

# Patient Centered Care Advocacy Group

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## Information Quality Appeal

### Frequency of EM Rash in Patients with Lyme Disease

July 16, 2019

On March 14, 2019, the Patient Centered Care Advocacy Group submitted an information quality request for correction (case #65) regarding information disseminated by the Centers for Disease Control and Prevention (CDC) about the frequency of erythema migrans (EM) rash in patients with Lyme disease. On July 10, 2019, we received a letter (dated June 17) from Lyle Petersen, MD, MPH, Director, CDC Division of Vector-Borne Diseases that denied our requested corrective actions. (Copies of our request and Dr. Peterson's response are attached.) We are appealing this denial decision as follows.

#### Description of Contested Information

The contested information includes statements in CDC publications, web pages and presentation materials that the erythema migrans rash "occurs in 70–80% of the patients with Lyme disease."

#### CDC Publications

In the CDC publication, *Tickborne Diseases of the United States, A Reference Manual for Healthcare Providers, Fifth Edition, 2018*, the section on Lyme disease includes the following statement:

*"The erythema migrans (EM) rash occurs in 70–80% of patients with Lyme disease."*

Corrections are needed in the print and PDF versions:

- Print: Page 28
- PDF: [www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf](http://www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf)

#### CDC Websites

Similar statements are found on the following web pages.

1. [www.cdc.gov/ticks/tickbornediseases/lyme.html](http://www.cdc.gov/ticks/tickbornediseases/lyme.html)

*"The erythema migrans (EM) rash occurs in 70–80% of patients with Lyme disease."*

2. [www.cdc.gov/ticks/symptoms.html](http://www.cdc.gov/ticks/symptoms.html)

*"This rash occurs in approximately 70-80% of infected persons and begins at the site of a tick bite."*

3. [www.cdc.gov/lyme/signs\\_symptoms/index.html](http://www.cdc.gov/lyme/signs_symptoms/index.html)

*"Erythema migrans (EM) rash: Occurs in approximately 70 to 80 percent of infected persons."*

#### Problems with CDC's Response

The letter from Dr. Lyle Petersen in response to the Information Quality Request requesting that the CDC revise information related to the frequency of erythema migrans (EM) rash in patients with Lyme disease, does not provide sufficient or adequate reasons why the contested information should not be revised or removed.

There are several assertions made in this letter that are inaccurate, incorrect, or based on opinion. Dr. Petersen begins by noting that the request for correction “refers to Hanrahan et al. (1984) as the source of CDC’s information about erythema migrans rash” and then states the use of that reference to be “incorrect.” As pointed out in the original request, all research studies published **previous** to this study showed the rate of EM in patients considered to have “Lyme disease” to be much lower than 70–80%. In the history of research on Lyme disease, the **first** publication that investigated the epidemiology of “Lyme disease” and concluded that the EM rash occurred in 70-80% of patients with Lyme disease was Hanrahan et. al. (1984). This oft-repeated statistic traces directly to this article. [1]

In addition, Dr. Petersen states:

“There are many sources of data supporting a erythema migrans (EM) frequency of 70% or more among patients with Lyme disease.” This assertion is rhetorical hyperbole to inflate the perception it is supported by published research. If there are in fact “many sources” they should have been included (and cited) in this response.

Dr. Petersen also asserts:

“These data, as well as the rare, small series claiming a lower rate of EM, are subject to varying degrees of ascertainment bias that may influence the relative distribution of symptoms.” Referring to other peer-reviewed, published research studies as “rare” and “small” is another rhetorical attempt to dismiss the outcomes of this research, which contradicts the prevailing dogma endorsed by the CDC. The much broader issue is that in general, there are **very few published research studies** available to cite, in which the true rate of association between EM and infection with *Borrelia burgdorferi* (i.e. Lyme disease) was objectively investigated.

In the next sentence, Dr. Petersen notes that, “The most reliable information, therefore, is derived from prospective cohort studies”

The article cited by Dr. Petersen as “reliable information” is actually a letter to the editor published in the New England Journal of Medicine. It is a less than 600 word overview of a “trial of vaccination against Lyme disease.”[2]

The data from the “prospective cohort study” were derived from a previous study by the same author (Steere), and includes “microbiologically confirmed” EM, systemic symptoms without EM or asymptomatic seroconversion.

