



Two Standards of Care

ILADS and IDSA guidelines reflect deeply divided opinions about treatment approaches, clinical judgment and patient preferences

By Lorraine Johnson, JD, MBA

Medically recognized standards of care are those accepted by medical experts as appropriate treatments for a disease or condition and commonly used by healthcare professionals. Medical recognition of standards of care is typically represented by publication in a peer-reviewed journal or some form of recognition by a professional medical society.(1) Multiple standards of care exist for over 25 medical conditions that have posted guidelines on the National Guidelines Clearinghouse.(2)

In Lyme disease, opinion within the medical community is deeply divided regarding the best approach for treating Lyme disease, particularly when patients remain ill after treatment with short-term protocols. This split has resulted in two standards of care — one advanced by the Infectious Diseases Society of America (IDSA) and the other by the International Lyme and Associated Diseases Society (ILADS).(1, 2) Both viewpoints are reflected in peer-reviewed guidelines and constitute medically recognized standards of care.

To increase the quality and trustworthiness of guidelines, in 2010 the Institute of Medicine (IOM) adopted standards that include the use of a rigorous evidence assessment scheme called GRADE, patient representation in the guideline development process, and regular updating of guidelines.(2) The National Guidelines Clearinghouse (NGC), which evaluates and lists evidence based guidelines now requires that guidelines listed be based on GRADE.

In 2014 ILADS published the first Lyme disease guidelines that conform with GRADE and included patient representation in development. These are now listed on the NGC. The IDSA guidelines, which were published in 2006, did not use GRADE and did not provide patient representation. These guidelines have been removed from the NGC because they are outdated and no longer conform to its quality standards for listing.

Guidelines reflect both the evidence base and value judgments of the guidelines panel. Factors associated with divergent guidelines include a weak evidence base, clinical experience, patient preferences, treatment availability, and clinician values.(3) The main difference between the IDSA and ILADS guidelines is that in the face of scientific uncertainty, ILADS defers to clinical judgment and patient preferences while the IDSA makes very strong recommendations against treatment and severely restricts the application of clinical judgment.

A recent study funded by the Centers for Disease Control and Prevention (CDC) surveyed a representative sample of people in the U.S. population and found that only 39% of those with Lyme disease were treated in accordance with blanket short-term recommendations in the IDSA guidelines. The majority were treated for longer periods.(4)

In 2013, the CDC dramatically revised its estimate of the annual incidence of Lyme disease from roughly 30,000 cases per year to over 300,000 cases, a ten-fold increase.(5) To put this in perspective, the annual incidence of Lyme disease is now 1.5 times more than the estimated number of cases of breast cancer and six times higher than the annual incidence of HIV/AIDS. Federal funding of Lyme disease research has been meager, however. For example, while Lyme disease occurs six times more often annually than HIV/AIDS, it receives less than 1% of the funding allotted to HIV/AIDS by the National Institutes of Health (NIH).(6)

Inaccurate diagnostic tests, based on technology over 20 years old, create medical uncertainty in both the diagnosis and treatment of Lyme disease. The primary diagnostic tests detect antibodies — past exposure to infection not active infection. Unlike tests for HIV/AIDS, which have a sensitivity and specificity of over 99%, Lyme tests are highly insensitive and miss more than half of cases.(7)

Further uncertainty results from the high rate of treatment failure for all stages of Lyme. According to the CDC, as many as 20% of patients remain ill after the short-term treatment protocol recommended by the IDSA.(8) Other studies suggest the treatment failure rate for early Lyme disease may be as high as 36%.(9) In late Lyme disease, treatment failure rates may exceed 50%.(10) When patients remain ill after treatment, antibody tests cannot tell us whether the bacteria persist or whether treatment is effective. Persistence has been demonstrated in both animal and human studies after treatment with antibiotics, however, when more invasive testing such as tissue and organ biopsies is performed.(18,19-21)

Only three NIH-funded trials have been conducted on the treatment of chronic Lyme disease (CLD).(11-14) Sample sizes were extremely small, ranging from 37 to 129 randomized. Just 20 to 55 patients completed the treatment arm in these trials. Critics have pointed out that studies this small lack sufficient statistical power to measure clinically relevant improvement.(2,3) Nevertheless, two of the three studies demonstrated that retreatment improved some patients' measures, such as fatigue and pain. In addition, a number of observational trials have demonstrated that most patients improve with continued treatment.(7, 15-18)

CLD can be long lasting and significantly impair patient quality of life. It also may be costly to patients, employers, healthcare systems, and society. In a survey of more than 5,000 patients with CLD, half report that they have been ill for more than 10 years. These patients suffer a worse quality of life than those with most other chronic illnesses, including congestive heart failure, diabetes, multiple sclerosis and arthritis.(19) Over 43% report that they had to stop working, and 25% report that they have been on disability at some point in their illness.(19) They are five times more likely to visit healthcare providers and twice as likely to be seen in emergency rooms compared to the general population.(19) The cost of this increased healthcare utilization continues until patients are restored to health.

In the face of scientific uncertainty, clinical decisions should be based on the best currently available evidence. Today's patients cannot wait for tomorrow's research. The IDSA guidelines

deny treatment options to seriously ill patients. This results in unnecessary suffering for patients and is inhumane and unjust.

