

Cardio-Immu-Knowledgy of Lyme & Associated Diseases

It's not just about the tick.

It's not just about the microbe.

It's all about you.

Lowell I Gerber MD MS FACC

Presentation at ILADS 2018

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Disclosure Statement:

I do not have any financial arrangements or affiliations with any commercial entities whose products, research, or services may be discussed in these materials.

Acknowledgments: *MANY*

- I want to thank my family, friends, health care providers (many of whom are here today), colleagues, and patients who have supported and helped me to achieve a healthy survival of Neurolyme.
- It is with deep gratitude that I thank the ILADS Board and members for allowing me to present this to you.
- This presentation is biased by my own personal journey to find the truth about heart disease and Lyme disease.

EXPERIMENTAL AND MOLECULAR PATHOLOGY 21, 123-137 (1974)

Mechanisms of Blood-Vascular Reactions of the Primate Lung to Acute Endotoxemia¹

JOHN U. BALIS,² LOWELL I. GERBER, EDWARD S. RAPPAPORT, AND
WILLIAM E. NEVILLE

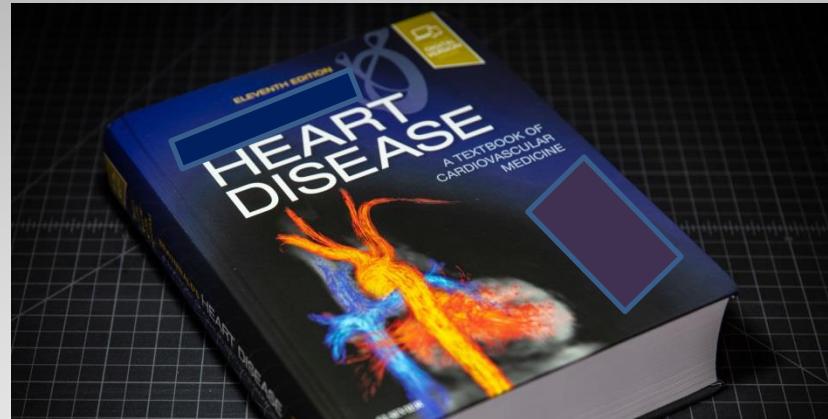
Department of Pathology, Loyola University Stritch School of Medicine, Maywood, Illinois
60153 and Veterans Administration Hospital, Joliet, Illinois 60141

Received November 21, 1973

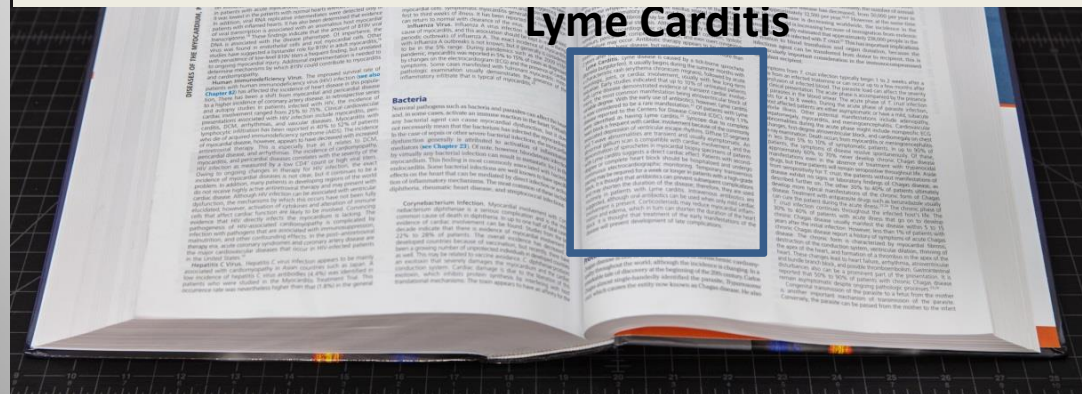
LEARNING OBJECTIVES

- **Re-thinking our concepts of “heart disease”**
 - Current “popular” view of cardiovascular disease
 - The “Diet-Heart Hypothesis” vs “A New Hypothesis”
- **Immunology of cardiovascular disease and Lyme carditis**
 - What have lipids got to do with it?
 - Mast Cells and Endotoxin
- **Heart manifestations of Lyme disease**
 - Conduction system issues
 - Cardiac inflammation
 - Valvular disease
- **Blood vessel manifestations of Lyme disease**
 - Atherogenesis, plaque formation, coronary artery problems
 - Hypercoagulation and Biofilms
- **Unifying comprehensive therapy**
 - Membrane medicine

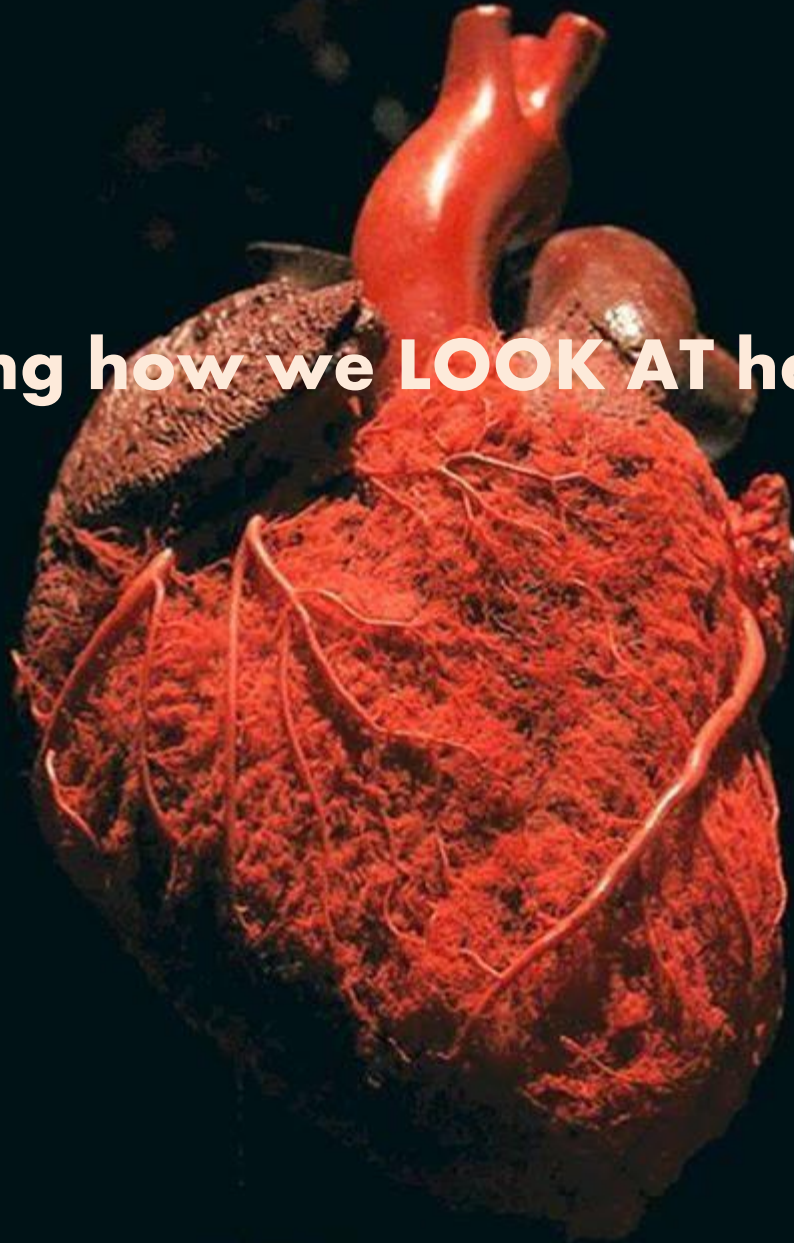
Cardio-Immu-Knowledge of Lyme & Associated Diseases



It is my opinion that the spectrum of the involvement of the cardiovascular system in Lyme and Associated Diseases is under recognized and underappreciated.



Rethinking how we LOOK AT heart disease

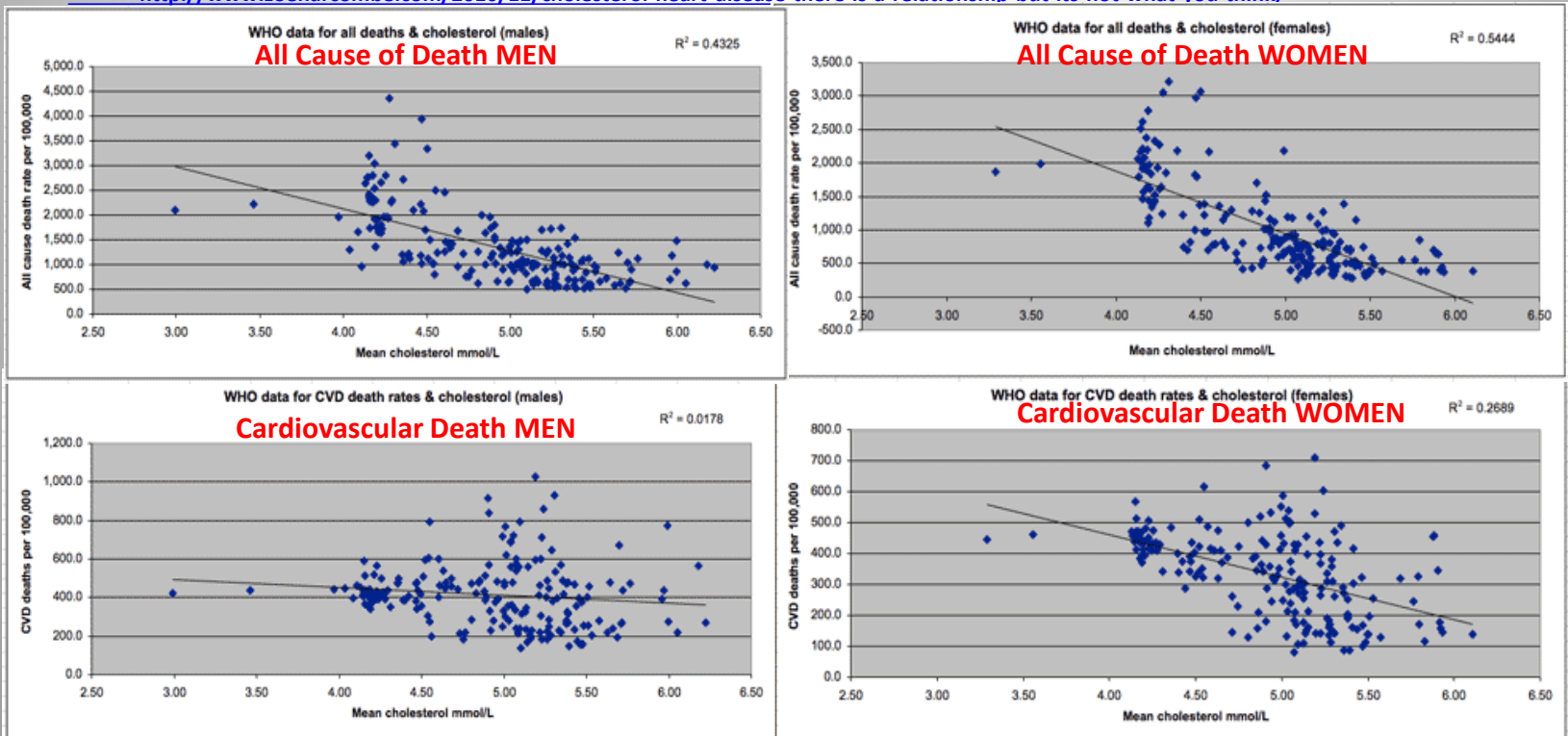


Cardio-Immu-Knowledge of Lyme & Associated Diseases

- Atherosclerotic Cardiovascular Disease is known as the **“leading killer”** in the USA. It is claimed that eating saturated fat causes abnormal elevation of cholesterol in the blood which then leads to blockages in the coronary (and other) arteries subsequently resulting in Heart Attacks, Strokes, Amputations, and Early Death.
- The Diet-Heart Hypothesis.**
- Consider the data from the World Health Organization which shows that high cholesterol is associated with lower heart disease and all cause mortality

