

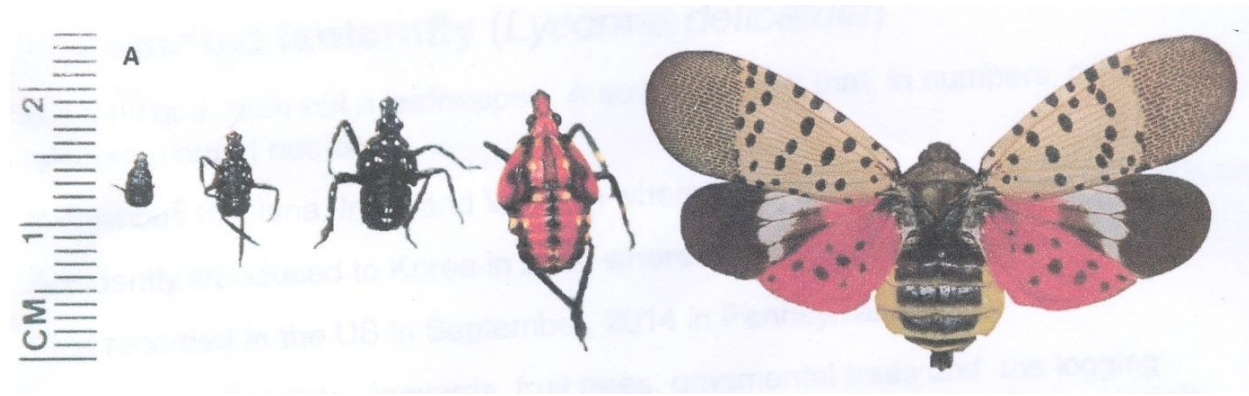
Are Hepatitis C and Lyme Chronic Diseases?

Chronic Disease Symposium

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Spotted Lanternfly (*Lycorma delicatula*)



Hepatitis C

A Chronic Disease?

- Need not be if...
 - Diagnosed
 - Treated
- Why Treat?
 - 8000-13000 deaths/year in USA
 - Major reason for liver transplantation

Hepatitis C Virus Background

- Identified 1989 as small RNA blood-borne virus
- Worldwide reservoir
- 6 Major Genotypes with subtypes
 - Each genotype has 30% or more difference at nucleotide levels giving viral diversity

Hepatitis C Virus Genotype Distribution

Location	Genotype
North America/Europe	1,2,3
Asia	1,2,3,6
Africa/Middle East	4
South Africa	5

Hepatitis C

Acute Infection

- Symptoms of fever, malaise occur in 6-7 weeks
 - Jaundice is rare
 - 80% are asymptomatic
- Lab Studies
 - ALT elevation may occur 4-12 weeks
 - HCV RNA appears at 1-3 weeks
 - HCV antibody appears at 8-9 weeks

Hepatitis C

- 15% Spontaneous remission
- 85% Chronic liver disease
 - 15-55% cirrhosis @ 20 years

Hepatitis C Risk Factors

Mode of Transmission	Transmission Rate
Transfusion <ul style="list-style-type: none"> • Clotting factors before 1987 • Blood products before July 1992 • after 	85% 5% <1%
Organ Transplants <ul style="list-style-type: none"> • Before July 1992 • Seropositive organs 	5% UNK
IVDU	80%
Sexual Contacts <ul style="list-style-type: none"> • Multiple partners • Single 	6% 3%
Needle stick	2%
Infant with Infected mother	<7%

Hepatitis C Virus Screening Strategies

- Baby Boomers
 - esp. Vietnam Vets -Experimentation without addiction
- Old tattoos/piercings
- Prior incarcerations
- HBV or HIV disease
- Body fluid exposures
- Unexplained ALT/AST elevations
- Standard risk factors

Hepatitis C Screening

Who?

- Anyone with risk factors- even if ALT/AST normal

How?

