Lyme Disease in 2013: Lessons Learned in Diagnosis

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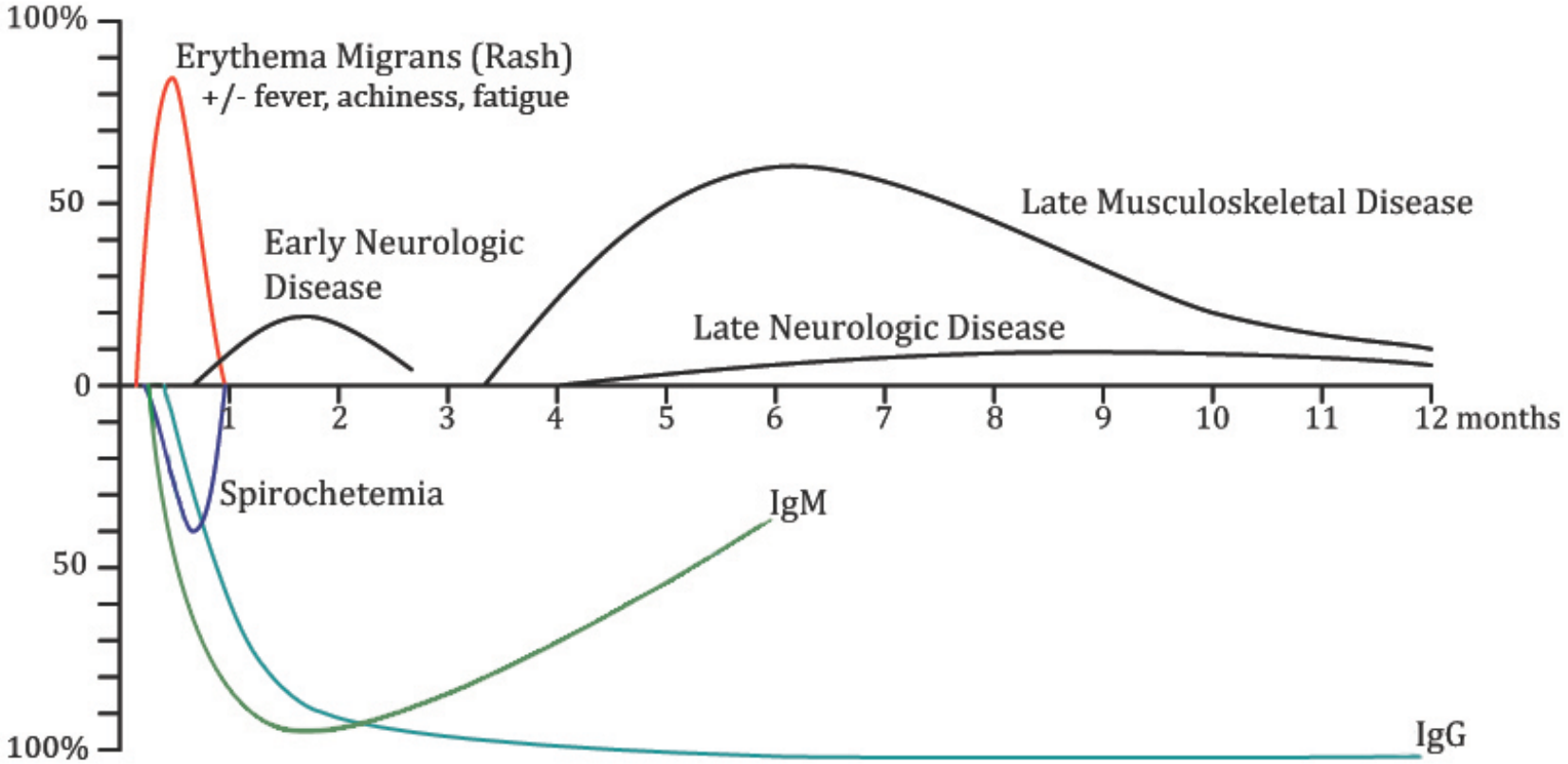
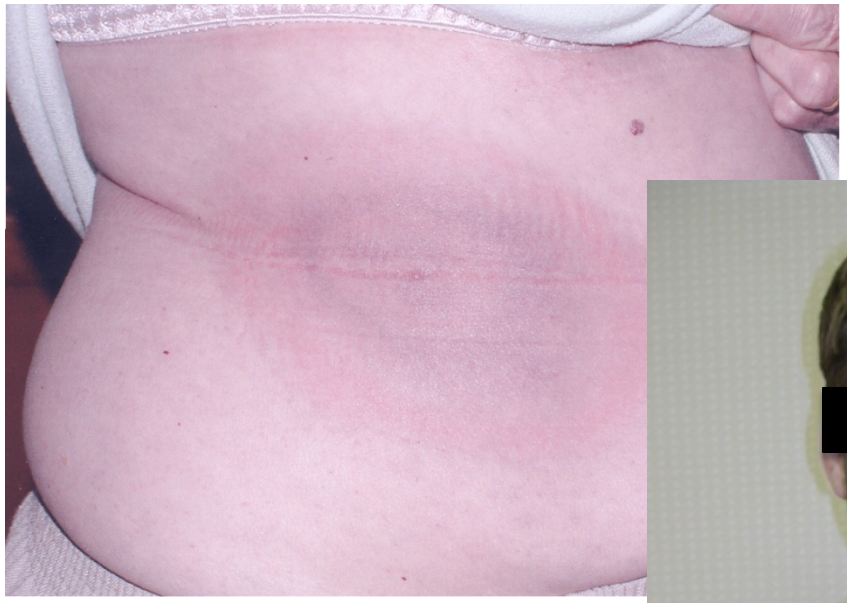
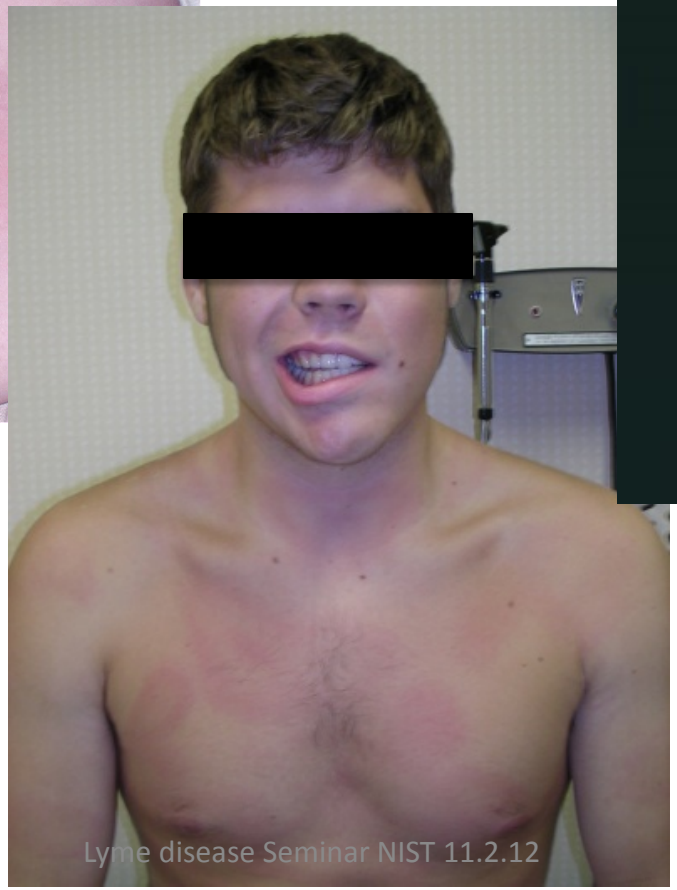
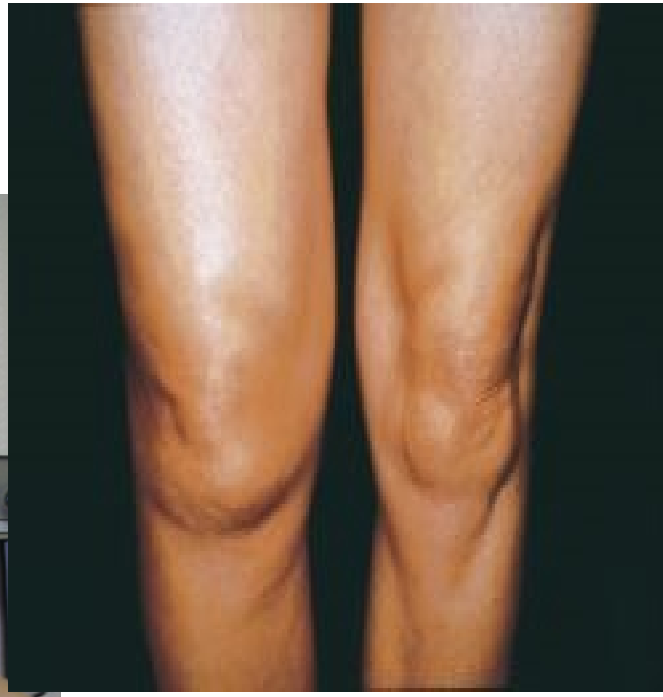
Untreated Lyme Disease is a Systemic Infection with both Early and Late Manifestations



