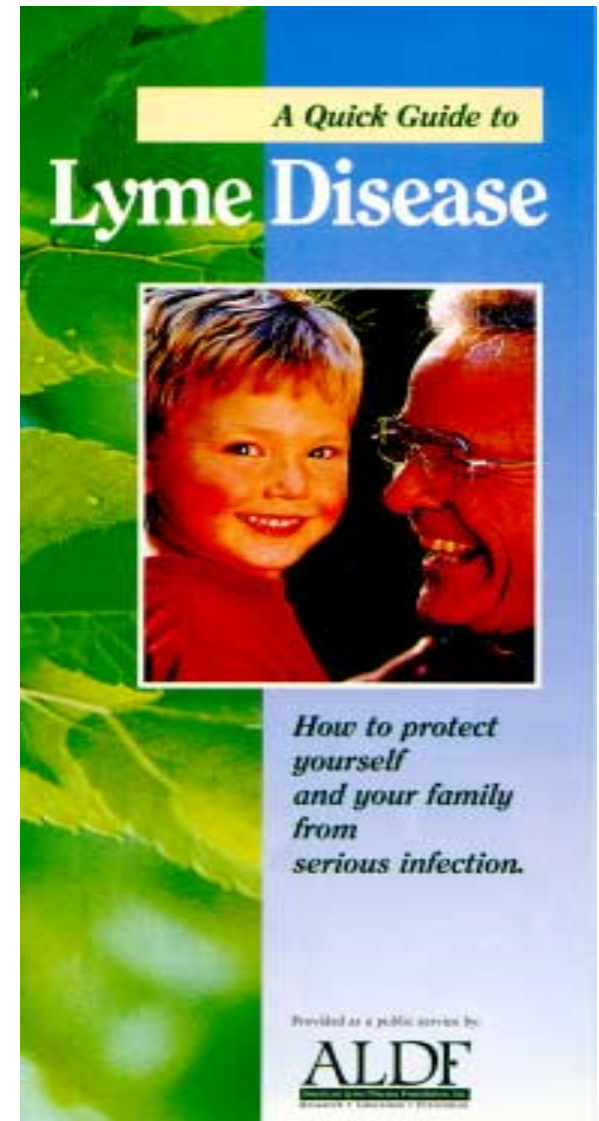


Ticks & Lyme Disease: California's Perspective

April 2004

Gary Green, MD
Infectious Diseases
Kaiser Medical Center
Santa Rosa, California

Credible Lyme Pamphlets



Ticks...

Local and Worldwide Vectors for:

- Bacteria
- Viruses
- Protozoa

Class Arachnida = **blood-sucking arthropods**
some ticks can survive 15 years without feeding

3 Families:

- **Ixodidae** (hard ticks)
- **Argasidae** (soft ticks)
- Nuttallielidae (features of hard and soft ticks)

Rationalists vs Empiricists (1)

Rationalists:

Use scientific studies to develop models of disease and appropriate diagnostic and therapeutic responses.

Empiricists:

Base models on community events, develop diagnostic and management schemas that are compatible with observations, but often at odds with scientific conclusions.

(1) Sigal LH. *Ann Int Med.* 2002. 136(5); 413-419

USA Tick Related Diseases

- Tick Paralysis *
- Relapsing Fever *Borrelia hermsii*
- Lyme Disease *Borrelia burgdorferi*
- Ehrlichiosis
 - HME *Ehrlichia chaffeensis*
 - HGE *Anaplasma phagocytophilum*
- Babesiosis *Babesia WA-1, B. microti*
- Rocky Mtn Spotted Fever *Rickettsia rickettsii*
- Colorado Tick Fever *Coltivirus*
- Tularemia *Francisella tularensis*
- Q Fever *Coxiella burnetii*
- Powassan Encephalitis Powassan virus

Lyme History

- 1977: First recognized in USA in cluster cases of JRA in Lyme, Connecticut

Steere AC, et al. *Arthritis Rheum.* 1977; 20:7-17.

- 1978: First reported case in California, Sonoma County

Naversen DN, Gardner LW. *Arch Dermatol.* 1978; 114:253-4.

- 1982: Etiologic spirochete isolated from tick *Ixodes scapularis* (*Ix. dammini*)* ; named after Willy Burgdorfer, Ph.D, public health researcher

(*) Burgdorfer W. et al. *Science.* 1982; 216:1317-1319.

Borrelia burgdorferi Nomenclature

3 pathogenic *genospecies* of
B. burgdorferi sensu lato complex: (1,2)

- *B. burgdorferi sensu stricto*
 - almost exclusive North America isolate, occasionally Europe
 - *B. garinii*
 - *B. afzelii*
- } more common in Europe and Asia

