



LYME DISEASE
ASSOCIATION OF AUSTRALIA
For Lyme Disease Awareness & Action

Ask the Doctor: A Six Part Series on Lifestyle Recommendations to Look After Your Nervous System

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Part 5: The Terrain, The Neuro Immune System & its interface.

'The terrain' is often referred to by integrative health practitioners as the background landscape of how healthy a tissue is. It is usually used in reference to how toxic a person is and is said to reflect the reasons for ongoing poor health and poor response to treatment of an infection. In this article, I describe the specific aspects to consider regarding 'the terrain' and how it is related to the nervous system and inflammation.

When we talk about an infection, the focus should not be just about the organism. It is in fact, a combination whereby microbial genes interact with our genes and this can then dictate the outcome of the mix. Just like in a relationship, this is a partnership where it takes two to tango with the pathogens that we carry. There are no two identical patients because the entire nature of this relationship involves life time environmental exposures (called the 'exposome') and biological components in our internal environment (called the 'interactome'). Hence it becomes less ideal to rely on protocols alone and may be much more conducive to work out what we need from first principles.

Since the days of the Human Genome Project, we have DNA technology that has broadened our scope of understanding how life time environmental exposures can affect an individual's risk of disease and also how all these components interact with each other. It is no

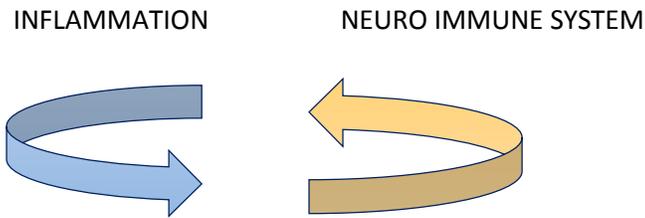
longer valid to consider our human DNA genome as a single static entity but instead, we should consider how it interacts with the ecological community of microorganisms in our body (called the 'microbiome') and all the biological triggers of inflammation (called the inflammasome). In relation to this, the popular gene mutations that are measured relating to vital metabolic repair processes (for example methylation), should be understood to be only a part of the whole picture.

For example, scientific literature describes how environmental pollutants such as mercury are playing a big role in altering the characteristics of the ecological community (or biome) leading to more complex and resistant human and animal infections.¹

Borreliosis gets many names and it is no wonder when you understand the nature of the biological components in our internal environment (the interactome) and how these dictate the outcome of the infection. Ultimately the underlying pathophysiology rests on inflammatory processes. Inflammation is normal at its core, but we are dealing with unresolved cycles of inflammation and that causes neuroimmune activation. These eventually lead to multiple levels of immune dysfunction and neurological dis-ease. (See figure 1)....

¹A study in Balance: How microbiomes are changing the shape of environmental health. Betts K. Environ Health Perspect 2011; 119: a340- a346

FIGURE 1.



A famous pathologist well known for describing pathogenic disease processes, towards the end of his work, said: "If I could live my life over again, I would devote it to proving that germs seek their natural habitat - diseased tissue - rather than being the cause of the diseased tissue." Rudolph Virchow (1821-1902)

Over 100 years on, this is what is being proven now. So what is it that governs whether inflammation is dealt with normally or whether it starts to become a burden on the neuro immune system? The answer lies in our various barriers which house our immunity and the role of mucosal immunity function is significant here. (I touched on this topic in part 2 of this series). Ideally, a way to prevent Lyme disease, apart from avoiding the tick bite, is to have a robust mucosal immune response to the spirochetes despite the fact that some immune dysfunction will be caused locally by the tick salivary proteins injected at the time of a tick bite.

A significant part of having a robust body-wide mucosal immunity is by having a diverse and full ecosystem of microbes in the gut. Studies show altered gut microbiota contribute to the chronic immune activation in patients with chronic infection namely HIV.² There may be no studies for this specific aspect in Lyme disease, but we cannot wait 30 years to do something about it when it applies directly to us now. In chronic