Lyme Disease is Defined by the Signs of Infection:
Rash is “Diagnostic”
Other Signs Require Serologic Confirmation





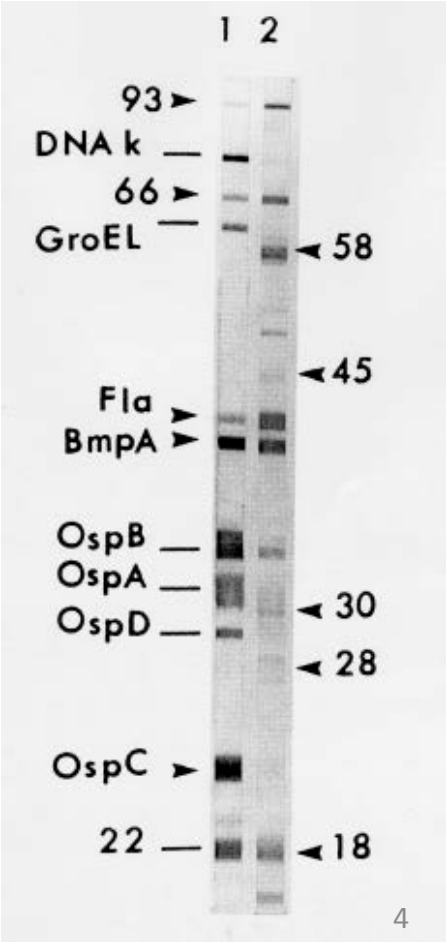


Antibody Testing is Used to Confirm Infection
CDC 2-Tier Strategy

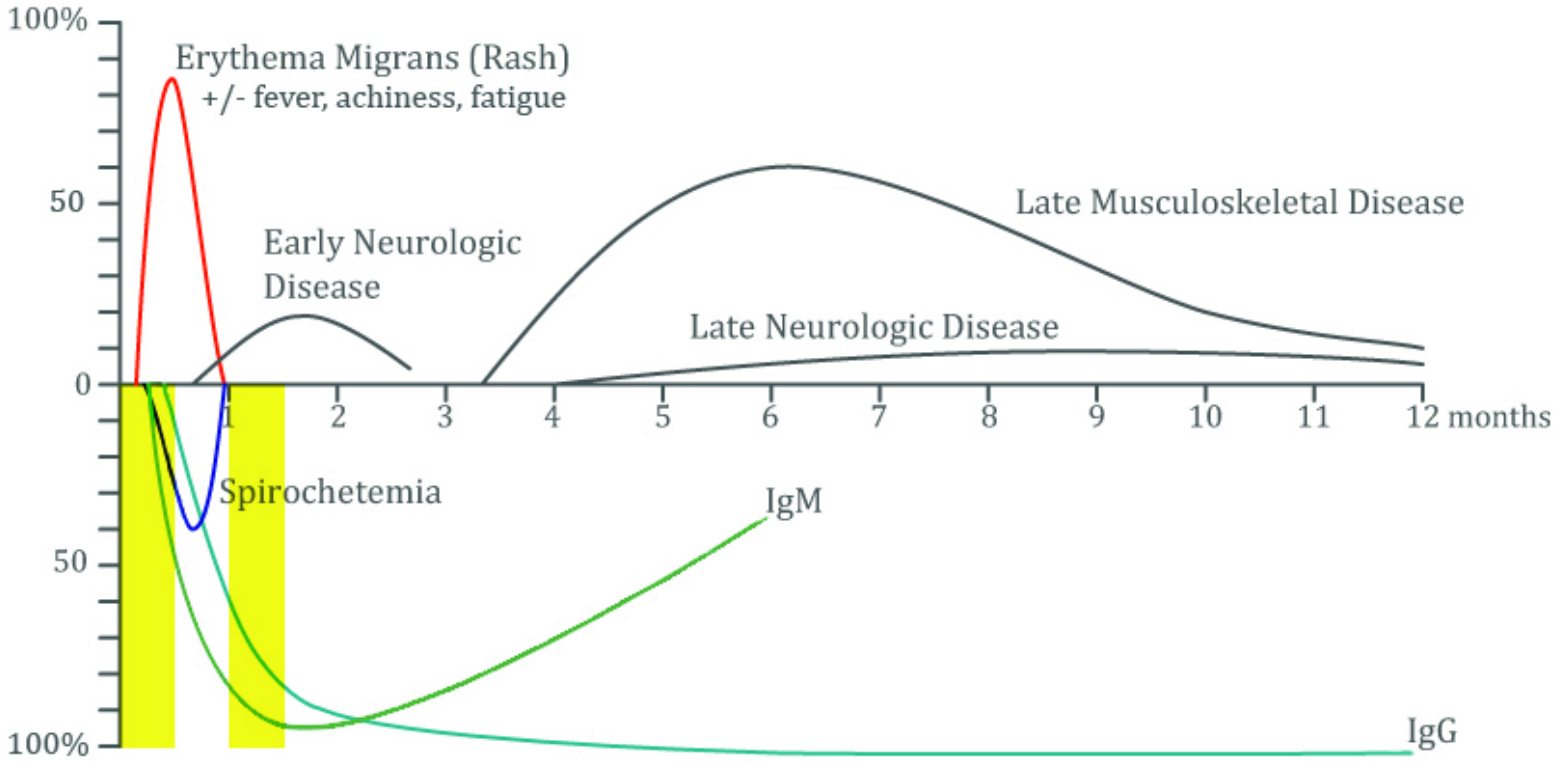
2-tier testing strategy is difficult for clinicians to understand and use