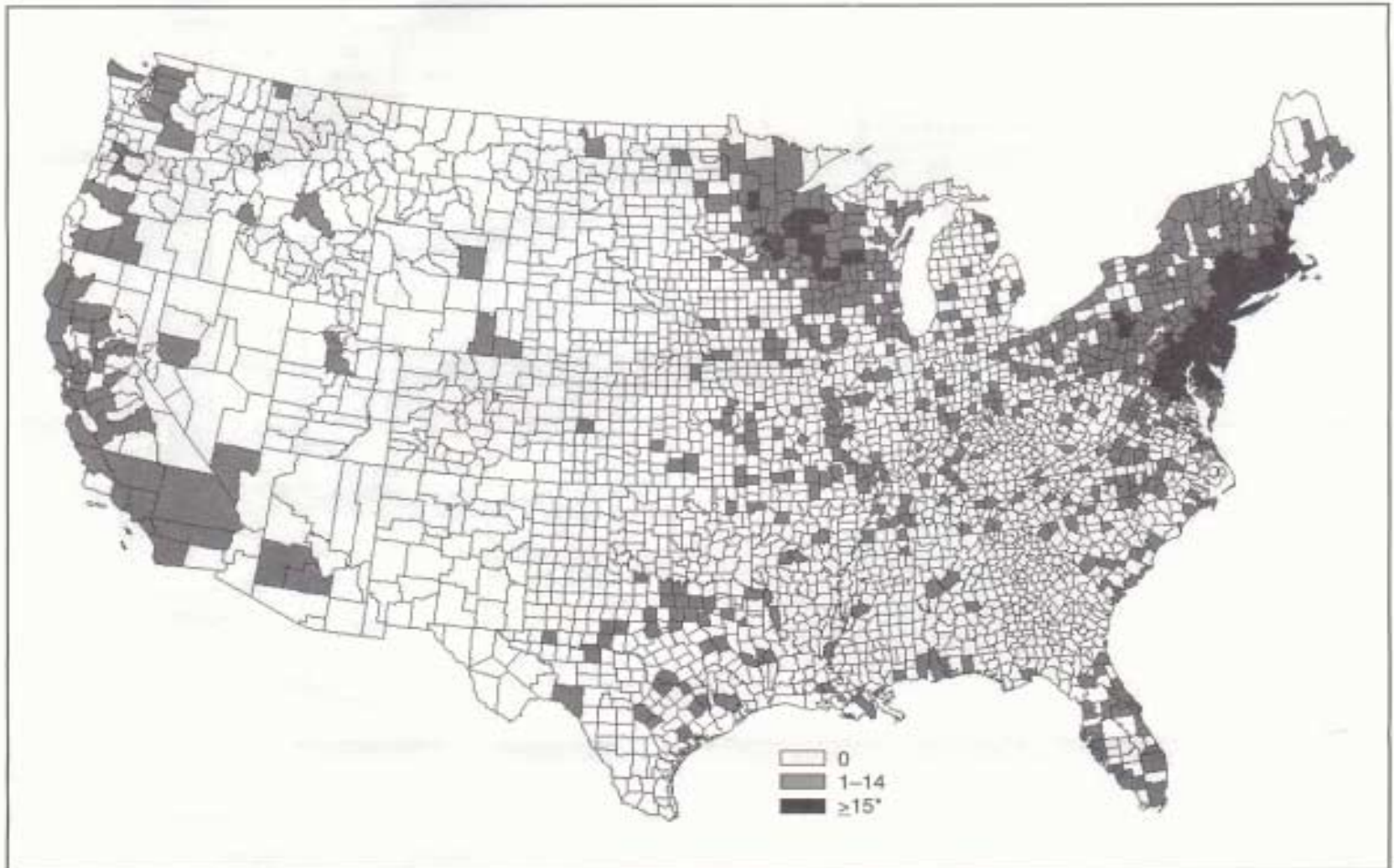
(1) Shapiro ED, Gerber MA. *CID*. 2000; 31: 533-542.

(2) Baranton G, et al. *Int J Syst Bacteriol* 1992. 42; 378-383.

US Lyme Prevalence

MMWR. Jan. 8, 2002; 51(2): 31

FIGURE 2. Number of cases of Lyme disease, by county — United States, 2000



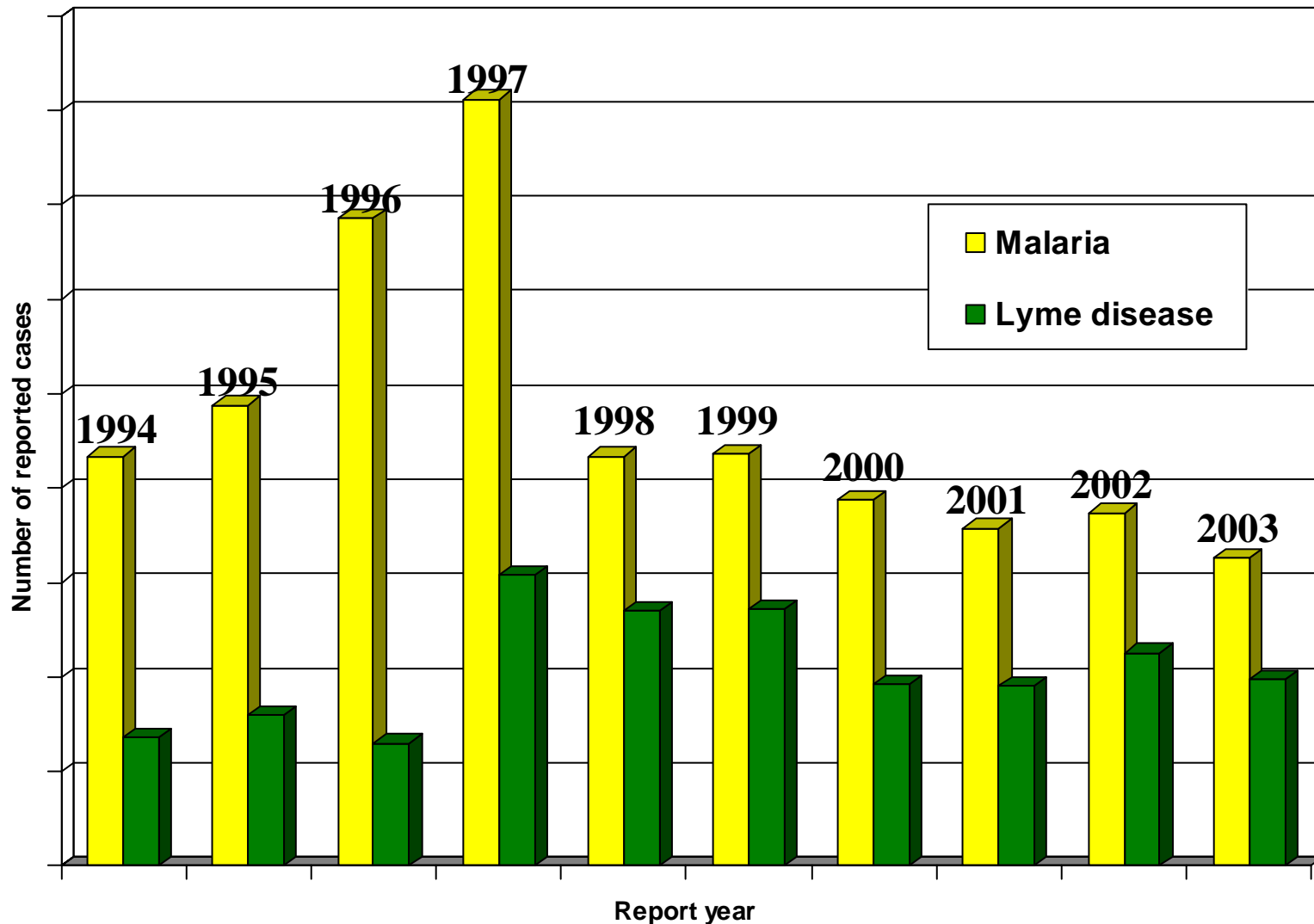
* Total number of cases from these counties represented 90% of all 2000 cases.

Arthropod Infections

Most common vector-borne California infection:

imported malaria

Reported Cases of Selected Vector-borne Diseases in California, 1994-2003*



*Internal data, CA DHS, courtesy of Curtis Fritz

Epidemiology

- Lyme disease most common tick-borne infection in USA(1)
- USA (1999) 16,273 cases reported to CDC (1, 2)
–92 % from NY, CT, MA, RI, PA, DE, NJ, MY, WI
- California (1999) 94 cases reported to DHS (3)
–16 reported exposure outside of CA

(1) CDC. Lyme disease - United States. *MMWR*. 2001; 50(10):181-185.