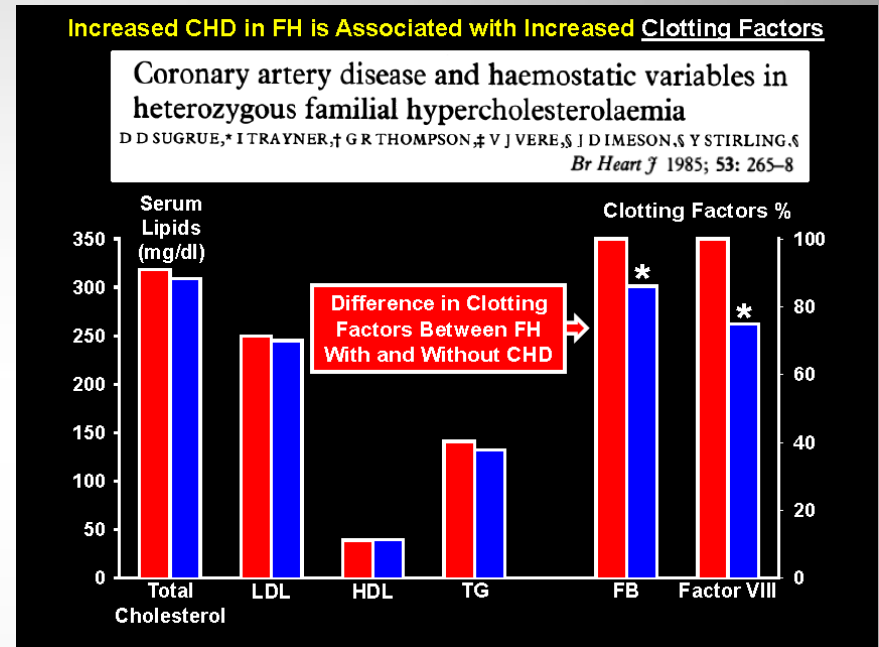
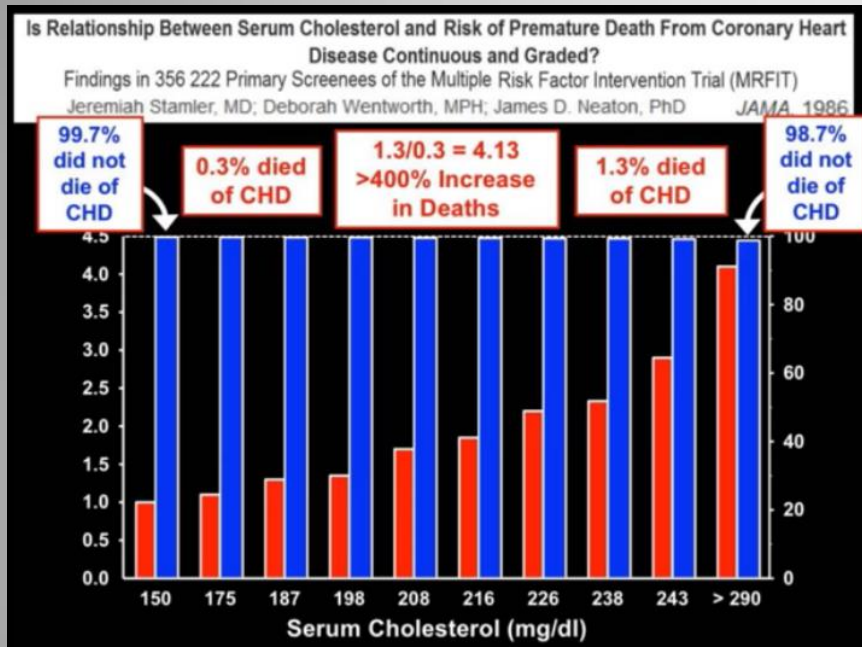
Data of 192 Countries (2002) calculated by Dr. Zoe Harcombe

<http://www.zoeharcombe.com/2010/11/cholesterol-heart-disease-there-is-a-relationship-but-its-not-what-you-think/>

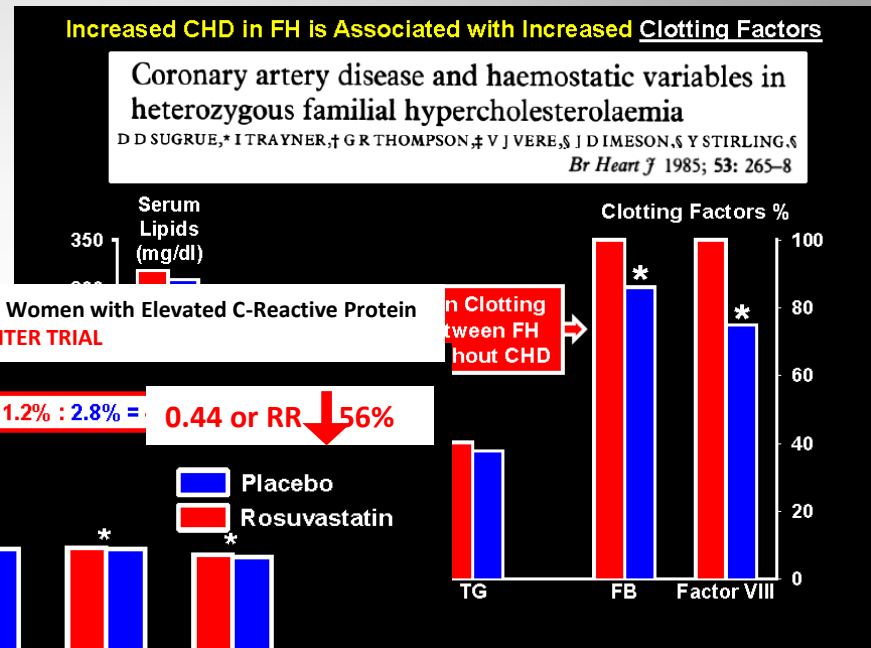
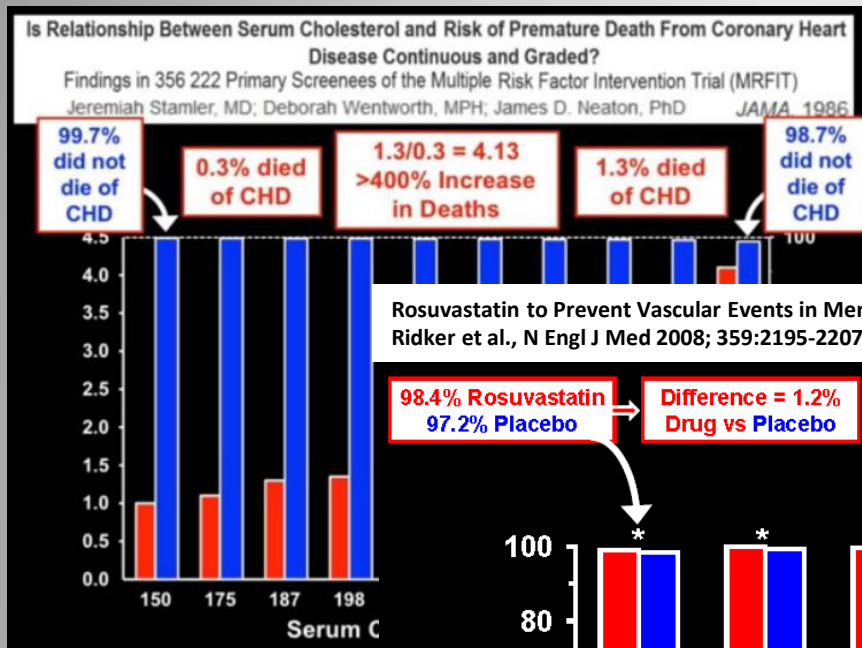


High Cholesterol is NOT associated with increased cardiac mortality.

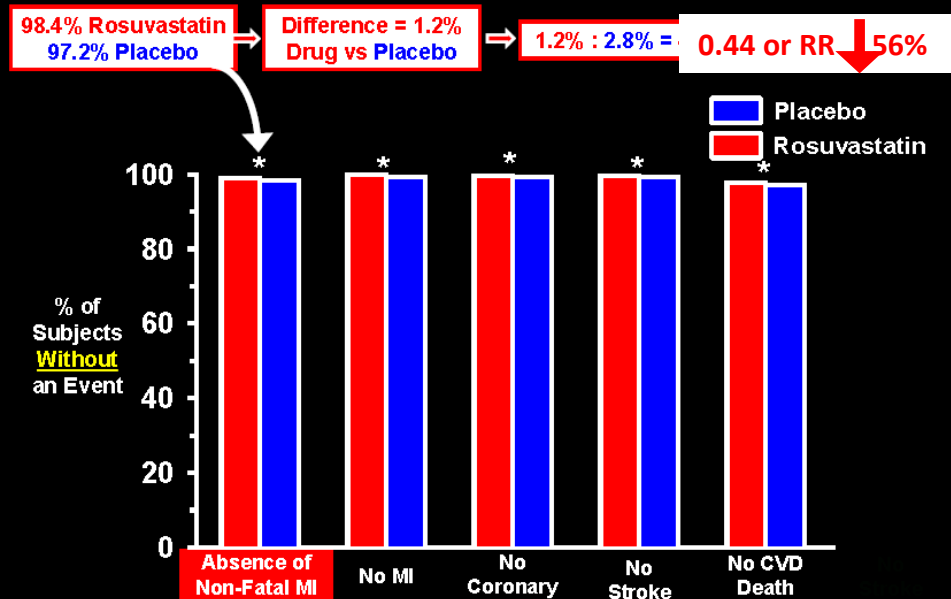
Lack of association of cholesterol levels with outcome



Lack of association of cholesterol levels with outcome



Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein
Ridker et al., N Engl J Med 2008; 359:2195-2207 JUPITER TRIAL



“The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue,” Dr. Horton commented in The Lancet.

www.thelancet.com Vol 385 April 11, 2015

<http://newswire.net/newsroom/news/00088806-world-s-top-scientists-agree-most-researches-findings-are-fraud.html>

- **High LDL-C is inversely associated with mortality in most people over 60 years.**

Ravnskov U et al., BMJ Open 2016;6: e010401.

- “Since elderly people with high LDL-C live as long or longer than those with Low LDL-C, our analysis provides reason to question the validity of the cholesterol hypothesis.”

- **Sudden death cases had more “favorable” levels of total cholesterol, LDL cholesterol, and non-HDL**

Hosadurg N et al., Mayo Clinic Proceedings: Innovations, Quality & Outcomes, 2018 2(3): 257 – 266

- Lack of association between traditional lipid CVD risk factors and sudden death.