- 2 step testing
  - Elisa screening, Western blot for (+) Elisa
- Criteria for (+) blot
  - **Weeks 1-4: IgM 2/3 bands**
  - **> 4 weeks: IgG 5/10 bands**
- Surveillance strategy emphasizes specificity over sensitivity
- 40% sensitivity in first weeks
- CDC criteria requires (+) IgG western blot to be considered positive in illness of greater than 4 weeks duration, which further decreases sensitivity

Western Blot



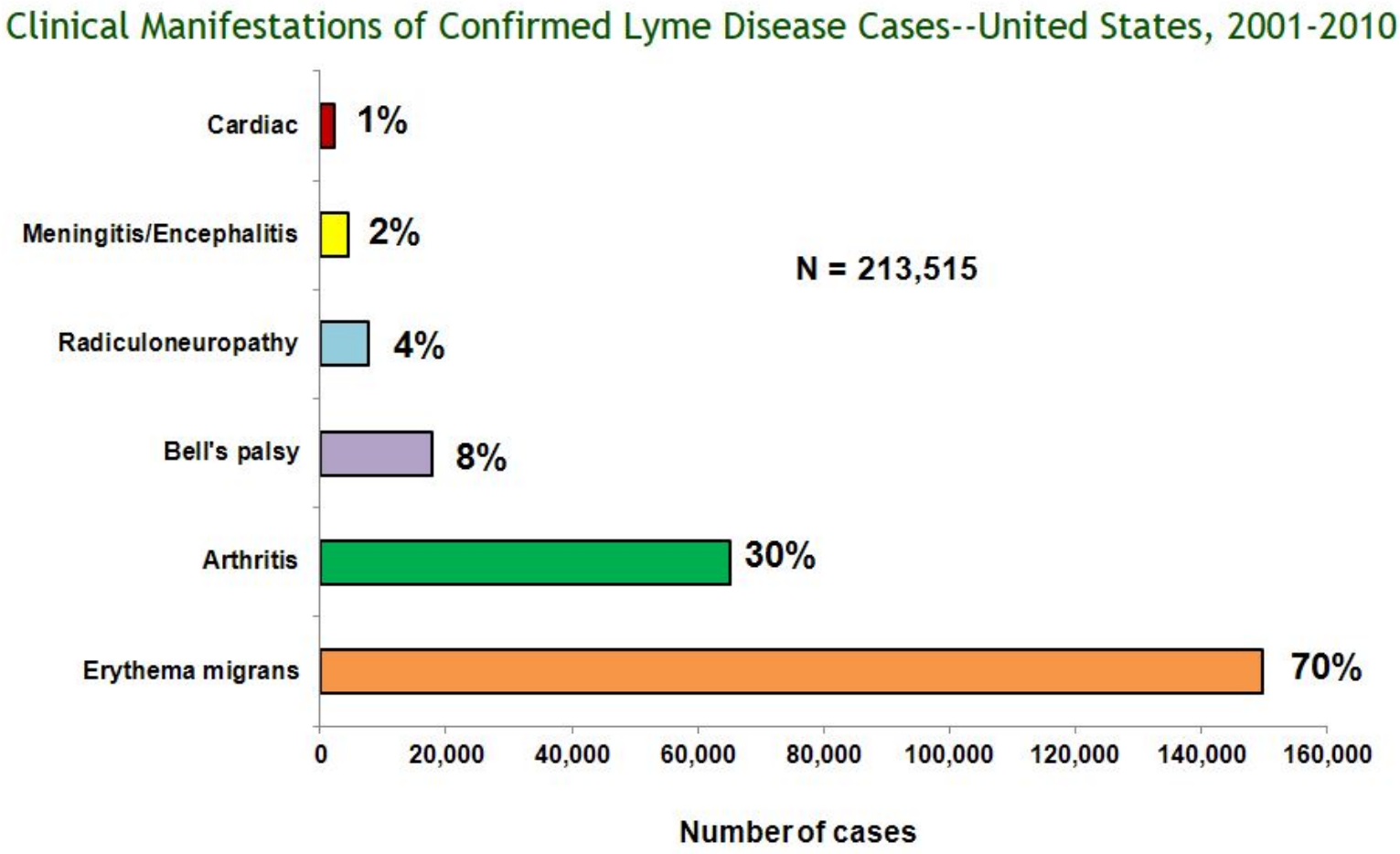
Seronegative Windows in IgM and IgG Antibody Responses in Untreated Lyme disease



Difficulties With Current Lyme Disease Diagnosis

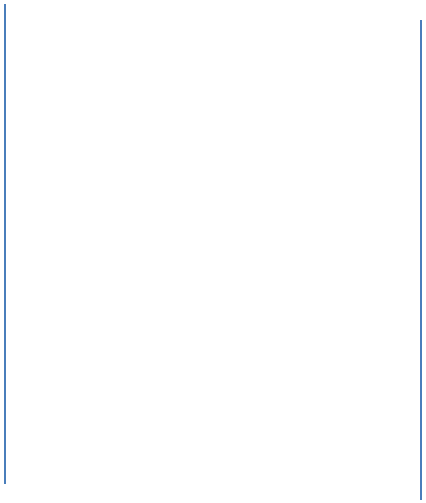
- Challenges of early Lyme diagnostics at initial physician visit:
  - Serologic tests are insensitive during acute phase
  - Early diagnosis is based on accurate clinician identification of EM
  - Rash is not always present or recognized
  - Other symptoms such as fever and myalgia are non-specific, and do not distinguish Lyme from other infections
- Diagnosis of Early Lyme Disease is based on the Physician's ability to recognize Erythema Migrans
  - When EM is present, often atypical without stereotypical target or bull's-eye appearance
  - Disseminated cutaneous skin manifestations not widely recognized
  - Atypical manifestations of rash possible
- Lack of recognition results in under diagnosis

40% of Early Cases Aren't diagnosed and go on to Develop Late Lyme Disease



Physician recognition of diagnostic EM rash is imperfect. Feder H. *Am J Med* ***99:41, 1995***

