



Is It a Lemon or a Lyme?

A Case Study on the Decision to Vaccinate or Not

by

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The immunology professor had just wrapped up the day's lecture. He was particularly well liked because he always found a way to make the topics in his class relevant to his students. He was friendly, with a nice smile that spread from the edges of his mustache to the sparkle in his blue eyes whenever he talked about something that really interested him. He didn't always have traditional views on the subjects he taught and was willing to listen to the students' views. The lecture had been on vaccines—the history of their development, how they work, a discussion of some of the more common ones. A lively discussion began, with many students raising their hands.

"Dr. Jim, how come you make it sound like vaccines are good things? Don't they cause autism and a lot of other problems?" asked Vicky, a young student in the class.

"Yeah, I heard that vaccines can cause gastrointestinal problems that can lead to autism," said Nadine, another young student.

"And I heard that the polio vaccine can cause polio!" said Thomas, an older student in the class.

"Well, I read somewhere that the new Lyme vaccine might cause arthritis," a student named Ian said. "I camp out a lot, and I've been exposed to ticks in areas where they have Lyme disease, but I would never take that vaccine!"

"It's the liberal press! They get all these young folk to believe that the establishment is out to hurt them. Vaccines are completely safe!" an older student shouted.

"So, Dr. Jim, what's the story? Are vaccines safe? Or are they dangerous?"

"Vaccines are like anything else that has been approved for medical use in this country," answered Dr. Jim. "They are generally very beneficial and have helped most of the people vaccinated. They have decreased the death rate due to infectious disease dramatically. Polio deaths and paralysis are almost nonexistent in this country now. Before a vaccine was developed, polio was a major worry for every family. Birth defects due to rubella were once common, but are now rare since a vaccine was developed to protect against the disease. Small pox has been wiped off the planet as a natural disease due to vaccine use. But vaccines, like any other medicine, have potential side effects, and some are useful for some people but not for others."

"How do you know which vaccines are good and which are bad? I don't want my baby to become

autistic," said an obviously pregnant student.

"Well," said Dr. Jim, "that one I can answer. But let me start with a question for you. You can see the light of the moon more brightly at night, can't you?"

"Yeah, but what has the moon got to do with vaccines," said an impatient student named John.

"Well, people drink more alcohol at night, don't they? But does the moon cause them to drink? No, the nighttime is just when more people have time to relax and consume alcohol. The moon doesn't cause it. That little story isn't to advocate drinking. It's to get you to realize that just because two things happen at the same time, doesn't mean they're related—one isn't necessarily the cause, or the effect, of the other," said Dr. Jim.

He continued: "The symptoms of autism become evident at about the same time a child receives the measles, mumps, and rubella (MMR) vaccine. However, there are no indications that there is any causal relationship. In fact, most cases of autism appear to be caused by an event while the baby is still in utero, or shortly after birth—many, many months before the baby has received his or her MMR vaccination. A vaccine safety study done by the Institute of Medicine¹ came to this conclusion last year. Fears about one vaccine or another can result in widespread panic and deaths, so the Centers for Disease Control are trying to prevent worries about this particular vaccine."

"What do you mean, worries about a vaccine can cause death. Aren't you overstating your message?" asked John.

"No, actually, a worry about the pertussis vaccine in Japan cut use of the vaccine to 10% and led to 13,000 cases of pertussis in children there and 41 deaths,"¹ replied Dr. Jim.

"So, are you telling us that all vaccines are safe?" asked Nadine.

"No," said Dr. Jim. "The use of a vaccine depends on several factors. Let's see how we would decide if a vaccine is good for us. Let's take the vaccine that Ian mentioned, LYMERix™, the relatively new vaccine for Lyme disease. Let's learn about it and then decide if it is a good choice for each of us."

"LYMERix™ is produced by SmithKline Beecham Pharmaceuticals. It's approved for use by people 15 to 70 years of age. Use of this vaccine, like any other, is reviewed by the Advisory Committee on Immunization Practices.² This committee suggests that the decision to be immunized should be based on individual risk—on where a person lives and works and plays and whether or not they engage in high-risk activities.² To make an informed decision, a person should weigh individual risk, disease pathology, effectiveness and side effects of therapy for the disease, and effectiveness and side effects of the vaccine. Are you in or are you going to be in a geographic area in which the disease is endemic? Do you engage in the kinds of activities by which the disease is spread (outdoor activities, in the case of Lyme disease)? How bad is the disease? Is the antibiotic therapy for disease treatment difficult or easy, expensive or cheap, with or without side effects, effective or sometimes ineffective? What about the vaccine—is the immunization protocol easy or difficult to follow, does it hurt, is it effective, does it have side effects? To answer these questions, we need to do a little work."

