**Management of Tick Bites and Investigation of Early Localized Lyme Disease: Flow Chart**

Introduction

The flow chart attempts to guide medical practitioners through a step-by-step course of action in handling patients who have been bitten by ticks or are symptomatic for Lyme disease.

The word "investigation" in the title implies that the author is unsure about the flow chart, and the information it contains. Unfortunately, the flow chart is stacked with discounting and dismissive information. From start to finish, it is erroneous and misleading. If this flow chart is adopted, it will be a thorn in the side of patients, and will be a health-care tragedy!

Blacklegged tick (no box number): The blacklegged tick, *Ixodes scapularis*, is a competent vector of the Lyme disease bacterium, *Borrelia burgdorferi*. However, the authors overlook the fact that other tick species have vector competency for *B. burgdorferi*. For instance, Scott et al. (2017) detected *B. burgdorferi* in 8 species of ticks in the Kenora area, and 5 of these species bite humans, and have vector competence for *B. burgdorferi*. These 5 human-biting species include *Ixodes angustus*, *Ixodes banksi*, *Ixodes cookei*, *Ixodes muris*, and *Ixodes scapularis*. Four of these five tick species are not mentioned in the flow chart.

Attachment time (no box number): The flow chart states that when the tick is attached for less than 24 hours, there is no risk of contracting Lyme disease. However, Cook (2015) indicates that when the tick salivary glands are infected with *B. burgdorferi*, accelerated transmission of Lyme disease spirochetes occurs in less than 24 hours. Also, *Anaplasma phagocytophilum* (human anaplasmosis), a tick-borne disease, can be transmitted in less than 24 hours (des Vignes et al., 2001), and is sometimes a co-infection of *B. burgdorferi*. In addition, Powassan virus can be transmitted in less than 15 minutes (Ebel et al., 2004). Then, again, who really knows how long the tick was attached? Less than 14% of Lyme disease patients remember a tick bite (Berger 1989). If, in fact, the person saw the tick at the point of entry, he/she would remove the tick immediately. I have seen multiple times where medical practitioners incorrectly judge the attachment time. This is one area of medicine about which they know nothing.

Wait and see approach to treatment (no box number)

The "wait-and-see" approach is precarious. First, ticks carry a multitude of tick-borne pathogens. Second, waiting 30 days allows *B. burgdorferi* to sequester and hide and persist in deep-seated tissues, namely ligaments, tendons and bone. Third, *B. burgdorferi* is known to enter the brain in 24 hours. Fourth, certain pathogens, such as *Anaplasma phagocytophilum* (human anaplasmosis) can be transmitted in less than 24 hours (des Vignes et al., 2001) and, similarly, Powassan virus can be transmitted from tick to host in less than 15 minutes (Ebel et al., 2004). Fifth, *B. burgdorferi* is known to be transmitted in less than 24 hours when the tick salivary glands are infected (Cook, 2015).

Wait 30 days (no box number)

In 30 days, *B. burgdorferi* has a chance to become well established in the body, especially in deep-seated tissue (i.e., ligament, tendon, bone, brain, eye). The Lyme disease bacterium is pleomorphic, and has 5 diverse forms (spirochetes, round bodies, blebs, granules, biofilms) (Meriläinen et al., 2015). Not only does *B. burgdorferi* have persister cells (Lewis, 2007), it can persist and survive after 28 days of treatment (Embers et al. 2017). Not only is a waiting period of 30 days precarious, it is a shortsighted approach to treating a stealth pathogen. Delay in treatment is a tragedy in the making. In fact, I have a list of peer-reviewed scientific references on the persistence of Lyme disease and, to date, I have 343 references.

There are far too many lives being destroyed because of the Centers for Disease Control and Prevention's proverb that "Lyme is hard to catch, easy to diagnosis, easy to cure." This by-line is certainly a simplistic and draconian approach to Lyme disease. We have young people who can't go to school, and end up in wheel chairs because of this backward, wait-and-see policy. Some young people have fatal outcomes (i.e., Ms. Chiara Divide) and, in addition, adults die from Lyme disease (Liegner et al., 1997).

Based on U.S. figures, we extrapolate that 50 Lyme disease patients in Ontario commit suicide annually (Adrion et al., 2015; Bransfield, 2017). Delays in prophylactic treatment are counterintuitive and, importantly, such delays are a waste of valuable time in getting successful treatment. Based on the current, antiquated treatment policy, it is no wonder that Lyme disease patients are in such dire straits in Ontario.

Travel to a risk area (no box number)

Whether a patient has travelled to a risk area or not can be a very misleading question. The person may live in an Lyme disease endemic area, and not know it. They may have been bitten by an *B. burgdorferi*-infected, songbird-transported tick dropped in their own backyard. Some areas in Ontario (i.e., Dundas, Rainy River, Kenora) are not included in the 2017 Lyme disease estimated risk map. This is another obvious oversight. I have a list of 43 Lyme disease endemic areas in Ontario, and only part of these are accounted for in box 5. In essence, the list is only a sample of all the established populations of *I. scapularis* and Lyme disease endemic areas.