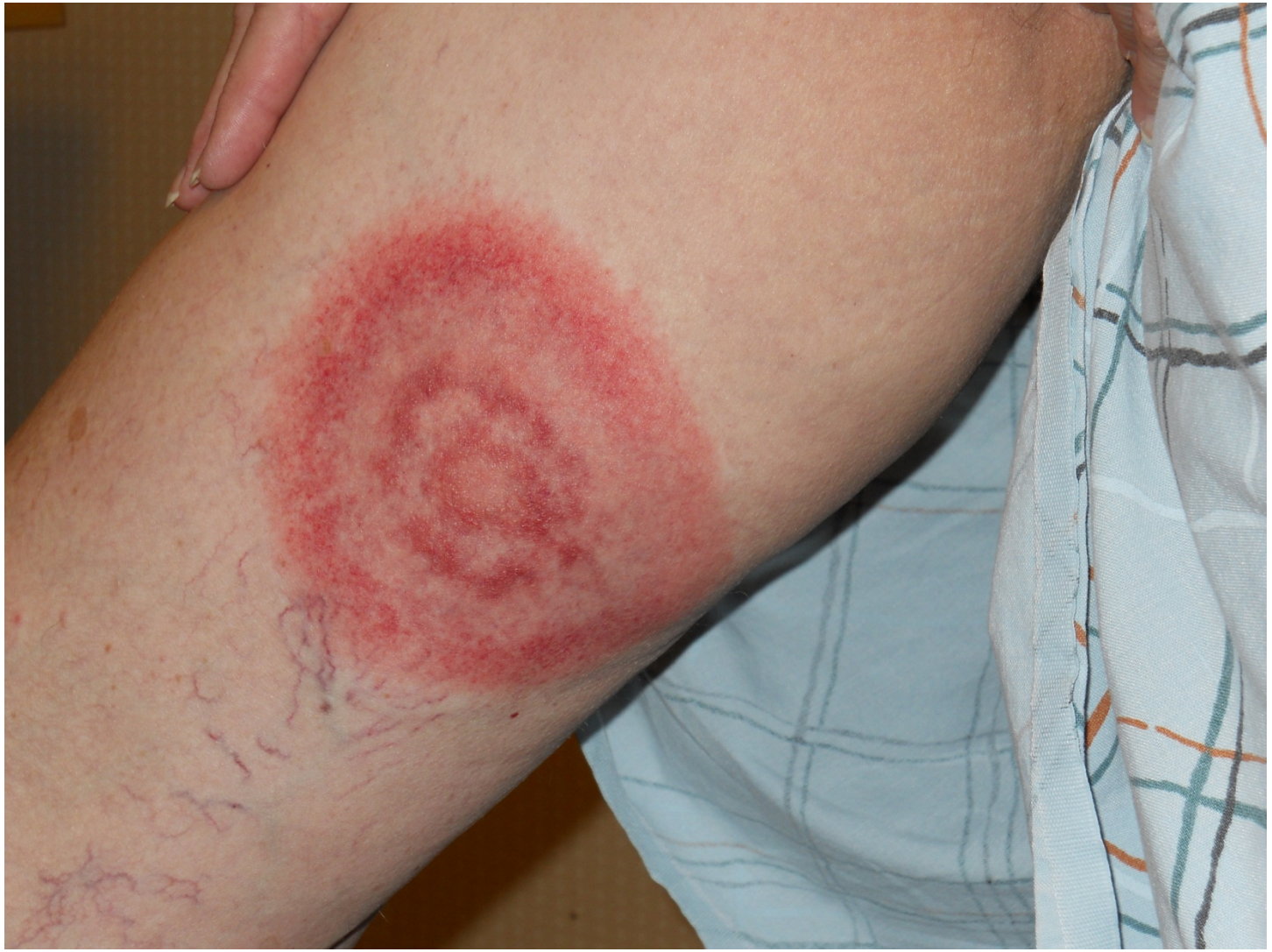
Internet Survey of Erythema Migrans Identification



Target EM

Atypical Lyme Rashes

Non-Lyme Rashes



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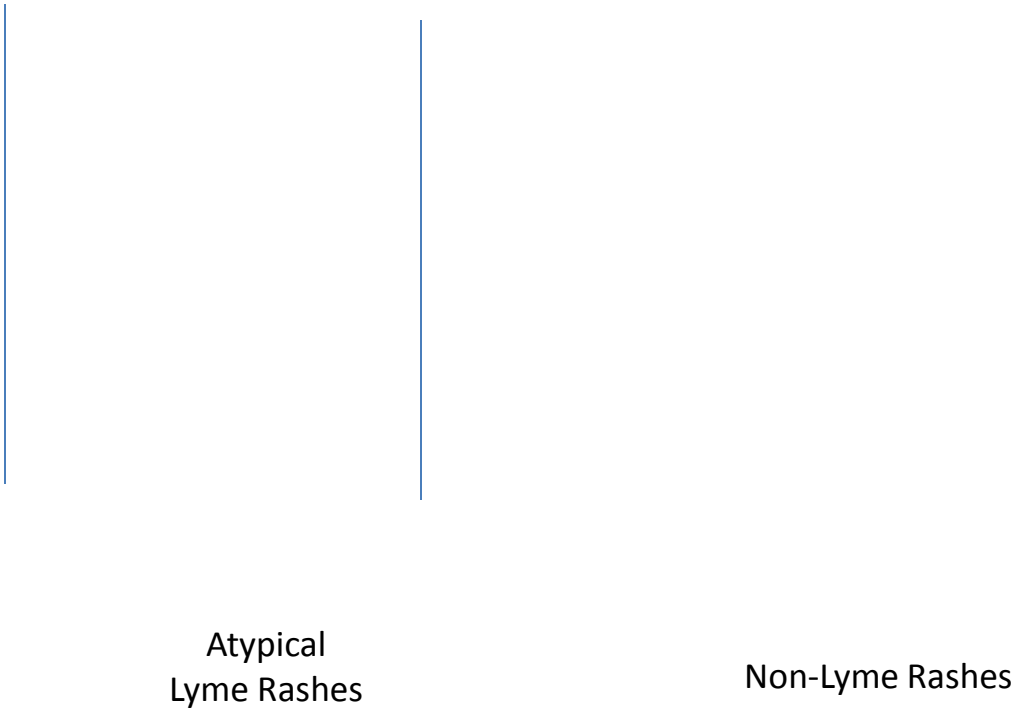
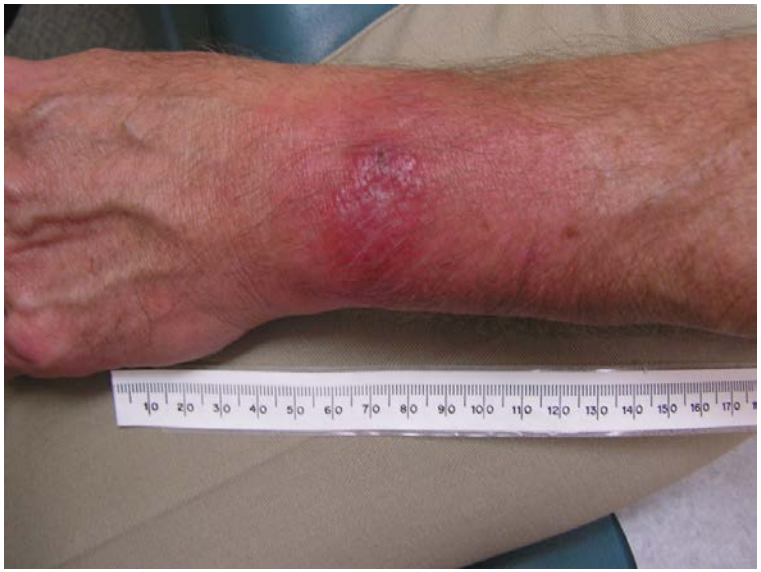
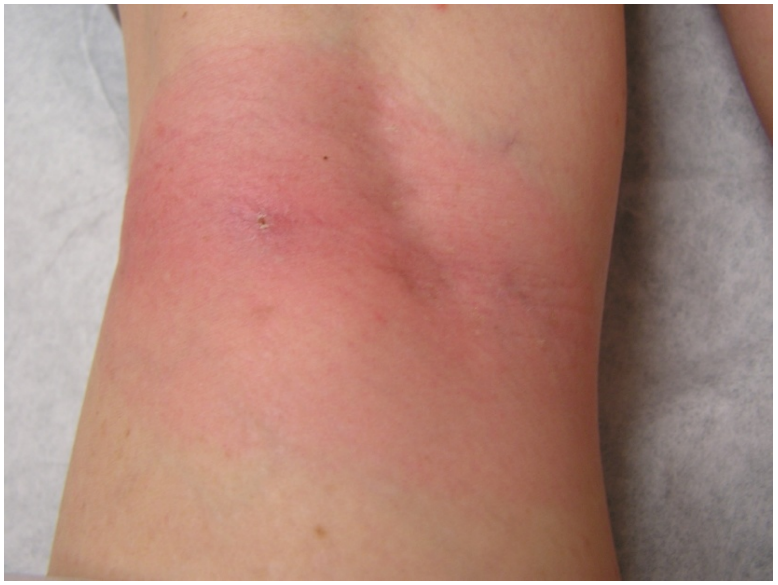
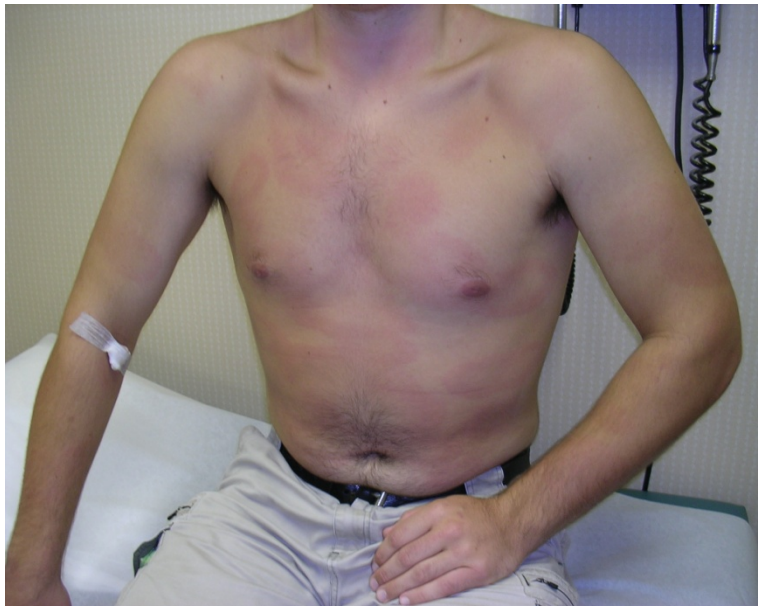
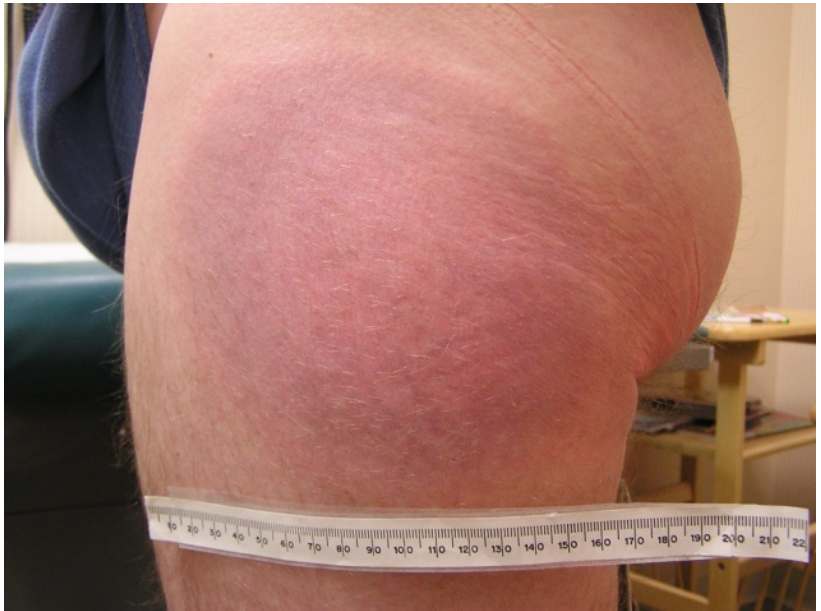