"Let me give you some background. Lyme disease was first reported in 1975 in Lyme, Connecticut. A woman named Polly Murray, her husband, and their four children had become ill with a variety of seemingly unrelated non-specific symptoms.³ The symptoms, when brought to the attention of a number of doctors, were dismissed as psychosomatic, but Polly was not so easily dismissed. She read the

literature, surveyed neighbors looking for similar symptomology, and, perhaps most importantly, she kept meticulous records. She finally found a sympathetic ear when she met Dr. Allen Steere at Yale. She also went to the public health department of the state of Connecticut and convincingly showed them that there was a health problem in Lyme. The media became involved and the disease, Lyme arthritis, was defined." ³

"Two years later, the causative organism was discovered by Burgdorfer. The organism that causes Lyme disease is a spirochete called *Borrelia burgdorferi*.⁴ The spirochete is spread to humans, usually in wooded areas, through the bite of deer ticks. Common early clinical symptoms of Lyme disease are the characteristic bulls-eye rash (called erythema migrans) and fever, fatigue, and muscle and joint aches. If left untreated, or if treatment is unsuccessful, the disease can develop secondary and tertiary manifestations that can be quite debilitating."⁵

Study Questions:

To determine whether or not you need and want to take the vaccine to prevent Lyme disease, you need to educate yourself. The class will break up into five groups of five students each. Each group is to find and summarize the material necessary to answer its question, below. To help you get started, each group will be given a summary and a list of suggested sources for finding additional information. In one week, each group will present its information to the class as a whole. These presentations will each be 10 minutes in length. The information presented will include the group's recommendation based only on the information it has gathered about whether or not to take the vaccine.

Click a Tick to Go to a Worksheet:



Group 1: Who is at risk for developing this disease? (Epidemiology)



Group 2: How bad is this disease? (Etiology and Pathology)



Group 3: What is the prevention for this disease? What is its treatment? Its side effects? (Prevention and Treatment)



Group 4: What are the laboratory assays that are utilized in the diagnosis of Lyme disease? How reliable are they? What is the likelihood of a misdiagnosis? (Laboratory Diagnosis)



Group 5: What is the vaccine like? What are its costs, risks, and benefits? (Vaccine)

References

1. The National Academies Institute of Medicine. 2001. "Immunization Safety Review: Measles-Mumps-Rubella Vaccine and Autism." Available at: <http://www.iom.edu/IOM/IOMHome.nsf/Pages/MMR+Autism+Summary>.
2. Modlin, J.F. *et al.* 1999. "Recommendations for the Use of Lyme Disease Vaccine, Recommendations of the Advisory Committee on Immunization Practices (ACIP)," *Morbidity and Mortality Weekly Report*, June 4, 48 (RR07): 1-17. Available at: <http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/rr4807a1.htm>.
3. Murray, P. 1996. *The Widening Circle: A Lyme Disease Pioneer Tells Her Story*. New York: St. Martin's Press.
4. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "CDC Lyme Disease Home Page." Available at: <http://www.cdc.gov/ncidod/dvbid/Lymeinfo.htm>.
5. Edlow, J.A. 1999. "Lyme disease and Related Tick-borne Illnesses." *Annals of Emergency Medicine* 33(6): 680-693.

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Epidemiology

Please use the following information as well as the material including charts, graphs, photographs and text from the cited web sites to prepare a 10-minute presentation to your classmates about the epidemiology of Lyme disease. Your group is of course welcome to supplement this material with material that you find on your own. Remember to consider the source of any information that you obtain. If you use a peer reviewed journal article, you can place more trust in it than in an unreviewed web site. If you use sources on the web, think about the owner or author of the site. Is there an agenda for this group or agency that may bias this material? Since this is health related material, where was the author educated about this topic? Is it a stable web site? If you send your classmates there, you want it to still be there. Is it a company owned site? Would this company have any reason for feeling biased about the material?

Geographic Risk Assessment

Prior to your collection of information on geographic risk, survey your class to find out the hometown areas of your fellow students. Be sure to research the risk in each of these areas.