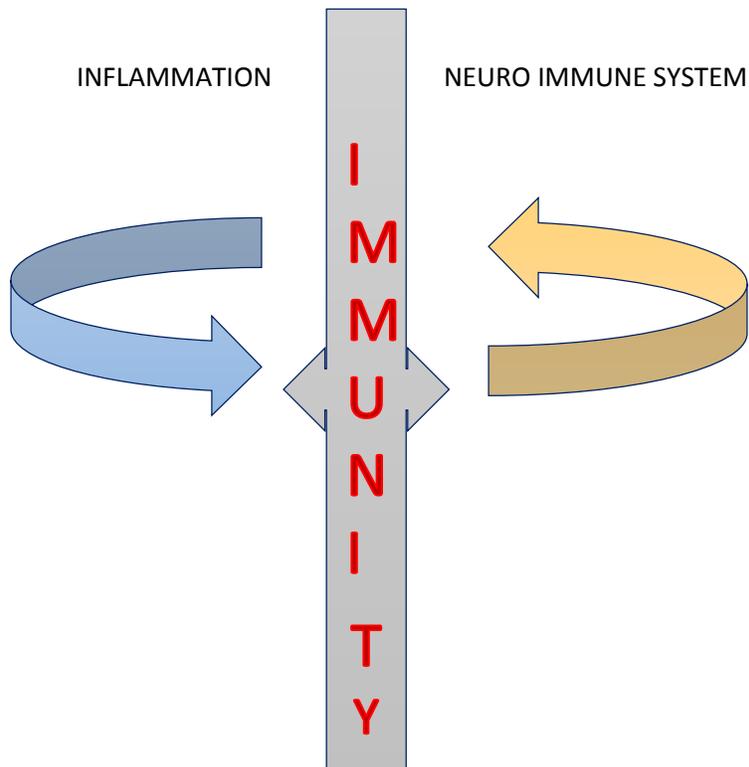
borreliosis, we are literally dealing with chronic immune activation, which is what I prefer to call an "Immune - mediated neuro immune disorder"

I will not dwell on the importance of improving the gut bacteria in this article, but it is an immensely important topic that requires sole focus. However I will emphasize that chronic usage of antibiotics leads to diminishing returns in terms of the immune system. Certain symptoms can be reduced with antibiotics but, it does not build resilience to the system. Entire myriads of immune education needs to occur with the microorganisms on and in our system. Furthermore, the body's natural antibiotics (called anti-microbial peptides) are produced by the microbial communities themselves that are in us and they are very beneficial in ongoing immunity. Thus all efforts to improve the density of immune building microorganisms and anti-microbial peptides are an essential component of lasting recovery.

However it is not just the gut we need to think about when addressing a chronic and difficult health challenge - we need to consider the whole interphase between infection, inflammation and our nervous system. This involves considering the skin, gut, blood brain barrier, mucus membranes, cell membranes and mitochondrial membranes. (See Figure 2)....

² Altered metabolism of gut microbiota contributes to chronic immune activation in HIV-infected individuals. Vázquez-Castellanos JF et al. *Mucosal Immunol.* 2014 Nov 19. doi: 10.1038/mi.2014.107

FIGURE 2



All of the environmental triggers hit us on our membranes (skin, gut, sinuses, throat, eyes, urogenital tract, bladder, lungs). These have to be interpreted by our nervous system and immune system. With dynamic balance and integration, we can maintain peace and smooth functioning on the insides of the membranes. We are then adaptive beings living in and on this planet and our nervous and immune systems are functioning to find ways to sense the environment and not only survive but preferably to thrive. With this in mind, it becomes no surprise that toxins in the environment impact severely on this balance.

Because the mucosal immune system is a body-wide organ, we need to maximise its improvement not just by treating the gut, but also improving the function of the skin. For example while dealing with a chronic infection, dermatitis and dry skin may be overlooked but it should be actively treated as it is a significant sign of poor mucosal immunity. On top of that, actively making your skin work for you as a protective organ means you want to support it in engaging its important detoxification functions of sweating and sensing the environment. To do this, it is best to not block it up with cosmetics and creams containing chemicals but instead, to stimulate its blood flow and lymphatic circulation using manual therapies, exercise, heat and infra-red sauna therapies, and of course feeding you skin with the nutrients it needs. This also means that the immune dendritic cells in the mucosal layer will function better with more robust immunity. We do this with lots of good fat in the diet (as Part 3 in this 'Ask the Doctor' series outlines). Other nutrients include phospholipids, butyric acid, vitamin A, vitamin D and zinc.

As for the blood brain barrier, its importance can be considered in comparison with the intestinal permeability barrier- which aim to keep toxins and infections at bay. How do you look after it? Chronic immune activation and inflammation is what worsens the integrity of the blood brain barrier.³ Hence, it is a whole approach of trying to identify all sources of neuro-immune activation.