- **LDL-C Does Not Cause Cardiovascular Disease: a comprehensive review of current literature**

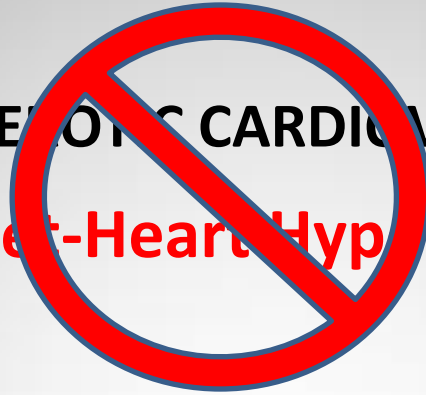
Ravnskov U et al, 2018 Expert Review of Clinical Pharmacology,

- The association between TC and CVD is weak or inverse.
- Statin benefits are exaggerated and adverse events are de-emphasized.
- Familial Hypercholesterolemia is associated with improved longevity.
- Studies have not adjusted for other factors: mental stress, coagulation, inflammation, infections.
- LDL participates in the immune system by inactivating microorganisms and toxic products.
- Infections incriminated as a possible causal factor of CVD.

Conclusion: there may be better methods than cholesterol lowering to prevent atherosclerosis and CVD

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

Diet-Heart Hypothesis



Consider an Alternate Hypothesis:

ATHEROGENIC CARDIOVASCULAR DISEASE

Non-Traditional Risk Factors Associated with Cardiovascular Disease
and Lyme Carditis:

Nutritionally depleted and corrupted food sources
Pollution of air, water, sound, and light
Mercury amalgams and heavy metals
Root canals
EMF and Electro-smog

Genetics
Environment
Infection

Excess Medications and poly-pharmacy
Vaccines
Emotional and Financial Stress
Infections

&

The Immune Response

“ATHEROGENIC” CARDIOVASCULAR DISEASE

CHRONIC INFLAMMATION AS A RESULT OF INJURY

in the presence of IMMUNOSUPPRESSION

Genetic Predisposition

Nutritional, Metabolic ,Hormonal Factors

INFECTIOUS & IMMUNE TRIGGERS

Bacteria/Parasites

Virus/Protozoa/ Mold/Mycotoxin

Cell Wall Deficient/Nano Bacteria

Endotoxin-Lipopolysaccharide (LPS)

METABOLIC ENDOTOXEMIA

ENVIRONMENTAL TOXINS

Endocrine Disruptors

Chemotoxins, Pollutants, Pesticides, Herbicides, Glyphosate

OXIDATIVE STRESS

ENDOTHELIAL DYSFUNCTION

**Lyme and
Co-
infections**

**Leaky Gut
Dysbiosis**

Cell membrane health is a reflection of genetic and epigenetic influences

The Red Cell Membrane Fatty Acid Analysis

Kennedy-Krieger Peroxisomal Lab / Johns Hopkins and Neurolinid.org

VLCFAs/Renegades =
Epigenetic insult
Damage from
SPIROCHETES
MOLD and VIRUS

BURN IT				BUILD IT			
TRANS ISOMERS		VLCFA'S		MYELINATION		STRUCTURAL	
		Lignoceric	59.66 H			Palmitic	-85.58 L
		Hexacosanoic	156.49 H			Stearic	-70.75 L
		Triacosanoic	50.00 H			Oleic	-124.92 L
						Palmitoleic	-81.13 L
SATURATED ODD		RENEGADES		SUMMATION			
		Phytanic	100.00 H	Total Saturates	-90.03 L		
		Pristanic	1950.0 H	Total w6	-175.02 L		
				Total w9	-48.92 L		
				Total Lipid Cont	-127.87 L		

Very Low Total
Lipid Content
POOR MEMBRANE
INTEGRITY

Endothelial Dysfunction is a result of Membrane Dysfunction
This is getting at the root cause of the pathophysiology

Severe
Omega 6:Omega 3
IMBALANCE
Affects Mitochondrial,
Cardiac, CNS function
& Immune Response

OMEGA 6			OMEGA 3		
Linoleic	-88.64	L	Alpha Linolenic	-79.69	L
Gamma Linolenic	-81.58	L	Eicosapentaenoic	377.04	H
Dihomo-γ Linolenic	-109.12	L	Docosapentaenoic	194.44	H
Arachidonic	-78.28	L	Docosahexaenoic	131.44	H
Adrenic	-111.72	L			

Gross overdose of
Heated Fish oil, suppressed
LA, GLA, DGLA, AA

INDEXES

Fluidity Index	-40.00	L	Odd Chain Index	-30.56	L
PR Index	173.00	H			

Gross overexpression
of DMAs indicative of
High Sphingomyelin
and Very Low
Phosphatidylcholine

STABILIZE IT

16:0 DMA	480.61	H	PR Index	173.00	H
18:0 DMA	414.01	H			
18:1 DMA	205.09	H			

Impaired Peroxisomal
Respiration + 173%
due to epigenetic insult

Conclusion: Valuable to introduce the concept that plasma lipoproteins belong in the realm of host immune response.

Plasma lipoproteins are important components of the immune system

Han R Microbiol Immunol 2010 54:246-253

- **Lipoproteins may prevent bacterial, viral, and parasitic infections**
- **Lipoproteins can detoxify lipopolysaccharide (LPS)**

HDL has protective immune functions

Murch O et al., Intensive Care Med 2007, 33(1) :13-24

- **Bind and neutralize LPS**
- **Modulate adhesion molecule expression**
- **Upregulate eNOS**

Arachidonic acid, other unsaturated fatty acids and some of their metabolites function as endogenous antimicrobial molecules

Das U., Journal of Advanced Research 2018, 11: 57-66

- **Polyunsaturated fatty acids (PUFAs) stimulate superoxide production** by macrophages, neutrophils, and lymphocytes to kill invading microorganisms.
- **AA, EPA, and DHA give rise to lipoxins, resolvins, protectins, and maresins that limit and resolve inflammation and have antimicrobial actions**

PUFAs such as LA, GLA, DGLA, AA, ALA, EPA, DHA
and their metabolites have broad
antibacterial, antifungal, antiviral and immunomodulatory actions

Vascular Infectology and Atherogenesis

Bacterial invasion of vascular cell types:

Kazarov E., Future Cardiol 2012; 8(1): 123-128

- **Vascular infectology is the study of the polybacterial atherosclerotic microbiome and the atherogenic sequelae of bacterial presence including endothelial activation and blood clotting.**

Infectious burden (IB) and atherosclerosis: A clinical Issue

Sessa R et al., World J Clin Cases 2014; 2(7): 240-249

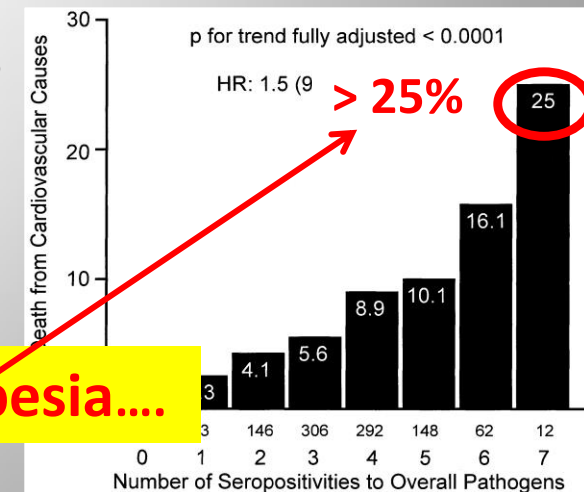
- Individual pathogens have local and/or systemic effects, and others result in molecular mimicry.
- The IB may be more involved in the pathogenesis than any single pathogen.
- The pro-atherogenic effect of each pathogen might be amplified in the presence of others.
- There is a complex interplay of multiple infectious agents and limitations of assessment methods.
- **The role of IB as a cause of atherogenesis may have been underestimated**

Percentage of mortality from cardiovascular causes according to infectious burden

Rupprecht H et al., Circulation. 2001;104:25-31

IgG seropositivities : HSV-1, HSV-2, CMV, H influenzae,

IgA seropositivities : C pneumoniae, M pneumoniae, H pylori, EBV

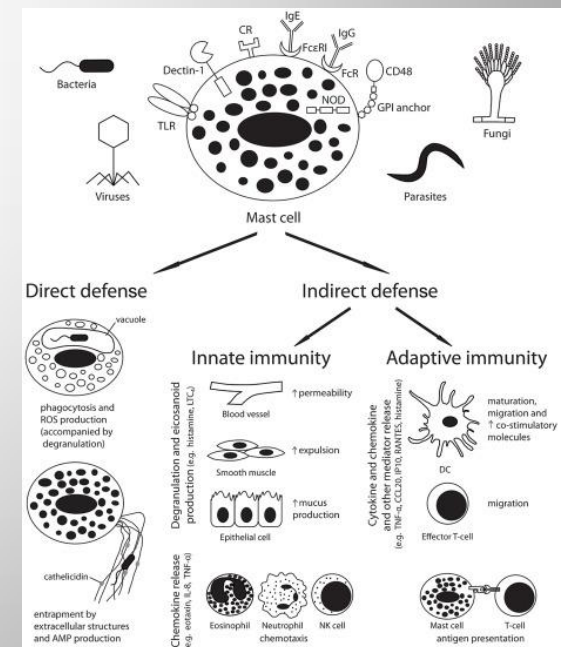
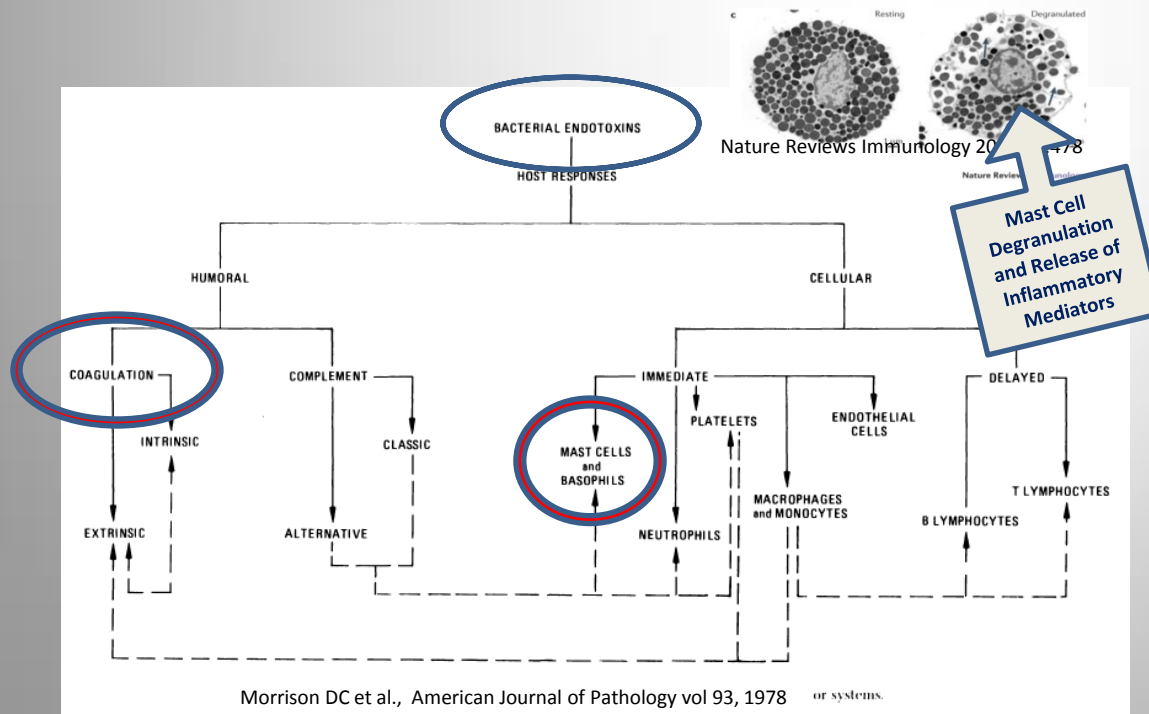


And now let's consider Borrelia, Bartonella, Babesia....