Lyme disease is endemic in 12 states in the United States. Endemic is a term that refers to a disease that occurs consistently in a particular region.¹ Ninety-five percent of the cases reported in 2000 in the U.S. were reported in the following 12 states, listed here in order of most cases to least: New York, Connecticut, Pennsylvania, New Jersey, Wisconsin, Rhode Island, Maryland, Massachusetts, Minnesota, Delaware, Vermont and New Hampshire.²

The latest map and information concerning the areas where ticks carry *Borrelia burgdorferi* is available on the CDC web site,³ which can be found at <http://www.cdc.gov/ncidod/dvbid/lyme/epi.htm>. There are about 4,000 cases of Lyme disease annually in New York State, with only six cases annually in Erie County.⁴ For other counties, see: <http://www.health.state.ny.us/nysdoh/cfch/nysmap.htm>.⁴ The disease incidence and geographic location are increasing because of the increased interaction of humans in areas that are favorable to deer. This has to do with the abandonment of farming in some areas of the U.S. and the reforestation of these areas, which border on suburban housing developments. To determine the number of cases in all the areas of interest to your class, the web sites at <http://www.geocities.com/HotSprings/Spa/6772/lyme.html#us>⁵ and <http://www.cdc.gov/mmwr/PDF/wk/mm5102.pdf>⁶ may be useful since these include other states and Canada. The web site at <http://www.utech.net/users/10766/lyme.htm>⁷ contains the U.S. Army's risk assessment for various states. In addition, you can find information by accessing the web sites of departments of health for the different states and then search on Lyme disease or on reportable communicable diseases.

A bite by a tick, even in an area in which Lyme is endemic, doesn't necessarily result in Lyme disease. Two factors that play a role in whether the disease develops are (1) the percentage of infected ticks in an area and (2) the duration of attachment. In the northeast about 50% of ticks are infected; this rate is 10% in the north central states and 3% in the south. For higher transmission rates the tick must be attached for longer than 72 hours, although a few percent of the ticks can transfer the spirochete faster. The amount of time the tick has been attached can be estimated by how engorged it is.⁷ Since the body size of the tick increases with its blood meal, the amount of time of tick attachment can be determined by measuring the ratio of the width of the scutum compared to the length of the body.⁷

Engorged**Nonengorged**

Sometimes the human-deer interactions are in neighborhoods, so it is not just hikers that are exposed to ticks and thus exposed to Lyme disease. Those at risk include those that live, work, or play in tick infested Lyme endemic areas.

Season and Infection Rate

Lyme disease cases have been reported in every month of the year, with the largest number of cases in June, July and August. This is most likely due to two reasons: the fact that the nymphal form of the tick is present during these months and the fact that these are the months when there is the greatest amount of time spent outdoors. The nymphal form of the tick is about 1/6 to 1/3 of the size of the adult tick. Nymphal tick attachment is more likely to go unnoticed for the required period of time, so most cases of Lyme disease are transmitted by this form rather than the adult form of the tick, although both stages can transmit Lyme disease.³

Risk Assessment by Age and Gender

Lyme disease occurs in men and women with almost the same frequency and occurs in any age group, with an apparent decrease in infection rate in individuals age 20 to 29. Children age 5 to 9 and adults age 45 to 54 have the highest disease incidence.⁷

End Notes

1. Stevens, C. 1996. "Spirochete Diseases," *Clinical Immunology and Serology, A Laboratory Perspective*, ch. 15. Philadelphia: FA Davis Co.
2. Centers for Disease Control. 2002. "Lyme Disease—United States, 2000." *Morbidity and Mortality Weekly Report* 51 (2):29-31. Available at: <http://www.cdc.gov/mmwr/PDF/wk/mm5102.pdf>.
3. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "Lyme Disease: Epidemiology." Available at: <http://www.cdc.gov/ncidod/dvbid/lyme/epi.htm>.
4. New York State Department of Health. "County Health Indicator Profiles." Available at: <http://www.health.state.ny.us/nysdoh/search/index.htm>.
5. Doherty, Art. "Lyme Disease in the United States and Canada." Available at: <http://www.geocities.com/HotSprings/Spa/6772/lyme.html>.
6. Orloski, K.A., E.B. Hayes, G.L. Campbell, and D.T. Dennis, Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases. "Surveillance for Lyme Disease—United States, 1992-1998." *Morbidity & Mortality Weekly Report* 49(SS03):1-11. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss4903a1.htm>.
7. Doherty, Art. "Lyme Disease Risk Assessments." Done by U.S. Army, 1983-1996. Available at: <http://www.utech.net/users/10766/lyme.htm>.

Etiology and Pathology

Please use the following information as well as the material including charts, graphs, photographs and text from the cited web sites to prepare a 10-minute presentation to your classmates about the etiology and pathology of Lyme disease. Your group is of course welcome to supplement this material with material that you find on your own. Remember to consider the source of any information that you obtain. If you use a peer reviewed journal article, you can place more trust in it than in an unreviewed web site. If you use sources on the web, think about the owner or author of the site. Is there an agenda for this group or agency that may bias this material? Since this is health related material, where was the author educated about this topic? Is it a stable web site? If you send your classmates there, you want it to still be there. Is it a company owned site? Would this company have any reason for feeling biased about the material?

