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Understanding L-form Bacteria

Posted By [Amy Proal](#) On August 15, 2007 @ 8:18 pm In [L-form bacteria](#), [essential](#), [horizontal gene transfer](#) | [Comments Disabled](#)

In a 2006 the Centers for Disease Control and Prevention (CDC) released a paper stating, "Infectious agents have emerged as notable determinants, not just complications, of chronic diseases. To capitalize on these opportunities, clinicians, public health practitioners, and policymakers must recognize that many chronic diseases may indeed have infectious origins."

According to the CDC, infectious agents likely determine more cancers, immune-mediated syndromes, neurodevelopmental disorders, and other chronic conditions than currently appreciated. In fact, they argue that the potential to avoid or minimize chronic disease by preventing or treating infections may yet be substantially underestimated. Those of us familiar with the Marshall Protocol know that they are absolutely correct. ^[1]

The same can be said for Dave Relman, PhD, assistant professor of medicine and of microbiology and immunology at Stanford University in California who argues, "The list of chronic inflammatory diseases with possible microbial etiologies is extensive; it includes sarcoidosis, various forms of inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, Wegener granulomatosis, diabetes mellitus, primary biliary cirrhosis, tropical sprue, and Kawasaki disease..... the concept of pathogenic mechanism should be viewed broadly." ^[2]

Fortunately, the stealth pathogens responsible for causing the vast majority of chronic diseases have already been identified.

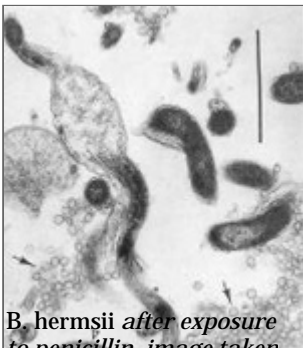
Almost all of us have suffered from a bacterial infection. Sometimes the forms of bacteria causing our symptoms can be killed by antibiotics that work by targeting their cell walls.

However, part of the life cycles of many bacteria include phases where they transform into small forms that lose their cell walls. This means that they can no longer be killed by many commonly used antibiotics. These bacteria are called cell wall deficient (CWD) or L-form bacteria.

Multiple studies have also shown that when one of the Beta-lactam antibiotics (a class of antibiotics that includes penicillin) are applied to wild-type bacteria in a Petri dish, small colonies of L-form bacteria form on the edges of the plate. "Treatment with penicillin does not merely select for L-forms (which are penicillin resistant) but actually induces L-form growth," states researcher Josep Casadesus in a paper about L-form bacteria published last month in the medical journal *BioEssays*. ^[3]



Granules of Borellia burgdorferi, Kersten 1995



B. hermsii after exposure to penicillin, image taken

L-form bacteria are pleomorphic, a term that refers to their ability to change in size and shape. During much of their lifetimes they are tiny, about 0.01 microns in diameter, and can be found clustered together inside the cells of the immune system.

Since they are smaller than viruses or fungal particles, they cannot be seen with a normal optical microscope. The small, individual forms of L-form bacteria are often referred to as coccoid bodies. Coccoid bodies sometimes group together, assuming the appearance of a string of pearls

Occasionally L-form bacteria break out of the cells. In the lab they can grow into long, thin biofilm filaments that can reach 60-70 microns in length. The biofilm filaments are composed of L-form bacteria and a protective protein sheath. For reasons still unknown, L-forms can also grow into large "giant" bodies.

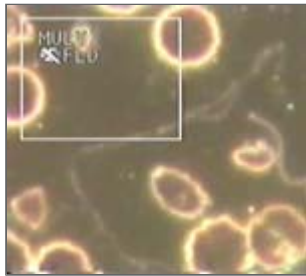
L-form bacteria replicate in various ways, including budding, filamentous growth and binary fission. Some species of L-forms such as *Proteus* can form large bodies that replicate by division. In other instances, granules bud from the body of the bacterium and give rise to small L-form colonies.

L-form bacteria also lack flagella, long slender appendages that allow some forms of bacteria to propel themselves forward by using a whip-like motion. Instead they glide to their destinations in a snail-like fashion.

Groups of L-form bacteria are often encased inside tubules. They are also separated from the environment inside the cell by a membrane or exoskeleton that keeps them from being digested by the cell.



T. pallidum inside a cell, Ovcinnikov 1971



Long L-form biofilm filaments between infected cells, picture by Andy Wright

Researchers have currently identified over 50 different species of bacteria capable of transforming into the L-form and it is likely that more species will be found in the coming years. "Probably most bacterial species can be converted into L-forms if treated with the antibiotics that inhibit cell wall synthesis," states Casadesus.

