Understanding the Chronic Controversy

Contentious disagreement continues over conflicting guidelines, the existence of chronic infection, and the benefit of extended treatment

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Conflicting guidelines are common. The Institute of Medicine (IOM) notes that the National Guidelines Clearinghouse, which lists most important treatment guidelines, has identified more than 25 health conditions with conflicting treatment guidelines, including those on the expected (breast cancer screening) and the unexpected (urinary tract infections or GERD). Dr. Gordon Guyatt, a key authority on evidence-based guidelines, explains why:

"What tends to happen to experts is that they develop strong beliefs and tend to select supporting evidence to back up their beliefs, and this is how you have people making absolutely opposite recommendations … Evidence is never enough — it is always evidence in the context of values and preferences that influence guidelines and clinical care."

The two most hotly contested guidelines are those related to colorectal cancer and Lyme disease.

IDSA guidelines are largely opinion-based. Two research studies performed by IDSA members found that the IDSA guidelines are not based primarily on evidence, but rather on expert opinion. So the contentious issues in Lyme disease are about how people fill in the gaps in the evidence base.

Lyme has a poor research base. In Lyme disease the research base is very sparse. Most research conducted today is funded by pharmaceutical interest in new patentable drugs. Lyme disease does not attract pharma interest because it is mostly treated with off-label generic drugs. There are only three or four (depending on how you count) NIH-funded studies on treatment of chronic Lyme disease (CLD).

Sample sizes are too small. The few NIH funded trials have very, very small sample sizes (ranging from 18 to 70 people in the treatment arm). Small trials are known for leading to false negative results because they lack sufficient statistical power to detect even important differences. According to Dr. Guyatt, sample sizes in the thousands are necessary to demonstrate a lack of effectiveness. Small trials also do not reflect the clinical population. For instance, patients in the Klempner trial were required to be diagnosed and treated with early Lyme (e.g., based on an EM rash), but almost all patients with chronic Lyme (86%) are not diagnosed until at least four months after symptom onset.

Mixed trial results. Of the three NIH trials, two found benefits from extended treatment, one did not. The results of these trials are, hence, mixed.

Klempner results refuted by parallel animal trial: The single NIH trial that found no benefit to extended treatment was conducted by Klempner. This study of humans was supposed to be conducted at the same time as a parallel one with non-human primates (because unlike people, you can autopsy monkeys in a study to get further details). That parallel study conducted by Monica Embers *et al* was finally released in 2011, an unexpected 10-year lag in publication. Embers found that 75% of the monkeys treated with the Klempner protocol still had persistent infection, determined at necropsy with intensive tissue sampling. This means that the antibiotic type or duration was insufficient to clear the infection, which is what we see in humans. Embers also found that the diagnostic tests were bad.

Non-randomized trials show treatment benefit. Treatment of chronic Lyme disease is supported by non-randomized trials. A treatment trial of 277 patients by Dr. Sam Donta found that 70% improved with longer treatment. Drs Oksi and Wahlberg reported improvement in their separate trials.

When evidence is uncertain, physicians and patients need treatment options. The need to offer treatment options is widely acknowledged in other diseases when evidence is uncertain. For instance, women with breast cancer can choose radiation, chemotherapy, lumpectomy and/or mastectomy. Men with prostate cancer can choose watchful waiting, radiation, hormone therapy, and/or surgery. Lyme patients should be able to choose between extended treatment approaches or doing nothing. This choice is especially important since there are no other treatment options available for them.

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