People often assume that with infections, chronic symptoms can improve with antibiotics alone to remove pathogens, but in a chronic situation, sometimes the neural dysfunction has gone too far down a spiral spin. Once this occurs, there is so much more that needs to be done for neuroimmune support. This is why adjunctive therapies and the diet play huge roles in

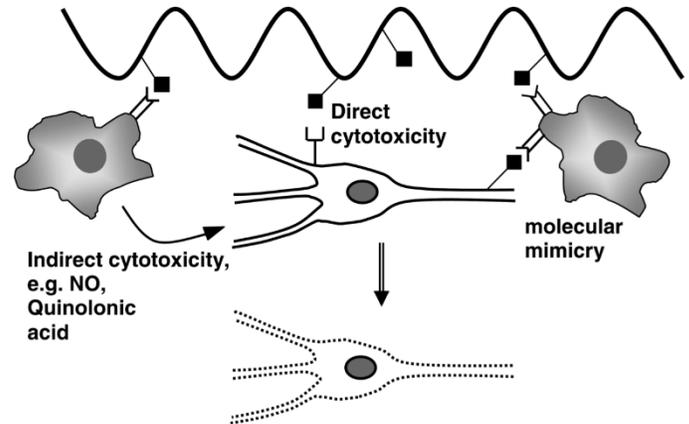
³ The blood brain barrier in health and chronic neurodegenerative disorders. Zlokovic BV. Neuron 2008; 57 (2): 178-201.

chronic infections. Recall that the diet can change the entire microbial genome in a very short span of time (for example three weeks) and because this changes the entire exposome and interactive factors, it is more powerful than one single drug which targets one single pathway.

Moving to the terrain of neuroimmune activation, studies show the different ways neural dysfunction can occur in Borreliosis.⁴ Figure 3 (to the right) is taken from this article, and it tells us where neural dysfunction occurs and how we need to identify and address the three different pathways of nerve damage. The first is by looking for factors triggering direct damage to nerves (called direct cytotoxicity). In this article, causes of direct cytotoxicity are identified as OSP A from *Borrelia* and also glutamate but, there are also other triggers of glutamate too including dietary factors such as artificial flavorings and monosodium glutamate. The second is looking for indirect triggers of nerve damage (called indirect cytotoxicity). This article describes the immune mediators and cytokines secreted by other immune cells that are also causing nerve damage indirectly (indirect cytotoxicity). This is usually caused by other infections such as viruses, toxins from the gut, triggers of nitric oxide and food allergies. The third factor described in this article pertains to the activated immune B cells which are producing antibodies. These attack the self-tissue (known as molecular mimicry) which is essentially a mechanism of auto immunity.

Here we need to understand what can trigger autoimmunity. This topic was touched on in part 2 of this series on immune-dysregulation. In a nut shell, the total load of environmental toxins and antigens which keep triggering the immune cell response has to be lowered in order to improve the autoimmune process. This includes food allergens, heavy metals & chemicals such as perfume, agricultural chemicals and many others. All these are contributing to the terrain of neurological dysfunction via driving the immune system

FIGURE 3: The neural dysfunction in neuroborreliosis. Three principle mechanisms



and activating the nerve cells to be sensitive, touchy and not integral in its function.

There is a great overlap of mitochondria and nerve cell function, particularly as nerve cells have the most mitochondria in them compared to any other cell in the body. Understanding the mitochondrial terrain is extremely important when dealing with neurodegenerative disorders. The mitochondrial terrain also leads us to differing activations of innate immune cells in the nervous system (called microglia). The understanding of mitochondria and cytokines is important in managing herxheimer reactions when treating infections. In the next article (Part 6), we will visit why it is important to treat mitochondrial dysfunction, how to protect neurons by addressing the state of the cell membrane and the problems that are produced by the inner lining of blood vessels when they get leaky (called endothelial dysfunction) and how to repair them.

I wish to follow Part 6 with an additional three articles to complete this "Ask the Doctor" Series. Part 7 will cover breathing, part 8 movement and finally, part 9 will explore sleep.

⁴ The Pathogenesis of Lyme Neuroborreliosis: From Infection to Inflammation. Rupprecht TA et al. Mol Med 2008; 14(3-4); 205-212.