(2) Lyme Disease Cases Reported to CDC by State Health Depts, 1990-1999. June 21, 2001. www.cdc.gov.

(3) Vector-borne Diseases in California. California DHS 2001 Annual Report, www.dhs.ca.gov/ps/dcdc/disb/disbindex.htm

Tick Entomology

Family: Ixodidae (HARD TICKS)

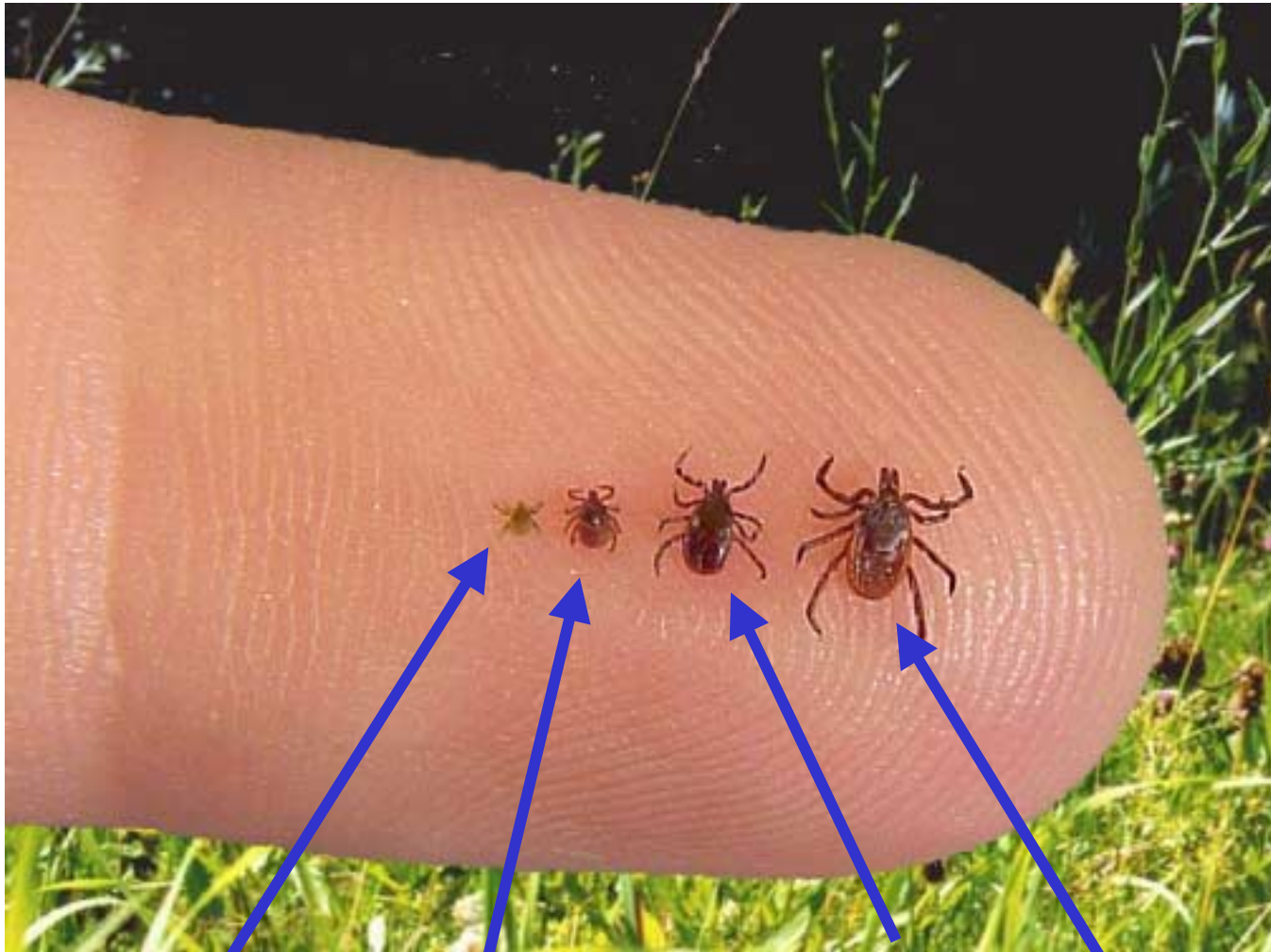
- Ticks feed slowly and continuously (2-72 hours)
- *More time is required to transmit infections*
- Adults ticks exhibit “*questing*” behavior:
 - Tick climbs to top of vegetation to wait for host
 - Vibration \pm CO₂ --> “wave” arms for host attachment
- Interface of forest & field is ideal tick habitat
- Hard ticks favor brushy, woody, leafy, weedy areas (many mammals are located in these areas)

“Questing” *Ixodes scapularis*



Ixodes pacificus

Western Black-legged Tick



larva

nymph

adult male/female

Ixodes pacificus

- “Western black-legged tick”
- Distribution: western Canada - northern Mexico
- Potential human infections:
 - Lyme Disease (*Borrelia burgdorferi*)
 - Ehrlichiosis (*A. phagocytophilum*)
- Only *nymph, adult-female* transmit lyme to humans *

Ixodes scapularis

- Formerly *Ixodes dammini*
- “Black-legged deer tick”
- Northern form (Ontario; NH - MD - WI/MN)
- Southern form (northern Mexico)
- Lyme disease (*Borrelia burgdorferi*)
- Babesiosis (*Babesia microti*)
- Ehrlichiosis (HGE) (*A. phagocytophilia*)

Tick Avoidance

- Remove leaf litter (nymphs attach to leaves)
- Check children often and thoroughly
- Wear light-colored clothing
- Wearing long sleeves and long pants
- Tuck pant legs into socks
- Apply DEET to clothing and exposed skin
- Apply permethrin to clothing (only)

American Lyme Disease Foundation. Lyme Disease brochure.

(www.aldf.com)

Tick Removal



- Remove tick with forceps/tweezers close to mouth parts
- Crushing ticks with bare fingers can theoretically be infectious
- Leaving embedded mouth parts in skin may result in “tick granuloma” (itchy bump)

Human Behavior - Tick Exposure *

UC Hopland Research Center (Mendocino county)

Activities increasing risk of *nymph* tick encounters:

- *sitting on log* 30% (≥ 1 tick encounters)
- *gathering wood* 19%
- *sitting against tree* 13%
- stirring then sitting on leaf litter 8%
- sitting on leaf litter 6%

ticks acquired independent of the type footwear worn (hiking boots, sandals, running shoes)

(*) Lane R, et al. *J Med Entomol.* 2004; 41(2): 239-248.

