

2. Bunyaratavej S, Rujitharanawong C, Kasemsarn P, Boonchai W, Muanprasert C, Matthapan L, et al. Skin scrapings versus standardized skin surface biopsy to detect *Demodex* mites in patients with facial erythema of uncertain cause – a comparative study. *Indian J Dermatol Venereol Leprol*. 2016;82:519–22, <http://dx.doi.org/10.4103/0378-6323.174423>
3. Blakley BR, Rousseaux CG. Effect of ivermectin on the immune response in mice. *Am J Vet Res*. 1991;52:593–5.
4. Schaller M, Gonser L, Belge K, Braunsdorf C, Nordin R, Scheu A, et al. Dual anti-inflammatory and antiparasitic action of topical ivermectin 1% in papulopustular rosacea. *J Eur Acad Dermatol Venereol*. 2017, <http://dx.doi.org/10.1111/jdv.14437>
5. Lacey N, Delaney S, Kavanagh K, Powell FC. Mite-related bacterial antigens stimulate inflammatory cells in rosacea. *Br J Dermatol*. 2007;157:474–81.
6. Gallo R, Drago F, Paolino S, Parodi A. Rosacea treatments: what's new and what's on the horizon? *Am J Clin Dermatol*. 2010;11:299–303, <http://dx.doi.org/10.2165/11537020-000000000-00000>
7. Parodi A, Paolino S, Greco A, Drago F, Mansi C, Rebora A, et al. Small intestinal bacterial overgrowth in rosacea: clinical effectiveness of its eradication. *Clin Gastroenterol Hepatol*. 2008;6:759–64, <http://dx.doi.org/10.1016/j.cgh.2008.02.054>
8. Agnoletti AF, DE Col E, Parodi A, Schiavetti I, Savarino V, Rebora A, et al. Etiopathogenesis of rosacea: a prospective study with a three-year follow-up. *G Ital Dermatol Venereol*. 2016.
9. Drago F, De Col E, Agnoletti AF, Schiavetti I, Savarino V, Rebora A, et al. The role of small intestinal bacterial overgrowth in rosacea: a 3-year follow-up. *J Am Acad Dermatol*. 2016;75:e113–5, <http://dx.doi.org/10.1016/j.jaad.2016.01.059>

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## Reply To: The Possible Combined Action of Different Trigger Agents in Rosacea



### Réplica a ‘‘Posible acción combinada de los diferentes agentes desencadenantes en la rosácea’’

Dear Editor,

I thank Ciccarese et al. for their comments and welcome their thoughts about my article on the successful therapy of papulopustular rosacea in an immunocompetent patient.<sup>1</sup>

Rosacea is a chronic inflammatory condition diagnosed clinically. In the absence of clinical findings suggestive of any underlying comorbidity, analytical assessment or histological study is largely unnecessary.<sup>2</sup> Skin surface biopsy technique and skin scrapings may help visualize mites from follicular canals, but the relevance of this finding to the management of the condition is unclear and it is not routine. Nevertheless, we agree with Ciccarese et al. that ivermectin might play a role not only as an acaricide drug but also as an immunodulatory agent in controlling rosacea flares. In fact, the mechanism of action of topical immunomodulators such as pimecrolimus and tacrolimus (that proved non-efficacious in our patient) is centered on diminution of inflammation rather than antimicrobial action.<sup>3</sup>

Several microorganisms have been hypothesized to play a role in the pathogenesis of rosacea, but their exact role is unclear. Ciccarese and colleagues have published two studies on the role of *Demodex folliculorum*, *Helicobacter pylori* and small intestine bacterial overgrowth (SIBO)<sup>4,5</sup> in rosacea pathogenesis, concluding that the eradication of such underlying triggers might be crucial in improving the disease and maintaining the long-term clinical remission. However, a recent systematic review and meta-analysis

found weak non-statistical significance associations between rosacea and *H. pylori* infection as well as the effect of *H. pylori* eradication on rosacea symptoms.<sup>6</sup> Additionally, the pathogenic role of SIBO in rosacea patients has been challenged.<sup>7</sup>

From a practical point of view, evidence-based therapy of rosacea is still limited and therapeutic decisions are often based on personal experiences and patient preference.<sup>8</sup> Although there is still a lack of randomized controlled trials, oral ivermectin has already proved useful and well tolerated in immunocompetent children with rosacea, providing long-term remission after monotherapy with one single dose.<sup>9,10</sup> I am aware that oral ivermectin has only been assessed for short-term safety, but these preliminary studies provide promising data about oral ivermectin as an innovative and inexpensive therapeutic approach.

Ciccarese's comments about a possible combined action of different trigger agents in rosacea are interesting and may contribute to elucidating the underlying pathogenesis of the condition. They do not however allow any definite conclusions to be drawn about the relevance of SIBO in rosacea management.

## References

1. Hernandez-Martin A. Oral ivermectin to treat papulopustular rosacea in a immunocompetent patient. *Actas Dermosifiliogr*. 2017.
2. Two AM, Wu W, Gallo RL, Hata TR. Rosacea: part I. Introduction, categorization, histology, pathogenesis, and risk factors. *J Am Acad Dermatol*. 2015;72:749–58 [quiz 759-60].
3. Two AM, Wu W, Gallo RL, et al. Rosacea: part II. Topical and systemic therapies in the treatment of rosacea. *J Am Acad Dermatol*. 2015;72:761–70 [quiz 771-2].
4. Agnoletti AF, DE Col E, Parodi A, et al. Etiopathogenesis of rosacea: a prospective study with a three-year follow-up. *G Ital Dermatol Venereol*. 2016.

5. Drago F, De Col E, Agnoletti AF, et al. The role of small intestinal bacterial overgrowth in rosacea: a 3-year follow-up. *J Am Acad Dermatol.* 2016;75:e113–5.
6. Jorgensen AR, Egeberg A, Gideonsson R, et al. Rosacea is associated with *Helicobacter pylori*: a systematic review and meta-analysis. *J Eur Acad Dermatol Venereol.* 2017.
7. Gravina A, Federico A, Ruocco E, et al. *Helicobacter pylori* infection but not small intestinal bacterial overgrowth may play a pathogenic role in rosacea. *United Eur Gastroenterol J.* 2015;3:17–24.
8. Schaller M, Almeida LM, Bewley A, et al. Rosacea treatment update: recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Dermatol.* 2017;176:465–71.
9. Noguera-Morel L, Gerlero P, Torrelo A, et al. Ivermectin therapy for papulopustular rosacea and periorificial dermatitis in children: a series of 15 cases. *J Am Acad Dermatol.* 2017;76:567–70.
10. Brown M, Hernandez-Martin A, Clement A, et al. Severe demodexfolliculorum-associated oculocutaneous rosacea in a girl successfully treated with ivermectin. *JAMA Dermatol.* 2014;150:61–3.

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