Etiology

Lyme disease is the major tick-borne disease in the U.S. today. It is transmitted by several genera of *Ixodes* tick. Descriptions and photographs of the various ticks are available at <http://www.cdc.gov/ncidod/dvbid/lymeinfo.htm>,¹ and a movie and other images of these ticks can be found at <http://www.ent.iastate.edu/imagegal/ticks/>.² The ticks that carry Lyme disease are *Ixodes scapularis* and *Ixodes pacificus*.³ These ticks take as hosts for their blood meals deer and the white-footed mouse, birds and other mammals. The reservoir for the Lyme bacteria is the white-footed mouse. Areas that are conducive to the spread of Lyme disease have an ample food source for the mice and have wooded areas for mice, deer and humans to be in close proximity.³

Lyme disease is caused by a spirochete named *Borrelia burgdorferi* that resides in the ticks. A photograph of the *Borrelia* can be seen at: <http://www.cdc.gov/ncidod/dvbid/lyme/bburgdorferi.htm>.⁴ It is 18 to 20 microns long and 0.2 to 0.3 microns in diameter. It has multiple flagella and divides by binary fission. It grows only in complex media; the medium of choice is modified Barbour-Stoenner-Kelly at 33°C.⁴

Pathology

Like syphilis, another disease caused by a spirochete, Lyme disease is a multi-symptom, multi-system disease. The disease begins after the bite of an infected tick. The tick must be attached for approximately 72 hours before the disease is transmitted. Three stages of Lyme disease can occur and any of these stages can have symptoms that overlap. The stages are cutaneous involvement, dissemination to multiple organ systems, and a chronic disseminated stage.⁵

The "cutaneous involvement stage" is characterized by the aptly named "bull's-eye" rash on the skin. The medical terminology for this rash is *erythema chronicum migrans* (ECM). Photographs of the rash can be seen at <http://www.lymenet.org/picture4.shtml>⁶ or <http://ourworld.compuserve.com/homepages/frankd/emrash.htm>.⁷ This type of rash occurs in 60 to 80% of the patients.

After this, the "dissemination stage" occurs and the disease can have a variety of different manifestations. Patients may experience headaches, muscle aches, bone and joint pain, swollen lymph nodes, fever and malaise.⁵ Patients may in addition have mild hepatitis with associated upper right quadrant tenderness.⁵ Neurologic and or cardiac involvement may occur.⁵ Bell's palsy, which is a peripheral neuritis affecting one side of a patient's face, may appear.⁵ Central nervous system

complications may develop with chronic confusion, memory defects and intellectual functioning defects. Double vision may also occur during a chronic disseminated infection. ⁵

After the "chronic disseminated stage" of the disease occurs, 50 to 60% of the patients may get brief attacks of arthritis. (See the accompanying figure for a summary of disease manifestations.) Only 10% of patients have continued chronic disease; in the other patients spontaneous remission may occur. The susceptibility to the chronic course may be related to the HLA DR4 type. Descriptions from individuals with chronic Lyme disease may be found at: <http://www.lyme.org/index2.html> ⁸ under the link "Faces of Lyme." Please remember that only about 10% of Lyme disease patients develop chronic Lyme.

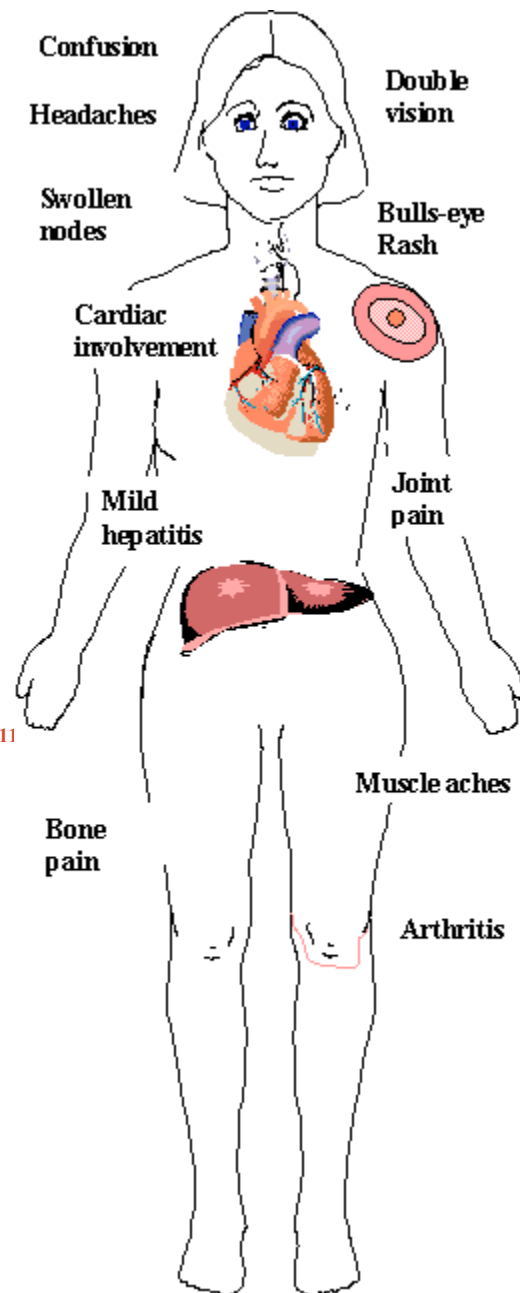
A general description of the disease may be found at:

<http://www.cdc.gov/ncidod/dvbid/lyme/index.htm>, ⁹

<http://www.wadsworth.org/databank/borreli.htm>, ¹⁰ and

<http://www.cdc.gov/ncidod/dvbid/lyme/diagnosis.htm>. ¹¹

The diagnosis of Lyme disease can be very difficult to make since the symptoms can vary widely and can mimic those seen in other diseases. In fact, Lyme disease has been dubbed "the great imitator" by some physicians. In patients where the bulls-eye rash has occurred and/or the tick bite was a known occurrence, the diagnosis of Lyme disease is based on these factors and additional clinical signs. In cases where the rash either did not occur or went unnoticed and the tick bite went unnoticed, the diagnosis can be facilitated by serologic tests. The CDC recommends a preliminary enzyme immunoassay and a confirmatory Western blot. These assays will be described by the laboratory diagnosis group and are available at <http://www.cdc.gov/ncidod/dvbid/Lymediagnosis.htm>. ¹¹ The assays show cross reactivity with other spirochetal diseases.



End Notes

1. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "CDC Lyme Disease Home Page." Available at: <http://www.cdc.gov/ncidod/dvbid/lyme/index.htm>.
2. Iowa State University Entomology Department. "Entomology Image Gallery: Ticks." Available at: <http://www.ent.iastate.edu/imagegal/ticks/>.
3. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "CDC Lyme Disease Home Page-Introduction." Available at: <http://www.cdc.gov/ncidod/dvbid/Lymeinfo.htm>.
4. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "Lyme Disease: The Bacterium." Available at: <http://www.cdc.gov/ncidod/dvbid/lyme/bburgdorferi.htm>.
5. Stevens, C. 1996. "Spirochete Diseases," *Clinical Immunology and Serology, A Laboratory Perspective*, ch. 15. Philadelphia: FA Davis Co.
6. The Lyme Disease Network of New Jersey. Lymenet Pictures Available at: <http://www.lymenet.org/picture4.shtml>.
7. Demarest, Frank. "EM Rash." Available at: <http://ourworld.compuserve.com/homepages/frankd/emrash.htm>.
8. Lyme Disease Foundation, Inc. "Tick Spread Diseases, Which is a Lyme Disease Rash?" Available at: <http://www.lyme.org/>.
9. Center For Disease Control. Lyme Disease Publications. Available at: <http://www.cdc.gov/ncidod/dvbid/pubs/lyme-disease-pubs.htm>.
10. New York State Department of Health Wadsworth Center. "Borrelia Burgdorferi." Available at: <http://www.wadsworth.org/databank/borreli.htm>.
11. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "Lyme Disease—Diagnosis." Available at: <http://www.cdc.gov/ncidod/dvbid/lyme/diagnosis.htm>.

Prevention and Treatment

Please use the following information as well as the material including charts, graphs, photographs and text from the cited web sites to prepare a 10-minute presentation to your classmates about the prevention and treatment of Lyme disease. Your group is of course welcome to supplement this material with material that you find on your own. Remember to consider the source of any information that you obtain. If you use a peer reviewed journal article, you can place more trust in it than in an unreviewed web site. If you use sources on the web, think about the owner or author of the site. Is there an agenda for this group or agency that may bias this material? Since this is health related material, where was the author educated about this topic? Is it a stable web site? If you send your classmates there, you want it to still be there. Is it a company owned site? Would this company have any reason for feeling biased about the material?