The Majority of EM Lack the Typical Bull's Eye Appearance

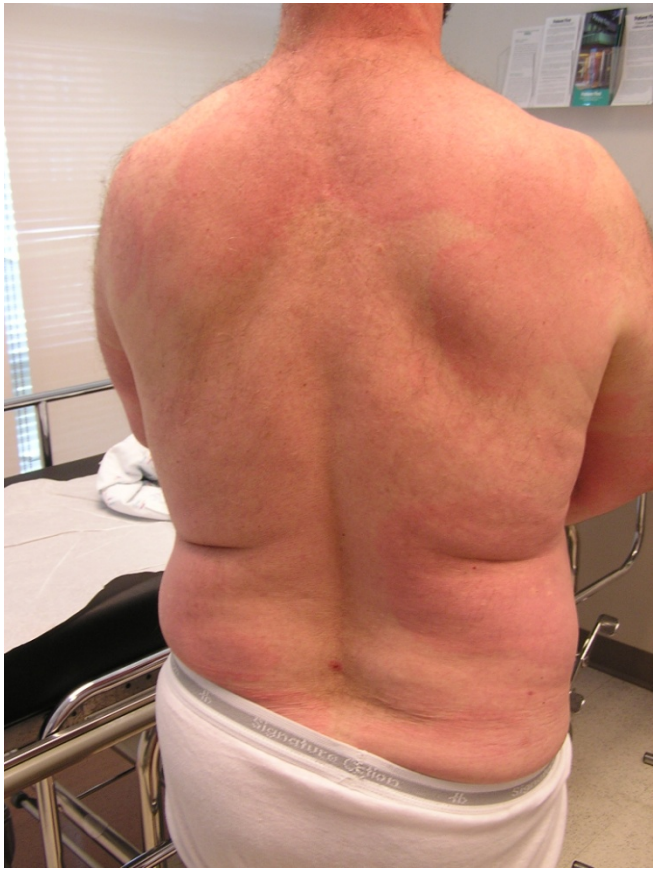


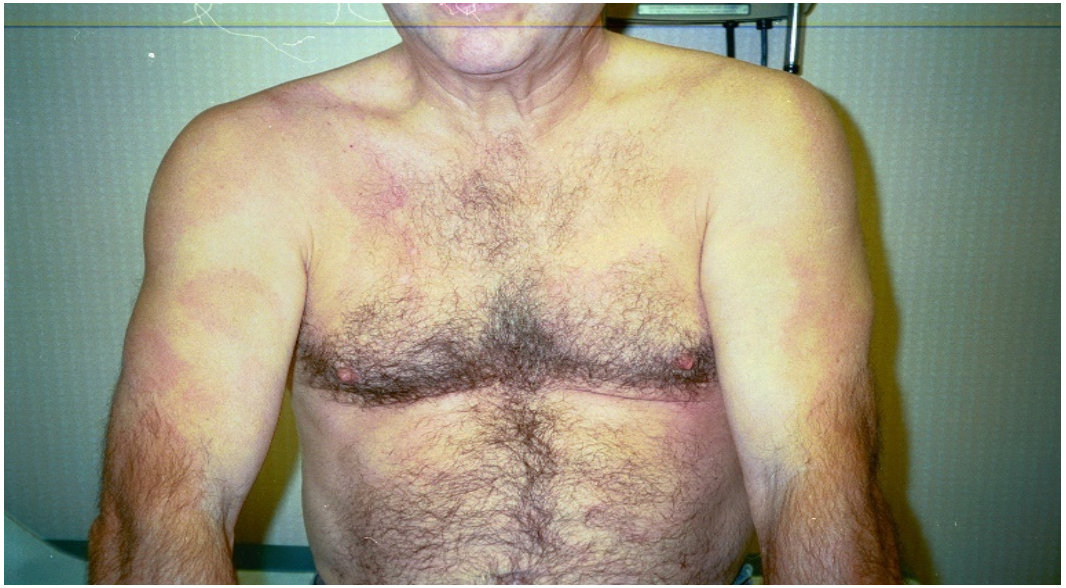






Disseminated Rash of Lyme Disease is atypical in appearance





Improving Diagnosis in Lyme Disease

- Accurate Identification of EM
  - Starts with patient awareness and seeking care
  - Patient “misdiagnosis” of EM as spider bites, bruises, poison ivy, other skin conditions
  - Increasing clinician sensitivity/specificity for diagnosis of EM
- Biomarker improvement/discovery for confirmation of clinical diagnosis

