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Reply to Italiano et al

Douglas H. Esposito[1], **Benjamin M. Rosenthal**[2], **Günther Slesak**[3], **Dennis Tappe**[4], **Ronald Fayer**[2], **Emmanuel Bottieau**[5], **Clive Brown**[1], **Martin P. Grobusch**[6], **Denis Malvy**[7], **Frank von Sonnenburg**[8], **Mark J. Sotir**[1], **Florian Steiner**[9], **Philipp Zanger**[10], and **Phyllis E. Kozarsky**[1,11]

[1]Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia [2]Beltsville Agricultural Research Center, US Department of Agriculture, Beltsville, Maryland [3]Tropenklinik Paul-Lechler-Krankenhaus, Tübingen, Hamburg, Germany [4]Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany [5]Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium [6]Centre of Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Academic Medical Centre, University of Amsterdam, The Netherlands [7]Division of Tropical Medicine and Clinical International Health, University Hospital Center, Bordeaux, France [8]Department of Infectious Disease and Tropical Medicine, University of Munich [9]Institute of Tropical Medicine and International Health, Charité–Universitätsmedizin Berlin [10]Institute of Tropical Medicine, Eberhard Karls University, Tübingen, Germany [11]Department of Medicine, Division of Infectious Diseases, Emory University, Atlanta, Georgia

TO THE EDITOR

We appreciate Italiano et al's [1] interest in our article [2] and agree that our case definition, described in our methods as "intentionally specific," may have excluded some travelers infected with *Sarcocystis nesbitti.* Nevertheless, we believe that published data from outbreak investigations in Malaysia offer ample evidence that peripheral eosinophilia and myositis are important distinguishing components of human acute muscular sarcocystosis (AMS) [2–8]. It is expected that some patients would not have these findings at any given point in their illness; indeed, our Figure 4 shows subthreshold laboratory values during the late phase of disease [2], a finding corroborated elsewhere [3–6]. We concur that some ill patients will not develop detectable eosinophilia or myositis at all. As in all infectious diseases, variations in the clinical manifestations, laboratory testing results, and the courses of illness should be expected. Such variation may stem from host factors, the infectious load, or the infecting *Sarcocystis* species [9] or even strain. In this light, performing serial clinical and laboratory investigations seems warranted when evaluating and managing patients with suspected AMS.

Correspondence: Douglas H. Esposito, MD, MPH, Division of Global Migration and Quarantine, Travelers' Health Branch, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd, NE, MS E-03 Atlanta, GA 30333 (hgj4@cdc.gov).

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Italiano et al express concern that we restricted “analysis to those persons who sought care after the fourth postdeparture week.” However, we excluded no data from patients presenting early. We did, however, confirm through a stratified subanalysis that the biphasic nature of AMS persisted after removing those patients who presented early, thereby strengthening the validity of that observation.

We believe that recommending routine use of expensive whole-body magnetic resonance imaging (MRI) to guide muscle biopsy in patients with suspected AMS [1, 3] must await evidence that MRI is superior to physical findings in locating areas of maximal inflammation in *Sarcocystis* species infections, that parasite encystation occurs preferentially in these same inflamed areas, and that biopsy itself is routinely indicated. We interpret the available MRI data as having confirmed edema at painful and visibly swollen sites but not necessarily as having found unsuspected occult edema [4, 5].We are unaware of published data attributing myositis to parasite encystation; the cause of myositis in AMS and its relationship to the local presence of tissue sarcocysts remains unknown. Although sarcocysts of some species predominate in cardiac, diaphragm, and tongue muscle [9, 10], there are no data demonstrating especially marked inflammation in these sites. The absence of inflammation immediately surrounding intramyocytic sarcocysts is well documented [2, 3, 8–10]. Finally, with no proven treatment, invasive muscle biopsy may be better reserved for the sickest patients or for those requiring investigation of other treatable conditions rather than as a routine diagnostic pursuit to be done “wherever possible,” as recommended by Italiano et al [3].

We agree with Dr Italiano that the manifestations of human AMS require more study and therefore caution against hasty definitions, conclusions, and recommendations. Careful and thoughtful consideration of all new human and animal data on this disease as they emerge is warranted.

References

1. Italiano CM, Wong KT, AbuBakar S, et al. Avoid haste in defining human muscular sarcocystosis. Clin Infect Dis. 2015; 60:1134. [PubMed: 25537869]
2. Esposito DH, Stich A, Epelboin L, et al. Acute muscular sarcocystosis: an international investigation among travelers returning from Tioman Island, Malaysia, 2011–2012. Clin Infect Dis. 2014; 59:1401–1410. [PubMed: 25091309]
3. Italiano CM, Wong KT, AbuBakar S, et al. *Sarcocystis nesbitti* causes acute, relapsing febrile myositis with a high attack rate: description of a large outbreak of muscular sarcocystosis in Pangkor Island, Malaysia, 2012. PLoS Negl Trop Dis. 2014; 8:e2876. [PubMed: 24854350]
4. Abubakar S, Teoh BT, Sam SS, et al. Outbreak of human infection with *Sarcocystis nesbitti* Malaysia, 2012. Emerg Infect Dis. 2013; 19:1989–1991. [PubMed: 24274071]
5. Lau YL, Chang PY, Tan CT, Fong MY, Mahmud R, Wong KT. *Sarcocystis nesbitti* infection in human skeletal muscle: possible transmission from snakes. Am J Trop Med Hyg. 2014; 90:361–364. [PubMed: 24420776]
6. Arness MK, Brown JD, Dubey JP, et al. An outbreak of acute eosinophilic myositis attributed to human *Sarcocystis* parasitism. Am J Trop Med Hyg. 1999; 61:548–553. [PubMed: 10548287]
7. Slesak G, Schäfer J, Langeheinecke A, Tappe D. Prolonged clinical course of muscular sarcocystosis and effectiveness of cotrimoxazole among travelers to Tioman Island, Malaysia, 2011–2014. Clin Infect Dis. 2014; 60:329. [PubMed: 25301217]

8. Tappe D, Ernestus K, Rauthe S, et al. Initial patient cluster and first positive biopsy findings in an outbreak of acute muscular *Sarcocystis*-like infection in travelers returning from Tioman island, peninsular Malaysia, in 2011. J Clin Microbiol. 2013; 51:725–726. [PubMed: 23224083]

9. Dubey, JP.; Speer, CA.; Fayer, R. Sarcocystosis of animals and man. Boca Raton, FL: CRC Press, Inc; 1989.

10. Wong KT, Pathmanathan R. High prevalence of human muscle sarcocystosis in south-east Asia. Trans R Soc Trop Med Hyg. 1992; 86:631–632. [PubMed: 1287922]