B. burgdorferi Host Relationships

Neotoma fuscipes
(dusty-footed woodrat)

Sceloporus occidentalis
(western fence lizard)

Borrelia burgdorferi
Borrelia bissetti

WOODRAT
lagamorphs
larger mammals
birds



Ixodes neotomae



Ix pacificus

Ix pacificus Life Cycle

Western-black legged tick = **LIZARD TICK**

3 year life cycle (1): egg - larva - nymph - adult

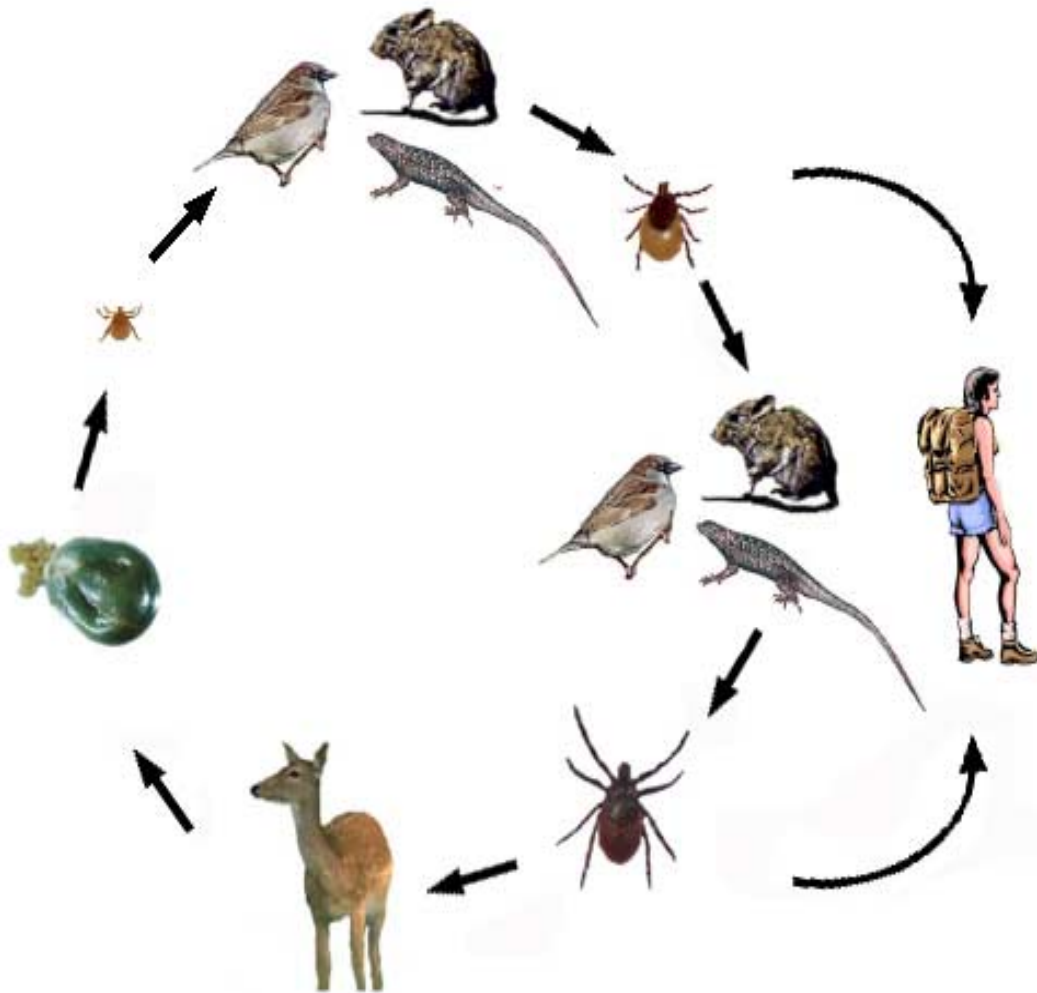
- Winter: female adult feeds -> lays ~800 eggs
- Summer: eggs hatch
- Spring: larvae feed on lizards (leaf litter)
- Spring: nymphs feed on lizards (leaf litter)
- Winter: adult tick quests in grass for mammals

B. burgdorferi **CANNOT SURVIVE** in lizard (2)
(complement-killing via alternate complement pathway)

(1) Padgett K, and Lane R. *J. Med Entomol.* 2001. 38(5):684-693.

(2) Kuo M, Lane R, Giclas PC. *J Parasitol.* 2000. 86(6):1223-1228.

Ix pacificus Life Cycle



Active Feeding Months

Nymphs: March-Aug
(peak April - June)

Adults: Oct - March
(peak Dec - Feb)

Eisen RJ et al. *Med Vet Entomol.* 2002; 16: 235-244.