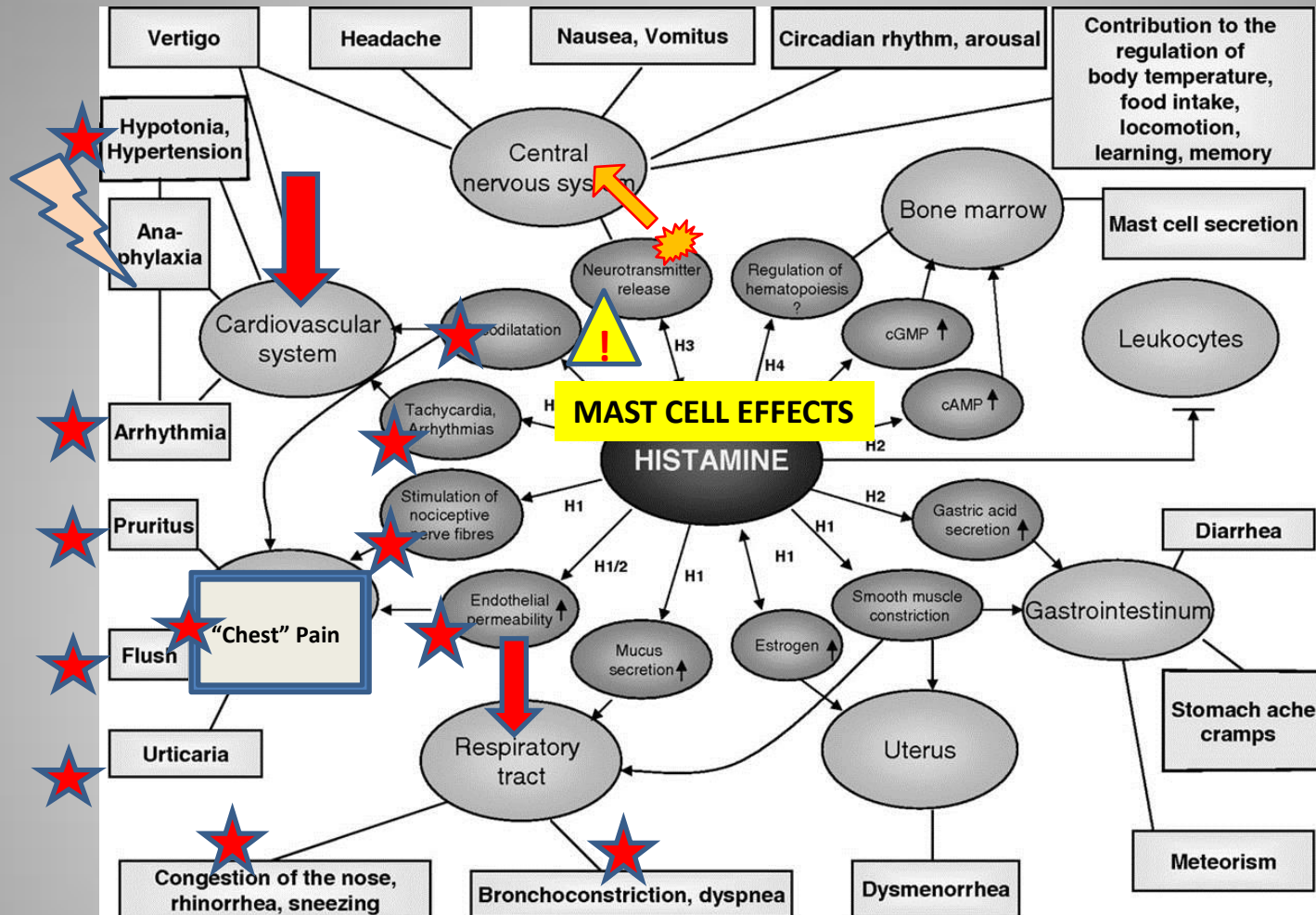
Infection and Cardiovascular Plaque

- **Many studies link infection with cardiovascular plaque**
 - Makris GC et al., Curr Vasc Pharmacol 2010 8(6):861-72
- **Bacteria and their DNA which may arise from the mouth and gut are detected in vascular biopsies from patients**
 - Arminoghar Z et al., Journal of Oral Microbiology 2014, 6: 23408 Kozarov EV et al., Arterioscler Thromb Vasc Biol, 25(3), pp. e17–e18
- **Direct effects of microbial invasion and indirect mechanisms via systemic inflammation by multiple organisms have been extensively reviewed**
 - Campbell LA et al., Arch Med Res. 2015 46(5): 339–350 and 2014 Front. Cell. Infect. Microbiol
- **Infections may be causal in the pathogenesis of atherosclerosis**
 - Ravnskov U et al., The American Journal of the Medical Sciences 2012; 344(5): 391 - 394
- **However causality not yet proven in clinical trials**
 - Few small trials were positive, but large antibiotic trials to treat C. Pneumoniae failed to show benefit
- **Problems similar to studies of antibiotic treatment for chronic Lyme:**
 - Advanced disease in the patient when extensive chronic complex plaques are already present.
 - Pathogen lifecycle with metabolically inactive intracellular forms not susceptible to antibiotics, induction of antibiotic resistance, persisters, induced persisters, and other immune defense mechanisms.
 - Presence of co-infections, many of which are not identified, no combined antibiotic trials.
 - Toxicity of the antibiotics
 - Effects of repeated courses of antibiotics on the microbiome

- **Intracellular Localization of *Borrelia burgdorferi* within Human Endothelial Cells** Ma Y et al., Infect. Immun 1991 59(2):671-678
- *Borrelia burgdorferi* **upregulates expression of adhesion molecules on endothelial cells and promotes transendothelial migration of neutrophils in vitro.** Sellati T et al., 1995. Infect. Immun. **63**:4439–4447
- *Borrelia burgdorferi* outer membrane protein A **induces nuclear translocation of nuclear factor-kappa B and inflammatory activation** in human endothelial cells. Wooten R et al. 1996. J. Immunol. 157:4584–4590
- *Borrelia burgdorferi* **lipopolysaccharide (endotoxin) inflammatory role in Lyme disease** Habicht G et al., Zentralbl Bakteriell Mikrobiol Hyg A 1986; 263(1-2),137-41
- *Borrelia burgdorferi* Spirochetes **Induce Mast Cell Activation and Cytokine Release** Talkington J et al., Infection and Immunity, 1999, 67(3): 1107-1115



Cardio-Immu-Knowledge of Lyme & Associated Diseases



Maintz. L et al , Histamine and histamine Intolerance Am J Clin Nutr 2007 85(5):1186-95

"Mast cells are the 'universal alarm cell" that starts the inflammatory cascade."
"They can be triggered by infection, allergens, environmental factors like pollution, or even emotional stress."

T Theoharides MD PhD



**Human mast cells are classified according to presence of both chymase and tryptase (MCTC).
 Ninety percent of the MCs in the human heart are of MCTC type.**

Kolck UW Transl Res 2016 Aug;174:23-32

Lyme Carditis Pathology in Humans

Postgrad Med J 1990 66:134 – 136, Am J Pathol. 2016 186(5):1195-205 Br Heart J 1990 63:162-8
Cardiovascular Pathology 2008 17(2):103–107.

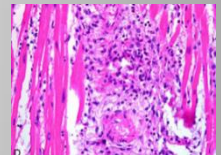
- Interstitial and perivascular lymphoplasmacytic infiltrate associated with myocyte damage and necrosis.
- The identification of morphological spirochetes or PCR necessary to confirm the diagnosis.
- **The extent of lymphocytic infiltrate is often out of proportion to the finding of only sporadic spirochetes is consistent with an immunological component of Lyme carditis.**
- Infiltrates and spirochetes in the base of the heart and above the AV node in patients with AV block who recover conduction, below the AV node may need permanent pacing.

Cardiac Involvement in Non-human Primates

Laboratory Investigation 2004 84:1439–1450 Am J Pathol 2018, 188: 672e682



- Carditis is very common in primates infected with *B. burgdorferi* but **more prominent infiltrate is present when the animals are immunosuppressed.**
 - Multifocal interstitial and perivascular collections of lymphoplasmacytic infiltrates and macrophages.
 - Increased IgG and IgM in the heart.
 - Pericardial inflammation only in animals with myocardial involvement.
- Individual immune response to bacterial inoculations varied in both untreated and treated primates
- Genetic diversity results in different immune responses to the same antigen correlating with our clinical problems when using antibody testing.
- Live spirochetes were found in the heart after 28 days of doxycycline, and late post treatment, indicating that limiting treatment duration to 28 days may not be effective.
- **Chronic Lyme disease symptoms can be attributable to residual inflammation in and around tissues that harbor a low burden of persistent host-adapted spirochetes and/or residual antigen with chronic immunosuppression.**



Infections and cardiovascular disease: is *Bartonella henselae* contributing to this matter?

Paola Salvatore et al, Journal of Medical Microbiology (2015),64, 799-809

- *Bartonella* **invades endothelial progenitor cells (EPCs)** which are key players of vascular repair
- *Bartonella* could **enhance susceptibility and worsen the prognosis** in CVD
- *Bartonella* infection could **favor the process of atherogenesis**.
- ***Bartonella* is more widespread throughout the world than *Borrelia*.**

This could have a HUGE impact on our understanding and management of atherogenic/atherosclerotic coronary artery disease!

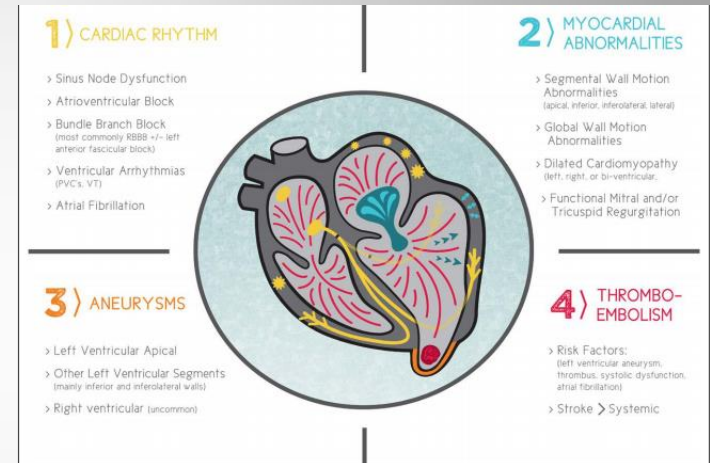
- **The *Bartonella* interaction with EPCs presents a broad spectrum of cardiovascular pathology:**
 - Vasculitis and/or thrombosis**
 - Myocarditis and/or cardiomyopathy resulting in Sudden Death**
 - May be a major pathogenetic factor in the development of ARVC-like disease.
 - Endocarditis, particularly culture negative endocarditis**
 - Aneurysm**
 - Vasoproliferative Disease:**
 - Verruga Peruana**
 - Bacillary Peliosis**
 - Epithelioid Hemangioendothelioma**