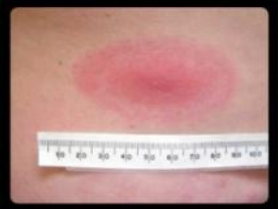
Strategy to Improve Early Diagnosis through increased recognition of Erythema Migrans

- Education with visual tools to show range of appearance of EM
- Protocol for thermal enhancement and photography for self diagnosis
- Use of photos to increase patient communication with physicians at earliest stage of Lyme disease

Looking for a bull's-eye rash? Look again – erythema migrans can take many forms.

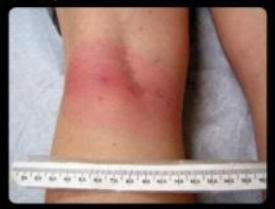
Most people do not see the tick that causes their Lyme disease. However, approximately 75% of patients with early Lyme disease will have the telltale skin lesion in the first 1-4 weeks of infection. The Lyme disease skin lesion is large, greater than 5 cm (2 inches), in size. It can be distinguished from an uninfected tick or bug bite because it lasts days or weeks and enlarges in size over time. When the skin lesion is present, it is a more accurate way to diagnose Lyme disease than by using the currently available blood tests.

Most clinicians recognize the classic target lesion or bull's-eye rash. However, most are not aware that the majority of Lyme disease skin lesions are uniformly red or reddish-blue. In late spring and early summer when early Lyme disease is most prevalent, any of the skin lesions shown here could be indicative of Lyme disease. Fever, chills, and muscular pain in the neck and extremities are common early Lyme disease symptoms. The presence of these symptoms with a rash should raise the suspicion of a Lyme disease diagnosis.



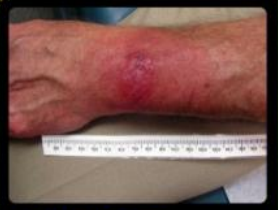
Central Clearing/ Target Lesions

The classic bull's-eye target lesion of Lyme disease occurs in the minority of patients. The majority of Lyme disease skin lesions lack the hallmark rings and central clearing. **Only about 20% of Lyme disease lesions have a bull's-eye appearance.**



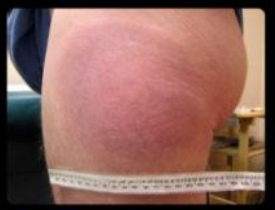
Uniformly Red Lesions

Most Lyme disease skin lesions are uniformly red without the rings or target appearance. They are distinguished from other skin rashes by their round or oval shape and sharply demarcated borders. Skin lesions often hide in difficult to see places such as behind the knee or in the groin or armpit.



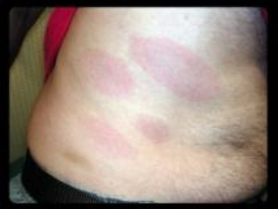
Blistering Lesions - It's not a spider bite.

1% of Lyme disease skin lesions have a central blistering or pustular appearance that is commonly mistaken for a spider bite. Why does this occur? It is likely a more severe inflammatory reaction to *Borrelia burgdorferi* that results in skin blistering.



Blue-Red Lesions

Some Lyme disease skin lesions have a blue-purple color and can be mistaken for a bruise. What distinguishes this from a bruise? The perfectly uniform circle and sharply demarcated border. They may be minimally pruritic or sensitive to touch but are not pruritic like poison ivy or extremely painful like shingles or cellulitis.



Disseminated Lesions

These are not multiple tick bites. The original skin infection of Lyme disease can spread through the bloodstream to other areas of the body, including the joints, nervous system and other areas of the skin. This results in multiple skin lesions that often have variable shapes and appear throughout different areas of the skin.

How to differentiate Lyme disease from other causes of fever and rash.

While viral illnesses and other bacterial infections can cause symptoms of fever, fatigue, and pain that mimic Lyme disease, they do not have large distinct round or oval rashes like Lyme disease. In addition, most viral illnesses have typical cold symptoms of runny nose or prominent cough which are not common in Lyme disease.

This project is a collaborative effort of the Maryland Department of Health and Mental Hygiene and the Lyme Disease Research Foundation of Maryland.

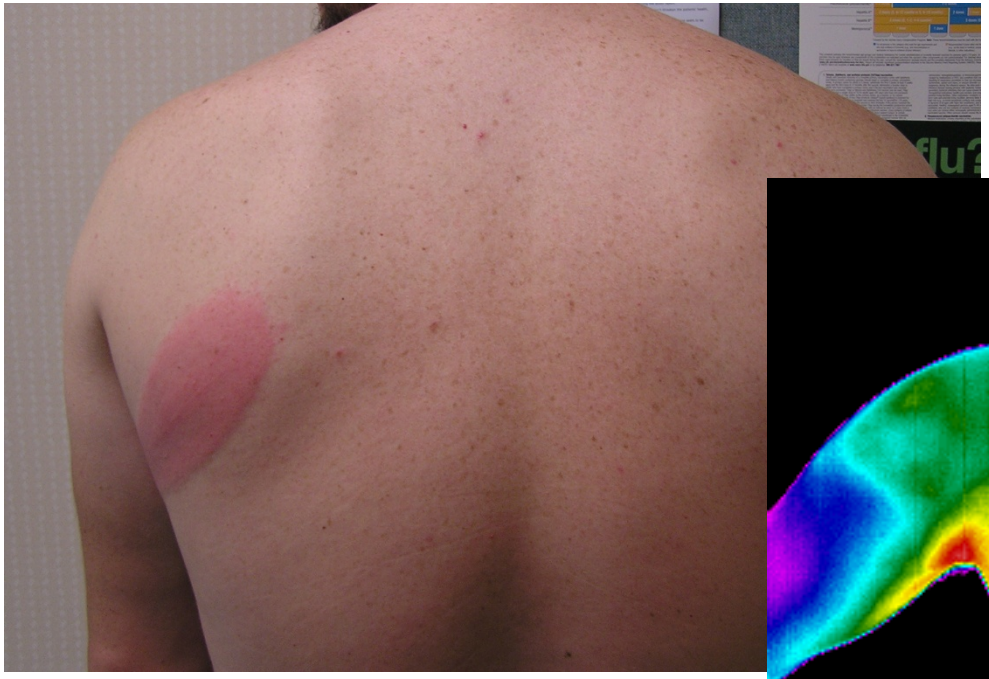
Maryland Department of Health and Mental Hygiene
Infectious Disease and Environmental Health Administration
Center for Zoonotic and Vectorborne Diseases