For any study investigating the correlation between infection and a surrogate marker, the only objective way to determine if a person is infected is to show direct evidence of the infection, by detection of either bacteria through culture, or bacterial DNA, RNA, or other cellular component. In this study, the only direct evidence of infection used was microbiological culture of the *B. burgdorferi* from the skin rash.

The data from the cohort study shows that of the 267 participants who were designated as having an EM, only 118 had a “microbiologically confirmed EM.” The association between *B. burgdorferi* infection and EM is therefore only 44%. This group (and only this group) of 118 microbiologically confirmed EM cases were additionally characterized in a companion article published as a peer-reviewed article the previous year.[3]

Serology, measured by laboratory test, does not provide direct evidence of infection and indicates only exposure, not infection. However, even if serology results are included in the data analysis, the rate of association between EM and Lyme disease is only 53%. The two criteria used in this study were EM noted by physician or EM noted by patient, which are in fact, subjective.

The assertion made in the official CDC response by Dr. Petersen stipulating that 73% of participants with EM showed “definite or possible *B. burgdorferi* infection” is not supported by the data presented in the study. The fact that this study and a lack of other research on the frequency of EM is enough for the CDC to contend that “the best available evidence supports an estimate of 70-80% as the frequency of EM among patients with Lyme disease” is concerning. Does this truly represent the CDC’s view of what qualifies as the “best available evidence” to support an opinion that profoundly impacts the diagnosis and treatment of patients with Lyme disease in the US?

### **Research that Supports Our Appeal**

The agency response dismisses existing evidence showing that the association between EM and *B. burgdorferi* infection (Lyme disease) is lower than what the CDC asserts. CDC surveillance data from 1992-2006 documented that 31% of surveillance cases lacked an EM rash.[4] Patient-derived data from the MyLymeData patient registry (a project by LymeDisease.org), noted that only 34% of 3,903 patients recalled having an EM rash.[5]

This appeal contends that the most objective and least biased studies done with non-human primates (NHP) to empirically investigate many of the clinical aspects of Lyme disease, provide definitive data on the rate of association between EM and infection by *B. burgdorferi*. NHP studies have previously demonstrated that the macaque model most closely resembles human borreliosis and provides the best experimental model to study Lyme disease.[6]

In a comprehensive study of the pathobiology of infection with *B. burgdorferi* in outbred non-human primates (NHPs), the rate of classic EM in NHPs infected by nymph tick bite and confirmed to be infected by culture or PCR, was only 10%.[6] It is also noted by the NHP researchers that nearly half of infected NHPs do not develop any erythematous rash (personal communication with the study authors) following infection.

Collectively, the limited research that has been done to investigate the frequency of EM in human Lyme disease patients—along with contradictory evidence from human studies and particularly the research done with non-human primates— does not support the opinion that 70-80% of Lyme disease patients show an EM rash as a result of infection by *B. burgdorferi*.

This statistic should not be cited or used until an objective and unbiased study of the true rate of occurrence of a typical or atypical EM rash in humans who can objectively be identified as being infected with *B. burgdorferi*, is conducted.

### **Impact**

Misinformation from CDC regarding an EM rash accompanying Lyme disease 70-80% of the time misleads patients and healthcare professionals. This can increase the likelihood that patients with Lyme disease may get misdiagnosed or go undiagnosed, accompanied by treatment denial or delay. Research shows that delayed treatment increases the rate of treatment failure.[7]

## Conclusion

In summary, misleading information from CDC stating that an EM rash accompanies Lyme disease 70-80% of the time can have a profoundly negative impact on the diagnosis and treatment of patients with Lyme disease across the United States. Therefore, it is in patients' best interests that this information be corrected, amended and/or updated on CDC publications, websites, and presentation materials.

Thank you for your reconsideration of this matter. We look forward to your response.

## Complainants



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## References

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[www.frontiersin.org/articles/10.3389/fmed.2017.00224/full](http://www.frontiersin.org/articles/10.3389/fmed.2017.00224/full)