Furthermore, migratory songbirds widely disperse Lyme disease vector ticks during northward spring migration, and people do not have to visit an endemic area to contract Lyme disease (Scott et al., 2010; Scott et al., 2012; Scott & Durden, 2015).

Alternative cause of symptoms (no box number)

Although another pathogen/diagnosis may be correct, there is no consideration given to the fact that Lyme disease can be persistent. Once *B. burgdorferi* becomes established in deep-seated tissues, it is hard to treat successfully.

Signs and symptoms (box 1)

In actuality, the "erythema migrans rash ~70%" is out-of-date, and highly misleading. Less than 40% of Lyme disease patients develop an erythema migrans (EM) rash (Stonehouse et al., 2010; Johnson et al., 2014; Schutzer et al., 2013) There is no mention that more than 50% of EM rashes are homogenous rashes; this is a gross oversight. Additionally, there is no mention that there are at least 19 different rashes associated with Lyme disease. The approach to EM rashes is myopic in scope, especially, for health-care providers.

Prevalence of symptoms in patients presenting with possible early localized Lyme disease (box 2)

Given the symptoms listed, it is likely that the patient also has a co-infection, such as human babesiosis. There is no mention of co-infections anywhere on the flow chart⎯a blatant oversight.

When it comes to "patient exposed to ticks," only 14% of Lyme disease patients recall a tick bite (Berger, 1989). Nymphs, in particular, are very covert, and take a blood meal, and drop off without a person knowing it. The statement, "If symptoms persist, consider an alternate diagnosis" overlooks the fact that Lyme disease is often persistent after antibiotic treatment (Embers et al., 2017; Middelveen et al., 2018).

Ticks and stages (box 3)

The flow chart assumes that medical practitioners know how to identify ticks. Plain and simple, they do not know how to identify ticks. Box 3 overlooks the fact that ticks change their appearance (shape, size, colour) dramatically when they become engorged. Anyone identifying ticks needs a stereoscopic microscope, and extensive training to identify ticks properly. Ticks have 4 developmental life stages (eggs, larvae, nymphs, adults [male, female]), and the 3 motile stages all look dramatically different.

There are over 40 species of ticks in Canada, and additional tick species are imported into Canada annually by migratory songbirds during northward spring migration (Scott et al., 2001; Morshed et al., 2005; Ogden et al., 2008; Scott et al., 2010, 2012; Scott & Durden, 2015; Scott & Durden, 2016). This flow chart only deals with 2 tick species, and leaves out other Lyme disease vector ticks.

The *I. scapularis* and *D. variabilis* ticks displayed in box 3 are twice their normal size. Not only is the size not accurate, the shape of the immature stages (larvae, nymphs) is not correct. The diagram overlooks the fact that engorged ticks look dramatically different than the unfed ticks in the diagram. None of the ticks in box 3 is engorged. A fully engorged *D. variabilis* female can be 3 cm in diameter (Chagnon et al., 2014). It can be overlooked by medical practitioners, especially if it is attached in the hair (Chagnon et al., 2014). Furthermore, it can cause tick paralysis (Chagnon et al., 2014).

Risk areas (box 4)

The authors contend that visiting a risk area is an important epidemiological criteria to determine whether a person has acquired Lyme disease. However, songbirds widely disperse Lyme disease vector ticks across Canada, and one does not have to go to an endemic area to contract Lyme disease (Scott et al., 2001; Morshed et al., 2005; Ogden et al., 2008; Scott et al. 2010, 2012; Scott & Durden, 2015). There is no mention of the fact that 35% of the *I. scapularis* nymphs collected from songbirds in central and eastern Canada are infected with *B. burgdorferi* (Scott & Durden, 2015).

If a person is bitten by a tick, prophylaxis treatment is warranted. Ticks, regardless of species, are notorious for harbouring tick-borne pathogens. Ticks are nature's dirty syringes. For example, the American dog tick, *Dermacentor variabilis*, is known to carry and transmit *Francisella tularenis* (tularema), *Rickettsia rickettsii* (Rocky Mountain spotted fever), *Ehrlichia chaffeensis* (human monocytic ehrlichiosis), and *Ehrlichia ewingii* (canine granulocytic ehrlichiosis). Each of these pathogens can be transported into Canada by bird-feeding, pathogen-laden *Amblyomma* ticks during northward spring migration and, after the molt, these ixodid ticks can bite humans.

Box 4 is nearsighted in its approach to the distribution of Lyme disease. In fact, the zoogeographic distribution reaches 4 continents, and includes at least 86 countries. There is no mention of Russia which has over 10,000 Lyme disease cases yearly. There is no mention of the fact that blacklegged ticks can harbour at least 10 different tick-borne pathogens.