We agree with the AMA, ACP and other professional medical organizations that informed shared medical decision-making enhances the exercise of the patient's right of self-determination — a cornerstone of medical ethics.(3, 20) Shared decision-making is a collaborative process in which the clinician offers options and describes their risks and benefits, and the patient expresses his or her preferences and values.(21) A goal of the U.S. Department of Health Services under the Healthy People 2020 program is to increase shared medical decision-making.

Since two standards of care exist for Lyme disease, we believe that:

- Physicians, insurers, patients and governmental agencies should be educated that two treatment approaches exist;
- Physicians should inform patients about the risks and benefits of all available treatment options, and engage in shared decision-making, taking into account patient preferences and values and the importance of autonomy in matters involving health related quality of life and functional capacity;
- Insurance reimbursement should be provided for treatment rendered in accordance with either standard of care; and
- Government agencies should provide unbiased public information regarding both standards of care and treatment approaches.

References

1. Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klemmner MS, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2006 Nov 1;43(9):1089-134.
2. Cameron DJ, Johnson LB, Maloney EL. Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Review Anti-Infective Therapy*. 2014 Sep;12(9):1103-35.
3. Institute of Medicine. *Clinical Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011. Available from: <http://bit.ly/1Cxulv6>.
4. Hook S, Nelson C, Mead P. Self-reported Lyme disease diagnosis, treatment, and recovery: Results from 2009, 2011, & 2012 Health Styles nationwide surveys. Presented at The 13th International Conference on Lyme Borreliosis and other Tick Borne Diseases, Boston, MA Aug 19, 2013. Available from: <http://bit.ly/1B2WrfZ>.
5. Centers for Disease Control and Prevention. CDC provides estimate of Americans diagnosed with Lyme disease each year. 2013; Available from: <http://1.usa.gov/1wW0HIQ>.
6. National Institute for Health. Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC). Table published March 7, 2014.: Available from: <http://1.usa.gov/18ksEnp>.
7. Stricker RB, Johnson L. Lyme disease diagnosis and treatment: lessons from the AIDS epidemic. *Minerva Med*. 2010 Dec;101(6):419-25.
8. Centers for Disease Control and Prevention. Lyme Disease: Treatment. Available from: <http://1.usa.gov/1w4iiTN>.
9. Aucott JN, Rebman AW, Crowder LA, Kortte KB. Post-treatment Lyme disease syndrome symptomatology and the impact on life functioning: is there something here? *Qual Life Res*. 2013 Feb;22(1):75-84.
10. Johnson L, Stricker RB. Treatment of Lyme disease: a medicolegal assessment. *Expert review of anti-infective therapy*. 2004 Aug;2(4):533-57.
11. Fallon BA, Keilp JG, Corbera KM, Petkova E, Britton CB, Dwyer E, et al. A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy. *Neurology*. 2008 Mar 25;99:992-1003.
12. Fallon BA, Petkova E, Keilp J, Britton C. A reappraisal of the U.S. clinical trials of Post-Treatment Lyme Disease Syndrome. *Open Neurology Journal*. 2012;6(Supp. 1-M2):79-87.
13. Klemmner M, Hu L, Evans J, Schmid C, Johnson G, Trevino R, et al. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. *The New England Journal of Medicine*. 2001 Jul 12:85-92.
14. Krupp LB, Hyman LG, Grimson R, Coyle PK, Melville P, Ahnn S, et al. Study and treatment of post Lyme disease (STOP-LD): a randomized double masked clinical trial. *Neurology*. 2003 Jun 24;60(12):1923-30.

15. Donta S. Tetracycline therapy for chronic Lyme disease. *Clin Infect Dis*. 1997 Jul;25 Suppl 1:S52-6.
16. Fallon BA. Repeated antibiotic treatment in chronic Lyme disease. *J Spirochet Tick-Borne Dis*. 1999;6(Fall/Winter):94-101.
17. Oksi J, Nikoskelainen J, Viljanen MK. Comparison of oral cefixime and intravenous ceftriaxone followed by oral amoxicillin in disseminated Lyme borreliosis. *Eur J Clin Microbiol Infect Dis*. 1998 Oct;17(10):715-9.
18. Wahlberg P, Granlund H, Nyman D, Panelius J, Seppala I. Treatment of late Lyme borreliosis. *J Infect*. 1994 Nov;29(3):255-61.
19. Johnson L, Wilcox S, Mankoff J, Stricker RB. Severity of chronic Lyme disease compared to other chronic conditions: a quality of life survey *PeerJ*. 2014; 2: Available from: <http://dx.doi.org/10.7717/peerj.322>.
20. Institute of Medicine: Evidence Communication Innovation Collaborative of the IOM Roundtable on Value and Science-Driven Health Care. Shared Decision-Making Strategies for Best Care: Patient Decision Aids. Washington, DC: National Academies Press; 2014. Available from: http://books.nap.edu/openbook.php?record_id=13058.
21. Informed Medical Decisions Foundation. What is shared decision-making?; Available from: <http://www.informedmedicaldecisions.org/what-is-shared-decision-making/>.