Babesia

- **Babesia invade and infect red blood cells.**
- **They significantly inhibit nitric oxide production in the body (the body's main defense against them).**
- **Distortion of the endothelial cells.**
- **Aggregates of red blood cells around those sites with subsequent coagulation and obstruction of the vessels.**
- **Severely affects endothelial cell function including mitochondrial function.**
- **“Mitochondriopathy” represents an early manifestation of endothelial cell dysfunction leading to metabolic hypoxia which is a factor in the common symptom of fatigue.**
- **Co-enzyme Q10 may interfere with the effectiveness of atovaquone and atovaquone+proguanil (Malrone/Mepron) and probably should be avoided.**
 - **Atovaquone is a competitive inhibitor of ubiquinol, specifically inhibiting the mitochondrial electron transport chain.**
- **Heparin has been proposed as a therapeutic agent, however there is limited published literature to support it.**

Other co-pathogens

- **Ehrlichia: Human Monocytic Ehrlichiosis and Human Granulocytic Anaplasmosis**
 - Myocarditis
- **Rickettsia (RMSF)**
 - Microcirculatory vasculitis
 - Myocarditis.
- **Mycoplasma**
 - CAD, myocarditis, cardiomyopathy
- **Toxoplasmosis**
 - Pericarditis and myocarditis
- **Coxiella (Q fever)**
 - Endocarditis
- **Chlamydia**
 - Atherosclerosis, myocarditis
- **Tularemia**
 - Endocarditis
- **H. Pylori**
 - CAD, atrial fibrillation
- **Yersinia enterocolitica**
 - Endocarditis
- **Funneliformis mosseae (Protomyxzoa rheumatica)**
 - Slime forming complex protozoan like organism, newly categorized
 - Low fat diet recommended because it grows better in cultures with fat.
- **Chagas, American trypanosomiasis**
 - Chagas disease now affects at least 300,000 residents in the U.S.
 - Dilated cardiomyopathy, arrhythmias, CHF
- **Syphilis The original GREAT IMITATOR**
 - Cardiomyopathy, Aortic aneurysm and stenosis, ostial coronary obstruction



- **Powassan**
 - Myocarditis
- **Heartland Virus**
 - Lymphocytic Myocarditis
- **HSVs (CMV, EBV)**
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It may be 2017, but syphilis is making a comeback in Maine

April 11, 2017 Home
By Jackie Farwell

200% increase in last ten years

Of all the sexually transmitted infections, syphilis typically falls pretty low on the list of concern. HIV/AIDS, HPV, and drug-resistant gonorrhea grab more headlines than an infection most of us consider a relic of history. You don't often hear sex ed teachers warning students about a disease believed to have stricken the likes of Vincent Van Gogh and Al Capone.

But syphilis is making a comeback, according to government health officials. The Maine Center for Disease Control and Prevention recently Tweeted about rising rates of the disease in Maine and across the country:

- **Powassan**
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Other co-pathogens

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Braunwald's Heart Disease, 11th edition

TABLE 79.3 Causes of Myocarditis

Modified from Elamm C, Fairweather D, Cooper LT: Pathogenesis and diagnosis of myocarditis. Heart J 2012;98:835.

VIRUSES AND VIRAL DISORDERS	BACTERIA AND BACTERIAL DISORDERS	CARDIOTOXINS	HYPERSENSITIVITY MEDIATORS AND FACTORS
Adenovirus*	<i>Chlamydia</i>	Anthracycline drugs*	Cephalosporins
B19V	Cholera	Arsenic	Clozapine
CVB*	Leptospirosis	Carbon monoxide	Diuretics
Cytomegalovirus*	Lyme disease	Catecholamines	Hypereosinophilia
Epstein-Barr virus	<i>Mycoplasma</i>	Chagas disease	Insect bites
Hepatitis C virus	<i>Neisseria</i>	Cocaine*	Kawasaki disease
Herpes simplex virus	Relapsing fever	Copper	Lithium
HIV*	<i>Salmonella</i>	Ethanol*	Sarcoidosis
Influenza virus	Spirochete	Heavy metals	Snake bites
Mumps	<i>Staphylococcus</i>	Lead	Sulfonamides
Poliovirus	<i>Streptococcus</i>	Leishmaniasis	Systemic disorders
Rabies	Syphilis	Malaria	Tetanus toxoid
Rubella	Tetanus	Mercury	Tetracycline
Varicella-zoster virus	Tuberculosis	Protozoa	Wegener granulomatosis
Yellow fever	Bartonella		

- **Powassan**
 - Myocarditis
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- **Coxsackievirus**
 - Myocarditis

The Lyme Literate world has increased awareness of “Lyme Carditis”

- For the purposes of this presentation the term “Lyme Carditis” refers to the spectrum of heart and blood vessel disorders related to the effects of pathogens related to Tick Born Diseases.
- We all recognize that the pathogens are transmitted by vectors other than ticks, and that there are many pathogens besides *Borrelia*, and many are not yet identified.

Table 10. Disease Manifestations of Chronic Lyme Disease and Chronic Co-infections (Overview)

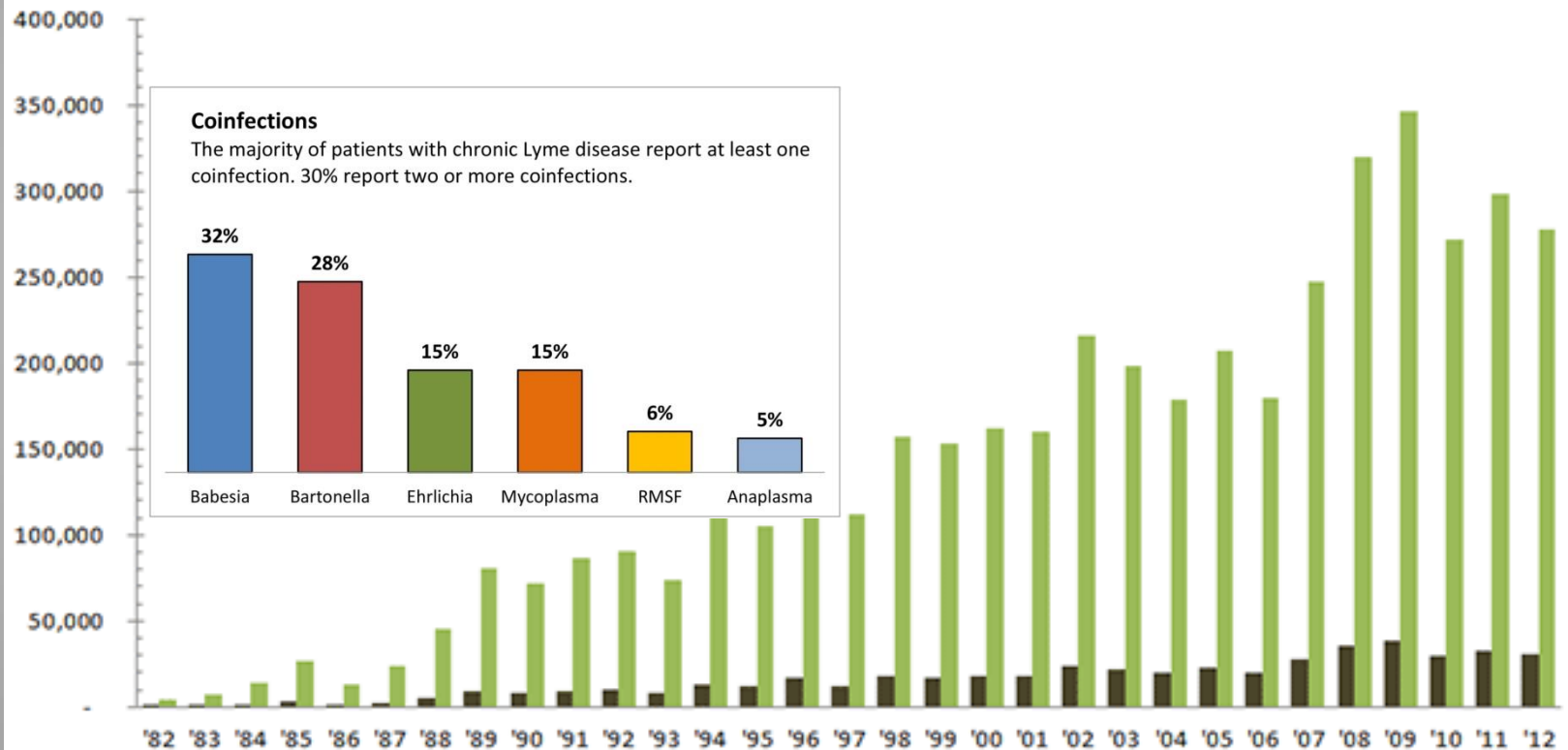
Disease	Symptomatology									GBS	LA
	GenS	MuSk	NS	Skin	Heart	Eye	GI	UG	rA		
Lyme disease	+	+	+	+	+	+	+	+	(+)*	+	+
Bartonellosis	+	+	+	+	+	+	+	+	+	+	+
<i>Y. enterocolitica</i>	(+)	+	+	+	+	+	+		+	+	
<i>M. pneumoniae</i>	(+)	+	+	+	+	+	+	+	+	+	
<i>C. pneumoniae</i>			+		+				+	+	
<i>C. trachomatis</i>							+		+	+	
<i>C. jejuni</i>									+	+	

Y. enterocolitica = *Yersinia enterocolitica*; *M. pneumoniae* = *Mycoplasma pneumoniae*; *C. pneumoniae* = *Chlamydophila pneumoniae*; *C. trachomatis* = *Chlamydia trachomatis*; *C. jejuni* = *Campylobacter jejuni*; GenS = general symptoms (fatigue, head aches, lassitude); MuSk = musculoskeletal symptoms (arthritis, arthralgias, myalgias); NS = symptoms of the nervous system (CNS, polyneuropathy, radiculopathy); Skin = skin lesions (erythema migrans, ACA in cases of Lyme disease e.g. infected skin injury); LA = lymphadenopathy; Heart = heart disease (myocarditis, cardiomyopathy, pericarditis); Eye = eye disease (uveitis, conjunctivitis, optic neuritis); GI = gastrointestinal complaints; UG = urogenital symptoms; rA = reactive arthritis; GBS = Guillain-Baré syndrome; + = positive; (+) = presumption based on general symptoms in cases of yersiniosis and *Mycoplasma pneumoniae* infection; +* = probably chronic infectious, hypothetical autoimmune origin (mimicry).

Annual Cases of Lyme Disease in the US

Bay Area Lyme Foundation

■ Number of CDC-Reported Cases ■ CDC-Estimated Total Diagnosed Cases



Estimated Prevalence of Lyme Carditis

- **ADULT** untreated patients with Lyme Disease in US: 1.5 to 10% vs Europe: 0.3 to 4%
 - 90% of patients with Lyme carditis develop cardiac conduction abnormalities.
 - 60% develop signs of perimyocarditis.
- A study on **PEDIATRIC** patients with Lyme disease found ECG changes indicative of myocardial involvement in approximately **30% of patients**.
- **Carditis was found in 16%** of children who had early disseminated Lyme disease and presented for acute management in another study. (Not every patient presenting with early disseminated Lyme disease received an electrocardiogram and cases of mild carditis may have gone undetected.)
- **Asymptomatic complete heart block has been identified in children presenting with Lyme disease, confirmed with diagnostic testing.**
- **AV block of unknown etiology in children, possibly failure to diagnose Lyme**

Cox J et al., Cardiovascular manifestations of lyme disease. Am Heart J 1991; 122: 1449–55.

Steere AC, et al.: Lyme carditis: cardiac abnormalities of lyme disease. Ann Intern Med 1980; 93: 8–16.

van der Linde MR: Lyme-carditis: clinical characteristics of 105 cases. Scand J Infect Dis 1991; 77: 81–4.

Woolf PK et al., Electrocardiographic findings in children with lyme disease. Pediatr Emerg Care 1991; 7:334–6.