Prevention

Articles addressing prevention can be found in many places, including the web site for the Centers for Disease Control ¹ (CDC) and the journal *Pediatrics*.²

To prevent infection an individual can take certain relatively simple precautions. The first level of prevention would be avoidance of areas that contain ticks, the second would be to avoid tick attachment, the third would be to do a tick check and removal after exposure, and the last would be to use prophylactic antibiotics after a bite.¹ To avoid areas that contain infected ticks, one must be aware of the endemic areas and avoid outside exposure in these areas.¹ In addition, ticks like moist areas with leaf litter, high grass and woodpiles, so these types of areas could be cleared or avoided. This strategy is not always possible, so avoidance of tick attachment can also be attempted. When in an area with ticks, the individual can wear clothing that does not allow access to the skin. This would include long pants tucked into socks and long sleeves. Rubber boots are also recommended by the CDC.¹ Light clothing may facilitate tick removal before they become attached.¹ DEET is a pesticide that can be applied to clothes and exposed skin to repel the ticks. Since it takes 24 to 72 hours for Lyme disease to be transmitted after a tick bite, another way to reduce the risk of Lyme disease is to thoroughly look for ticks after exposure and remove them.^{1,2,3} The best way to remove the tick is by pulling straight back and out with forceps, taking care not to crush the mid-gut region.¹ In most areas, physicians will not treat a patient with antibiotics just because they have had a tick bite, but they will observe the patient for signs and symptoms of infection and rapidly treat if necessary.^{1,2,3} This, however, is not an approach set in stone, and some physicians may treat with prophylactic antibiotics if the patient displays anxiety or if the geography and season and length of time of tick attachment all indicate that Lyme disease could have been transmitted.⁴

Strategies are being considered to either reduce the number of ticks in an area, to reduce the number of ticks on deer through pesticide application at baited stations, or to reduce the number of deer. These ideas have not yet received general use or acceptance.⁴

Treatment

To be successful it is important to begin treatment of Lyme disease in the earliest stage possible. Antibiotics chosen include penicillins, cephalosporins, macrolides and tetracyclins.³ The antibiotics chosen vary with the stage of the disease. A table that lists these antibiotics is given in end note [4](#) below, and a summary is given in end note [3](#).

Antibiotics are chosen by how effective they are on the *Borrelia*, how much they cost, what their side effects are, efficacy on possible co-infecting organisms, and whether the patient in question has experienced any reaction to a specific antibiotic in the past.⁴ Antibiotic choice can also be limited by whether the patient is pregnant and by the age of the patient.⁴ Later stage disease is more difficult to cure and can require antibiotics to be given by injection for 2 to 4 weeks.⁴ Patients with severe systemic disease may require more than one course of antibiotics for successful treatment, and in some patients the therapy may not be effective and may result in persistent infection.⁵ Lyme disease is rarely fatal, however.⁵

The web site at <http://www.aldf.com/templates/Lyme.cfm#PARA5> discusses therapy as does the web site at <http://www.geocities.com/HotSprings/Oasis/6455/antibiotics-links.html>. On http://www.aldf.com/templates/Lyme_TreatmentTable.cfm you will find a table of drug doses suggested for different stages of Lyme disease. The site at <http://www.infomed.org/100drugs/amoxtoc.html> is a good site to check for the side effects of antibiotics as is <http://www.druginfonet.com/index.html>.

End Notes

1. Centers for Disease Control: Division of Vector-Borne Infectious Diseases. "Prevention and Control." Available at: <http://www.cdc.gov/ncidod/dvbid/lyme/prevent.htm>
2. Committee on Infectious Diseases. 2000. "American Academy of Pediatrics: Prevention of Lyme Disease." *Pediatrics* 105 (1):142-147.
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4. Edlow, J.A. 1999. "Lyme Disease and Related Tick-borne Illnesses." *Annals of Emergency Medicine* 33(6):680-693.
5. Modlin, J.F. *et al.* 1999. "Recommendations for the Use of Lyme Disease Vaccine, Recommendations of the Advisory Committee on Immunization Practices (ACIP)," *Morbidity and Mortality Weekly Report*, June 4, 48 (RR07): 1-17. Available at: <http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/rr4807a1.htm>.

Laboratory Diagnosis

Please use the following information as well as the material including charts, graphs, photographs and text from the cited web sites to prepare a 10-minute presentation to your classmates about the laboratory diagnosis of Lyme disease. Your group is of course welcome to supplement this material with material that you find on your own. Remember to consider the source of any information that you obtain. If you use a peer reviewed journal article, you can place more trust in it than in an unreviewed web site. If you use sources on the web, think about the owner or author of the site. Is there an agenda for this group or agency that may bias this material? Since this is health related material, where was the author educated about this topic? Is it a stable web site? If you send your classmates there, you want it to still be there. Is it a company owned site? Would this company have any reason for feeling biased about the material?