“Questing” *Ixodes pacificus*



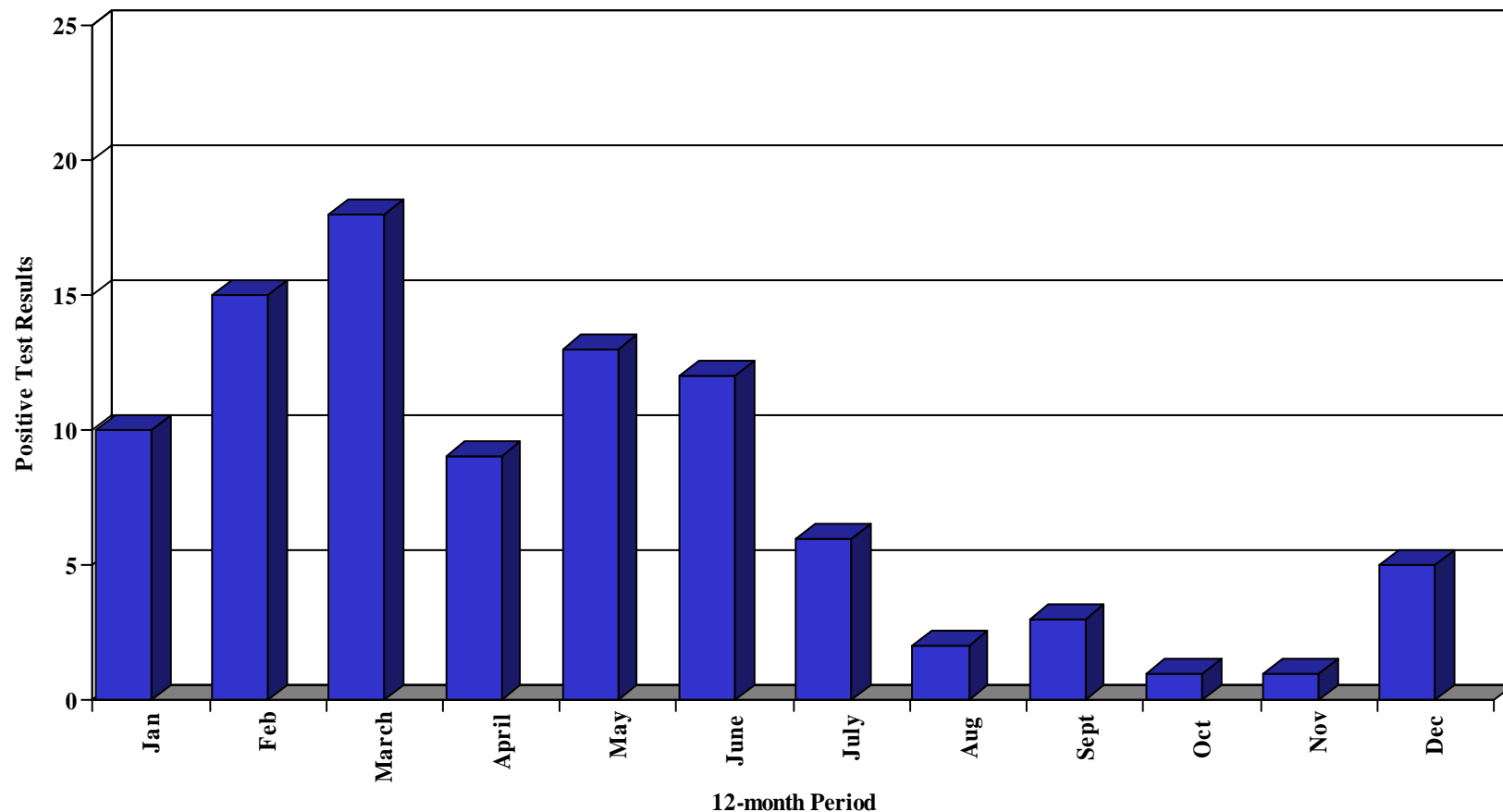
Sonoma County Tick Testing

Ticks brought to Public Health laboratory by public since 1993, >95% of tick submitted/tested were *Ixodes* species *Ixodes* ticks tested for *B. burgdorferi* by IFA

<u>1998-2001 data</u>	<u>adults</u>	<u>nymphs</u>
# ticks <i>Ixodes spp</i>	5129	1161
# (+) <i>B. burgdorferi</i>	97	16
% (+) <i>B. burgdorferi</i>	1.9%	1.4%

Sonoma County Public Health Laboratory,
David Yong, Ph.D., and Michael Ferris.

Seasonal (+) *B. burgdorferi* Tick Testing, Averaged 1992-1996*



*Sonoma County Public Health Laboratory,
David Yong, Ph.D., and Michael Ferris.

Ix pacificus Nymph Infection Rates Mendocino County*

3.4% (234)	<i>A. phagocytophilum</i> (HGE)
3.9% (234)	<i>B. burgdorferi</i>
0	<i>E. chaffeensis</i>
15.4 % (2)	coinfected HGE/ <i>B.burgdorferi</i>

*Lane R, et al. *J Med Entomol.* 2004; 41(2): 239-248

Ix pacificus Lyme Transmission

- animal model: deer mice (*Peromyscus maniculatus*)
- *B. burgdorferi* strain CA4 (highly infectious)
- deer mice exposed to nymph *Ix pacificus* 24, 48, 72 hours, or until ticks feed to repletion (>96 hrs)

<u># mice infected</u>	<u>tick exposure time</u>
0/8 (0%)	24 hrs
1/9 (11%)	48 hrs
2/8 (25%)	72 hrs
8/10 (80%)	≥96 hrs

Infectivity Varies by Strain

- animal models:
 - deer mice (*peromyscus maniculatus*),
 - hamsters,
 - Swiss Webster mice
- Bb isolates evaluated: CA2, CA3, CA4, CA7, CA8, CA9
- CA4 appeared most infectious to rodents
- CA3, CA4, CA7, CA8 infectious by Cx to all 3 rodents
- CA2 lower infectivity by Cx (only Swiss Webster mice)
- CA9 not recovered from any rodents

California Lyme Risk After Tick Bite

- “in California, the average risk for spirochete transmission from a recognized *Ix. pacificus* bite ranges 0.0005 to 0.004.” (1)
- *B. burgdorferi* infection risk is 4 chances/1000 to 5 chances/10,000 if the correct tick is identified (undetermined period of tick attachment)
- tick identification and IFA testing for *B. burgdorferi* is available at many PH labs, but not recommended in recent IDSA guidelines (2)

(1) Fritz C, Vugia D. *Infect Dis Rev.* 2001; 3(3): 111-122.

(2) Wormser GP, et al, *CID.* 2000. 31(1); S1-S14

Prophylactic Lyme Treatment

- Prospective Placebo-Controlled Study in Westchester County (New York)
- *hyper-endemic zone*
- single 200mg dose doxycycline vs placebo
- pts > 12 years age, attached *I. scapularis*
- EM developed: 0.4% doxy, 3.2% placebo
- no asymptomatic seroconversions
- nausea and vomiting common in doxy patients
- cost-effective if risk of infection > 3.6%
- Prophylaxis for 40 deer tick attachments would be needed to prevent 1 case EM

Nadelman RB, et al. *NEJM*. 2001; 345:79-84

Controversies in TRANSMISSION

- Transmission through sexual activity ? *NO!!*
 - *B. burgdorferi* as Sexually Transmitted Disease ?
 - failed transmission in hamster model research (1)
- Perinatal transmission to fetus in pregnancy? (rare)
 - 2 infants deaths 1st wk of life, mothers with Lyme disease during pregnancy, data inconclusive (2,3)
 - failed transmission in hamster model research (1)
 - single case perinatal transmission HGE (4)

(1) Woodrum JE, Oliver JH. *J Parasit.* 1999; 85:426-430.

(2) Schlesinger PA, et al. *Ann Intern Med.* 1985; 103:67.

(3) Weber K, et al. *Pediatric Infect Diseases.* 1988; 7: 286.

(4) Horowitz HW, et al. *NEJM.* 1998; 339:375-378.

