What's New In Tick-borne Disease?

Lyme Disease

Relapsing Fever

and beyond…

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Objectives

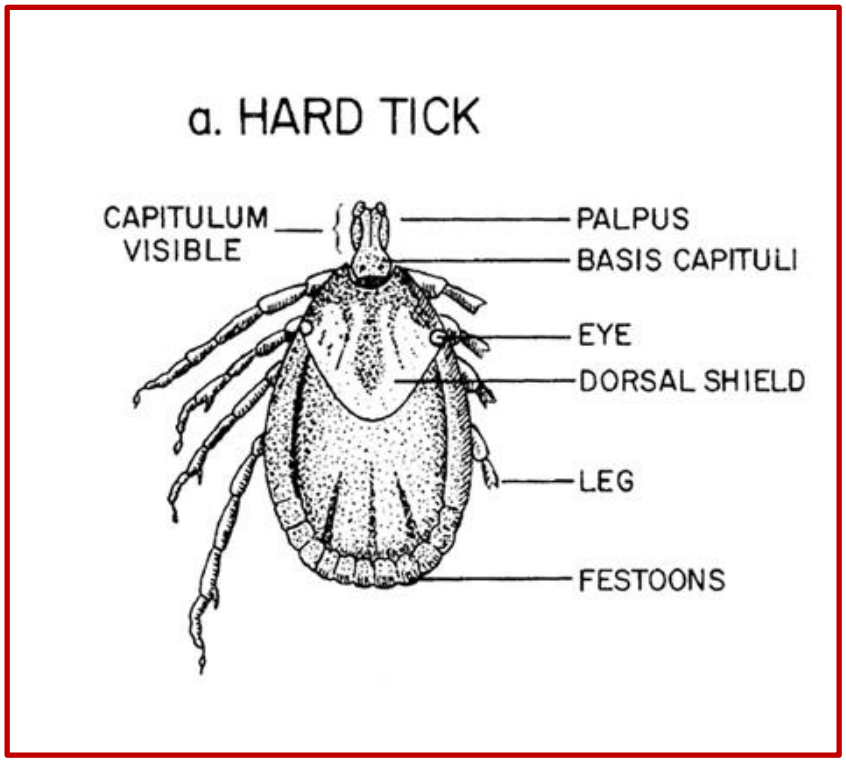
1. Understand the epidemiology of tick-borne diseases and the ticks that vector the diseases.

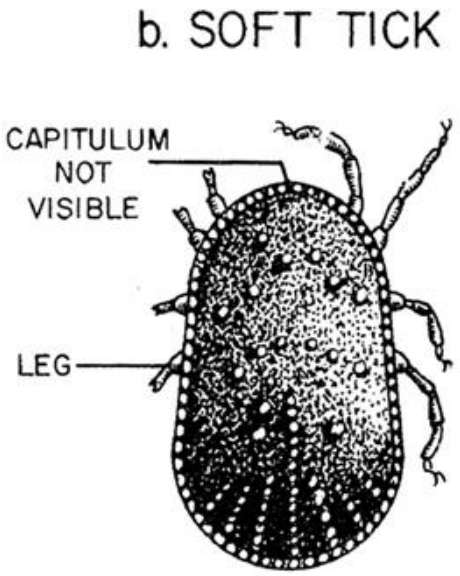
2. Recognize the growing list of tick-borne diseases.

3. Recall the testing available for detection of tick-borne diseases.

Anatomy of the tick…

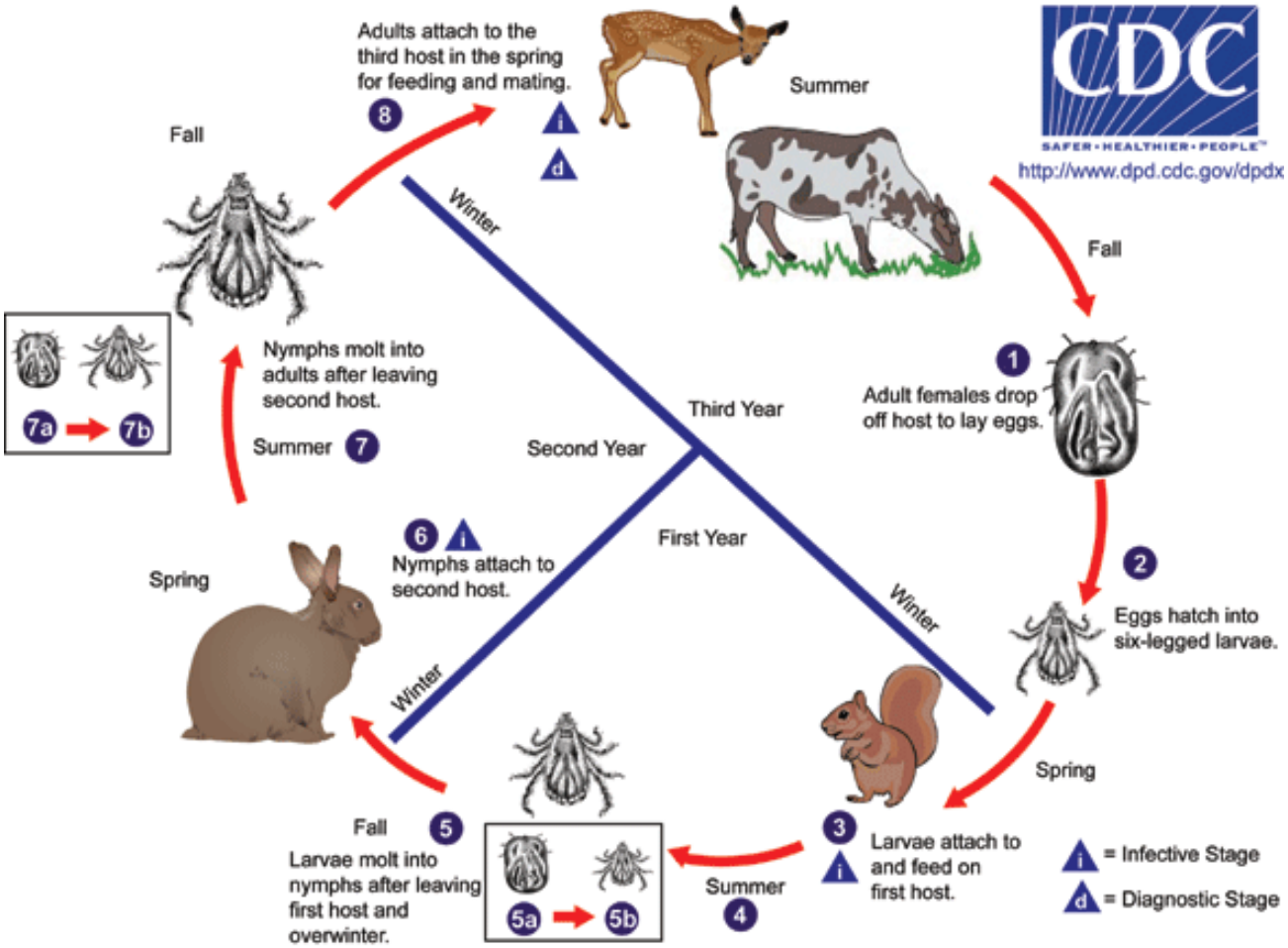
Hard Shell Tick (Ixodid) vs Soft Shell (Agasid)





https://www.cdc.gov/dpdx/ticks/index.html

Hard Ticks-Life Cycle



https://www.cdc.gov/dpdx/ticks/index.html

Ixodid Ticks – male vs. female

female

male

https://www.cdc.gov/dpdx/ticks/index.html

Hard Shelled Ticks of the Northeast

Ixodes scapularis
"Deer tick or black-legged tick"

Rhipicephalus sanguineus
"Brown dog tick"

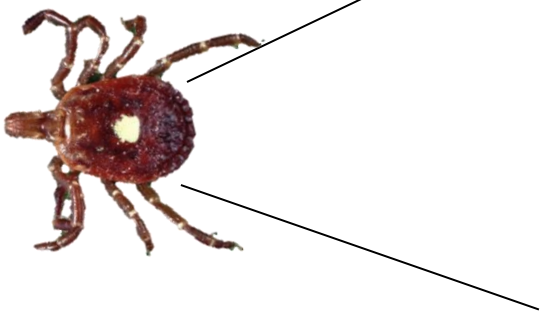
Dermacentor variabilis
"American Dog Tick"

Amblyomma americanum
"Lonestar Tick"

https://www.cdc.gov/dpdx/ticks/index.html

Amblyomma americanum

Amblyomma americanum



- *Ehrlichia ewingii*
- *Ehrlichia chaffeensis*

} Human monocytic ehrlichiosis

- *Francisella tularensis*
- STARI (Southern Tick Associated Rash Illness)
- Heartland virus

Rhipicephalus sanguineus

Rhipicephalus sanguineus

- *Rickettsia rickettsii* (Rocky mountain spotted fever)