Setting the *B. burgdorferi* infection prevalence greater than 20% for treatment is a counterproductive and dangerous precedent. There should never be an arbitrary figure for treatment because no one knows for sure whether any given tick is infected or not. Furthermore, there is no justification for this level of *B. burgdorferi* prevalence (Eisen et al., 2016).

Post-exposure prophylaxis (box 5)

The "1−3%" figure has no validity. Using this range of figures plays Russian roulette with Lyme disease patients. In central and eastern Canada, 35% of the *I. scapularis* nymphs collected from songbirds were infected with *B. burgdorferi* (Scott & Durden, 2015). Furthermore, on Corkscrew Island, in Lake of the Woods in northwestern Ontario, 41% of the unfed *I. scapularis* nymphs were infected with *B. burgdorferi* (Scott et al., 2016). Adults had an infection prevalence of 73%, the highest ever reported in Canada (Scott et al., 2016). For some strange reason, this endemic area was not posted on last year's (2017) Lyme disease estimated risk map for Ontario.

Laboratory testing (box 6)

The statement "Laboratory testing is not indicated for asymptomatic patients" is a unqualified statement and, in some cases, a moot point. Typically, patients are not going to consult a health-care provider unless they are symptomatic or have had a tick bite. If there was a tick bite, and the patient is within the timeframe for elevated serology, testing should be mandatory.

If one intimate partner in a relationship has Lyme disease, *Borrelia* testing is warranted for the asymptomatic partner (Middelveen et al., 2015). If the mother has Lyme disease, all the children should be tested regardless of whether they are asymptomatic or not. Their future is at stake. Congenital Lyme disease is a fact of life (MacDonald, 1989; Gardner, 2001; Vanderhoof-Forschner, 1997).

The two-tier Lyme disease testing is highly unreliable. In fact, the methodology only has a sensitivity of 48.6% in late Lyme disease (Fallon et al., 2014). Alternatively, the in-house Western blot in one U.S. laboratory has a sensitivity of 97% (Shah et al., 2014). This test has double the sensitivity of the two-tier Lyme disease serology test. Again, this very important point was overlooked.

Sensitivity of serological (two-tier) testing in patients with Lyme disease (box 7)

There is no provision given to the fact that *B. burgdorferi* is a stealth pathogen, and can slip past the immune system, and lodge in deep-seated tissues. This pathogenic trick is one reason why the two-tiered system fails miserably. The reference that is cited in box 7 (Aguero-Rosenfeld et al., 2005) selected patients who were already positive for Lyme disease and, consequently, generated inflated results. Such tactics constitute circular reasoning, and is no different than stacking the deck before the card game begins. This study is misleading and is highly flawed. It is junk science. It is no wonder that Lyme disease patients are "falling through the cracks." For years, they have been obtaining negative results when, in fact, they are infected with *B. burgdorferi*. Lyme disease patients have been duped by a flawed testing system.

When frontline allopathic physicians order a Western blot as the first screening test, they are told by PHO officials that there are "too many false positives." Such statements are highly fallacious because species-specific bands for *B. burgdorferi* don't lie. Based on the species-specific bands, it would be rare to have a false-positive Western blot (personal communication, Dr. Charles Ray Jones, New Haven, Connecticut).

Treatment (box 8)

The source of the treatment guidelines is not cited⎯a glaring omission. The Infectious Diseases Society of America (IDSA) guidelines for Lyme disease have been delisted by the National Guideline Clearinghouse, and are no longer valid. The International Lyme and Associated Diseases Society (ILADS) guidelines, which are the only authorized guidelines, have been completely overlooked in box 8. The drug recommendations in box 8 appear to be IDSA guidelines incognito. Once again, Lyme disease patients have been duped by Public Health Ontario officials.

Based on empirical experience, the "1 dose of doxycycline 200 mg, by mouth" for prophylaxis treatment has shown to be inadequate in most cases.

Conclusion

At almost every step of the flow chart, the boxes take a dismissive and discounting approach in handling tick bites and the diagnosis and treatment of Lyme disease. The author of this flow chart plays Russian roulette with patients' health at almost every step of the two-page flow chart. Overall, the flow chart is highly sceptical, and provides misinformation regarding Lyme disease. It is no wonder that Ontario residents have an enormous health-care problem with Lyme disease patients becoming completely disabled and, in many cases, beyond the point of recovery. We have far too many young people who can't go to school and adults who can't work. Some patients are bedridden or in wheelchairs. Others are suicidal and homocidal (Bransfield, 2018). Tragically, we have patients dying from persistent Lyme disease.

Currently, over 3,000 Canadian patients are having to go out-of-province or out-of-country for diagnosis and treatment of Lyme disease and associated tick-borne diseases. We have a health-care calamity!

Again, the flow chart is playing Russian roulette with peoples' lives! Timing is of the essence in treating Lyme disease! Early treatment is paramount!

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