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Bacterium that causes Q fever linked to non-Hodgkin lymphoma

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The bacterium that causes Q fever, an infectious disease that humans contract from animals, is associated with an increased risk of lymphoma, according to a study published online today in *Blood*, the Journal of the American Society of Hematology (ASH).

Q fever is caused by infection with *Coxiella burnetii*, a bacterium primarily transmitted through the excrement of cattle, sheep, and goats. Approximately 3 percent of healthy adults in the United States and 10-20 percent of those in high-risk occupations such as veterinarians and farmers have antibodies for *C. burnetii*, suggesting previous infection. Symptoms of Q fever vary from person to person and can be acute and resolve spontaneously, or chronic and persistent. Because some patients have been reported to also suffer from lymphoma, researchers believed that this type of cancer could be a risk factor for Q fever. However, the experience of one patient prompted doctors to consider the opposite - that the infection might actually cause the lymphoma.

"During a follow-up scan in a patient we had successfully treated for Q fever, we observed a tumor close to the location of the previous infection," said senior study author Didier Raoult, MD, PhD, of Aix-Marseille University in Marseille, France. "The discovery that it was a lymphoma tumor containing *C. burnetii* encouraged us to consider that the infection might have contributed to the development of the cancer."

In order to better understand the association between *C. burnetii* and lymphoma, Dr. Raoult and colleagues screened 1,468 patients treated at

the French National Referral Center for Q Fever from 2004 to 2014. Investigators conducted imaging of patient tissue samples to identify seven people, including the initial patient, who developed lymphoma after *C. burnetii* infection (6 patients were diagnosed with diffuse large B-cell lymphoma and one with follicular lymphoma). Of all the Q fever patients included in the study, 440 presented a persistent infection concentrated to one area.

To determine if patients with Q fever have a higher risk of lymphoma than the general population, researchers compared the incidence of lymphoma in the Q fever registry to the incidence reported in France's general population. Based on this analysis, researchers conclude that patients with Q fever are 25 times more likely to develop diffuse large B-cell lymphoma than those without the infection. In addition, the odds of lymphoma in patients with persistent concentrated infections are higher than those with other forms of Q fever.

Upon further imaging of the patient samples, investigators observed that Q fever patients with lymphoma demonstrate overproduction of the critical anti-inflammatory pathway interleukin-10 (IL-10), suggesting that suppression of the immune system may have allowed the lymphoma cells to evade immune detection and multiply.

"As we continue to learn more about the association between *C. burnetii* and lymphoma, these results should encourage clinicians to survey high-risk patients as early as possible for potential cancer," said Dr. Raoult. "Ultimately, this early diagnosis and treatment would improve outcomes for Q fever patients who subsequently develop lymphoma, particularly those with B-cell non-Hodgkin lymphoma."

Provided by American Society of Hematology