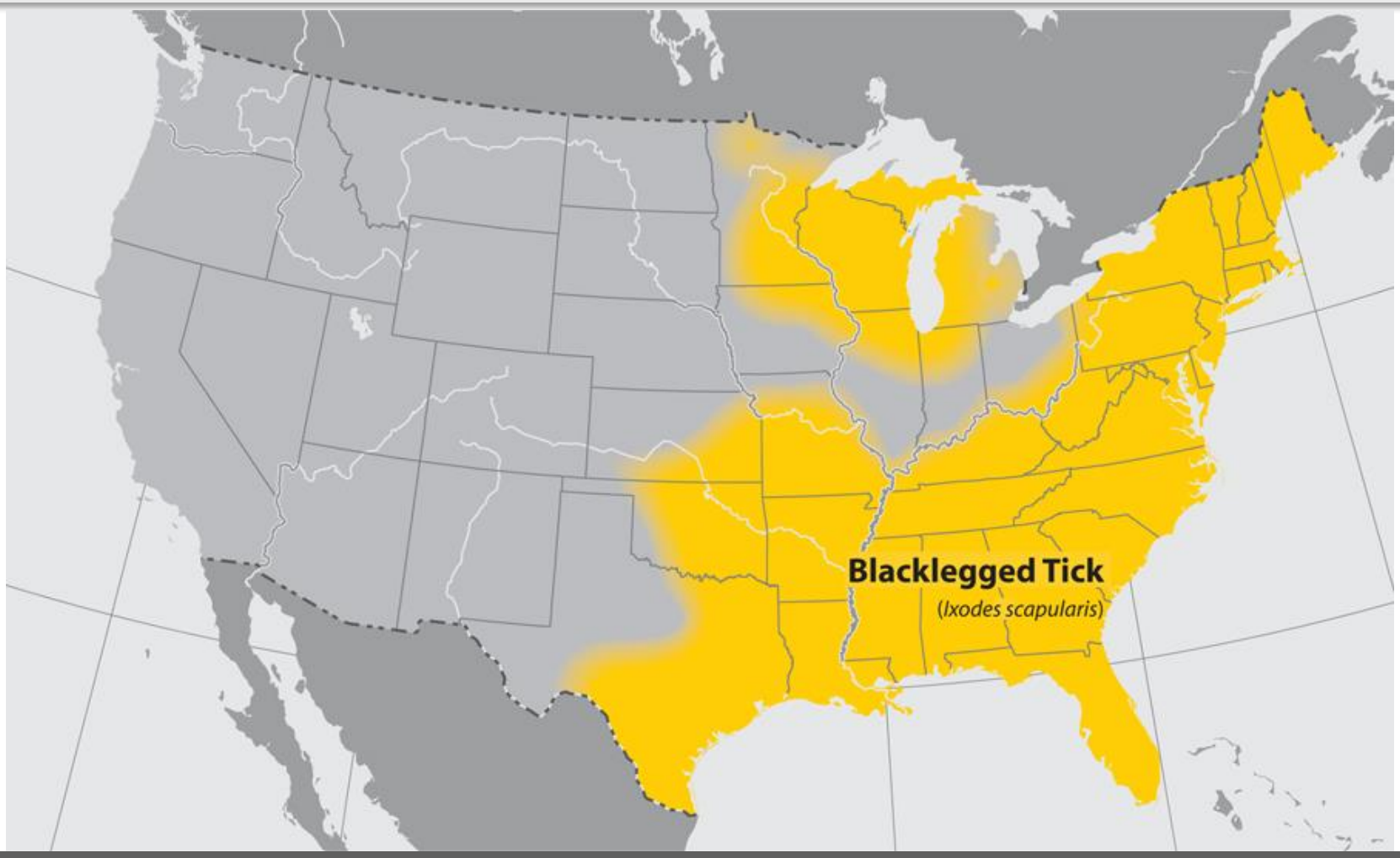
  In the southern USA only

Dermacentor variabilis

Dermacentor variabilis.

- *Ehrlichia* spp. (Human monocytic ehrlichiosis)
- *Rickettsia rickettsii* (Rocky mountain spotted fever)
- *Francisella tularensis* (Tularemia)

Ixodes scapularis



Ixodes scapularis

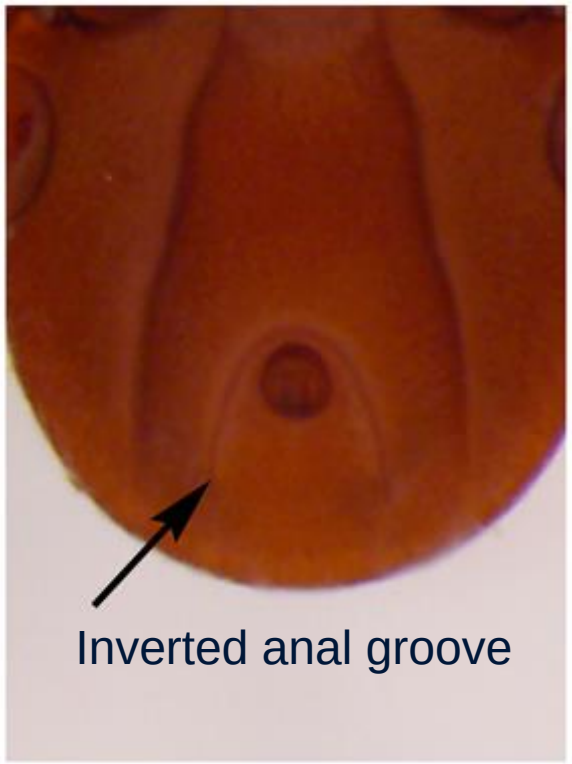
- *Borrelia burgdorferi*
- *Borrelia mayonii*

} Lyme disease

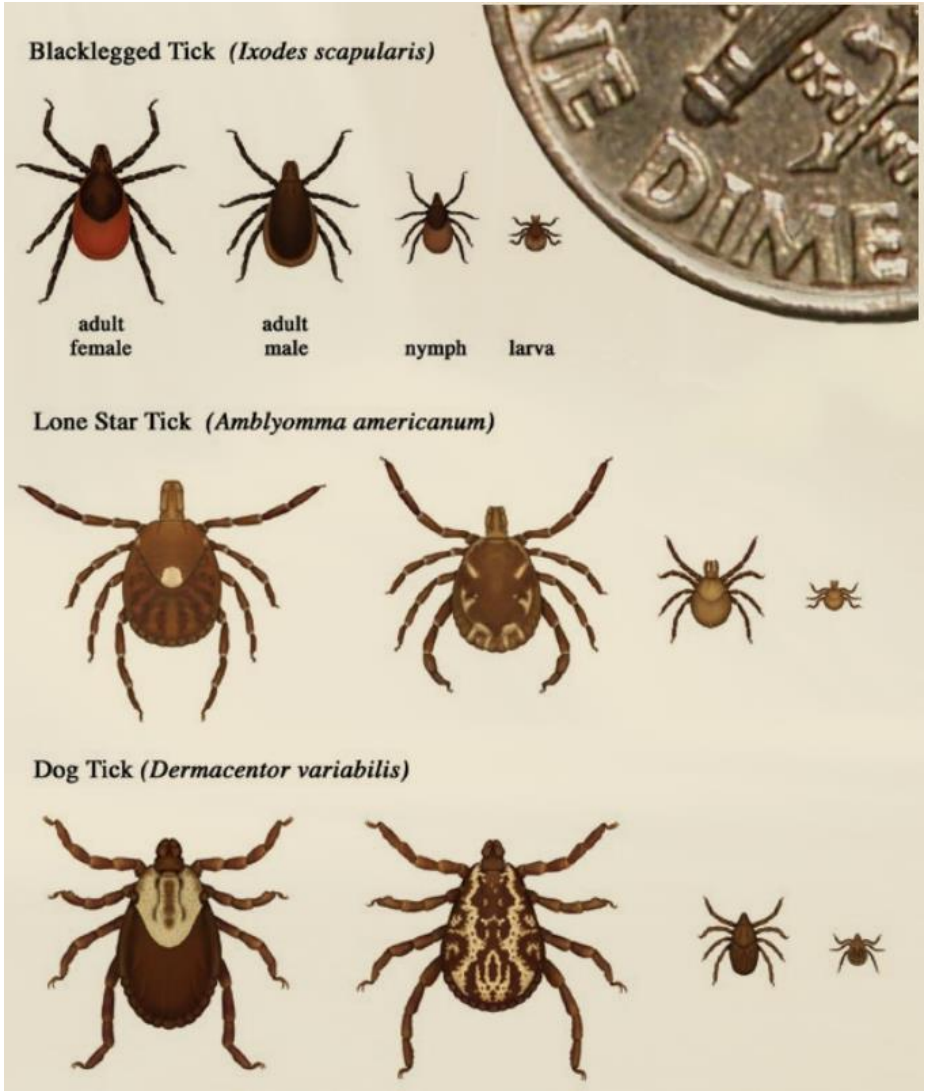
- *Borrelia miyamotoi* (Tick-borne relapsing fever-like)
- Deer tick virus (Powassan virus, lineage II)
- *Babesia spp.*
- *Anaplasma phagocytophilum*