Although scientists have known about L-form bacteria for over a century, many of them have not detected them in tissue and blood samples because they are very difficult to culture. However an increasing body of research has shown that these bacteria are responsible for causing a wide array of chronic diseases including rheumatoid arthritis, Chronic Fatigue Syndrome, Lyme disease, sarcoidosis, and Crohn's disease.

Some of the species of L-form bacteria that have been implicated in chronic disease include *Bacillus anthracis*, *Treponema pallidum*, *Mycobacterium tuberculosis*, *Helicobacter pylori*, *Rickettsia prowazekii*, and *Borrelia burgdorferi*.

Survival mechanisms

Classical forms of most bacterial species can be found in the bloodstream. However L-form bacteria have figured out how to successfully infect and live inside the very cells of the immune system whose job is to kill bacteria. Once inside these cells, they can no longer be detected by the immune system and are able to persist in the body over long periods of time. L-form bacteria can infect many types of cells but prefer to infect white blood cells called macrophages.



A macrophage

Several very recent studies have confirmed the fact that bacteria can live inside the cells of the immune system. In a paper published in the *Journal of Immunology* by a team at the University of Michigan Medical School, Gabreil Nunez, senior author of the paper, stated "In our study, the presence of bacterial microbes inside the cell is what triggers the immune response."

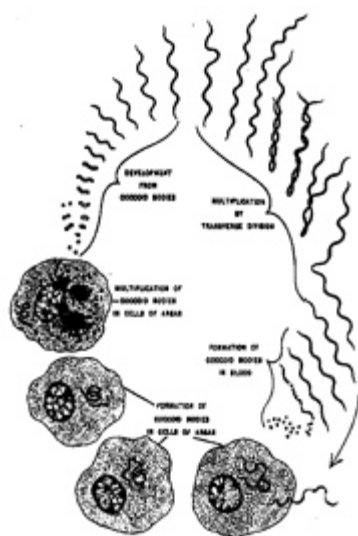


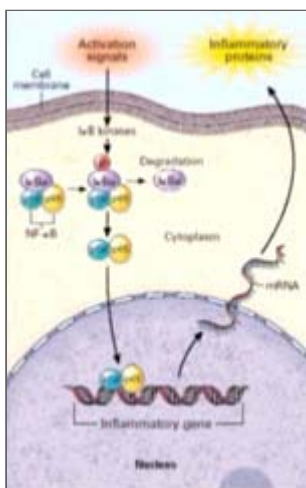
Diagram 4. The life cycle of *Spirochaeta gallinerum* (diagrammatic).

The life cycle of Spirochaeta gallinerum, Hindle 1912

are too small to be filtered during the purification processes used in pharmaceutical manufacturing procedures, they can be transmitted through injectable medicines. They have even been cultured from dry soil.

Once macrophages and other cells have been infected with L-form bacteria, the bacteria circulate in the blood and tissues. In some cases they cluster together in clumps called granulomas. In other cases, they accumulate in regions such as the joints.

Once L-form bacteria have successfully invaded a cell, they begin to use the nutrients inside the cell to their own advantage, disturbing the cell's delicate chemical balance. They are also able to take control of the host's genetic material, which allows them to create proteins that enhance their ability to survive.



A diagram of Nuclear Kappa Factor B entering the nucleus

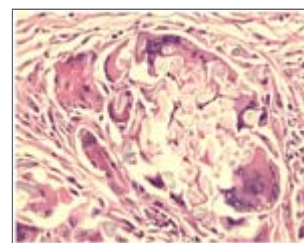
The CDC concurs, stating, "The epidemiologic, clinical, and pathologic features of many chronic inflammatory diseases are consistent with a microbial cause."

Similarly, a team of researchers at the Bacterienne Institute in France released a paper detailing how the bacteria *E. coli* is able to live inside the cells of the immune system. The researchers state that *E. coli* are "true invasive pathogens, able to invade intestinal epithelial cells and replicate intracellularly. Strains also survive and replicate within the macrophages."

Infection with L-form bacteria

People are exposed to L-form bacteria in many places. Not all species cause disease.

Because they cannot be killed by pasteurization or chlorination, L-form bacteria can be found in milk, food, and water. They can be transmitted via sperm, intimate contact, and can be passed from mother to child during childbirth. Since they



A granuloma

L-form bacteria cause inflammation and painful symptoms by taking control of a protein called Nuclear Factor Kappa B. They are able to activate proteins that increase the activity of Nuclear Factor Kappa B, which subsequently moves to the nucleus or center of the cell. Once there, it turns on a variety of genes that cause the release of inflammatory cytokines, proteins that generate pain and/or fatigue. These cytokines include interferon gamma and TNF alpha.