Diagnosis

- **CLINICAL DIAGNOSIS** based on explicit objective evidence in the proper setting and geographic region (1,2)
 - NOT histologic diagnosis
 - NOT serologic diagnosis
 - NOT a diagnosis of exclusion
- Serology developed as *adjunct* to clinical Dx (3)
- (+) serologic test is NOT diagnostic of active infection, only represents an *immune response* to *B. burgdorferi* (2)
- 10-20% US pts have asymptomatic infections (3, 4)

(1) Shapiro ED, Gerber MA. *CID*. 2000; 31: 533-542.

(2) Sigal LH. *Ann Int Med*. 2002. 136(5); 413-419

(3) Steere, A. *NEJM*. 2001. 345(2); 115-125.

(4) White DJ, et al. *JAMA*. 1991: 266: 1230.

Erythema Migrans

- important *objective* specific diagnostic sign
- 80-90% patients develop EM lesions (1,2,3,4)
- rash is warm to touch, *not* typically painful
- Early Localized Infection
 - EM location at tick bite
 - ~30% patients recall tick bite at site of EM (1)
- Early Disseminated Infection
 - rash(s) distant from site of tick bite

(1) Shapiro ED, Gerber MA. *CID*. 2000; 31: 533-542.

(2) Sigal LH. *Ann Int Med*. 2002. 136(5); 413-419

(3) Gerber MA, et al. *NEJM*. 1996. 335;1270-1274.

(4) Steere, A. *NEJM*. 2001. 345(2); 115-125.

Erythema Migrans



Schwartzberg

Standard Serologic Testing

Standard 2-Test Serologic Evaluation: (1, 2, 3)

Step (1) EIA (or IFA)

- if EIA (or IFA) (-) --> stop
- if EIA (or IFA) “+” or equivocal --> step 2 WB

Step (2) IgG and IgM WESTERNBLOT

- endorsed by: CDC, ACP, FDA, ASTPHLD (2)

(1) Tugwell P, et al. *Ann Intern Med.* 1997;127: 109.

(2) CDC. *MMWR.* 1995; 44:1-591.

(3) Steere A. *NEJM.* 2001. 345(2); 115-125

Lyme Serologic Testing

- Sensitivity of 2-test EIA-WB approach: (1, 2)
 - Acute Infection (EM) 30 - 40 % (+) serology
 - 2-4 weeks after Sx's 60 - 70 % (+) serology
 - 4-6 weeks after Sx's \geq 90 % (+) serology
- 10-20% US pts have asymptomatic infections (2,3)

(1) Steere, A. Mandel et al. Principles & Practices of Infectious Dis. 5th ed. 2000. pp. 2504-2518.

(2) Steere A. *NEJM*. 2001. 345(2); 115-125

(3) White DJ, et al. *JAMA*. 1991; 266: 1230.

Lyme Diagnostic Tests

- Standard ELISA antibody testing

B. burgdorferi ELISA II

Diamedix Corp

BioMerieux VIDAS

MarDX Diagnostics, Inc

Meridian Premier Lyme EIA

Sigma Diagnostics

Wampole (Zeus) EIA

Wampole ELISA

Wampole PreVue

Zeus Scientific EIA

- Kinetic EIA

- C6 ELISA Test (Specialty Laboratory, Santa Monica)

- IFA

- Westernblot (IgG and IgM)

(similar # tests/labs as above for ELISAs)

Lyme Serologic Testing

- False (+) EIAs (1,2)

T. pallidum

H. pylori

B. hermsii

Varicella

mouth treponemes

Pregnancy

Lupus

Rheumatoid Arthritis

non-pathogenic *Borrelia* spp

(1) Barka NE, et al. [Letter] *JID*. 1990; 161: 1312

(2) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42.

Different *Borrelia* Species

PATHOGENIC species (1):

- *B. hermsii*
- *B. recurrentis*
- *B. burgdoferi*
- *B. lonestarii*

(1) Shapiro E, Gerber M. *CID*. 2000.
31: 533-42.

NON-pathogenic species (2):

- *B. andersoni*
- *B. bissetti*
- *B. japonica*
- *B. lusitaniae*
- *B. balasiana*

(2) Steere, A. Mandel, et al. Principles & Practices of Infectious Diseases.
5th ed. 2000.

Westernblot Lyme Criteria (1,2,3)

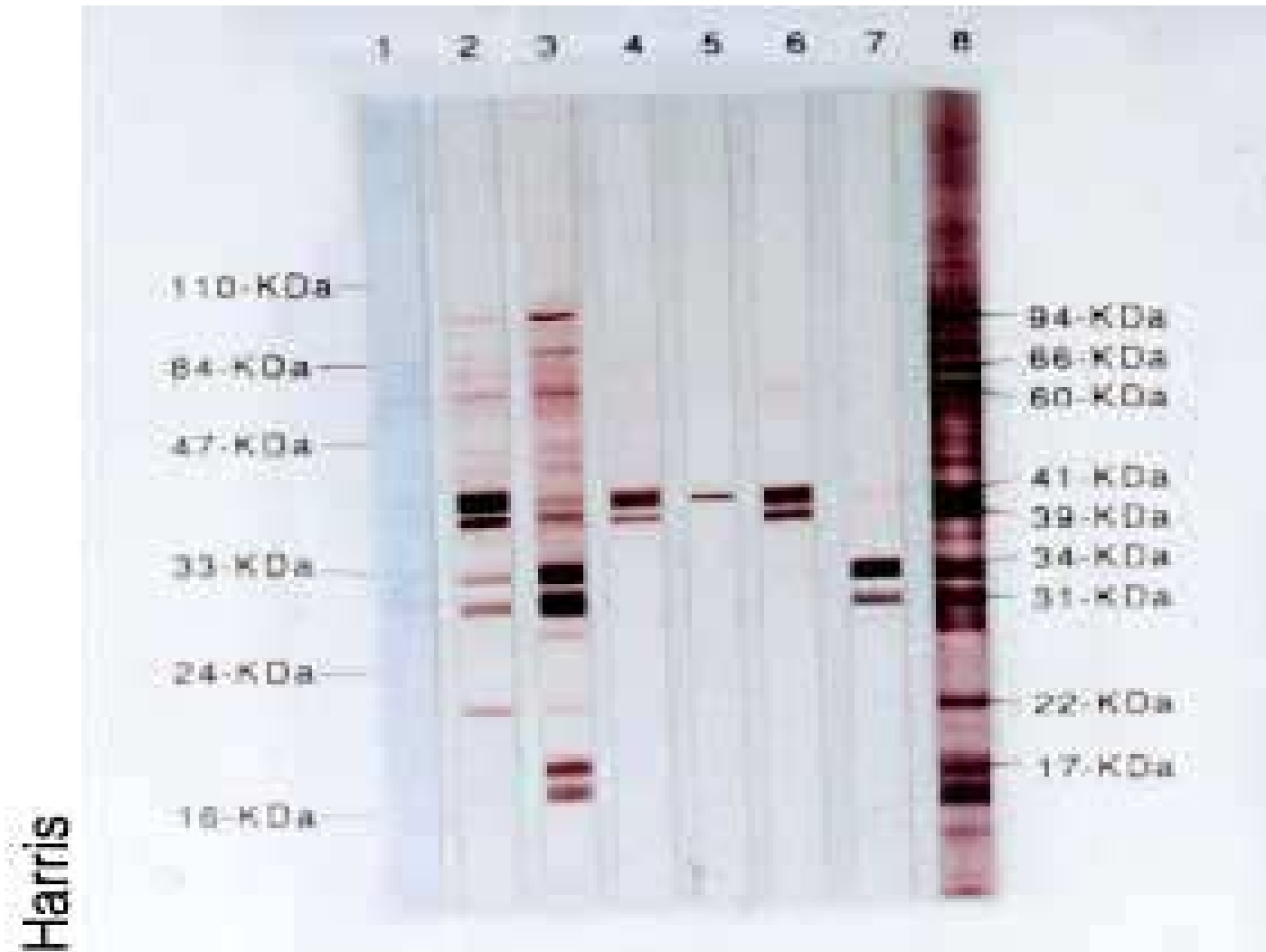
- WB is designed to confirm EIA, limit false (+) results (2)
 - (+) **IgG Westernblot** = 5 of 10 (+) bands
18, 23, 28, 30, 39, 41, 45, 58, 66, 93 kD
 - (+) **IgM Westernblot** = 2 of 3 (+) bands
23, 39, 41 kD
(+) single 23 and 41 may still be a *false* (+)
- equivocal bands (“+/-”) are NOT positive (2)

