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Review article

# Role of phrenic nerve in respiratory distress secondary to Lyme neuroborreliosis

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ABSTRACT

*Introduction:* Critical importance of phrenic nerve, in patients with Lyme disease is discussed.
*Aim:* This paper addresses the critical importance of phrenic nerve and Lyme disease.
*Material and methods:* Medline searches were conducted in context of phrenic nerve, Lyme neuroborreliosis, thoracic diaphragm, and respiratory distress.
*Results and discussion:* The advancements in treatment options in Lyme disease were reviewed using current literature. Applied anatomy of the phrenic nerve and its dysfunction in neuroborreliosis is described in the article.
*Conclusion:* This paper reviews the literature pertaining to the importance of the phrenic nerve in Lyme disease.


## 1. Introduction

The phrenic nerve descends from the 3rd, 4th, and 5th cervical nerves to innervate the lung, heart and diaphragm. This nerve carries motor, sensory and sympathetic nerve fibers for diaphragmatic function that is essential in respiration. Breathing occurs because sensory and motor information are exchanged between the phrenic nerve and the diaphragm. Diseases and dysfunction of phrenic nerves result in respiratory distress. One of the most rare manifestations of phrenic nerve disorder is neuroborreliosis, which may present itself with Lyme disease.[1]

## 2. Aim

This paper addresses the critical importance of phrenic nerve and Lyme disease.

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*Abbreviations:* DHI, diaphragmatic height index; CDC, Centers of Disease Control and Prevention.

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## 3. Material and methods

Medline searches were conducted in context of phrenic nerve, Lyme neuroborreliosis, thoracic diaphragm, and respiratory distress.

## 4. Results and discussion

### 4.1. *Anatomy*

Large contribution of the phrenic nerve comes from the C4's ventral ramus, but the nerve receives contributions from the C3 and C5 as well. The accessory phrenic nerve serves as the branch to the subclavius and joins the phrenic nerve in the thorax. Due to phrenic nerve's extensive anatomy, it can be divided into the cervical and thoracic portions. The cervical portion of the nerve stretches from the cervical plexus to the anterior surface of the scalenus anterior muscle. The right phrenic nerve descends through mediastinum, parietal pleura and the pericardial sac. It passes along the superior vena cava, travels next to the right atrium, and leaves through the inferior vena cava opening. The nerve may pass near the right superior pulmonary vein. The left phrenic nerve descends behind the innominate vein, passes near the aortic arch, pulmonary trunk, left atrial appendage, and then travels along the lateral border of the left ventricle to innervate the diaphragm.[2]

### 4.2. *Relation to Lyme disease (Lyme neuroborreliosis)*

Lyme neuroborreliosis is defined as neurological involvement of manifested Lyme disease. Lyme disease is a bacterial infection elicited by tick-borne bacteria spirochete, *Borrelia burgdorferi*. This double-membrane bacterium is primarily injected into the skin by bites of the genus *Ixodes* ticks. Thus, the disease is commonly diagnosed in patients who reside in densely wooded area, where human to deer contact often occurs. During the early-localized infection stage, the infection is detected by skin rash.

The early disseminated stage of Lyme disease infection comes weeks to months after the bite. The infection typically spreads through hematological or lymphatic routes to distant sites. Weeks to months after the infection, about 15% of untreated patients exhibit neurological conditions such as meningitis and cranial neuritis. In 5–10% reported cases, patients exhibit Lyme neuroborreliosis. The chronic stage symptoms primarily arise from rheumatologic and neurological disturbances.

Lyme neuroborreliosis is divided into categories of early, late, or chronic stages. It is in later stages of the disease that neurological symptoms begin to manifest. Three to six weeks after infection, Lyme neuroborreliosis results as lymphocytic meningoradiculoneuritis.[3]

Diaphragmatic complications from Lyme neuroborreliosis are unusual cases of Lyme disease. Diaphragmatic or respiratory disturbances in the presence of Lyme neuroborreliosis are recorded in only a few published cases. Most of these cases involve elderly patients with a few middle-aged patients who exhibit respiratory weakness or failures. *B. burgdorferi* infection was detected through serological testing for Lyme disease.

Lyme neuroborreliosis symptoms are caused by painful radiculitis. The pathogenesis is axonal injury of nerve segments caused by lymphocytic perineuritis. Lymphocytic inflammation is confirmed by the presence of meningeal and root inflammation in cerebrospinal fluid. The central nervous system becomes more involved in the late stage of Lyme neuroborreliosis (Tables 1 and 2).[3]

### 4.3. *Epidemiology*

Analyses of cases between 1991 and 2005 in the Northeastern United States had high incidence of Lyme disease.[40] Another region of high incidence of Lyme disease was prevalent in Nova Scotia, Canada.[41]

### 4.4. *Clinical presentation*

Patients who suffer from phrenic dysfunction secondary to Lyme neuroborreliosis manifest with severe pain in their abdominal, neck, or upper back. Dyspnea, diplopia, dysuria and flu-like symptoms have been presented as well. Tick head or bite marks were recovered from some, while others had no tick bites. Unilateral or bilateral facial palsy indicates cranial symptoms. In children, the primary symptoms are of meningitis (Table 3).[3]

### 4.5. *Treatment*

Treatment of phrenic nerve dysfunction in relation to Lyme neuroborreliosis is intravenous ceftriaxone that ranges up to 30 days. Depending on the severity of the patient's respiratory performance, mechanical or non-invasive ventilation is also administered as necessary. Tetracyclines (such as doxycycline) are used extensively because of their various antimicrobial uses and relatively safe properties. Oral doxycycline has also been used as a treatment option and is preferred over

**Table 1 – Diagnosis of phrenic dysfunction and Lyme neuroborreliosis.**

| Diagnosis of phrenic dysfunction | Diagnosis of Lyme neuroborreliosis – eMedicine |
|---|---|
| • Diaphragmatic height index (DHI)[4] | • Early stage, clinical presentation |
| • Introcardiac echocardiography (early detection during cryoballoon pulmonary isolation)[5] | ○ History of tick exposure or bite |
| • Fluoroscopy[6] | ○ Presence of erythema migrans |
| • Electrophysiological phrenic nerve testing after cardiac surgery[7] | • Positive anti-*B burgdorferi* antibody index |
| • Hemidiaphragm elevation | |

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