Thus, an inflammatory response is correlated with diseases caused by L-form bacteria. "An inflammatory immune response—one of the body's primary means to protect against infection—defines multiple established infectious causes of chronic diseases, including some cancers," argues Relman. "Inflammation also drives many chronic conditions that are still classified as (noninfectious) autoimmune or immune-mediated (e.g., systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease). Both [the innate and adaptive immune systems] play critical roles in the pathogenesis of these inflammatory syndromes. Therefore, inflammation is a clear potential link between infectious agents and chronic diseases.

Detecting L-form bacteria

Once bacteria have transformed into the L-form they can no longer be detected by many standard laboratory procedures.

Regular forms of bacteria can be easily grown outside the body (grown in-vitro). However L-form bacteria have great difficulty surviving in a foreign environment. In order to grow them successfully in the lab, conditions must be similar to those in the human body (grown in-vivo). Consequently they can be cultured on a medium called blood agar at very specific temperatures and at a certain pH.

The concept that some bacteria cannot grow in-vitro is not new. Scientists have known for decades that neither (*Syphilis Treponema pallidum*) nor leprosy (*Mycobacterium leprae*) cannot be easily cultivated outside the body.

L-form bacteria take several measures to ensure they can survive for as long as possible inside a cell. They are able to infect all types of white blood cells, but prefer to infect macrophages, the type of white blood cell with the longest life span (about 45 days.)

Several studies have shown that once inside a macrophage, L-form bacteria are able to delay the process of apoptosis, or programmed cell death, allowing them to thrive inside the cell for a period of time even longer than 45 days.

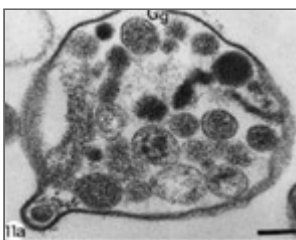
Classical bacterial forms can be detected by a lab test called Polymerase Chain Reaction (PCR). PCR identifies and amplifies the proteins and DNA of bacteria that have been killed. However since L-form bacteria are able to persist inside the macrophages for such extended periods of time, few of them die and only tiny amounts of L-form bacterial proteins and genetic material reach the bloodstream at any given time; an amount so small that the PCR test cannot pick them up.



T. pallidum inside a fibroblast, Lauderdale 1972

Even if a few small fragments from L-forms that have been killed are identified by PCR testing, the remains are often not from the bacterial species causing the most harm to the patient. This is because the most well adapted, persistent bacterial species are the ones who have developed the most effective survival mechanisms and are consequently least likely to die.

L-forms can also not be detected with antibody testing. Antibodies are Y-shaped proteins that are found in blood. They are used by the immune system to identify and neutralize foreign objects including bacteria.



Granules of B. burdorferi, Hayes 1993

However antibodies only form in response to bacteria that have died. Since L-form bacteria are able to persist for such long periods of time inside the cells, very few antibodies are created in response to their presence.

Gaining acceptance

Scientists such as Lida Mattman at Wayne State University have worked extensively with the L-form and figured out new ways to grow and view the pathogens. These techniques include a variety of special staining techniques.

British clinician Andy Wright and Danish researcher Marie Kroun have used a Dark Field Bradford Microscope to view L-forms in the bloodstream.

Nevertheless, many doctors and researchers still question whether the L-forms actually exist.

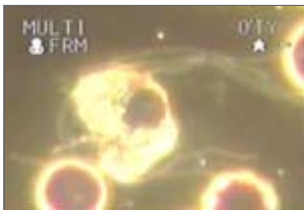
Mattman and other researchers have spent decades figuring out how to correctly culture the L-form. Applying their techniques correctly requires rigorous adherence to specific guidelines. Mattman has said that, over and over again, researchers misinterpreted just one of the steps required to correctly grow the bacteria. They then report to the medical community that no L-forms appear in their samples.

As Gerald Domingue, a (retired) professor at the Tulane University School of Medicine stated, "Unfortunately, in the area of L-form or cell wall-defective bacteriology, too often there have been conclusions (anecdotal) drawn without supporting scientific data. In my opinion, many of these studies have hampered progress in the field and especially the role of these cryptic organisms in bacterial persistence and expression of disease."

"Features of a number of important but poorly explained human clinical syndromes strongly indicate a microbial etiology," states Relman. "In these syndromes, the failure of cultivation-dependent microbial detection methods reveals our ignorance of microbial growth requirements." [2]

There is also little incentive for scientists to study the L-form. Since the bacteria can be killed by simple low-dose antibiotic therapy, drug companies have little interest in investing money into related research. Researchers studying the L-form often find themselves with very little grant money but must still work long, tedious hours in the lab.