Diagnosis

Diagnosis of the Lyme patient is primarily based on clinical signs and symptoms, and on the evident risk of the patient being exposed to infected ticks. Laboratory analysis can yield supportive information. The laboratory diagnosis of Lyme disease is complicated. It is usually performed using a two-step analysis, with the first analysis a screening assay with either an indirect enzyme immunoassay or an indirect immunofluorescent assay. These analyses are often performed with class specific anti-globulins to determine the amount of antigen specific IgM and IgG produced by the patient. If the screening assay is positive, it is followed by a Western blot. This two-step analysis method was suggested by the CDC in 1994. Please describe these assays to the class.

A general description of an indirect enzyme immunoassay and indirect immunofluorescent assays can be found in your text: *Clinical Immunology and Serology* by Christine Stevens.¹ See <http://www.phppo.cdc.gov/cdcrecommends/>² for a discussion of the use of laboratory testing. See <http://www.cdc.gov/ncidod/dvbid/lyme/diagnosis.htm>³ for a photo of the Western blot for Lyme disease. The Western blot is considered positive for IgM if there is staining on at least 2 of the following antigen bands: OspC, BmpA and Fla. The Western blot is considered positive for IgG if there is staining on at least 5 of the following antigen bands: 18kDa, OspC, 28kDa, 30kDa, BmpA, Fla, 45 kDa, 58 kDa, 66 kDa and 93 kDa. For discussion of this, see CDC MMWR on Lyme serologic diagnosis.⁴

A person who is treated for and recovers from Lyme disease may continue to have a positive serologic result for Lyme disease, so a positive laboratory result does not necessarily indicate a current infection. Positive results can also be due to cross-reacting antibodies from other spirochetal diseases or from autoimmune diseases. An IgM only positive result may be suspect as the specificity of the IgM reaction is low. A positive IgM assay should be confirmed with a later IgG assay. Positive IgM only results in an illness of greater than 1 month duration is especially suspect. In addition, a person with early Lyme disease may not have developed antibodies, so a negative result may also be false. False negative results can also occur in chronic Lyme disease if a patient's antibody response to the *Borrelia* has decreased or if a patient with early Lyme has been treated with antibiotics (see <http://www.fda.gov/medbull/summer99/lyme.html>).⁵

A further complication in using these assays is that recipients of the Lyme vaccine will have antibody to the OspA surface protein of the *Borrelia*. Careful interpretation of the Western blots should be performed and if the patient only has antibodies to the OspA surface protein, this is more likely a result of vaccination than of infection (see <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm4837a8.html>).⁶

Other false positives and false negative reactions can occur. A discussion of these can be found at <http://www.geocities.com/HotSprings/Spa/6772/false-neg-pos.txt>.⁷ Please present to the class the reasons that false negative and false positive laboratory tests can occur.

B. burgdorferi can also be cultured from biopsies of the rash using a special media called Barbour-Stoenner-Kelly media. PCR analysis for the pathogen can also be performed, and reverse Western blots can be performed to find the ag from the Borrelia in the patients urine. Please describe these tests.

See <http://www.igenex.com/>⁸ for discussion of a Lyme dot blot assay and a reverse Western blot (looking for ag rather than ab), the lyme eia, pcr for lyme disease, Western blot for neurologic lyme and how to make a decision on which tests to perform.

See <http://www.mdlab.com/fees&servs/serv-ticks.html#lyme>⁹ for a discussion of the various assays for Lyme disease, <http://www.geocities.com/HotSprings/Oasis/6455/testing-links.html#labsBBI>¹⁰ for a listing of various laboratories that perform Lyme disease testing, and <http://www.igenex.com/timeb.htm>¹¹ for how time after infection affects which laboratory test is the best choice.

End Notes

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5. U.S. Food and Drug Administration. 1999. "Lyme Disease Test Kits: Potential for Misdiagnosis." *FDA Medical Bulletin*, Summer. Available at: <http://www.fda.gov/medbull/summer99/lyme.html>.
6. Centers for Disease Control. 1999. "Erratum to 'Notice to Readers Recommendations for Test Performance and Interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease'." *Morbidity and Mortality Monthly Reports* 48(37):833. Available at: <http://www.cdc.gov/mmwr/PDF/wk/mm4837.pdf>.
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8. Igenex, Inc. State-of-the-Art Research and Reference Laboratory. Available at: <http://www.igenex.com/>.
9. Medical Diagnostic Laboratories. "Diagnostic Services: Tick-Borne Diseases." Available at: <http://www.mdlab.com/fees&servs/serv-ticks.html#lyme>.
10. Doherty, Art. "Testing for Lyme Disease." Available at: <http://www.geocities.com/HotSprings/Oasis/6455/testing-links.html>.
11. Igenex, Inc. "Persistent/Recurrent Disease." Available at: <http://www.igenex.com/timeb.htm>.

