PATIENT-FOCUSED SOLUTIONS IN ROSACEA MANAGEMENT: TREATMENT CHALLENGES IN SPECIAL PATIENT GROUPS

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Hardware/Software Requirements: High speed internet connection, any web browser

Statement of Need

Reports show 16 million individuals in the US are affected by rosacea and account for up to 3% of all cases seen in dermatology practice. Recent reports show rosacea is more common in patients with darker skin types than previously recognized and in skin types III-VI, rosacea may be more difficult to distinguish in the early stages; these patients may not seek treatment until their symptoms are quite severe. Rosacea has a considerable psychosocial impact and is the cause of embarrassment, anxiety, and low self-esteem. Men are more likely than women to feel ridiculed for their appearance despite higher disease prevalence in women. Current treatments aid in the management of rosacea signs and symptoms and therapeutic goals and decisions should include individual, patient-identified issues. Current recommendations for achieving optimal treatment results include achieving clear/almost clear skin and improving key patient-reported outcomes. Therefore, there is need for increased medical knowledge on features, benefits, and limits of available treatment modalities, their effect on minimizing rosacea symptoms, and formulation of optimal individualized rosacea treatment plans in special patient groups often not always considered to be at high risk. Dermatology providers of all levels of training and experience require tools to establish ongoing clinician-patient communication relating to the identification of patient-reported disease impact and the burden of the condition on daily life.

Educational Objectives

The overall information and educational goals of this enduring activity are to expand awareness of the impact of rosacea on quality of life of patients of all ages and genders and skin types including those with darker skin, summarize current rosacea treatment strategies and the unique challenges rosacea presents when treating patients with darker skin types, men versus women, and other special patient types, and formulate effective, individualized rosacea treatment regimens that address patients' self-reported concerns on the impact of their disease on their overall quality of life.

Upon completion of this continuing education activity participants should be able to:

- Recognize the impact of rosacea on various patient populations including skin types III-IV, younger men, and others
- Define rosacea treatment strategies based on individual diagnosis, disease classification, and patients' self-reported issues
- Identify challenges to early diagnosis and treatment in patients with darker versus lighter skin, male versus female patients, and other select patient types
- Develop and implement ongoing clinician-patient dialogue to assess the impact, extent, and the burden of rosacea on the individual patient to enable better personalized treatment outcomes

Target Audience

This activity is intended for dermatologists, residents, and fellows in dermatology, and physician assistants, nurse practitioners, and other healthcare providers with an interest in cutaneous diseases and disorders affecting patients of all skin types.

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Patient-focused Solutions in Rosacea Management: Treatment Challenges in Special Patient Groups

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ABSTRACT

Rosacea is among the most common facial skin conditions diagnosed by dermatologists. Typical clinical features include erythema, flushing, telangiectasia, papules, and pustules distributed on the central face. While the prevalence of rosacea is highest among white populations of Northern European descent, recent reports have found that rosacea frequently occurs in people from a broad range of racial/ethnic backgrounds and skin types. When rosacea presents in darker skin types, the diagnosis is often more challenging due to masking of features by increased epidermal melanin. As such, under-diagnosis and underreporting may contribute to misconceptions about the prevalence of rosacea in populations with skin of color. Recognizing the unique presentations and complications associated with darker skin types is necessary to reduce the disparities in rosacea treatment, especially as the American population continues to become increasingly heterogeneous. Although rosacea is most common in middle-aged females, patients of other demographics may have more negative impacts on quality of life due to their disease. In this article, we review rosacea management with a focus on special patient groups: people with skin of color, and less common forms of rosacea, in order to diminish the physical and psychosocial burden of rosacea in all patient groups. Due to the variability inherent to rosacea, we advocate for an individualized, patient-centered approach to disease management.

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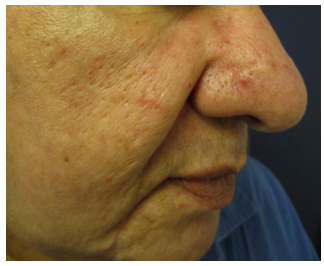
INTRODUCTION

Rosacea is a common, chronic facial condition presenting with various combinations of erythema, flushing, telangiectasia, edema, papules, and pustules most often affecting fair-skinned individuals.[1,2] Although most prevalent in light-skinned populations with Fitzpatrick skin types I-II, rosacea affects a broad spectrum of populations, including those with skin of color. The prevalence of rosacea in nonwhite racial/ethnic populations is less studied, but recent data suggest that it is more prevalent than previously reported.[3] In order to effectively diminish the physical and psychosocial burden of rosacea, considering the diverse populations groups affected by this condition is paramount.