As Domingue states, "It is generally agreed among scientists that L-form bacteria are extraordinarily intriguing, interesting tools for biological study, yet the most neglected area of research has been on the role of these organisms in disease, particularly in host-pathogen interactions."



A neutrophil infected with L-form bacteria, picture by Andy Wright

Another problem rests with the fact that many researchers rely on a series of rules called "[Koch's Postulates](#)" when interpreting research data. The postulates state that only one pathogen can cause a given disease. But research has shown each chronic disease is the result of infection with multiple species of L-forms.

This means that separate teams of researchers often detect different L-forms in patients with the same disease. For example both *Borrelia burgdorferi* and *Rickettsia helvetica* have been detected in patients with sarcoidosis. These findings make little sense to researchers still bent on adhering to Koch's Postulates.

Hopefully as the medical community begins to better understand the role of the L-form in chronic disease, more and more researchers will take the time to learn how to correctly culture and interpret these forms of bacteria.

Most importantly, now that L-form bacteria can be effectively killed by the Marshall Protocol, the opportunity to curb chronic disease is groundbreaking. According to the CDC, chronic diseases represent the major health burden of established economies (>90 million people in the United States) and are a rapidly growing burden in developing economies.

"If a mere 5% of chronic disease is attributable to infectious agents, in the United States alone 4.5 million of the 90 million people living with chronic disease might benefit from strategies designed to prevent or appropriately treat selected infections. Worldwide, the impact could be far greater," states the 2006 CDC report.

SOURCES

Bisset, K.A., & Bartlett, R. (1978). [The isolation and characters of L-forms and reversions of *Bacillus licheniformis* var. *Endoparasiticus* \(Benedek\) associated with the erythrocytes of clinically normal persons.](#) *J Med Microbiol*, 11(3), 335-349.

Domingue GJ, S., & Woody, H. (1997). [Bacterial persistence and expression of disease.](#) *Clin. Microbiol. Rev.*, 10(2), 320-344.

Butler, H.M., & Blakey, J.L. (1975). [A review of bacteria in L-phase and their possible clinical significance.](#) *The Medical journal of Australia*, 2(12), 463-7.

Dienes, L. (1947). Further observations on the reproduction of bacilli from large bodies in *Proteus* cultures. *Proc Soc Exp Biol Med*, 66, 97-98.

Domingue, Sr, G., & Woody, H. (1997). [Bacterial persistence and expression of disease.](#) *Clin Microbiol Rev*, 10(2), 320-344.

Kagan, Y. (1968). Some aspects of investigations of the pathogenic potentialities of L-forms of bacteria. In *Microbial Protoplasts, Spheroplasts and L-forms*. Baltimore: Williams & Wilkins Co. (pp. 422-443).

Klieneberger-Nobel, E. (1951). [Filterable forms of bacteria.](#) *Bacteriol Rev*, 15(2), 77-103.

Klieneberger-Nobel, E. (1951). The L-cycle; a process of regeneration in bacteria. *Journal of general microbiology*, 5(3), 525-30.

Klieneberger-Nobel, E. (2005). [The natural occurrence of pleuropneumonia-like organism in apparent symbiosis with *Strrptobacillus moniliformis* and other bacteria.](#) *The Journal of Pathology and Bacteriology*, 40(1), 93-105.

Marshall, T., Fenter, B., & Marshall, F. [Antibacterial Therapy Induces Remission in Sarcoidosis.](#) *Journal Of Independent Medical Research*.

Mattman, L.H. (2000). [Cell Wall Deficient Forms: Stealth Pathogens.](#) CRC Press.

Onwuamaegbu, M., Belcher, R., & Soare, C. [Cell Wall-deficient Bacteria as a Cause of Infections: a Review of the Clinical Significance.](#) *J Int Med Res*, 33(1), 1-20.

Pfeiffer, R. (1895). Differential Diagnose der vibrionen de cholera asiatica mit hulfe der immunieserung. *Z Hyg Infekt Kr*, 19, 75-77.

Pratt, B. (1966). Cell-wall deficiencies in L-forms of *Staphylococcus aureus*. *J Gen Microbiol*, 42, 115-122.

REFERENCES

1. O'Connor SM, Taylor CE, Hughes JM. (2006). [Emerging infectious determinants of chronic diseases.](#) *Emerging Infectious Diseases*. [□]
 2. Relman, D. A. (1998). [Detection and Identification of Previously Unrecognized Microbial Pathogens.](#) *Emerging Infectious Diseases*, 4(3). [□] [□]
 3. Casadesús, J. (2007). [Bacterial L-forms require peptidoglycan synthesis for cell division.](#) *BioEssays : news and reviews in molecular, cellular and developmental biology*, 29(12), 1189-91. [□]
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