- Serum HCV antibody- if reactive confirm with quantitative HCV PCR

Remember:

HCV Antibody Positive + HCV PCR Negative =

Prior exposure and resolution

or

False positive antibody test

Chronic Hepatitis C Timeline

- Rapid Progressors 10 years
 - Stage 4 Fibrosis (cirrhosis)
- Intermediate Progressors 30 years
 - Stage 4 Fibrosis
- Slow Progressors 50 years
 - Stage 2-3 Fibrosis

Chronic Hepatitis C

Decompensation with Cirrhosis

- Ascites
- Portal hypertension, Variceal bleeding
- Encephalopathy
- Hepatocellular carcinoma
 - 3% year after dx

Chronic Hepatitis C

Extrahepatic Manifestations

- Hematologic
 - Cryoglobulinemia
 - Aplastic anemia
 - Thrombocytopenia
 - B-cell lymphoma
- Renal
 - Nephrotic syndrome
 - Glomerulonephritis

Chronic Hepatitis C

Extrahepatic Manifestations

- Dermatologic
 - Vasculitis
 - Porphyria cutanea tarda
 - Lichen planus
- Endocrine
 - Insulin resistant diabetes
 - Antithyroid antibodies
- Misc.
 - Sialadenitis
 - Uveitis
 - Corneal ulcer

Chronic Hepatitis C

Risks for Disease Progression

- Male
- Acquisition over age 40
- Co-infection HIV, HBV
- Duration of disease
- Immunosuppression
- Over 2 drinks of alcohol daily

Chronic Hepatitis C

Factors Influencing Outcome

Host	Virus	Environment
Gender	Genotype	ETOH
Age	High Viral Load	IVDU
Genetics		HIV,HBV
Race		
NASH		
Immunosuppression		

Chronic Hepatitis C Treatment Targets

- NS 5A Inhibitors
 - Protein required for viral replication
- NS 5B Inhibitors
 - RNA Polymerase
- NS 3/4A Inhibitors
 - Protease required for viral replication

Chronic Hepatitis C Common Treatment Regimens

Ledipasvir (NS 5A)/ Sofosbuvir (NS 5B)
(Harvoni)

Glecaprevir (NS 3/4A)/Pibrentasvir (NS 5A)
(Mavyret)

Chronic Hepatitis C

Barriers to Treatment

- Undiagnosed
- Patient
 - Alcohol and drug use
 - Uncontrolled HIV, HBV
 - Non-compliance
 - Behavioral issues
 - Lack of social support
- Financial
 - Drug Costs 26k-100k
 - No insurance overage
 - High co-pays
 - Formulary benefit plans