Epidemiology

The prevalence of rosacea is estimated at about 10 percent of predominantly fair-skinned populations and affects approximately 16 million American adults.[4,5] The onset of rosacea is often after 30 years of age and displays a female predominance with the exception of phymatous rosacea (Figure 1), which is more common in older males.[4] In younger populations with rosacea, this female predilection is amplified.[1] Prevalence of rosacea in Germany and Russia based on general population screening found 18% of subjects with rosacea were aged 18-30 years.[6] Though more common in adult females, studies evaluating disease severity support the prevalence of more severe disease in subjects of male gender and less than 60 years of age.[7]

FIGURE 1. Type IV skin with rhinophyma.



Until recently, rosacea was widely considered to be a disease almost exclusively affecting light-skinned individuals. However, the prevalence of rosacea in skin of color populations is increasingly being recognized. A study analyzing data from the National Ambulatory Medical Care Survey from 1993-2010 to determine racial and ethnic makeup of patients with rosacea found that of all patients diagnosed with rosacea, 2% were black, 2.3% were Asian or Pacific Islander, and 3.9% were Hispanic or Latino.[8] These findings challenge the long held belief that rosacea is a disease largely limited to white individuals of Northern European heritage with Fitzpatrick skin types I-III.

The lower prevalence rates of rosacea in non-white populations is likely due to a combination of factors including under-reporting, under-recognition (due to a low index of suspicion and

diagnostic challenges), protective effects of melanin from ultraviolet (UV) radiation, and a lower incidence of genes conferring susceptibility in diverse populations.[3,4] Recognizing diagnostic challenges posed by masking of clinical features by increased epidermal melanin are necessary to prevent delayed diagnosis, disease progression, and advanced disease, which result in greater morbidity and even disfigurement.[3]

Pathophysiology

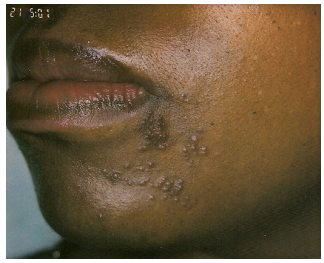
Pathophysiology of rosacea is likely multifactorial, involving abnormal responses to environmental stressors in individuals with genetic predispositions leading to immune and neurovascaular dysregulation.[9] Genetically predisposed individuals have an abnormal response to environmental stressors such as UV exposure, temperature changes, microbial antigens (eg, Demodex folliculorum, Heliobacter pylori), and emotional stress that results in Th1/Th17 polarization.[4]

Studies finding increased risk with positive family history, twin studies with high concordance, and genome association studies support the important role of genetics in rosacea.[4] A cohort-based twin study evaluating the role of genetics and environmental factors in rosacea calculated the genetic contribution to rosacea development to be 46%.[9] Genome-wide association studies isolated three human leukocyte antigen (HLA) alleles with known association to autoimmune disease including type I DM and celiac disease within a large population of European descent.[10] Additional studies are needed to further elucidate the complex interplay of genetics and environment in rosacea.

Diagnosis and Classification

Rosacea is a clinical diagnosis based on physical exam and history that can have a wide range of presentations.[5] Guidelines from the National Rosacea Society (NRS) published in 2012 pioneered criteria for rosacea diagnosis and categorization defined by the presence of one or more primary features: flushing, persistent erythema, papules, pustules, and telangiectasia with variable presence of secondary features: burning, stinging, erythematous plaques, dryness, edema, ocular manifestations, and phymatous changes.[2] Furthermore, the NRS identified four rosacea subtypes: erythematotelangiectatic (ETR), papulopustular (PPR), phymatous, and ocular, with one variant: granulomatous based on presence of combinations of various primary and secondary disease features.[2] Though this classification of rosacea is still currently in use and enabled the development of significant clinical and therapeutics advancements in rosacea management, it falls short in its failure to accurately address the broader scope of clinical presentations.[5] Oversimplification of the disease into distinct categories overlooks the fact that often features of multiple subtypes are present simultaneously creating a more complex clinical picture and furthermore, there is often progression from one subtype to another over time.[5,11] These shortcomings were addressed by the global ROSacea COncensus (ROSCO) consensus panel, which put forth the first set of guidelines for phenotype driven management, which will be further discussed in the management section of this paper.[11]

FIGURE 2. Granulomatous rosacea in black skin.