Costello JM et al., Lyme Carditis in Children: Presentation, Predictive Factors, and Clinical Course Pediatrics 2009 123(5):e835–e841

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ECG should be obtained on all patients with known or “suspected” Lyme Disease

PR>300ms Prolonged QTc

Cox J et al., Cardiovascular manifestations of lyme disease. Am Heart J 1991; 122: 1449–55.

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Cardio-Immu-Knowledge of **Lyme & Associated Diseases**

Lyme Carditis: Cardiac Abnormalities of Lyme Disease

Steere AC et al., Lyme carditis: Cardiac abnormalities of lyme disease.
Ann Intern Med 1980; 93: 8–16.

We studied 20 patients, mostly young adult men, with cardiac involvement of Lyme disease. The commonest abnormality (18 patients) was fluctuating degrees of atrioventricular block; eight of them developed complete heart block. Thirteen patients had evidence of more diffuse cardiac involvement: electrocardiographic changes compatible with acute myopericarditis (11 patients), radionuclide evidence of mild left ventricular dysfunction (five of 12 patients tested), or frank cardiomegaly (one patient). Heart involvement was usually preceded by erythema chronicum migrans and sometimes accompanied by meningoencephalitis, facial palsy, arthralgias, and some left testicular

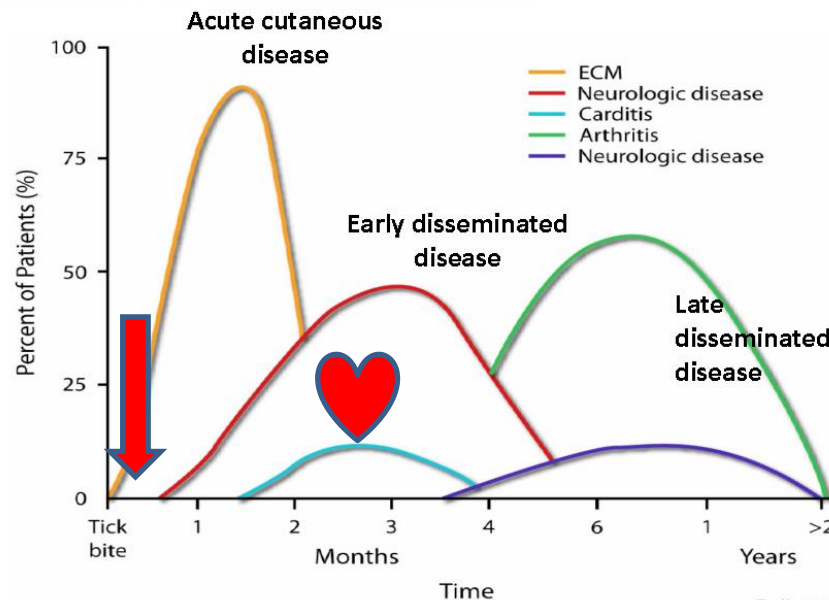
Materials and Methods

Lyme disease was diagnosed in 19 of the 20 patients by the occurrence of erythema chronicum migrans. The lesion was defined by its gross appearance: a red macule or papule that expands to form a large annular lesion, usually with a bright red outer border and partial central clearing (2). Although one patient lacked this lesion, his remaining findings were like those of the other 19 patients.

Sixteen patients (one with onset of the illness in 1975, one in 1976, three in 1977, two in 1978, and nine in 1979) were studied prospectively through December 1979 according to the protocol outlined previously (2, 10). Patients with high-degree atrio-

BC Centre for Disease Control
An agency of the Provincial Health Services Authority

Lyme Disease Clinical Course



Cardiovascular *Symptom* Manifestations

- Palpitations: THE MOST FREQUENT SYMPTOM
- Fatigue
- Effort intolerance
 - May simulate “Angina” (chest discomfort with effort, relieved by rest)
- Shortness of breath,
 - Gradual unexplained
 - When sudden onset with myocarditis mimics heart attack
 - Heart failure signs and symptoms when progress to cardiomyopathy
 - Pericardial effusion and tamponade
- Chest pain
 - May or may not have postural or phasic variation with respiration
 - May be associated with chest wall pain
 - Typical or Atypical Angina
 - **May present as Acute Coronary Syndrome or Acute Myocardial Infarction**
- Dizziness , faintness, syncope
 - Dizziness regardless of posture : Heart block, Ventricular tachycardia, seizures
 - Postural symptoms, consider POTS
- Raynauds associated with vasculitis
- New Heart Murmur
- TIA, Stroke
- **Hypertension, particularly when it is new onset and/or difficult to control**

Mast Cell Activation can explain many of these symptoms

Palpitations are the most frequent symptom of Lyme carditis

- **Confirm rhythm with 12 lead ECG and/or ambulatory recording**
 - AV block
 - Premature atrial contractions
 - Atrial fibrillation
 - Atrial flutter
 - Sick sinus syndrome
 - Junctional ectopic tachycardia
 - Premature Ventricular Contractions
 - Ventricular Tachycardia
 - Torsades de Pointes
 - Ventricular fibrillation/Electrical Storm
- **Sudden Death**
- **Electrocardiogram for all patients**
- **ALWAYS calculate QTc (antibiotic risk and risk of sudden death)**
- **Holter, Telemetry , “Personal recording devices” are often indicated**

Mast Cell Activation can be involved in all of these

AV block is the most common and well known manifestation of Lyme Carditis

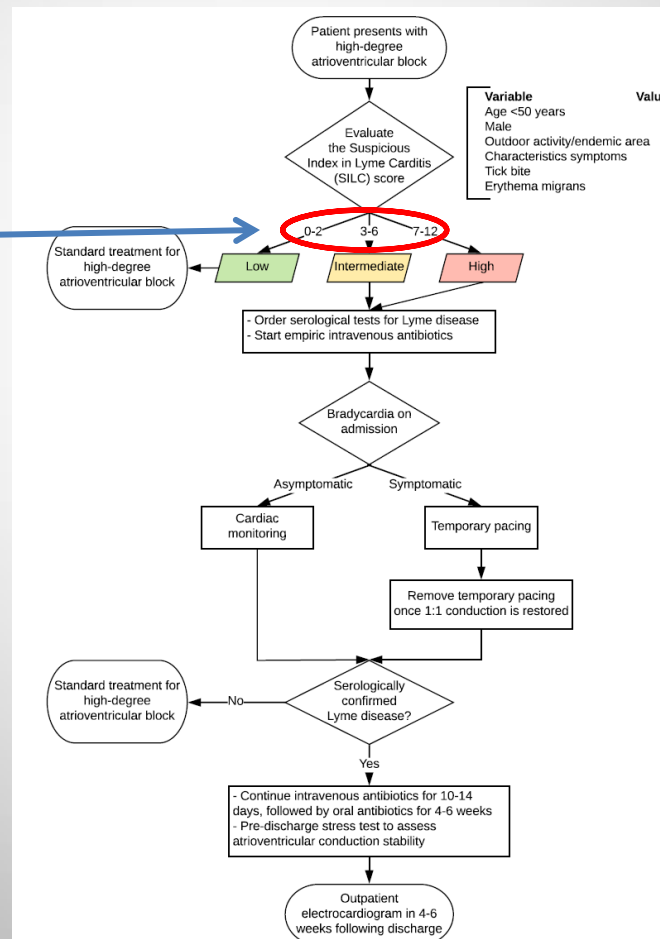
Systematic Approach to the Diagnosis and Treatment of Lyme Carditis and High-Degree Atrioventricular Block

- First, Second, and Third Degree block, can progress while being observed— **reverse with antibiotics**
- If PR > 300 ms: close observation and consider pacer
- IV: 10-14 days Ceftriaxone 2 g or injectable penicillin G benzathine 1.2 million units
- Oral: 4-6 weeks doxycycline alone or in combination with other antibiotics

SILC Score: COSTAR

Suspicious Index of Lyme Carditis

Risk Factor	Score
C – Constitutional Symptoms arthralgia, neurological, fever, malaise, dyspnea, pre-syncope, and syncope	2
O – Outdoors activity/Endemic area	1
S – Sex: Male	1
T – Tick Bite	3
A – Age < 50 years old	1
R – Rash / Erythema Migrans	4



Chest pain in Lyme disease may arise from numerous causes:

- **Cardiac Structures:**
 - Myocarditis, pericarditis, angina, myocardial infarction
 - **Mitral Valve Prolapse**
 - Inflammation of the valve may resolve with treatment
 - **Rhythm disturbances may be described as chest “discomfort” or even chest pain**
 - Most frequently described as “palpitations” or “fluttering”
 - **Airways and Lungs**
 - Asthma or bronchitis
 - **Musculoskeletal and chest wall inflammation and arthritis**
 - Common causes are periostitis of the ribs, pectoral myositis and tendonitis, sternoclavicular and costochondral arthritis
 - **GI tract**
 - GERD, esophagitis, esophageal spasm, and gastritis
 - **Women**
 - Mastitis
- Mast cells can be involved in all of these!**

Cardio-Immu-Knowledge of **Lyme & Associated Diseases**

- **When the cause of chest pain is uncertain, and coronary artery blockage is suspected:**
 - In the ER serial ECGs and/or cardiac enzymes may be suspicious for heart injury
 - An “imaging study” may be recommended such as:
 - an echo, stress echo or nuclear study, after serial enzymes and/or 24 hours of observation
 - or cardiac catheterization with coronary angiograms, often done ‘emergently’.
- **These “imaging tests” are designed to show “significant” blockages in the coronary arteries.**
- The “Invasive” Coronary Angiogram shows only the lumen and not the vessel wall, and the three dimensional object can be viewed in only two dimensions, leading to under or over estimation.



- **Coronary artery vaso-spasm can occur without or with blockages.**
- **Mast cells have been detected at the site of vasospasm:** Allergic Acute Coronary Syndrome “Kounis syndrome”.
- **Myocarditis can occur with ECG and enzyme abnormalities not seen on an angiogram.**

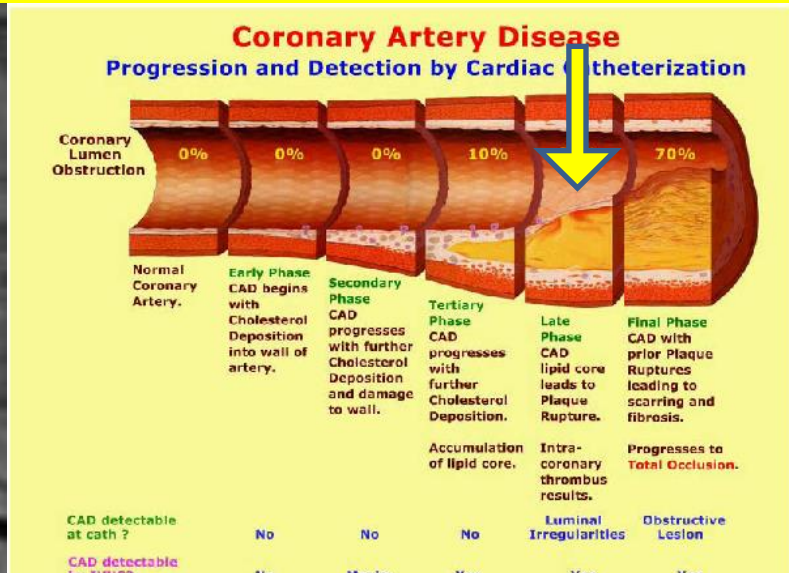
Hollander JE et al., Circulation. 2016;134:547–564