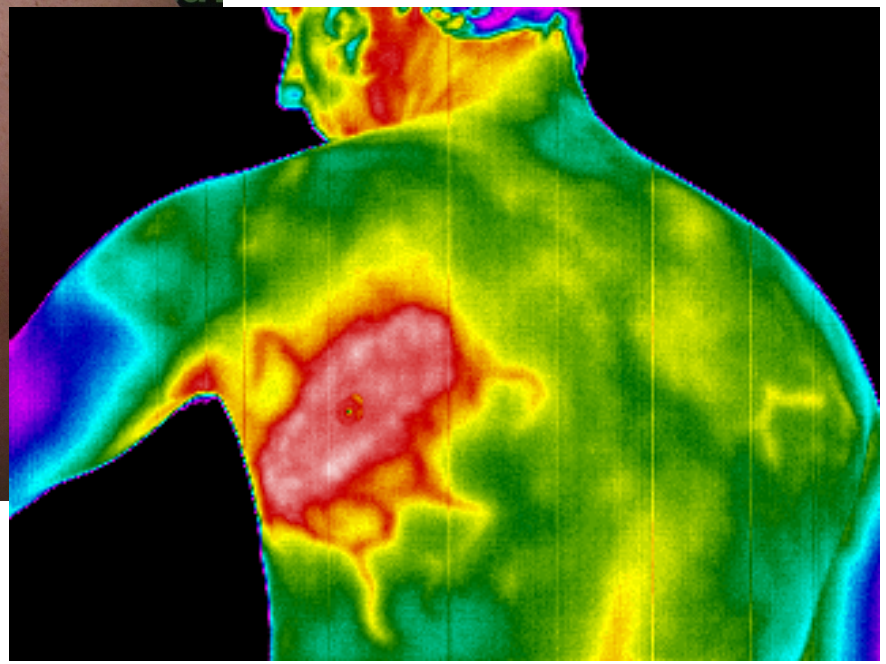
Martin O'Malley, *Governor*
Anthony G. Brown, *Lt. Governor*
Joshua M. Sharfstein, M.D., *Secretary, DHMH*

Provider Education

MARYLAND
Department of Health and Mental Hygiene

What makes the EM rash easily visible
Why don't most EM have the Target appearance
Comparison of Infrared photo vs. Visible light



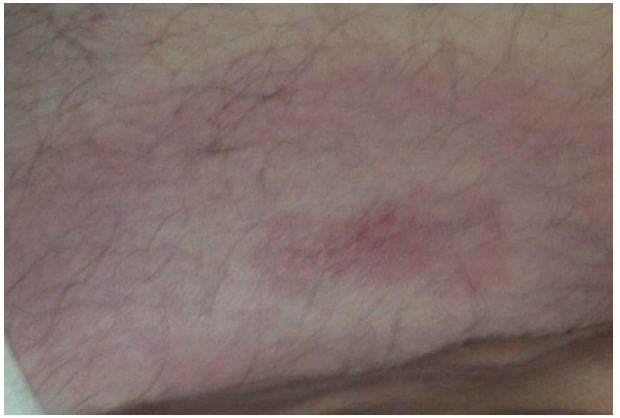


Thermal Enhancement Example

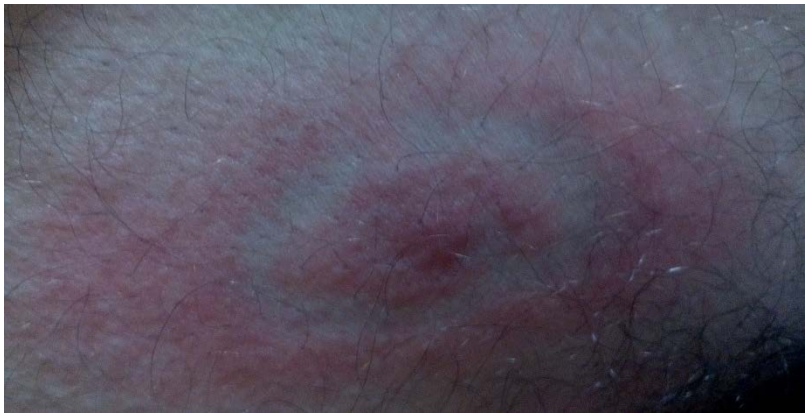
Anecdotal stories of rashes that only appear after hot shower or in the direct sun light

Possible use of “hot and cold shower” to bring out otherwise unseen EM rash

Room Temperature



After Warm Shower



Pictures courtesy of Henry G Taylor MD MPH. Used with permission and permission of patients.