Overall, ETR is the most common subtype of rosacea, followed by PPR.[2] Important differences in skin of color include higher reported frequency of PPR compared to ETR (likely due to difficulty recognizing features of ETR in dark skin), as well as increased prevalence of the granulomatous subtype (Figure 2).[3] Phymatous changes, most often seen in older males, are frequently observed in combination with ETR or PPR.[2] Ocular rosacea is frequently diagnosed when other features of rosacea are present to aid in the diagnosis, with nearly 50% of patients experiencing onset of cutaneous symptoms prior to ocular symptoms.[5]

Recently, there has been a shift towards a phenotype-led approach, which more accurately reflects patients seen in clinical practice and has important therapeutic implications, further discussed in the treatment portion of this review.[11] This is especially significant in patients with disease not fitting the prototypical descriptions such as those with skin of color who are less likely to be identified as having predominant telangiectasia and erythematous changes in the skin. Additionally, the current classification system perpetuates the lack of evidence-based research and investigation of less prevalent, but high morbidity subtypes such as phymatous and ocular rosacea.[11]

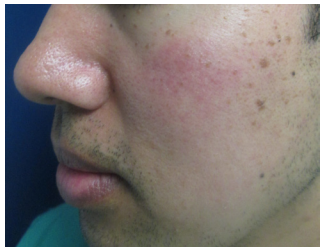
Rosacea remains under recognized in skin of color, however, there are tools readily available to assist with this oftentimes-challenging diagnosis. Patient history can provide vital information that is not obtainable on exam: this can include a description of burning or stinging sensations, a family history of rosacea or mixed heritage, and even a history of acne that failed to respond to standard treatments.[3] On exam, it may be difficult to appreciate features of erythema and telangiectasia due to masking by constitutive skin pigmentation, but other features such as dryness and edema may be visible on the central face or acneiform papular and pustular lesions in

the absence of comedones or acneiform lesions on the body (Figure 3).[3] Furthermore, strategies to further assess erythema and telangiectasia in darker skin include use of dermoscopy, diascopy to test for blanching, and photography against a dark blue background.[3]

Diagnosis of rosacea requires exclusion of differential diagnoses that may present with centrofacial erythema and must be excluded on a case-by-case basis including seborrheic dermatitis, malar rash of acute cutaneous lupus or systemic lupus erythematosus, chronic photodamage, contact dermatitis, carcinoid syndrome, and niacin ingestion.[3,5] Given the high prevalence of systemic lupus erythematosus and sarcoidosis in individuals of African descent, black patients presenting with central facial erythema sparing the nasolabial folds or edematous plaques should undergo appropriate work up in order to rule out these conditions including serological evaluation (eg, antinuclear antibody or angiotensin converting enzyme, respectively), punch biopsy, and referral to rheumatology or pulmonology colleagues if indicated.[12]

FIGURE 3. Rosacea in non-white populations (Skin type IV-VI).

(3A)



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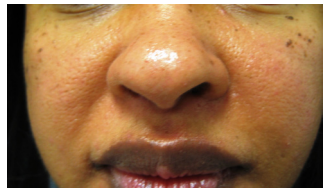

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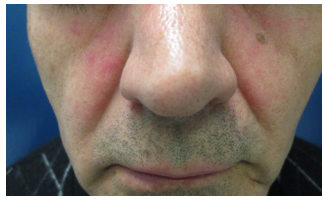

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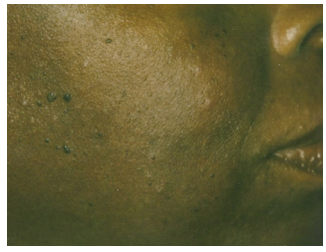


