259/IJDVL_1789_2024

extreme sense of localised heat. This adds to the discomfort and embarrassment of the prolonged flush. A typical history may present in a young to middle-aged woman performing aerobics. While the red colouration on everyone's face subsides, hers is deeper and lasts longer. As opposed to the fixed erythema, the flush of rosacea may extend to the scalp, but more commonly to the ears, neck, and upper chest. One exclusion that should be ruled out by history is the flushing caused by the ingestion of alcohol by a patient using tacrolimus or pimecrolimus for the treatment of seborrheic dermatitis or other central facial disorders.[4]

Clinical definition #6

Papules and pustules, cited in the 2002 NRS publication as a primary feature, are helpful for diagnosis when limited to the centrofacial skin.[3] However, one needs to state that gram-negative folliculitis may also manifest in such a geographically limited distribution.[5] While lesions between the upper lip and the nose or those clustered perinasally are most common in gram-negative folliculitis, they are often present only in rosacea-prone areas. Such patients have a history of long-term oral antibiotic treatment. While primarily seen among acne patients it is now less observed due to the American Academy of Dermatology emphasising limiting oral antibiotic treatment. However, many still use long-term treatment for rosacea, and as there is no guideline specifying limitations for the disease it may occur "incognito" and cause complications.

Clinical definition #7

Clinical trials often report that medications that act on papules, pustules, and nodules improve redness as well. Usually, the type of redness is not specified but later inferred as fixed long-lasting centrofacial erythema. However, trials usually score the redness of peri-inflammatory papules and pustules, which obviously improves once the inflammatory lesions are calmed. While patients are somewhat distressed by perifollicular inflammation-induced redness, this is easily treated due to the excellent therapeutic armamentarium available for papules, pustules, and nodules. What they want is something for the long-term red redness that antibiotics do not alleviate.

Clinical definition #8

Papules, pustules and nodules? The 2002 NRS report and most publications about rosacea did not include nodules in their descriptions.[3] In our 2004 article, we discussed their presence in mostly older men with thick, sebaceous skin.[1] This is the group that frequently develops rhinophyma. They usually have a history of acne and scarring. This group is distinctly different from young to middle-aged women with thin, telangiectatic skin. The latter are usually the ones affected by flushing and sun damage, while the former are likely not to flush or have telangiectasia. My sense about their fixed erythema is that it is a result of scarring and damage to lymphatic vessels, leading to a low-grade inflammatory process like that seen in stasis dermatitis.

Following are the implications of using precise clinical definitions

Implication #1

These observations allow an understanding of patients vulnerable to rhinophyma. It is not the young women with thin skin. It is rather those older men with thick sebaceous-type skin in whom this complication may occur.

Implication #2

Some recent publications by the ROSacea CONcensus group in Europe state that the erythrotelangiectatic rosacea (ETR) subtype can eventuate into the phymatous type and vice-versa.[6] This is not true; the patient's basic skin composition is different and no "progression or reversion" can occur.

Etiologic considerations

The updated 2018 NRS publication specifies that rhinophyma is due to a "subclinical neuroinflammation and adaptive or innate immune responses that then progress to fibrosis and glandular hyperplasia".[2] I am unaware of any model system showing that this process occurs. Is there an alternate explanation? Yes. Rhinophyma almost exclusively occurs in men with sebaceous type of skin. We know that androgens influence glandular overgrowth. I hypothesize that these men have a condition like acne vulgaris causing inflammation and both this and their phymas are a result of such hormonal stimulation.

Implication #1

The uncommon woman with thicker skin and acneiform papules, pustules, and nodules should be investigated for an androgen disorder such as polycystic ovarian disease. Additionally, 19 patients were reported to have had rhinophyma-like noses, which on biopsy were confirmed as B-cell lymphomas.[7] Eighteen of the 19 were women. Biopsy of the nodular excrescences is a secondary investigation that should be undertaken in a woman with rhinophyma.

Implication #2

Patients with such thick skin and acne-like lesions do not have the tendency to have the easily irritated skin that we commonly associated with the thin-skinned flushing woman. They tolerate conventional benzoyl peroxide and, in fact, may use it several times daily on their oily sebaceous skin. I have taken many older men off oral antibiotics for their recurrently inflamed, pustular noses by simply having them use topical benzoyl peroxide gel.

Implication #3

Women with thickened skin and a history of acne and scarring have inflammatory lesions that respond well to spironolactone, obviating the need for oral antibiotics in this less common subgroup.

Myth

The red scrotum syndrome may be due to a process like the redness and flushing seen in rosacea. I believe this is false. I have not seen a rosacea patient with such a complaint, and have not seen a man with a burning red scrotum who also has rosacea. I have tried rosacea therapy in these men, and they are not positively affected by the intervention.

I hope that by elaborating these 15 less-appreciated clinical concepts, implications, and myths that understanding of rosacea will be positively influenced and help patients get better treatment.

Key take home points

Precision in defining various clinical signs and symptoms that afflict rosacea patients will help in the critical reading of the literature, assist in designing better treatment options, and be a more compassionate physician.

Understanding how qualities of the underlying skin type influence signs and progression of rosacea allows for better education of patients, work-up of potential underlying diseases, and treatment.

Declaration of patient consent: Patient's consent not required as there are no patients in this study.

Financial support and sponsorship: Nil.
Conflicts of interest: There are no conflicts of interest.
Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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