Rodrigues MCL et al., Rev Bras Anesthesiol 2013; 63(5):426-428

Dedic A et al., AJIR 2013; 200:W26-W38

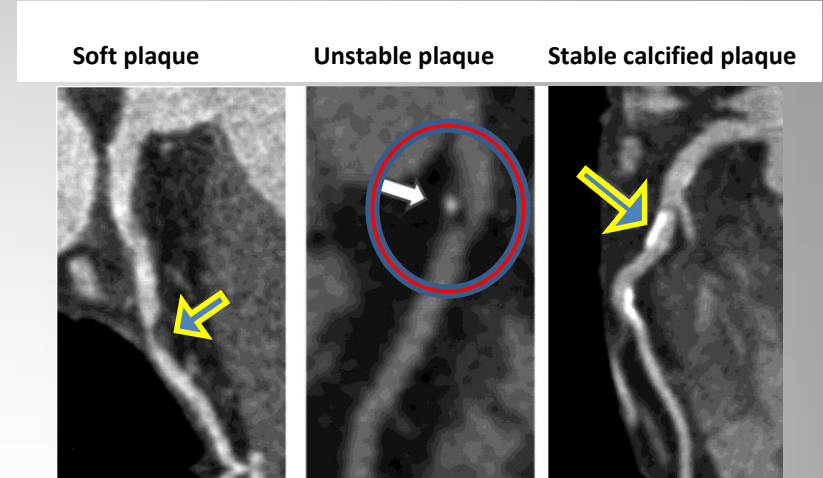
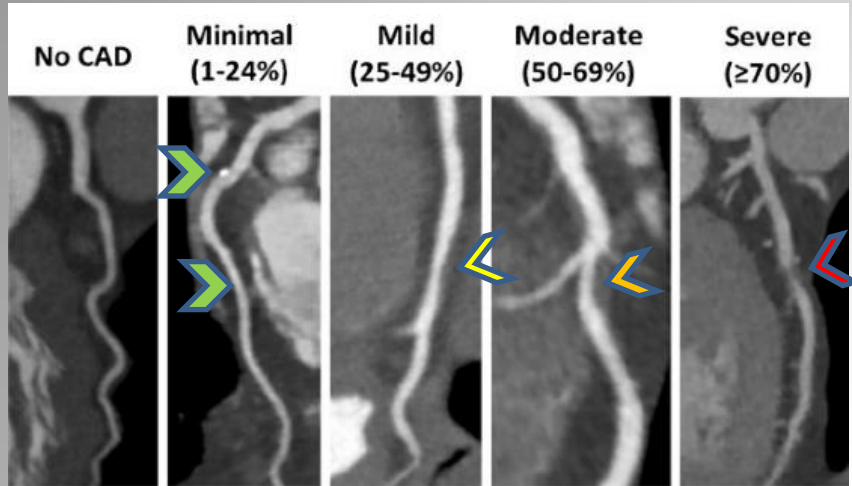


- **Nonobstructive Coronary Artery Disease is NOT Normal**
- The “Invasive” Coronary Angiogram shows only the lumen and not the vessel wall.

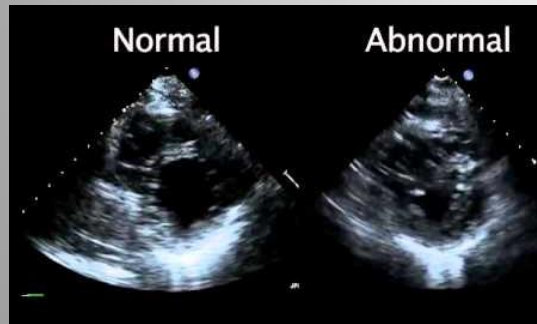


- **Most “Heart Attacks” occur where there is LESS THAN 50% blockage.**
- Can be reported as “No significant stenosis,” or even “Normal”.
- Less than 50% blockage is NOT a normal vessel.
- And a normal vessel is not an indicator that ALL is normal.

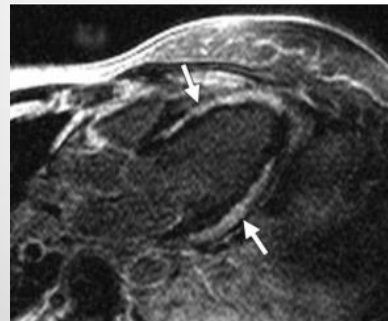
Cardio-Immu-Knowledge of **Lyme & Associated Diseases**



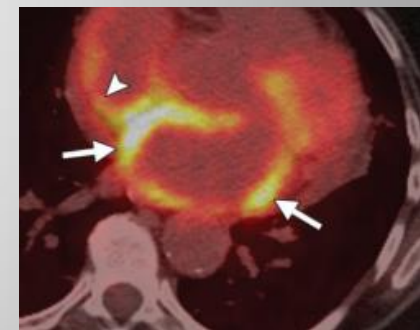
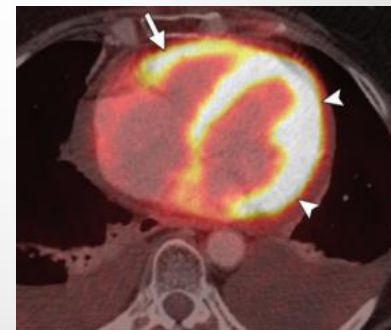
Coronary CT Angiograms



Echocardiogram



Cardiac MRI



FDG PET/CT

FDG = fluorine 18 fluorodeoxyglucose

Myocarditis Imaging

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:16120895>

James OG et al **RadioGraphics** 2011; 31:1271-1286

Myocardial Infarction With Nonobstructive Coronary Arteries (MINOCA): It's Time to Face Reality!

Jacqueline E. Tamis-Holland, MD; Hani Jneid, MD

Although the occurrence of an acute myocardial infarction (AMI) without significant coronary artery disease (CAD) was initially reported almost 80 years ago,¹ the term *MINOCA* (myocardial infarction with nonobstructive coronary arteries) has been used only recently to describe these patients.² A

were also comparable between the 2 groups. This multicenter study, in which sex-specific data were collected prospectively, outlines some key concepts related to MINOCA. First, MINOCA is not an uncommon presentation of AMI. It is more frequent in younger women and nonwhites, is associated with fewer

“Nonobstructive CAD” compared with “no apparent CAD” was associated with a significantly greater 1-year risk of MI and all-cause mortality.

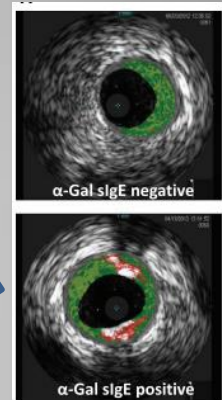
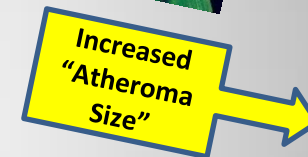
a blossoming body of literature on MINOCA has examined this unique syndrome to guide clinicians caring for such patients.

It is in this context that the work by Safdar and colleagues¹² in this issue of the Journal of the American Heart Association (*JAHA*) should be viewed. The authors reported on the incidence, etiologies, and outcomes of patients with MINOCA included in the VIRGO (Results From the Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study. They demonstrated that in young patients (aged <55 years) presenting with AMI, MINOCA is relatively frequent, occurring in >10% of the population. Although the characteristics of patients with MINOCA and their counterparts with AMI and CAD (AMI-CAD) were different, the mortality rates at 1 month

populations and heterogeneity in its definition, MINOCA is also more common in younger patients and women.^{3–7} This explains to a large extent why the current study, examining adult AMI patients aged <55 years, with a 2:1 enrollment ratio of women to men, reported a higher prevalence of MINOCA than earlier reports. In this study, women with AMI had 5-fold higher odds of having MINOCA than men with AMI, and 1 in 8 women with AMI were found to have MINOCA. It is also noteworthy that in the VIRGO study, all patients with spontaneous coronary artery dissection were categorized as MINOCA. However, some patients with spontaneous coronary artery dissection have obstructive disease, and this may have resulted in a larger-than-expected number of reported cases of MINOCA in the current study.

Manifestations of Lyme Carditis Continued

- Myocarditis +/- Pericarditis
 - Chest pain mimicking acute Myocardial Infarction with ST segment elevation
 - Acute Coronary Syndrome with ST segment changes and/or T wave changes/inversions
- Cardiomyopathy
 - Shortness of breath mimicking heart failure
 - Post transplant patients mimicking rejection
- Valve infection including vegetations, prolapse, and perforations
 - Culture negative endocarditis
- Endothelial invasion accelerates atherogenesis and plaque formation
 - Vasculitis and athero-thrombosis/atherosclerosis
 - Coronary, Carotid, Femoral and Aortic Plaque
 - **Red Meat Allergy from the bite of the Lone Star Tick results in sensitization to α -Gal**
 - Associated with a greater burden of atheroma which has unstable characteristics,
often without any symptoms!
- Aneurysms
 - Aortic and Coronary (? peri-stent)
- Hypertension, Hypotension, Postural Orthostatic Tachycardia Syndrome (POTS)
 - Mast Cell Activation Syndrome (MCAS) is often the underlying mechanism, auto-immune
 - **Beta blockers may be (relatively) contraindicated for hypertension in MCAS, consider ivabradine/corlanor for Heart Rate**
- Coagulation and Hypercoagulable state
 - **May be THE determinant of adverse outcomes in atherogenic cardiovascular disease patients**
 - Check for PFO if transvenous pacer leads are present or being placed
- Biofilm Formation:
 - Multiple organisms form biofilms which shield from antibiotics and the immune system
 - The biofilm can block flow in a small vessel, or break loose and lodge into smaller vessel
 - **Rapid dissolution of biofilm can result in wide dissemination of pathogens and “herx” reactions**



Arterioscler Thromb Vasc
Biol 2018; 38:1665-1669

Lyme Carditis: Points to Remember

- Lyme carditis (LC) may be an early manifestation of Lyme disease
- High index of suspicion required for diagnosis at first presentation.
 - **All patients should have an ECG and QTc calculation.**
 - **Patients with known or suspected cardiovascular disease should be evaluated for Lyme diseases**
- Lyme carditis can rapidly progress to unstable and potentially fatal rhythms or AV block
- Management includes prompt cardiac monitoring, and possibly temporary pacing
- Comprehensive echocardiographic evaluation is usual first imaging study.
 - TEE when clinically indicated, consider PFO study
 - MRI is the ideal imaging modality when myocarditis and/or cardiomyopathy is suspected.
 - Coronary CT to rule/out coronary disease is my preference over invasive coronary angiogram
 - FDG-PET/CT, SPECT, Gallium Scans individually selected
 - EndoMyocardial Biopsy is an elective, scheduled procedure.
- Antibiotic therapy for myocarditis and advanced AVB: Usually IV then transition to oral
- Allow adequate time for treatment before implanting a permanent pacemaker: not usually required.
- If no pacemaker implanted: Stress test at discharge to assess stability of AV node conduction.
- Usually benign course when treated early, but long term sequelae can vary .
- **Consider co-infections, mast cell therapies, immune system support, detox and drainage pathways**

Lyme Carditis: Points to Remember

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**There are NO RANDOMIZED TRIALS TO GUIDE CHOICE, DOSE, OR DURATION
of ANTIMICROBIAL THERAPY**

**Keep in mind the possibility of co-infection, need for combined therapy,
and possibility of late persistence.**

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- If no pacemaker implanted: Stress test at discharge to assess stability of AV node conduction.
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Educate Patients, Parents, Providers & Prevention
Oral Hygiene and Dental Care

A Unifying Therapy: Membrane Medicine

- **Facilitates recovery of all cellular and sub-cellular membrane function by restoring membrane composition and electrical potential**