Quality of Life

Rosacea has significant adverse effects on quality of life (QOL). Physical discomfort due to symptoms such as irritation, itching, burning, or stinging understandably affect an individual's well-being.[13] Psychosocial affects related to skin changes of rosacea that are typically highly visible and have a substantial effect on physical appearance have been shown to cause shame, embarrassment, low self-esteem, low self-confidence, negative body image, and anxiety.[14,15] Physical appearance has been shown to have a significant impact on a wide variety of social outcomes from personal relationships and mate selection to workplace success.[14] A German study using willingness to pay as a correlate for disease burden found women and those with more extensive facial involvement willing to pay more, and likely to experience greater negative QOL due to their rosacea than their counterparts who are of male gender or have less facial involvement.[16]The associated stigmatization and frustration experienced by patients are well documented, as are increased rates of psychiatric comorbidities such as social anxiety, depression, and social phobia.[14] Notably, males are more susceptible to stigmatization in setting of rosacea, possibly due to more severe phenotypes such as rhinophyma.[14] Increased stigmatization from rosacea has also been associated with higher rates of depression and social avoidance behaviors.

The psychosocial impact on QOL is often underestimated by physicians, likely in part due to the fact that the objective disease severity does not correlate with the magnitude of effect on QOL, with the exception of depression.[13,14] A web-based cross-sectional study of 600 adults with ETR and PPR cohorts, respectively, found that 45 and 53 percent disagreed that they were satisfied with their appearance due to rosacea, 42 and 27 percent agreed that they "worry how people will react when they see my rosacea," and 43 and 59 percent strongly agreed that they feel their rosacea is unattractive to others despite more than 90% of both cohorts self-identifying as having mild to moderate disease.[15] Another important finding in the literature is the reversal of psychological symptoms with therapy; though the number of studies evaluating this outcome are limited future studies will likely continue to evaluate these changes as important measures of treatment success.[16]

Management

Diagnosis of rosacea should promptly be followed by education regarding the chronicity and relapsing nature of the disease as well as the importance of gentle skin care, regular photoprotection with sun protection factor 30 or greater, and trigger avoidance.[4,5,11] Identification of patient-specific triggers is essential to preventing disease flares.[17] Use of gentle skin cleansers, frequent use of emollients, and avoiding exacerbating factors such as sunlight, temperature changes, and emotional stress, are primary interventions for managing secondary features namely dry, itchy, painful, burning skin.[11] Counseling should be provided in a culturally sensitive manner, taking into account that recommendations may differ significantly from traditional cultural practices in non-white populations such as regular consumption of spicy foods, aggressive exfoliation, or regular use of abrasive skin brightening and lightening products.[3] Many darker skinned individuals report not using sunscreen out of unfamiliarity or cultural discordance and may struggle to find a cosmetically suitable product.[18]

Evidence-based guidelines for rosacea are limited by the fact

FIGURE 4. Summary of ROSCO panel guidelines.

	Transient Erythema	Persistent Erythema	Papules Pustules	Telangiectasia	Phyma
General Skincare*	X	X	X	X	X
Topical alpha adrenergics	X	X			
Oral Beta Blocker	X				
Topical Azaleic Acid			X**		
Topical Ivermectin			X		
Topical Metronidazole			X**		
Oral Doxycycline (40 mg)			X		X***
Physical Modalities				X	X
Isotretinoin			X		X***
Laser therapy		X		X	

*Gentle skin care, trigger avoidance, sun protection with minimum SPF 30, moisturizers
** Monotherapy in mild to moderate disease only
*** Inflamed phyma

that most rosacea clinical trials rely on the 2012 NRS subtypes for inclusion criteria and assess efficacy based on outcome measures specific to the disease subtype rather than the phenotype, which more accurately reflects the constellation of features that would ideally be treated simultaneously.[11] Recognizing the lack of concordance between the archetypal NRS subtypes and real world patients, the ROSCO panel established consensus treatment guidelines (Figure 4) that encourages targeting individual features of rosacea and use of multiple therapies to achieve desired results.[11]