Vaccine

Please use the following information as well as the material including charts, graphs, photographs and text from the cited web sites to prepare a 10-minute presentation to your classmates about the vaccine for Lyme disease. Your group is of course welcome to supplement this material with material that you find on your own. Remember to consider the source of any information that you obtain. If you use a peer reviewed journal article, you can place more trust in it than in an unreviewed web site. If you use sources on the web, think about the owner or author of the site. Is there an agenda for this group or agency that may bias this material? Since this is health related material, where was the author educated about this topic? Is it a stable web site? If you send your classmates there, you want it to still be there. Is it a company owned site? Would this company have any reason for feeling biased about the material?

LYMERix™

LYMERix™, manufactured by SmithKline Beecham, was licensed for use in individuals aged 15 through 70. Since the original publication of this article, the production of LYMERix™ by GlaxoSmithKline has been discontinued,¹ but we will continue discussion of this vaccine so that the reader can understand how vaccine choices are made. For 85% (85% of vaccinated people protected from the disease) efficacy, a 3 immunization regime of LYMERix™ is required with vaccinations at 0, 3, and 12 months. The antigen in the vaccine is a lipidated derivative of the Outer surface protein A (Osp A) of *Borrelia burgdorferi*. The Osp A used is a recombinant protein that was expressed in *E. coli* for large-scale production. The vaccine contains the rOsp A absorbed onto aluminum hydroxide.² Aluminum hydroxide binds the antigen in an insoluble complex and increases the immune response to the antigen. A substance that increases the immunogenicity of an antigen is called an adjuvant. The increase in immunogenicity is in part due to the increase in the likelihood of phagocytosis, in part due to the ability to prolong the time the antigen remains in the body and finally in part due to the stimulation of the production of the cytokine, Interleukin-1.^{3, 4, 5} Aluminum hydroxide is also used in the diphtheria, pertussis and tetanus (DPT) vaccine. Since the LYMERix™ vaccine contains this adjuvant it must be administered intramuscularly rather than subcutaneously, otherwise skin necrosis may occur.

The CDC recommendations for use of the LYMERix™ vaccine are listed at: <http://www.cdc.gov/ncidod/dvbid/lyme/vaccine.htm>.⁶ The use of this vaccine has been controversial for several reasons. There are questions concerning the long-term efficacy, since SmithKline's research trials had only followed the patients for 20 months. This is addressed at <http://www.lymenet.org/files/sbv0526.htm>.⁷ Further research will be required to determine if additional booster immunizations are needed after the third vaccination.

In addition, there are concerns about immunopathology caused by the vaccine. This is addressed at: <http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/rr4807a1.htm>.⁸ This concern stems from the fact that some of the pathology seen in chronic Lyme disease is in patients that have developed high levels of antibody to the Osp A antigen. In these patients, the antibody to Osp A is not protective. Antibody to the C-terminal region of the Osp A was correlated with the severity and clinical duration of the chronic arthritis. This association is related to the presence of the HLA type, HLA-DR4, in the infected individuals. A suggested reason for the immunopathology is a cross reaction between the Osp A molecule and LFA-1, which is a molecule on white blood cells. SmithKline's efficacy and safety trials did not report any immunopathology in vaccinated individuals, but the recommendation is that individuals with antibiotic resistant Lyme disease not be vaccinated.⁸

In addition, reports have surfaced that individuals involved in the SmithKline trials may have actually developed side effects, although this appears to be still in litigation and is not proven. For more information about this, see

http://www.abcnews.go.com/sections/living/DailyNews/lyme_vaccine0516.html.⁹ Current information concerning the status of the safety issues is available at <http://www.lyme.org/index2.html>.

The cost/benefits determination for vaccine use must also include the financial cost of the vaccine. The vaccine cost is about \$100/year with an efficacy of 85%. The CDC estimates that this yields approximately a \$5,700/case averted and approximately \$35,000 per complicated neurologic or arthritic case averted.⁸

GlaxoSmithKline has recently withdrawn marketing and sales of LYMERix™ vaccine. Studies continue towards the development of a vaccine with fewer side effects.¹⁰ The information concerning epidemiology, etiology and pathology, prevention and treatment, laboratory diagnosis and vaccines can be used to evaluate whether or not to be vaccinated with whatever new vaccine becomes licensed.

End Notes

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2. Thanassi, W.T., and R.T. Schoen. "The Lyme Disease Vaccine: Conception, Development, and Implementation." *Annals of Internal Medicine* 132(8):661-8.
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7. LymeNet. 1998. "FDA Advisory Committee Recommends LYMERix for Approval." Available at: <http://www.lymenet.org/files/sbv0526.htm>
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