(Human granulocytic Anaplasmosis)

Easiest way to identify

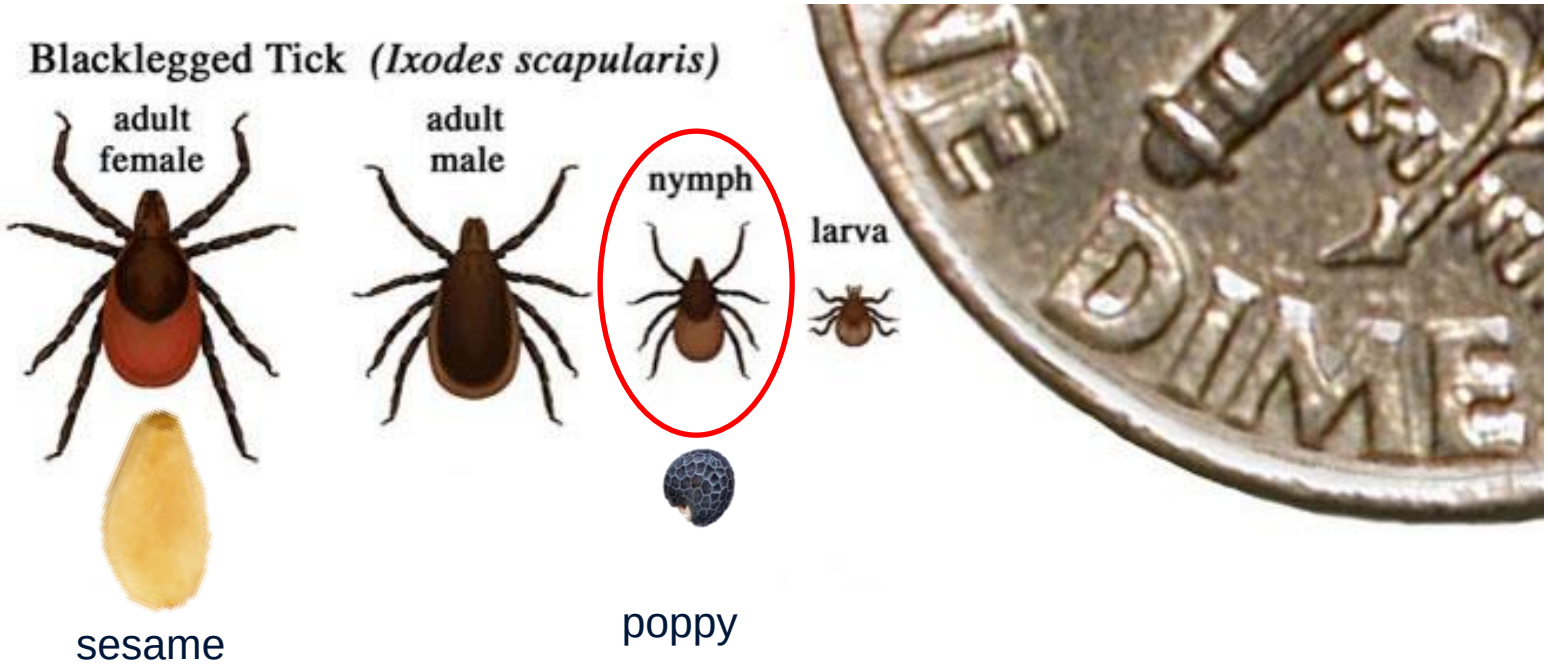


Smaller than you may expect



https://www.cdc.gov/lyme/resources/tickbornediseases.pdf

Smaller than you may expect



https://www.cdc.gov/lyme/transmission/index.html

Harder to identify when “full”

https://www.cdc.gov/dpdx/ticks/index.html

Why are the ticks so bad this year?

A song of humans, hosts, forests, and food!

http://www.commonweeder.com/the-harvard-forest/

http://www.commonweeder.com/the-harvard-forest/

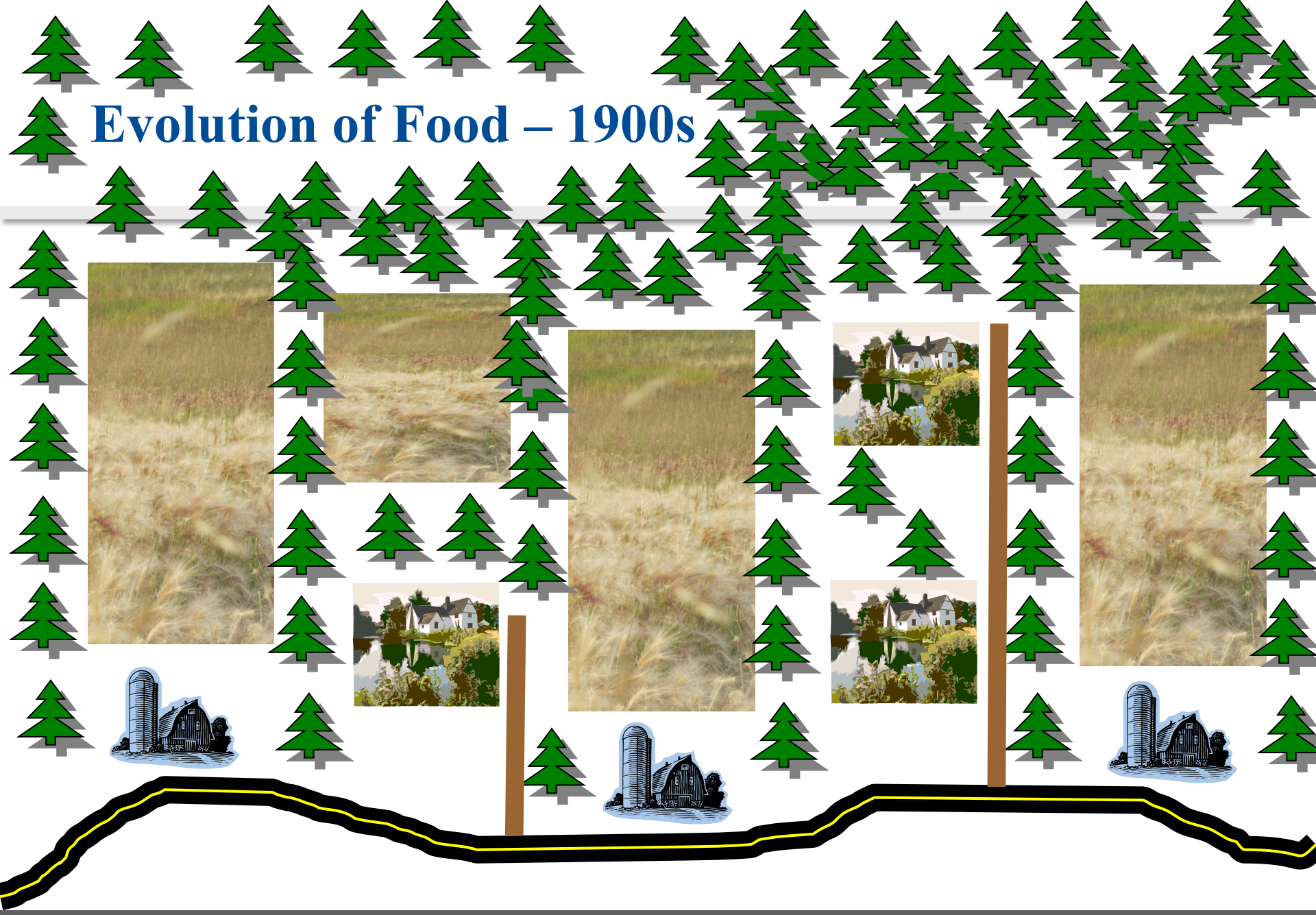
http://www.commonweeder.com/the-harvard-forest/