(1) Tugwell P, et al. *Ann Intern Med*. 1997; 127: 109.

(2) CDC. *MMWR*. 1995; 44:1-591.

(3) Steere A. *NEJM*. 2001. 345(2); 115-125

Lyme Disease Western Blot



(+) EIA should be confirmed with WB

Serologic Testing

- Selection of a *reliable laboratory* is *essential*
 - Kaiser Permanente Regional Laboratory
 - Sonoma County Public Health Laboratory
 - Santa Monica (regional) Lab - C6 ELISA tests
 - L2 Diagnostic Research Laboratory (Yale Univ.)
- Sonoma County Public Health Laboratory
 - *100 % proficiency* for Tick-Transmitted Disease testing for 12 years (Lyme, Babesia, Ehrlichia) (1)

(1) Personal Communication: David Young Ph.D. Director, Sonoma County Public Health Laboratory, DHS. Internal Documentation. Nov 2003.

C6 *B. burgdorferi* (Lyme) ELISA Kit

- Immunogenetics, Inc (Cambridge, MA)
- FDA approved May 2001 (1)
- antigen derived from VlsE protein
 - specific and highly immunogenetic
 - less cross-reactions, even in LYMErix vaccinated pts
- overall 97% sensitivity (1)
- potential future utility in following disease response (like RPR)

(1) www.FDA.gov

Lyme Serology Key Points

- Serology is always adjunctive data to clinical picture (a)
- (+) result represents *immune response* to *B. burgdorferi* (b),
(+) result is NOT diagnostic of active/ongoing infection (b)
- single result should NOT be sole criterion for diagnosis (c)
- should only ordered in *appropriate* clinical settings (d)
when there is reasonable positive predictive value
- NOT appropriate for patients with nonspecific symptoms
only (e.g., Chronic Fatigue Syndrome or Fibromyalgia) (e)

(a) Steere, A. *NEJM*. 2001. 345(2); 115-125.

(b) Sigal LH. *Ann Int Med*. 2002. 136(5); 413-419

(c) Hedberg CW, Osterholm MT. *Ann Int Med*. 1990; 150: 732

(d) FDA Public Health Advisory. 07-07-97. Assays for antibodies to *B. burgdorferi*.

(e) Rusk MH, Gluckman SJ. Serologic testing for Lyme disease. *JAMA* 2000;283:609

IgM EIA and WB Persistence (1)

- *IgM persistence does not indicate ongoing infxn*
10-20 year follow up New England Study
(all patients treated per standard protocol)

Early Lyme disease:

83% initially (+) IgM EIA & WB, 48% (+) EIA IgG

10% had (+) IgM WB @ 10-20 yrs post-Tx (no Sx's)

Late Lyme disease (arthritis):

38% initially (+) IgM EIA & WB, 100% (+) IgG EIA/WB

15% had (+) IgM WB @ 10-20 yrs post-Tx (no Sx's)

Controversies in DIAGNOSIS

- Westernblot testing *without* EIA/IFA
- Lyme Antigen Urine Test (LAUT)
 - high rate of false (+) results *
- Lyme DOT-BLOT Assay (not FDA approved)
- Lyme Multiplex PCR (not FDA approved)
- Reverse WB Antigen test (not FDA approved)

(*) Klempner MS, et al. Intralaboratory reliability of serologic and urine testing for Lyme disease. *Am J Med.* 2001, 110(3):217-219.

Clinical Definition

- Lyme disease is a multi-system inflammatory infection which may involve skin, heart, peripheral and CNS, musculo-articular system (1,2)

Three Potential Stages of Infection:

- Early Localized Disease
- Early Disseminated Disease
- Late Disease
- **CLINICAL DIAGNOSIS** (1,2)

(1) Shapiro ED, Gerber MA. *CID*. 2000; 31: 533-542.

(2) Sigal LH. *Ann Int Med*. 2002. 136(5); 413-419.

Early Localized Lyme Disease

- *B. burgdorferi* spirochetes incubate 3-32 days after tick transmission (1)
- *Erythema Migrans*
 - develops at site of tick bite
 - only ~30% patients recall tick bite at site of EM (2)
 - 80-90% patients develop EM (2,3,4)
- occasional regional Lymphadenopathy (1,2)

(1) Steere, A. Mandel, Douglas and Bennett's Principles and Practices of Infectious Diseases. 5th ed. 2000. Churchill Livingstone. 2504-2518.

(2) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42.

(3) Sigal LH. *Ann Int Med*. 2002. 136(5); 413-419

(4) Nadelman RB, Wormser GP. *Lancet*. 1998. 352; 557-562.