- Cell Fluidity
- Receptor function
- Signaling and release functions
- Balances anti inflammatory and pro- inflammatory mediators

- **Antidote for Antibiotic Induced Mitochondrial Injury**

- **Protects and repairs injured endothelial cells**

- Improves cardiovascular function
- Retards atherosclerosis

- **Facilitates Enterohepatic Bile Circulation**

- Repairs damage to hepatic cells.
- Elimination of toxins

- **Aborts and repairs nerve myelin injury**

- **Facilitates GI function and recovery**

- Repairs epithelial damage from pathogens and anti-biotics
- Provides needed nutrient for mucous lining
- Restores Healthy Microbiome
- Facilitates epithelial cells and tight junctions
- Improves the Gut-Brain Axis AND the Gut-Heart Axis

- **Gently breaks down biofilm**

- **Deters pathogen cellular invasion**

Nutrient Therapy

- Membrane Stabilizing Diet: Paleo/keto
- Concentrated phospholipids-PC,PE, PI
- BioActive Lipids/Essential Fatty Acids
 - Omega 6/Omega 3 4:1 ratio
 - Linoleic-cardiolipin support
 - GLA from Evening Primrose Oil
 - Anchovy, Caviar-Resolvins, Protectins
- Butyrate / Na Phenylbutyrate (PB)
- Co Q10
- Minerals, Vitamins, Amino Acids
- TUDCA. Ox Bile
- Nutrigenomics
- IV Nutrients

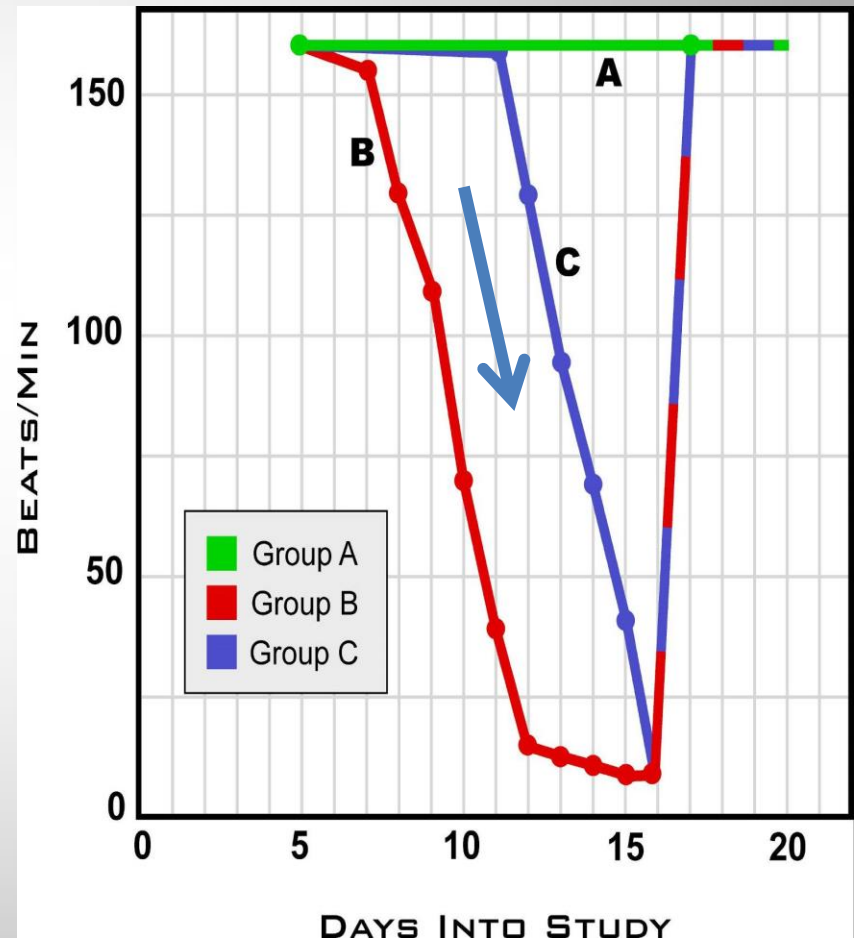
Alternative Therapies

- **Quantum Physics/Energy modalities**
- HRV/HeartMath/Acupuncture
- Homeopathics and Drainage Therapies
- Herbal therapies
- Essential oils
- Infra-red light/Sauna/Hyperthermia
- Ozone: blood (MAH), IV saline, Rectal
- Laser enhanced detoxification
- Prayer and Meditation

Phosphatidylcholine(PC) and Myocytes

Relationship between membrane lipid composition and biological properties of rat myocytes

- Rat myocytes plates on standard culture media contract at 160 bpm
- 3 groups:
 - **Group A** plated on PC starting day 6 to the end of the study.
 - **Group B** plated on standard media and not given PC until day 16 to the end of study
 - **Group C** Given PC days 6-11 then withheld until day 16.



Phosphatidylcholine(PC) and Myocytes

Relationship between membrane lipid composition and biological properties of rat myocytes

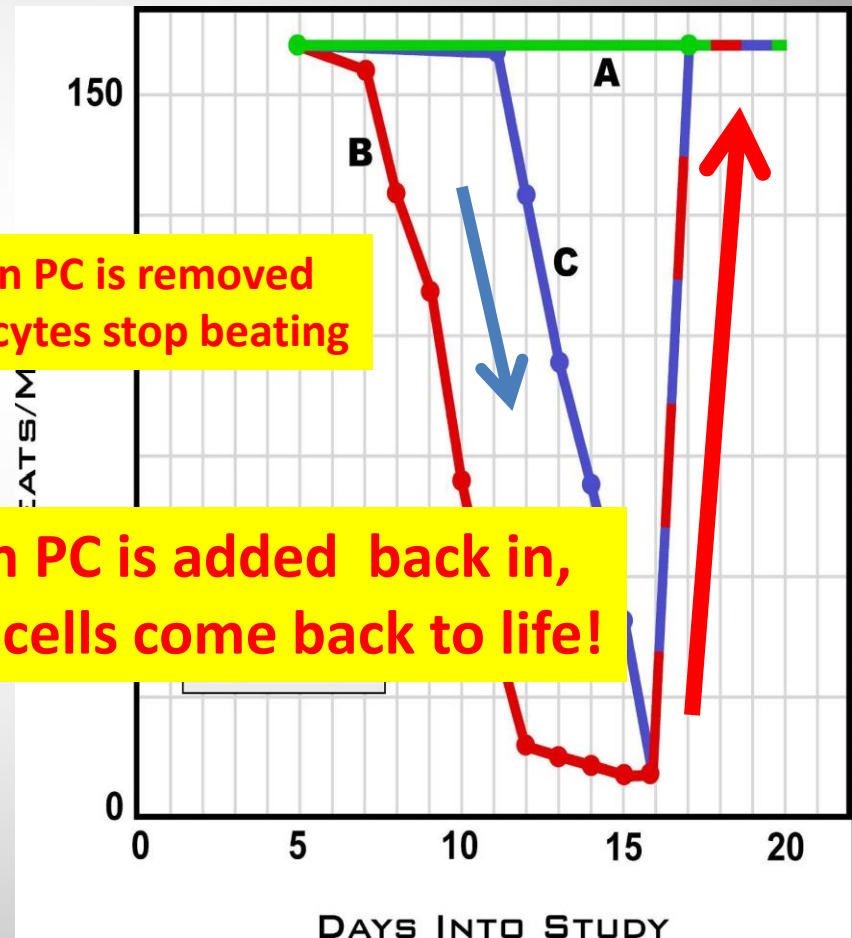
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- **Group A** plated on PC starting day 6 to the end of the study.
- **Group B** plated on standard media and not given PC until day 16 to the end of study
- **Group C** Given PC days 6-11 then withheld until day 16.

When PC is removed myocytes stop beating

When PC is added back in, dying cells come back to life!



New CDC Reports Spotlight Staggering Number of CV Deaths and Hospitalizations

Sep 06, 2018

ACC News Story

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Myocardial infarction, strokes, heart failure and other largely preventable conditions caused 2.2 million hospitalizations in 2016, resulting in \$32.7 billion in costs, and 415,000 deaths occurred, according to a [Vital Signs report](#) released Sept. 6 by the Centers for Disease Control and Prevention (CDC).

Using data from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project databases and the National Vital Statistics System, the report found that hospitalization and death rates were highest among men, non-Hispanic blacks and increased with age.

Further, state-level variation occurred in rates of emergency department visits, hospitalizations and death. The researchers predict that without preventative interventions, "approximately 16.3 million events and \$173.7 billion in hospitalization costs could occur during 2017–2021."

A second [Vital Signs report](#) used data from the National Health and Nutrition Examination Survey, the National Survey on Drug Use and Health, and the National Health Interview Survey to look at the prevalence of key cardiovascular disease risk factors. Researchers found that:

- 9 million adults are not taking aspirin as recommended
- 40 million adults have uncontrolled hypertension
- 39 million adults are not managing their cardiovascular disease risk through recommended statin use
- 54 million adults are smokers, and could benefit from cessation interventions
- 71 million adults are not physically active

New CDC Reports Spotlight Staggering Number of CV Deaths and Hospitalizations

Sep 06, 2018

ACC News Story

Share via: [f](#) [t](#) [in](#) [e](#) [+](#) [Print](#)

Font Size A A A

Heart disease and stroke are largely preventable

2.2 million hospitalizations in 2016, resulting in \$32.7 billion in costs, and 415,000 deaths occurred, according to a [Vital Signs report](#) released Sept. 6 by the Centers for Disease

However, despite decades-long improvement in outcomes, they remain leading **causes of morbidity, mortality, and health care costs** in the United States

hospitalization and death rates were highest among men, non-Hispanic blacks and increased with age.

Further, state-level variation occurred in rates of emergency department visits, hospitalizations and death. The researchers predict that without preventative interventions,

Moreover, recent evidence shows that heart disease and stroke **event rates are increasing** among certain demographic groups, including adults aged 35–64 years.

Survey to look at the prevalence of key cardiovascular disease risk factors. Researchers found that:

- 9 million adults are not taking aspirin, **Aspirin** recommended
- 40 million adults are not taking BP pills, **BP pills** recommended
- 39 million adults are not taking statins, **Statin** recommended
- 54 million adults are smokers, and could benefit from cessation interventions
- 71 million adults are not physically active



MORE

This just does not work!

New CDC Reports Spotlight Staggering Number of CV Deaths and Hospitalizations

Sep 06, 2018

ACC News Story

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Size A A A

Heart disease and stroke are the leading causes of death in the United States.

2.2 million

occurred

However, despite the fact that heart disease is the leading cause of death, the CDC reports that the number of deaths from heart disease has declined over the past several decades.

hospitalizations

with age.

Further, studies have shown that the risk of heart disease increases with age, and that the risk of heart disease is higher in people who have other risk factors, such as high blood pressure, high cholesterol, and smoking.

When treating any patient for Heart Disease, think about Lyme Disease

When treating any patient for Lyme Disease, please think about The HEART

that heart disease is increasing among certain demographic groups, including adults aged 35–64 years.

survey to look at the prevalence of heart disease and stroke among adults aged 35–64 years. Researchers found that:

- 9 million adults are not taking aspirin, which is recommended.

Is it time to consider an alternative hypothesis?

IS INFECTION THE NEW CHOLESTEROL?



Thank you for your attention!

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lgerber@bihmd.com
www.bihmd.com

207 869-9010

Proverbs 4:23
Above all else,
guard your
heart , for
everything you
do flows from
it.



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Slide 3:

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Slide 5:

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