Evolution of Food – 1800s

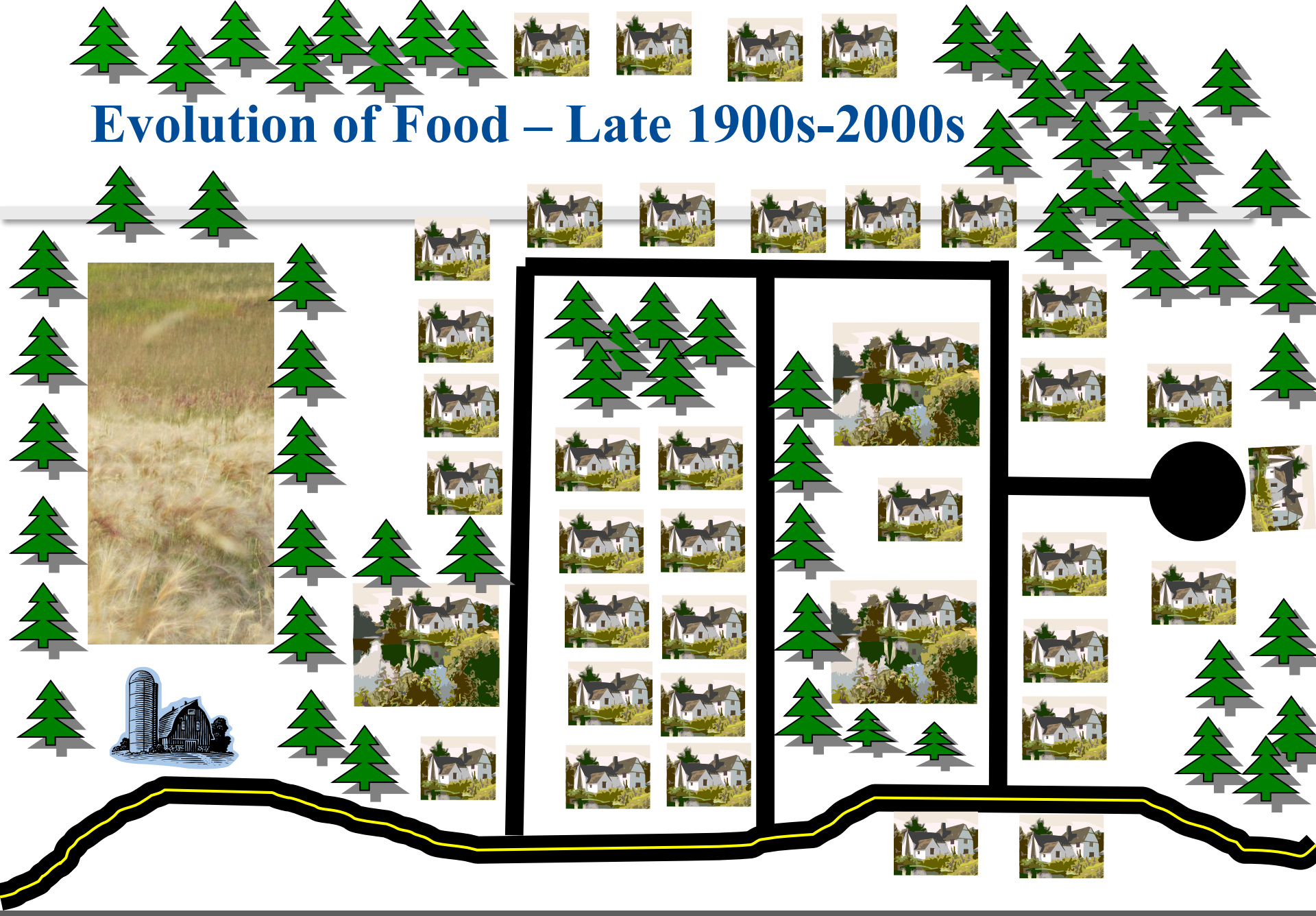




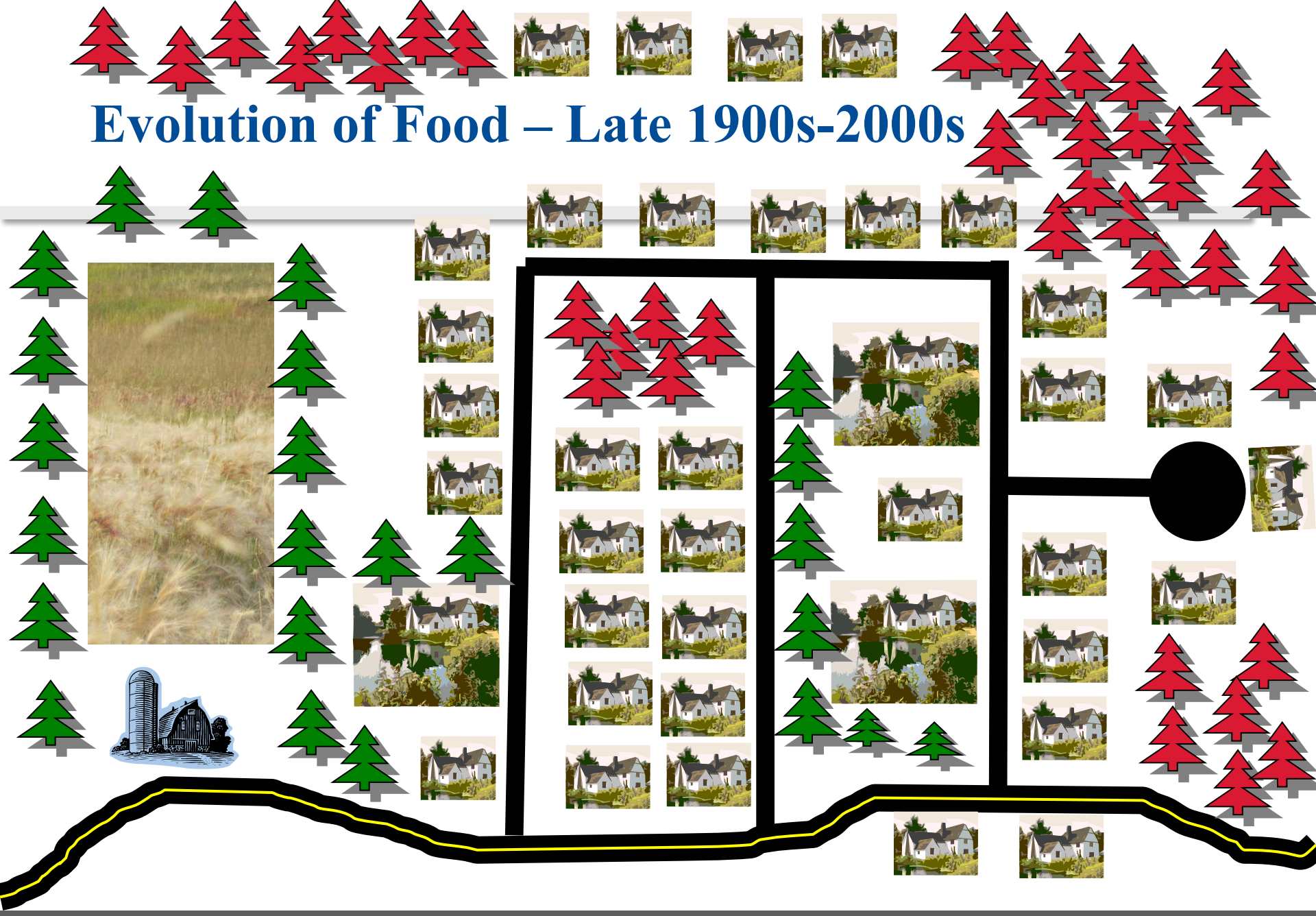
Evolution of Food – 1900s



Evolution of Food – Late 1900s-2000s



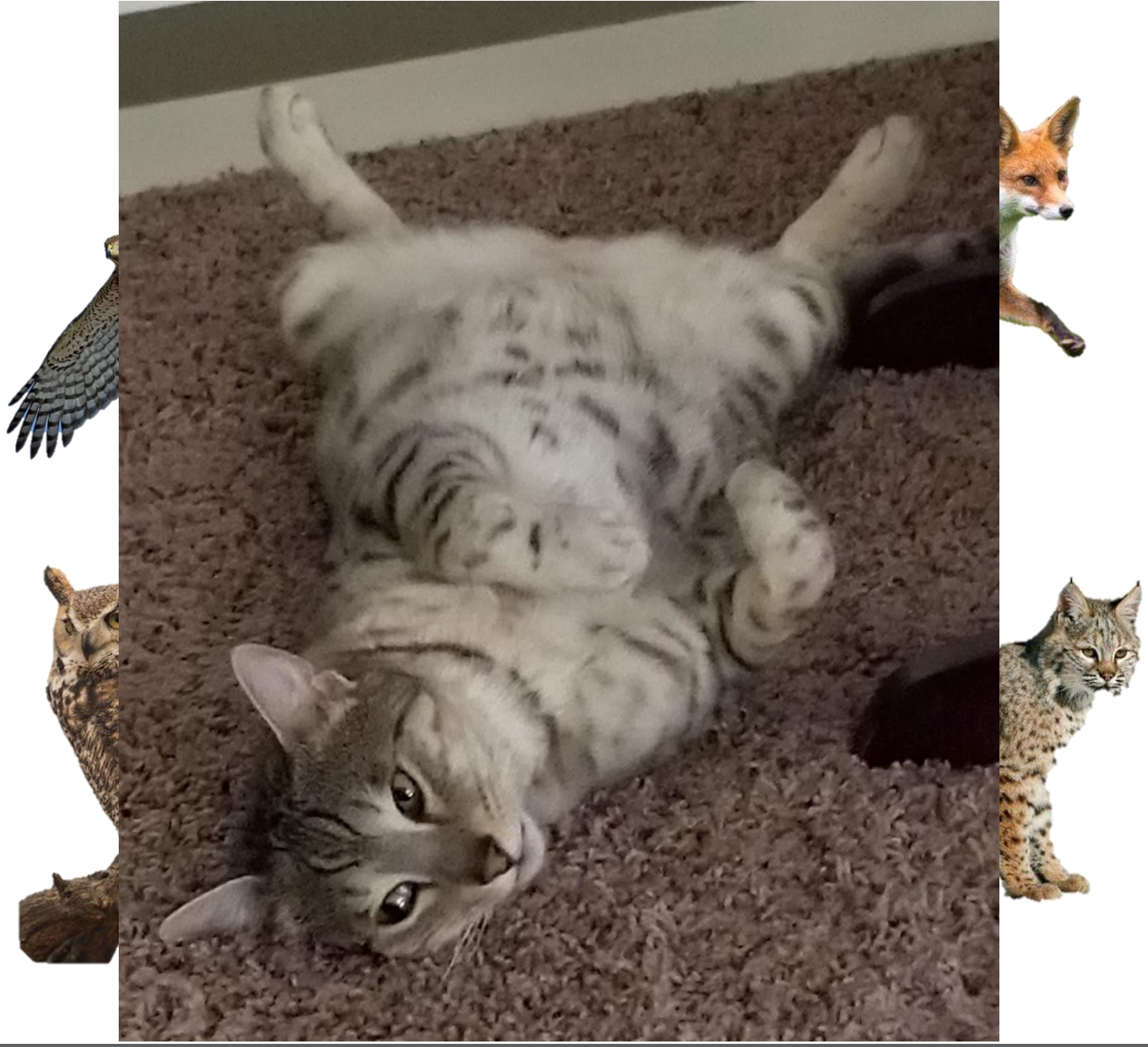
Evolution of Food – Late 1900s-2000s




Mast Year


White-footed mouse

http://www.npr.org/sections/goatsandsoda/2017/03/06/518219485/forbidding-forecast-for-lyme-disease-in-the-northeast

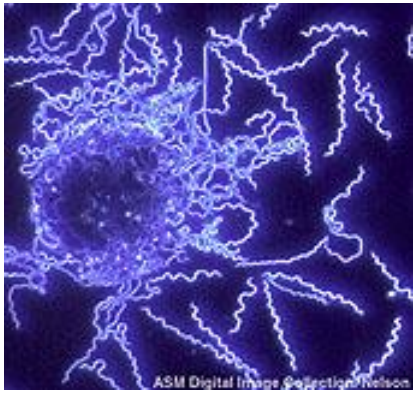


http://www.npr.org/sections/goatsandsoda/2017/03/06/518219485/forbidding-forecast-for-lyme-disease-in-the-northeast

- *Borrelia burgdorferi* (Lyme disease)
- *Borrelia mayonii* (Lyme disease)
- *Borrelia miyamotoi* (Tick-borne relapsing fever-like)
- Deer tick virus (Powassan virus, lineage II)
- *Babesia spp.*
- *Anaplasma phagocytophilum* (Human granulocytic Anaplasmosis)

Lyme Disease

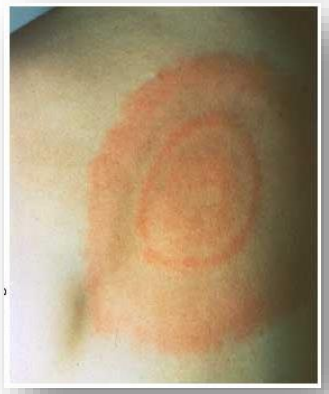
Lyme disease (LD)

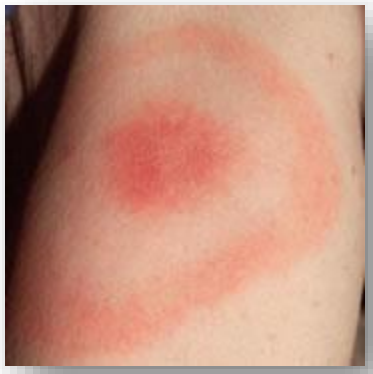


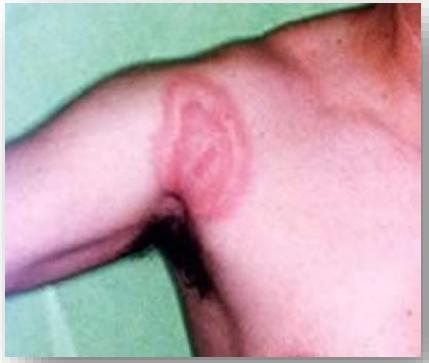
- *Borrelia burgdorferi* and *B. mayoni* (in N. America)
  - Gram-negative spirochete, motile by polar flagella
- Fastidious, not cultured in the clinical laboratory
- Vector
  - *Ixodes scapularis* (eastern/central)
  - *Ixodes pacificus* (west coast regions)
  - Infected Ixodes (nymph & mature adult) MUST feed >24 hours for transmission
    - @24 hours 5% of infected ticks will transmit
    - @48 hours 50% of infected ticks will transmit