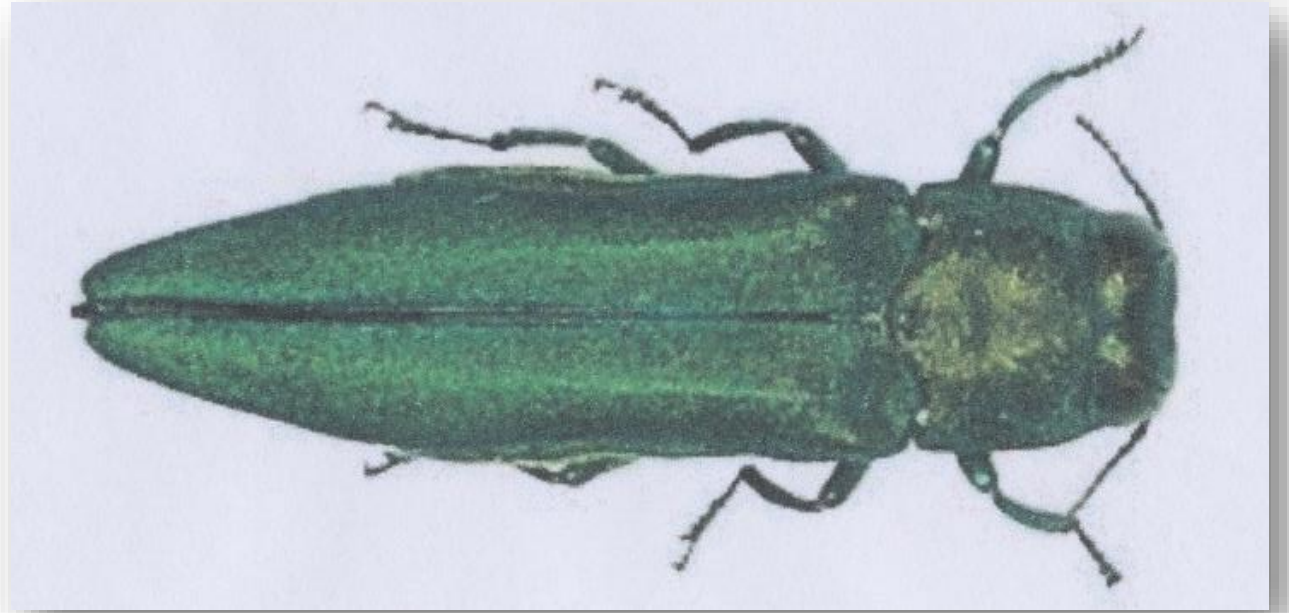
Chronic Hepatitis C

Does Treatment Work?

95% sustained viral response

- Halt disease progression? Yes
- Reverse disease damage? Maybe
- Provide immunity? Probably not

Emerald Ash Borer



Lyme Disease History

- 1909 Afzelius (Europe)
 - Correlates tick bite with erythema migrans
- 1921 Lipshitz (Europe)
 - Identifies *Ixodes ricinus* as vector
- 1940's in Europe
 - EM associated with neurologic and dermatologic conditions
- 1948 Lenhoff (Europe)
 - Spirochete-like structures in skin bx of EM

Lyme Disease History

- 1970 Scrimenti (Wisconsin)
 - First documented EM case in USA
- 1970's Steere (Connecticut)
 - EM associated with arthritis
 - Children and adults in Old Lyme, CT
- 1982 Burgdorfer
 - Isolated new borrelia species

Lyme Disease Agents

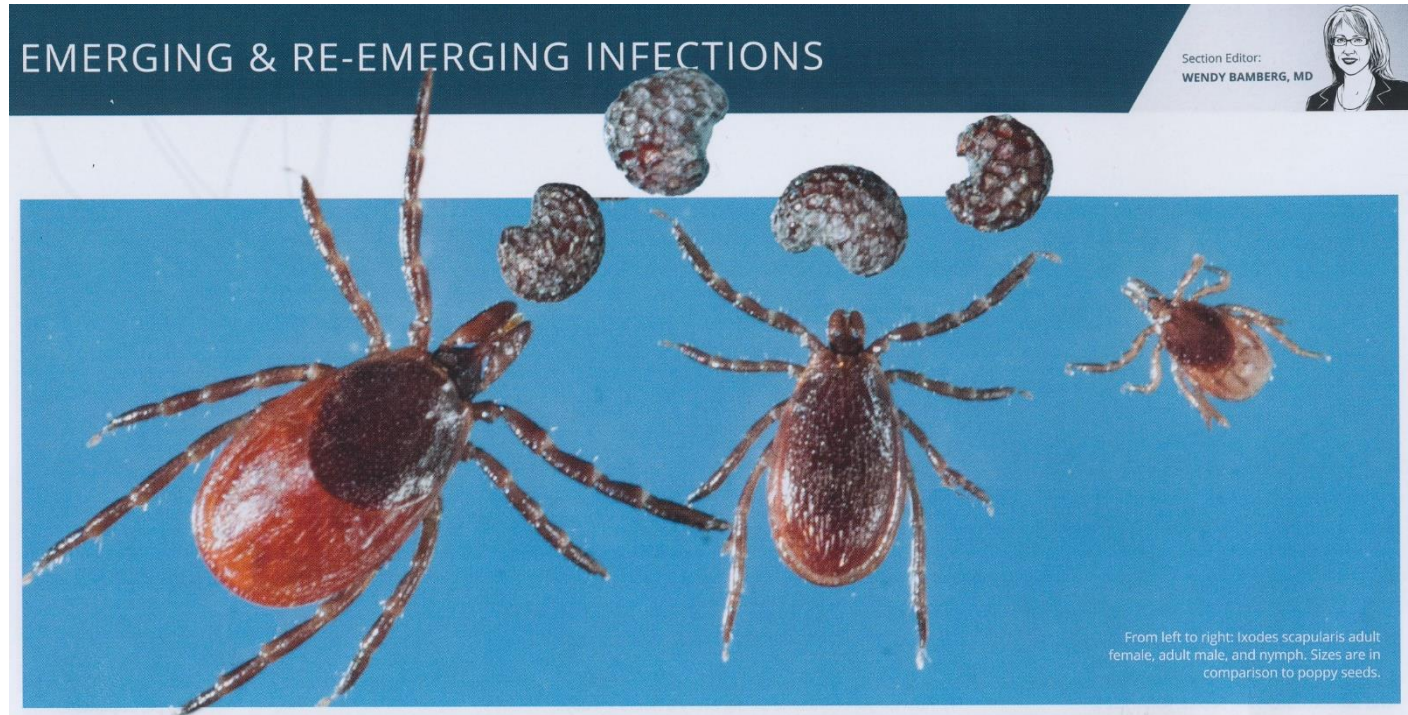
Borrelia burgdorferi	USA, Europe
Borrelia afzelli	Asia, Europe
Borrelia garinii	Asia, Europe
Relapsing Fever Agents	
Borrelia miyamotoi	
Borrelia hermsii	
Borrelia recurrentis	