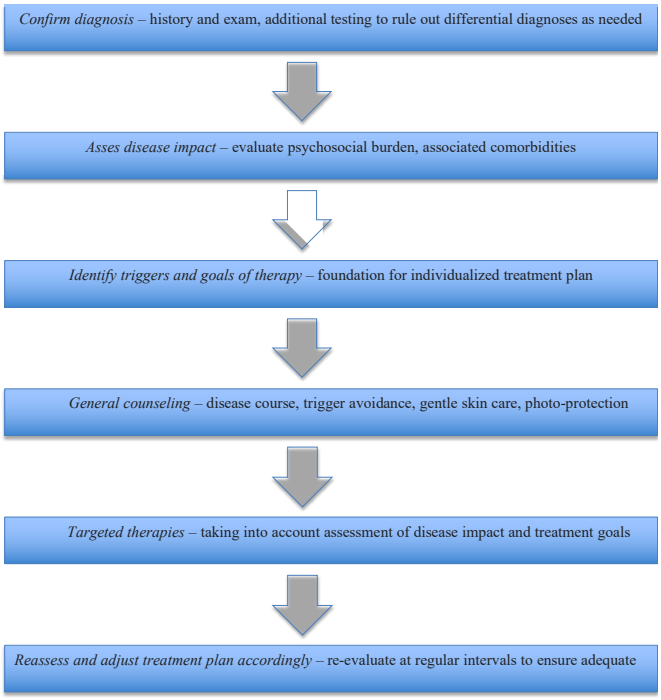
Randomized control trials (RCT) are an integral part of evidence based medicine, and their data support the use of topical azelaic acid, metronidazole, and ivermectin, as well as oral doxycycline for the treatment of mild to moderate PPR and the use of topical ivermectin and oral doxycycline for severe PPR.[19,20] Inflammatory lesions of PPR, active phyma, and ocular features can be managed with doxycycline 40 mg as an anti-inflammatory at subantimicrobial doses.[11] Effective treatments targeting the erythema of ETR include topical alpha-adrenergics (eg, oxymetazoline, briminodine), as well as intense pulsed light (IPL), and pulsed-dye laser (PDL) at 585-595 nm.[11] Telangiectasia require physical modalities for eradication such as electrodessication, IPL, or laser therapies.[11] Importantly, the 2015 Cochrane review found no difference in efficacy of IPL and PDL for erythema and telangiectasia (moderate quality evidence).[11]

High quality RCTs in rosacea are increasing and improving our therapeutic arsenal, however there remains a large gap in knowledge in less common subtypes, namely phymatous and ocular rosacea, as well as the spectrum of rosacea in skin of color.[11] The lack of large controlled trials for the treatment of less common phymatous and ocular subtypes is exemplified by the 2015 Cochrane review of rosacea interventions, which found no RCTs for phymatous rosacea and concluded that more studies are warranted to evaluate treatments for ocular rosacea.[19] ROSCO recommends treatment of inflamed phymatous rosacea with lasers, oral doxycycline, or isotretinoin; therapies for non-inflamed phymas can include CO2 lasers, microdermabrasion, and surgical excision based on patient preferences.[4,11] Initial treatments for ocular rosacea include education on eye care and lid hygiene, use of lubricating drops, and increased dietary intake or supplementation with omega-3 fatty acids. Collaboration with ophthalmology is recommended for more advanced cases.[4,11]

Treatment approach for rosacea in non-white populations is the same as that used in white populations, with the exception that special consideration must be given to avoid post inflammatory hyperpigmentation.[3,12] Few rosacea studies have significant numbers of subjects with skin of color as the general dearth of non-white subjects in clinical trials is amplified in rosacea, which is less prevalent in these populations. Individual studies for oral doxycycline and topical oxymetazoline showed equivalent efficacy in subjects with Fitzpatrick skin phototypes I-III and phototypes IV-VI.[3,21] Vascular lasers are effective in the treatment of vascular components of rosacea in skin of color, however IPL is generally not advised in types IV-VI due to higher risks of dyspigmentation.[3,12] Use of longer wavelengths and lower fluence in skin of color is advised to minimize the risk of pigmentary alterations or scarring.[3]

Given the heterogeneity of rosacea, there is no single best therapy, and often multiple treatment modalities including gentle skin care, trigger avoidance, topical agents, oral medications, and laser- or light-based therapies targeting specific disease manifestations are employed in order to achieve desired results.[4,5] Use of multiple therapies should be based on the patient's desire for treatment of multiple disease features, and should target specific complaints rather than disease severity given the large role of patient perception on disease impact.[11] Maintenance therapy is dependent on treatment modality and patient preference.[11] A comprehensive approach is appropriate (Figure 5). This model highlights the importance of communication with patients to shape personalized treatment plans. Patients should be reassessed regularly to maintain an optimal treatment plan as the disease presentation may change over time.