    - @96 hours 100% of infected ticks will transmit

Symptoms

- Early LD or Stage 1 (3-30 days post bite)
  - Red, expanding rash called erythema migrans (EM) or “bull’s eye rash” (7-14 days)
    - Present in up to 80% of cases
  - Fatigue, chills, fever, headache, muscle and joint aches, and swollen lymph nodes
    - All cases present w/combinations of these symptoms







Symptoms

- Early disseminated LD or Stage 2 (days to weeks)
  - Additional EM lesions in other areas of the body
  - Facial or Bell's palsy
  - Severe headaches and neck stiffness due to meningitis
  - Pain and swelling in the large joints
  - Shooting pains that may interfere with sleep
  - Heart palpitations and dizziness due to changes in heartbeat
- Symptoms will resolve over weeks without treatment but can lead to serious complications

Symptoms

- Late disseminated LD or Stage 3 (months to years)
  - Can occur even after treatment for Lyme
    - Muscle & joint pain
    - Cognitive defects (“slow”)
    - Sleep disturbance
    - Fatigue

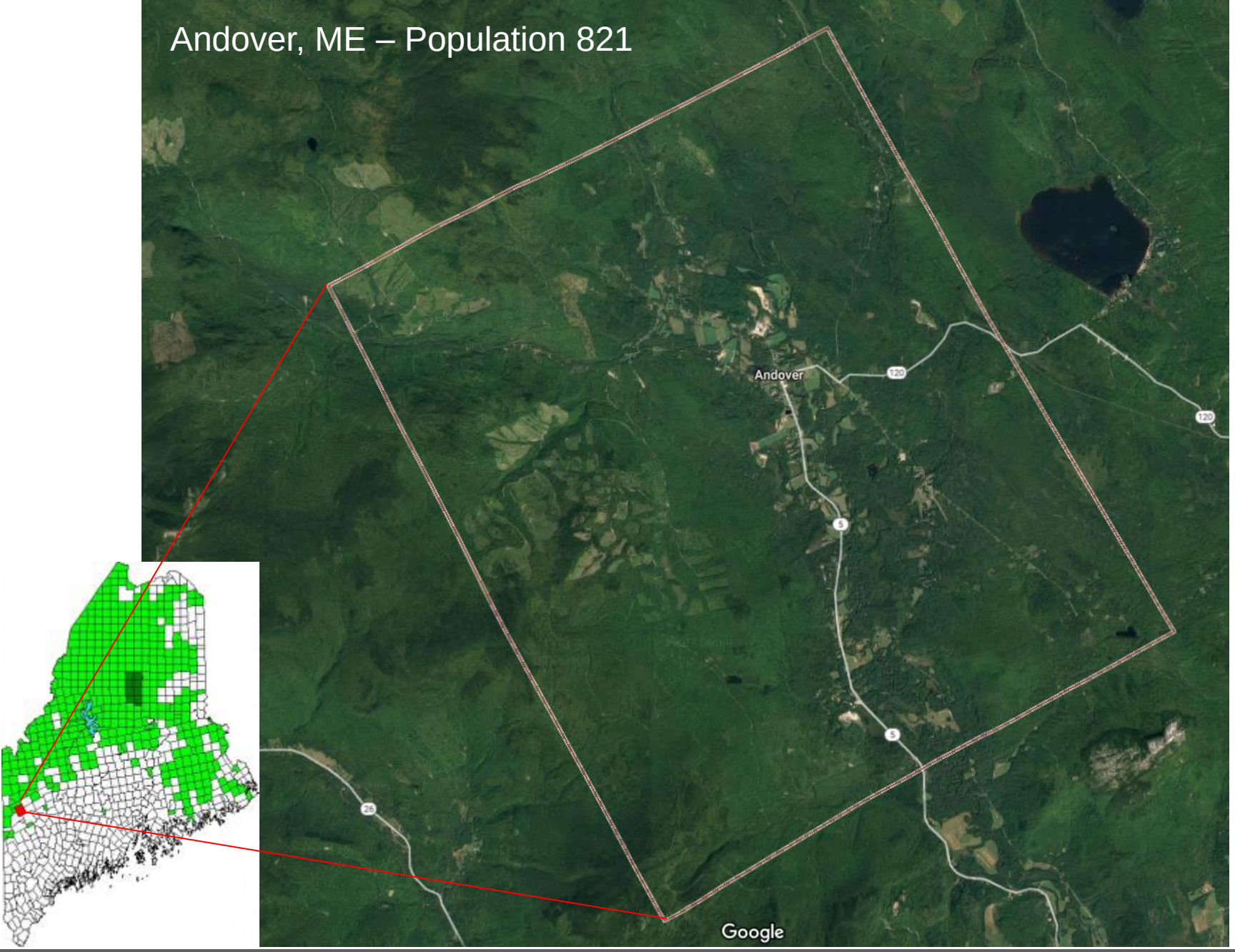
Diagnostic tests

- Shortly after bite –
  - Silver stain (not diagnostic)
  - PCR from lesion biopsy
- Second stage of disease (dissemination)
  - *Serology (may be negative due to therapy)*
  - PCR from joint fluid, lesion
    - Blood and CSF are poor samples
- Late stage of illness
  - *Serology testing only*