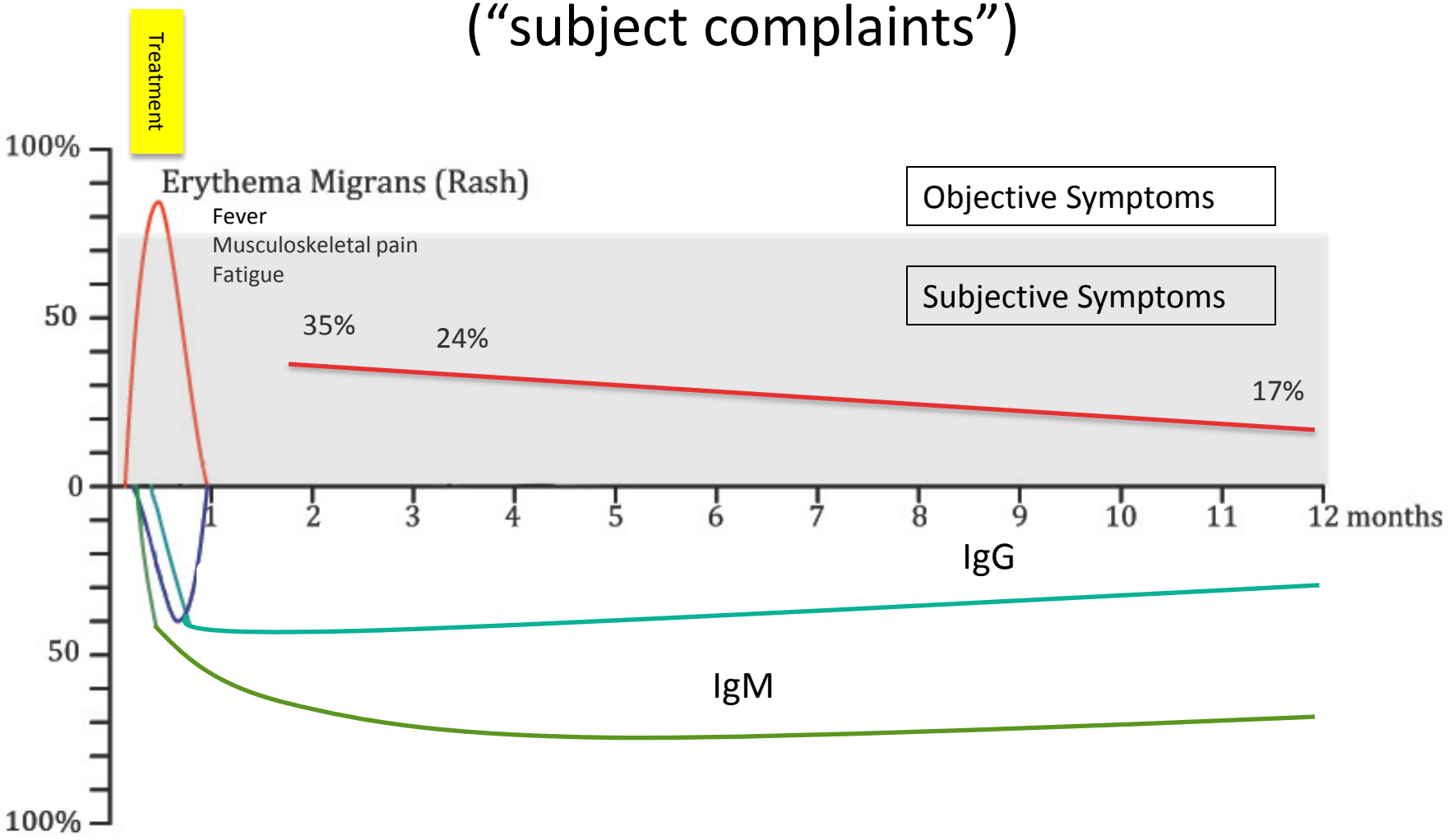
Thermal Enhancement of Erythema Migrans

protocol of Henry G Taylor MD MPH.

- Expose to room air for five minutes to even out skin temperature and pressure marks.
- Take a cell-phone picture at room temperature
- Take a warm shower. Warm enough to make your skin feel flushed, but NOT scalding!
- Pat rash dry – DO NOT RUB or irritate rash.
- Take second cell-phone picture
- Take a cool shower. It should feel cold and skin should look more pale than usual.
- Pat rash dry – DO NOT RUB or irritate rash.
- Take third cell-phone picture
- Email the pictures to your doctor

Post-Treatment Lyme Disease Syndrome:

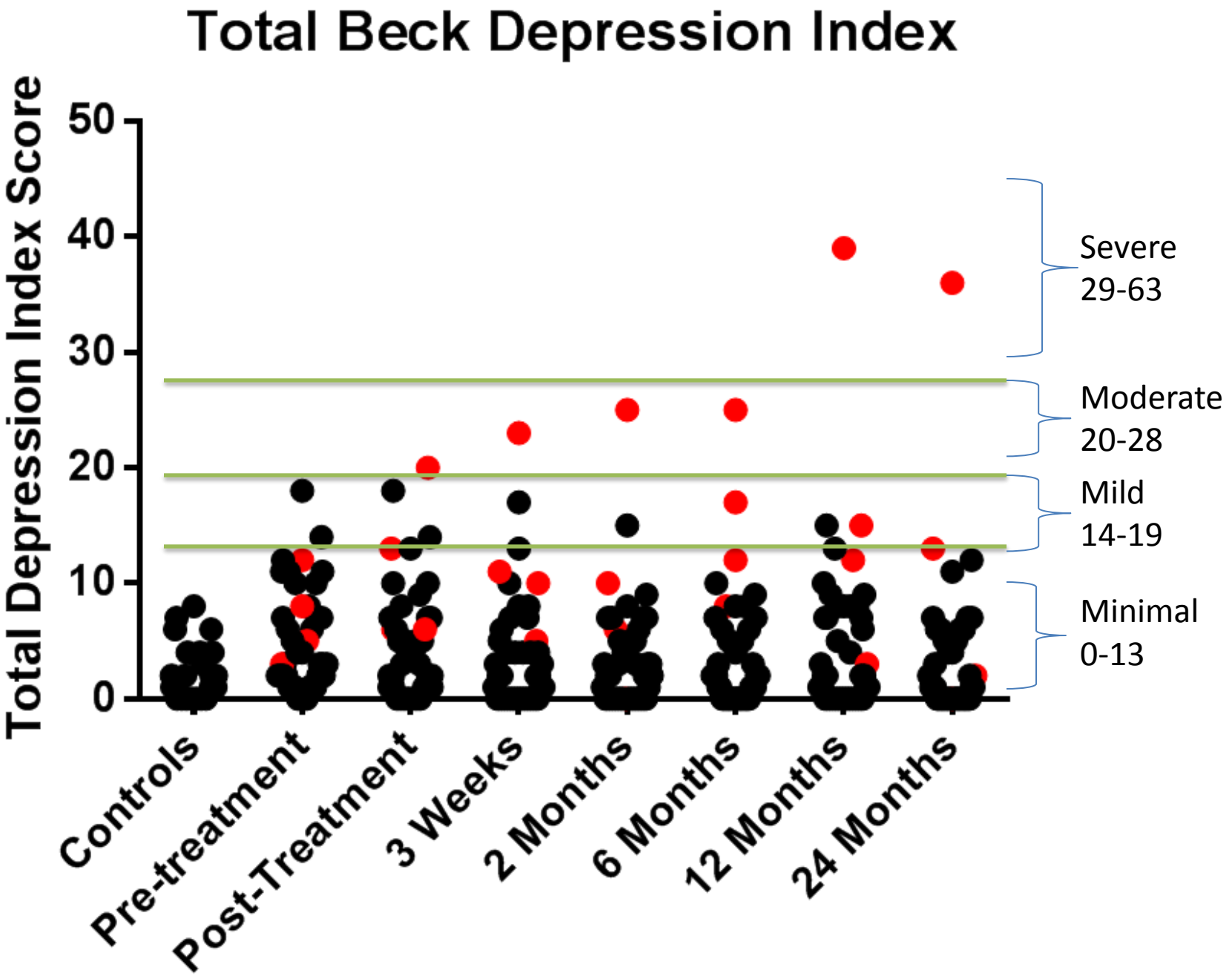
Fatigue, widespread pain, cognitive difficulties ("subject complaints")



Post Treatment Follow Up

- Measures of cure based on physical exam to document resolution of rash
  - Serology not biomarker for “proof of cure”
- Follow up visits
  - What to look for
    - Persistence of rash or other findings
    - Evidence of neurologic complication
    - Post treatment symptoms
- Expectations of post treatment health
  - Anticipatory guidance for patients on how symptoms are likely to resolve

Severe Fatigue
Cutoff = 20


Total Beck Depression Index
Total Depression Index Score
50
40
30
20
10
0
Controls
Pre-treatment
Post-Treatment
3 Weeks
2 Months
6 Months
12 Months
24 Months
Severe
29-63
Moderate
20-28
Mild
14-19
Minimal
0-13

Line Indicates
A Composite
Score of 45

Patient Follow Up after Treatment of Lyme Disease

Anticipatory Guidance

- Treat with Doxycycline for three weeks. Further antibiotics not needed unless there are obvious signs or symptoms of continued illness.
- Follow-up in 3 weeks to confirm rash cleared and assess symptoms/relapse.
- Empathetic Non-Judgmental listening to elicit patient beliefs and goals.
- Self-Care is important, especially rest and moderate exercise.
- Follow-up in 7 weeks to discuss persistent symptoms and potential benefit of exercise, lifestyle changes and/or Integrative Medicine treatments.

Developed in collaboration with Henry G Taylor MD MPH.

National Institute of Standards and Technology Workshop on Measurement in Lyme Disease

- Discussion of a variety of promising technologies and techniques for addressing the measurement of Lyme disease.
- Promotion of awareness, research collaboration and creative solutions
- Accelerate the time to development of effective biomarkers needed for more reliable diagnosis and management of the different stages of Lyme disease.

http://www.nist.gov/mml/nist-workshop-on-lyme-disease.cfm