Tick Borne Diseases



Source: CDC/James Gathany

The Asian longhorned tick has been reported in nine states.



From left to right: Ixodes scapularis adult female, adult male, and nymph. Sizes are in comparison to poppy seeds.

Lyme Disease Vectors (Tick)

Species	Location
Ixodes scapularis “deer tick” “black-legged tick”	USA East Coast
Ixodes dammini	USA East Coast, Midwest
Ixodes pacificus	USA West Coast
Ixodes ricinus	Europe
Ixodes persulcatus	Asia

Lyme Disease

Reservoirs

- Rodents
- Fowl



Disseminators

- White-footed mice
- White-tailed deer



Lyme Disease Blood Tests

- Screening for any antibody
- Western blot specific molecular weight antibodies
- Specific C₆ peptide antibody (IgG)
- Blood smears for borrelia on RBC's
 - Not standardized

Lyme Disease Tests

- CSF-RNA PCR
- Synovial Fluid-RNA PCR
- Skin biopsy- borrelia difficult to visualize

Lyme Disease Antibodies

- May stay reactive for life
 - Sequential testing not useful
- Indicate exposure not immunity
- May not help with re-infection
- Some people don't develop good antibody response
- Take time to develop

Lyme Disease

Common Symptoms

- Constitutional
 - Fatigue, headache, anorexia, fever
- Neurologic
 - Dysesthesias, weakness
- CNS
 - Bell's Palsy, ataxia, cognitive impairment
- Cardiac
 - Bradycardia, heart block, palpitations
- Orthopedic
 - Arthritis, arthralgia, myalgia
- Dermatologic
 - Rashes

Lyme Disease Stages

- Early
 - EM within one month
- Early disseminated
 - Cardiac, Neurological
- Late
 - Arthritis, CNS involvement

Lyme Disease

Standard Antibiotic Therapies

- Oral for 14-28 days
 - Doxycycline 100mg B.I.D.
 - Ampicillin 1000mg B.I.D.
 - Cefuroxime 500mg B.I.D.
- IV for 21 days
 - Penicillin 20,000,000 units daily
 - Ceftriaxone 2gm daily

Lyme Disease

Causes for Chronic Disease

- Undiagnosed
 - Alternative diagnosis
 - Seronegative *
- Treatment failure
 - Borrelia related
 - Dormant phase *
 - Resistant *

* Controversial

Lyme Disease

Causes for Chronic Disease

- Antibiotic related
 - Poor tissue penetration *
 - Poor GI absorption
- Patient related
 - Allergic to antibiotics
 - Poor compliance
 - Co-morbid conditions
 - Co-infections

* Controversial

Lyme Disease

Recurrent Symptoms Post Treatment

- Relapse due to inadequate initial Rx
- Reinfection
- Post Lyme Syndrome
- Co-morbid conditions

Lyme Disease

Post-Lyme Syndrome

- Persisting symptoms after treatment
- Damage from initial infection

Lyme Disease

Chronic Symptoms 6 months After Treatment

Post-Lyme Syndrome

vs

Unremitting Infection

plus

Co-morbid conditions

Lyme Disease Treatment Controversies

- Multiple antibiotics
- Duration of antibiotics
- Complimentary therapies
- Symptomatic therapies