Case Presentation

- 21 year old male from central Nova Scotia
- Experienced outdoorsman, hiker, hunter, and fisherman
- 3 day fishing and camping weekend in Andover, Maine
  - Memorial Day, 2002
- Noted tick attached to calf (unknown duration), removed with fishing pliers, cauterized pliers and wound with whiskey
- Continued fishing and camping

Andover, ME – Population 821

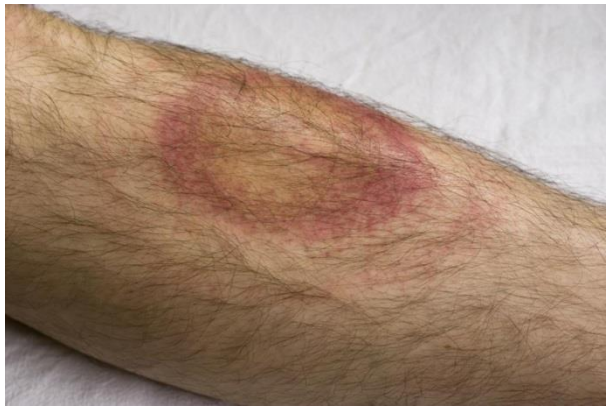


Case cont.

Lovejoy Bridge, Ellis River

Case cont.

- 3 days post-camping trip developed rash on right calf



(not the actual rash)

- No other symptoms
- No physician seen (remember it is 2002)

Fast Forward

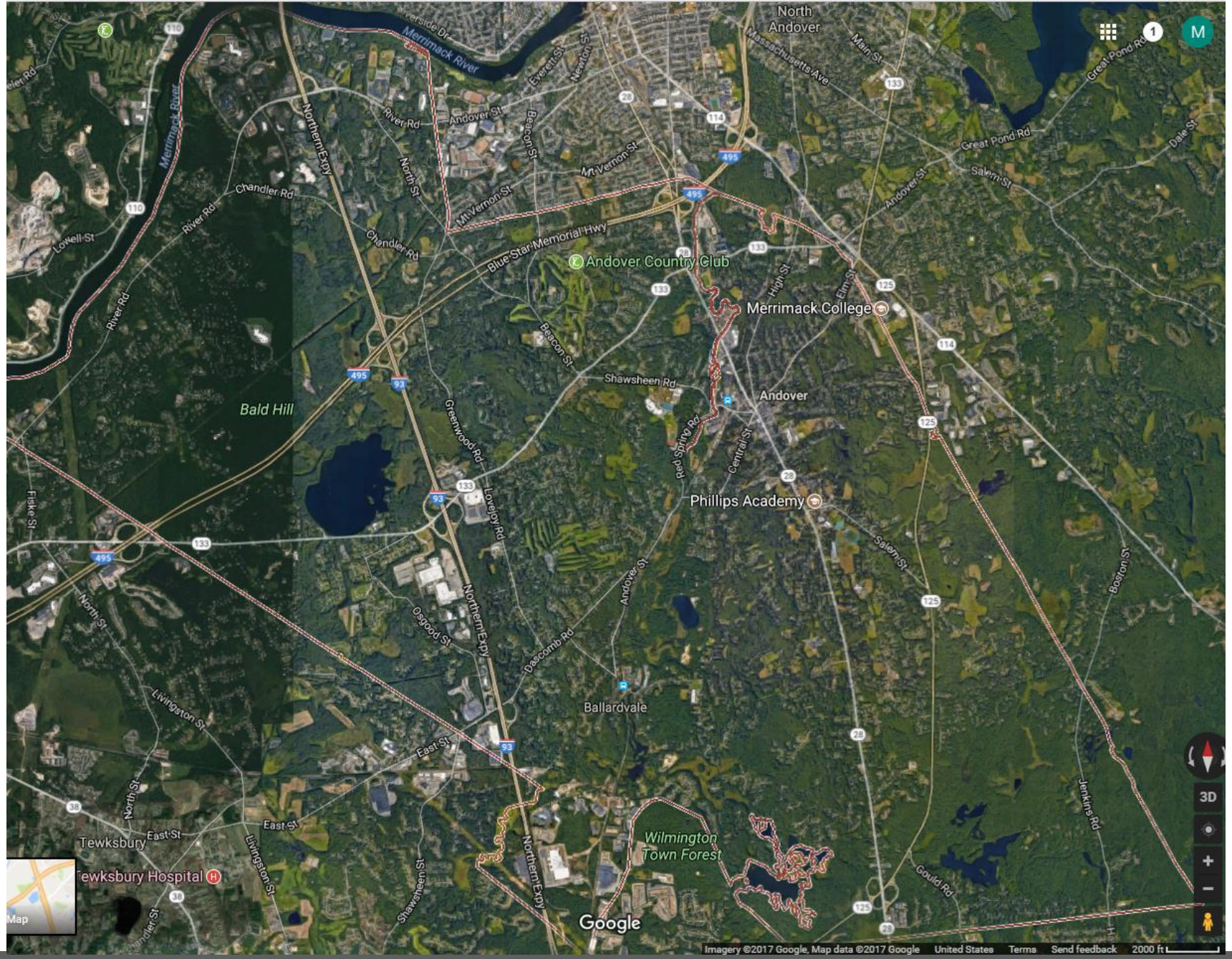
- 2012 – Now 31 year old microbiologist (and laboratory director)
- Participates in lab blood draw for QC purposes as “negative serum sample” for Lyme disease ELISA and Western blots
- + total antibody ELISA (screen)
  - Not a great negative QC point…
- Just for fun…
  - IgM blot – negative
  - IgG blot positive 7 of 10 bands
- Does this patient have Lyme disease?

No…but it is not always that easy

- 2003-2009 – Patient lived in Edmonton, Alberta Canada
  - Not a lyme endemic region
  - One vacation to lyme endemic region in 2006 & 2009
    - No observed tick bites, no rashes, no other symptoms
- 2009-2017 – Patient lived in Salt Lake City, UT
  - Not a lyme endemic region
- Patient grew up in central Maine

Case 2.

- 37 year old male from Andover, Massachusetts
- Never hikes, hates camping, generally disgusted by insects and nature
- Enjoys sitting in his back yard drinking, BBQing, and entertaining friends and family
- Enjoys golfing (2-3 rounds/week) – but he's not very good at it
- Does not recall a tick bite
- No rash
- Develops flu-like illness; body aches, headache, low grade fever


North Andover
Merrimack River
Andover Country Club
Merrimack College
Andover
Phillips Academy
Ballardvale
Bald Hill
Wilmington Town Forest
Tewksbury
Tewksbury Hospital
Google
Imagery ©2017 Google, Map data ©2017 Google
United States
Terms
Send feedback
2000 ft