Erythema Migrans at Tick Bite Sites



Previous tick bite



embedded tick, early EM

Early Disseminated Lyme Disease

- Spirochetes disseminate hematogenously
- other annular rashes may develop days after EM (distant from site of previous tick bites)
- “flu”: fever, chills, HA, fatigue, malaise
- Without Treatment: (1, 2)
 - GI: ~20% mild hepatitis
 - CNS: 15% lymphocytic meningitis (rare encephalitis), cranial neuropathy (CN VII palsy), or radiculoneuritis
 - CV: ~5% 1st-2nd-3rd AV nodal (heart) block, occasional myopericarditis, LV dysfxn

(1) Steere A. *NEJM*. 2001. 345(2); 115-125.

(2) Steere A. *NEJM*. 1989. 321; 586-596.

Erythema Migrans



Schwartzberg

Late Disseminated Lyme Disease

Without Treatment:(1,2)

- Arthritis (knee) ~**60%** patients, months later
 - joint *swelling* and pain, intermittent/episodic
 - joints warm but not hot to touch (not “septic”)
 - ~10% pts (especially (+)HLA-DRB1*0401) arthritis many persist for months-years even after antibiotic Tx.
- autoimmune mechanism: molecular mimicry between OspA T-cell epitope from spirochete and a synovial adhesion molecule (hLFA-1 alpha) (3)

(1) Steere A. *NEJM*. 2001. 345(2); 115-125.

(2) Steere A. *NEJM*. 1989. 321; 586-596.

(3) Gross DM, et al. *Science*. 1998. 281; 703-706.

Late Disseminated Lyme Disease

WITHOUT TREATMENT:

- Subacute Encephalopathy (1)
 - impaired memory, mood, sleep, language
- Polyneuropathy (1,2)
- Acrodermatitis Chronica Atrophicans (1,2,3)
 - more common in Europe, may occur years later
 - associated with *B. afzelii* or *B. garinii* infections

(1) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42

(2) Steere A. *NEJM*. 2001. 345(2); 115-125.

(3) Steere A. *NEJM*. 1989. 321; 586-596.

Achrodermatitis Chronicus Atrophicans



Masters

More common in European Lyme Disease.
ACA lesions remain PCR and Cx (+) for years
(Asbrink E, Hovmark A. *Acta Pathol Microbiol Immunol Scand.* 1985. 93: 161-163)

Late Lyme Disease

Post-Infectious Syndrome (1,2,4)

- Symptoms similar to fibromyalgia and CFS
- New England study: frequency in Sx of pain and fatigue after Lyme disease was no different than age-matched controls (lyme-negative) (4)
- post-infectious lyme syndrome: no difference in Sx relief after additional prolonged antibiotics vs placebo (additional 28d IV Ceftriaxone, 60 d PO Doxycycline) (3)

(1) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42

(2) Steere A. *NEJM*. 2001. 345(2); 115-125.

(3) Klempner MS et al. *NEJM*. 2001. 345; 85-92.

(4) Seltzer EG, et al. *JAMA*. 2000. 283; 609-616.

Lyme Treatment

Early Localized *and* Early Disseminated (1,2,3)

- Doxycycline 100mg PO BID, 14-21 d
 - age <8 yrs, or cannot tolerate Doxy, or Pregnancy
 - Amoxicillin 50mg/kg PO div TID, 14-21d
 - Pregnant, PCN allergic
 - Cefuroxime axetil 500 mg PO BID, 14-21 d
 - less effective 4th line agents:
 - Erythromycin, Clarithromycin, Azithromycin

(1) Wormser GP, et al, *CID*. 2000. 31(1); S1-S14 (IDSA Tx Guidelines)

(2) Steere A. *NEJM*. 2001. 345(2); 115-125

(3) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42.

Lyme Treatment (1,2,3)

Lyme Arthritis (NOT persisting arthralgias only)

- Doxycycline (100mg PO BID, x 28 days)

Meningitis or Cardiac Disease

- Ceftriaxone 2 gm IV q 24, 14-30 d
- Penicillin G 20 million units IV div q 6, 14-30 d

(1) Wormser GP, et al, *CID*. 2000. 31(1); S1-S14 (IDSA Tx Guidelines)

(2) Steere A. *NEJM*. 2001. 345(2); 115-125

(3) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42.

Treatment Controversies

- Repeated or Prolonged Antibiotic Tx
 - exposes patients to risks of antibiotics
(eg., drug rxn, photosensitivity, esophageal ulcers, BM suppression, serum sickness, *C. difficile* diarrhea, etc)
 - no benefit is clinical trials (1,2)
- Using serial WB analysis as indicator of response to antibiotic treatment

(1) Shapiro E, Gerber M. *CID*. 2000. 31: 533-42.

(2) Klempner MS et al. *NEJM*. 2001. 345; 85-92.

Controversies in TREATMENT

- Malariotherapy (1)
 - historically based on pre-antibiotic era of syphilis Tx
 - inoculation of *Plasmodium vivax* malaria (Mexico),
 - then Tx with chloroquine.
- Intracellular Hyperthermia Therapy (2,4-dinitrophenol)
- Hyperbaric Oxygen (HBO)
- Colloidal Silver. Warning: may result in argyria (grey or blue discoloration of skin/conjunctiva/internal organs) (2)

(1) *MMWR*. 1990; 39:873-875 Imported malaria associated with malariotherapy of Lyme disease.

(2) Federal Register. Colloidal Silver. 1996; 61: 53685-53688.

TREATMENT Risks & Complications

- Potential Complications of IV Antibiotic Tx:
 - Deep Vein Thrombosis at CVC site
 - Bone Marrow Suppression from beta-lactam therapy
 - Antibiotic Associated Diarrhea (*C. difficile* colitis)
 - Line Sepsis
 - recent death 30 year old female, IV antibiotic Tx > 2 yrs for unsubstantiated “chronic Lyme disease” (1)
 - Ceftriaxone biliary precipitation
 - cholelithiasis -> bile duct obstruction
 - 25 cases reported to CDC in 1995 (2)

(1) Patel R, et al. *CID* 2000; 31: 1107-1109.

(2) Ettestad PJ, et al. *JID* 1995; 171:356-361.

Reliable Lyme Information Sources:

- US Centers for Disease Control and Prevention
- National Institute Arthritis & Infectious Diseases (NIAID)
- Food and Drug Administration (testing info)
- American Lyme Disease Foundation, Inc. (ALDF)
- Infectious Diseases Society of America (IDSA)
- University of California, Berkeley
- California Department of Health Services
www.dhs.ca.gov/ps/dcdc/disb/disbindex.htm
- American College of Physicians
- National Institute of Allergy & Infectious Disease (NIAID)