FIGURE 5. Personalized rosacea management plan.



Rosacea treatment aims to eliminate and maintain clearance of signs and symptoms of the disease in order to eliminate negative effects the condition has on an individual's QOL. Communication with patients is necessary to reveal an individual's personal concerns, goals, and desires, which often differ from that predicted by clinicians.[14] For example, erythema has been described as the most troublesome symptom, however, these findings come from predominantly fair-skinned populations and it is plausible that erythema is not as bothersome in non-white populations. Alternatively, erythema may not be appreciated by clinicians, but nonetheless can be bothersome to patients, highlighting the need for individually tailored patient care reflecting the patient's wishes.[14] Optimal results and improved patient outcomes are achieved by understanding the patient's subjective disease severity and goals of treatment prior to initiating therapy.[11] Choice of therapy should incorporate patient preferences and values that can include cost of procedural therapies that are typically not covered by health insurance or preference for topical vs oral or frequency of administration.[11]

CONCLUSION

Rosacea is a chronic inflammatory skin condition due to immune and neurovascular dysfunction that has significant effects on QOL. Though more prevalent in patients with fair skin, rosacea occurs in people of all races and ethnicities and until recently has been largely under recognized in nonwhite populations. In order to optimize treatment of rosacea, recognizing more subtle or less typical features in special patient groups is essential. A patient centered approach targeting disease features most bothersome to patients contributes to improved outcomes including QOL. Future studies should continue to evaluate efficacy in diverse populations to accurately reflect the patients in need of treatment.

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1. What is the estimated prevalence of rosacea globally (inclusive of white and non-white populations)?
   a. 1%
   b. 2%
   c. 10%
   d. 20%

2. Which subtype of rosacea has a male predominance?
   a. Erythematotelangiectatic
   b. Papulopustular
   c. Phymatous
   d. Ocular

3. A 36-year-old female with skin type VI presents with an erythematous plaque on the central face, which condition is the least likely diagnosis?
   a. Lupus
   b. Tinea faciei
   c. Rosacea
   d. Sarcoidosis

4. Which treatment option is best for a patient with Fitzpatrick skin type IV requesting treatment for telangiectasia?
   a. Doxycycline
   b. Oxymetazoline
   c. IPL
   d. PDL

5. Which of the following adverse psychosocial effects is correlated with disease severity?
   a. Stigmatization
   b. Anxiety
   c. Depression
   d. Social anxiety disorder

6. Which of the following therapies is contraindicated in a rosacea patient with type IV skin?
   a. Brimonidine
   b. Oxymetazoline
   c. IPL
   d. PDL

Evaluation Form

PATIENT-FOCUSED SOLUTIONS IN ROSACEA MANAGEMENT: TREATMENT CHALLENGES IN SPECIAL PATIENT GROUPS

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Please answer the following questions using the appropriate rating:

1 = Strongly Disagree	*2 = Disagree*	*3 = Neutral*	*4 = Agree*	*5 = Strongly Agree*

1. The information presented was timely and will influence how I practice.

1 2 3 4 5

2. The information presented enhanced my current knowledge base

1 2 3 4 5

3. The information presented addressed my most pressing questions

1 2 3 4 5

4. The activity provided new ideas or information I expect to use

1 2 3 4 5

5. The activity addressed competencies identified by my specialty

1 2 3 4 5

6. The activity avoided commercial bias or influence

1 2 3 4 5

Impact of the Activity

1. Name one new strategy you learned as a result of completing this activity:

_____

2. Name one thing you intend to change in your practice as a result of completing this activity:

_____

3. Please provide any additional comments onthis activity:

_____

4. Please list any topics you would like to see addressed in future educational activities:

_____