Case 2. Continued

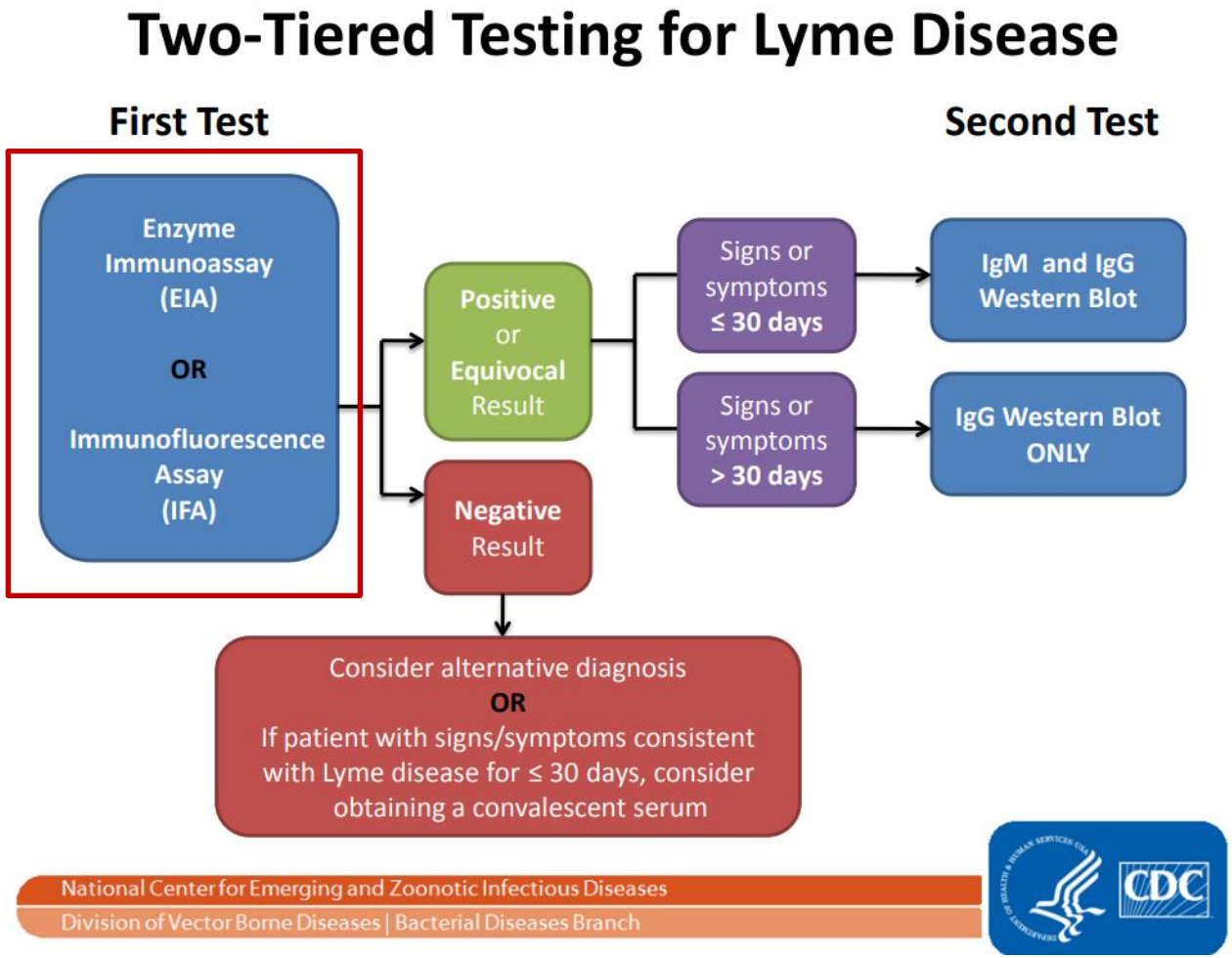
- Patient tested for LD
- Screen: ELISA +
- Immunoblot:
  - IgM + (3 of 3 bands)
  - IgG + (6 of 10 bands)

- Is this LD?
- YES. Clear cut LD

Quiz: What activity is the highest risk for LD in New England?

1. Camping
2. Hiking
3. Golfing
4. Yard work
5. Sleeping in cabins

Current State of LD Testing



Screening Assays

- Classic:
  - Whole Cell Lysate antigen source ELISA
- Evolved:
  - C6 peptide ELISA (26-amino acid recombinant region of VslE)
    - Immunetics/Oxford/Quest
  - VslE Chemiluminescent Immunoassay (CIA)
    - Diasorin (FDA clearance 2007)
  - rVslE1/pepC10 (OspC) ELISA
    - Zeus (FDA clearance 2013)

Screening Assay Performance

"Standard"

"Newer"

TABLE 1 Select studies that evaluated the performance characteristics of the WCS, VlsE, C6, and pepC10 immunoassays alone or in combination with supplemental Western blot testing

	Sensitivity (%)		Specificity (%)	
Assay[a]	Early (stage 1)	Late (stages 2, 3)	Healthy donors[b]	Patients with non-LD infections or conditions
WCS ELISA	74.9	97.7, 98.4	96.4	89.3
WCS ELISA + WB	35.2	77.3, 95.9	99.5	99.2
C6 ELISA	66.5	88.6, 98.4	98.8	99.5
C6 ELISA + WB	34.5	75, 95.1	99.5	99.5
VlsE CIA[c]	69.8	100	99.5	93.7
pepC10 kELISA	47.3	46.1, 10.3	100	98.0
VlsE/pepC10 kELISA	67.2	88.5, 94.1	99.2	96.7

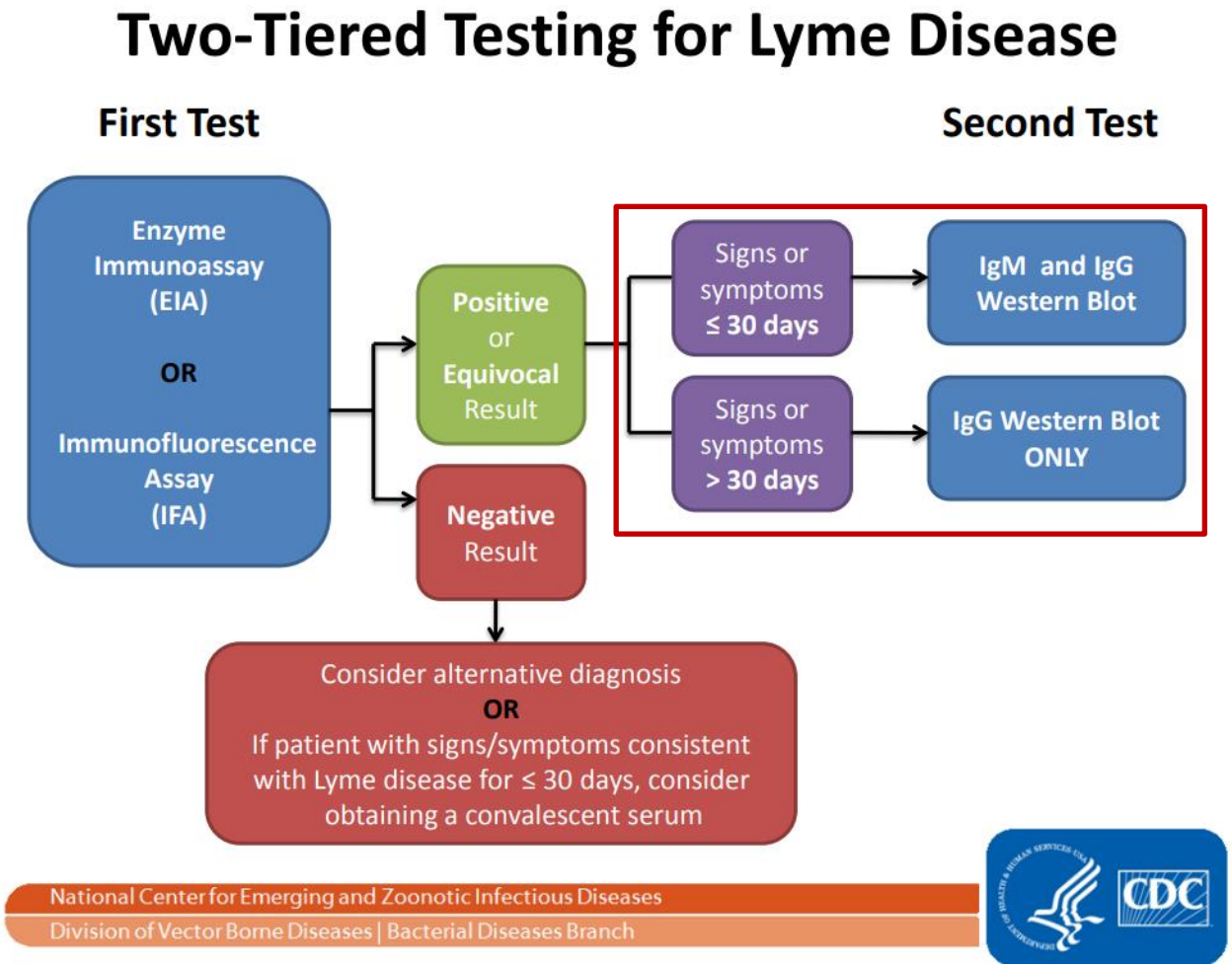
[a] WCS, whole-cell sonicate; VlsE, variable major protein (Vmp)-like sequence, expressed; WB, Western blot; ELISA, enzyme linked immunosorbent assay; CIA, chemiluminescent immunoassay; kELISA, kinetic ELISA.

[b] Data from healthy donors from regions in which Lyme disease is endemic and from those in which it is not endemic were combined.

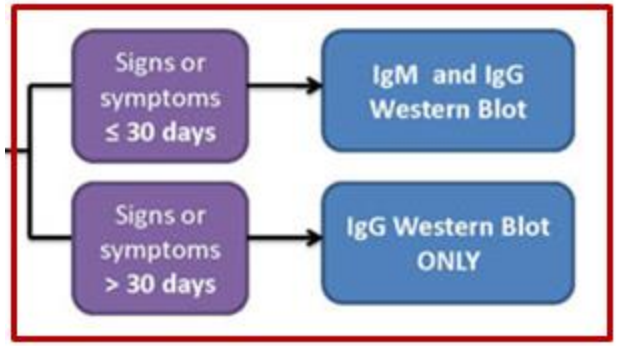
[c] Lyme disease stages 2 and 3 were not separated out in this study.

Theel. J Clin Micro. 2016 54(5), 1191-1196.

Back to the Algorithm



Details on the Blots



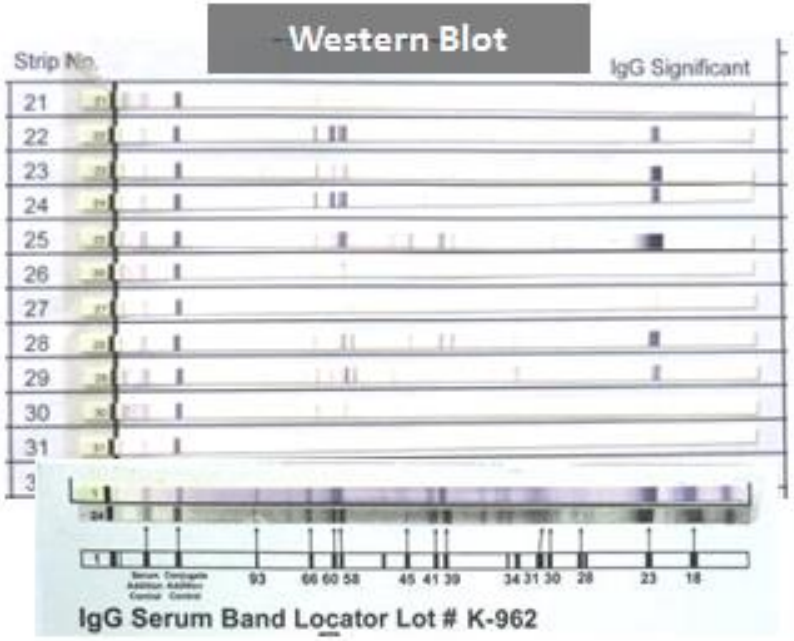
- IgM blot: 2 of 3 conserved bands*
  - Only run on patients with suspected symptom onset <30 days
  - If positive and IgG blot is negative after 30 days = false positive
  - Blot criteria do not apply after 30 days of symptoms

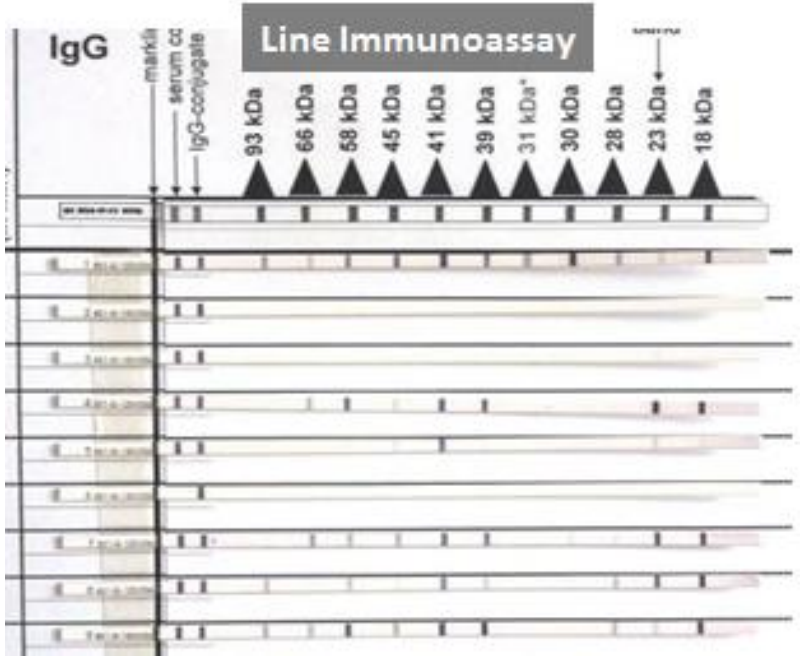
Unchanged since 1995

- IgG blot: 5 of 10 conserved bands*
  - Difficult to interpret in patients from endemic regions with unclear history
    - Think case 1 ☺

CDC. Morb Mortal Weekly Rep. 1995. 44(31);590-591

Blots


Western Blot
Strip No.
IgG Significant
21
22
23
24
25
26
27
28
29
30
31
93
66 60 58
45 41 39
34 31 30
28
23
18
IgG Serum Band Locator Lot # K-962


IgG
Line Immunoassay
93 kDa
66 kDa
58 kDa
45 kDa
41 kDa
39 kDa
31 kDa*
30 kDa
28 kDa
23 kDa
18 kDa

Automated Immunoblotting & Densitometry

Test: Borrelia B31 ViraStripe®IgG Strip: LGG0627178715-16

Bands:

93	66	58	45	41	39	30	28	23	18
104	-	118	-	086	-	122	090	081	136

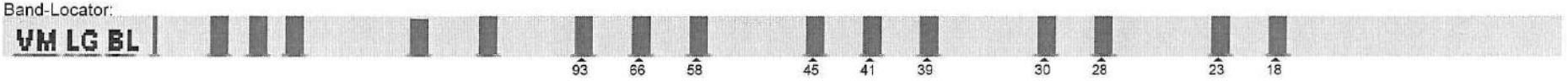
kDa

Intensity to Cut-off

Patient Strip: 16

Cut-Off Strip:

Band-Locator:



Do we really need blots?

Alternative Two-Tier algorithm

TABLE 2 Comparison of the traditional TTTA to a 2-EIA TTTA and the C6 ELISA alone in sera from patients with well-characterized Lyme disease[a]

	Sensitivity (%)			Specificity (%)	
Testing algorithm	Stage 1 (n = 114)	Stage 2 (n = 26)	Stage 3 (n = 29)	Healthy donors[b] (n = 1,246)	Patients with a non-LD infection or condition (n = 54)
Traditional[c]	42.1	73.1	100	99.4	100
C6 ELISA alone	56.1	100	100	98.4	98.1
2-ELISA[d]	52.6	100	100	99.4	100

[a] Adapted from reference 17.
[b] Data from healthy donors from regions in which Lyme disease is endemic and from those in which it is not endemic were combined.
[c] Traditional TTTA, WCS ELISA followed by Western blot analysis.
[d] 2-ELISA, WCS ELISA followed by C6-ELISA.

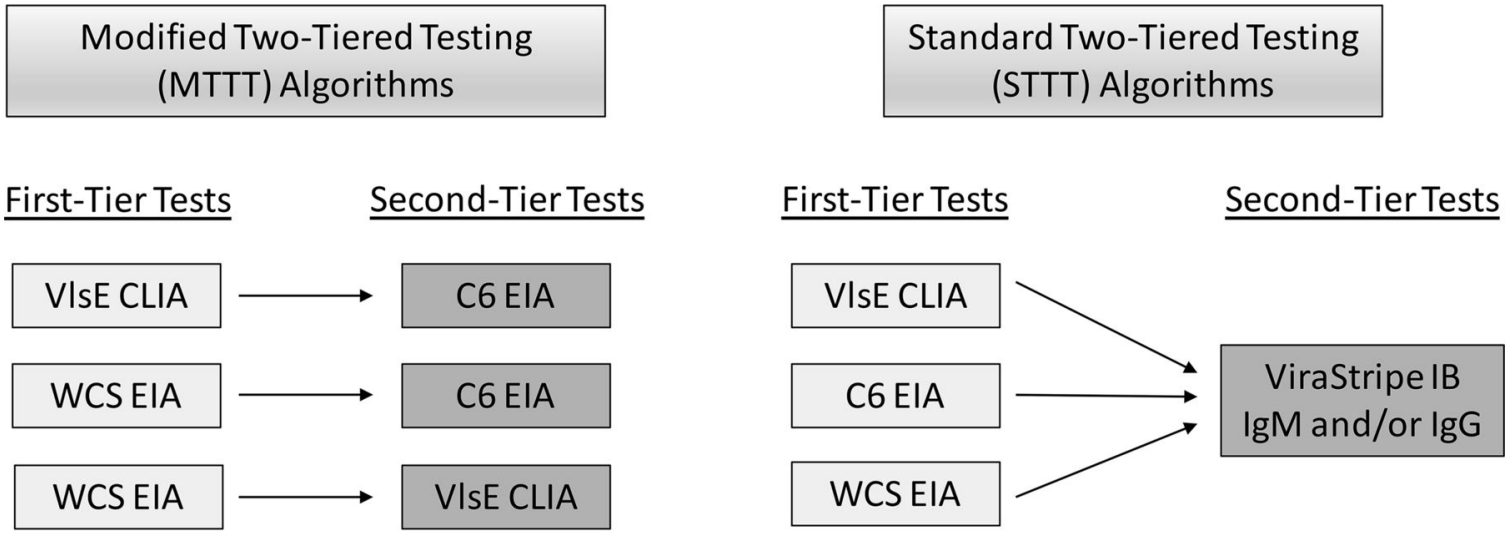
ELISA→ELISA

↓$ (27-44%)

↑ Accuracy (27%)

Reference 17 in figure: Branda et al. 2011. Clin Infect Dis 53:541–547.

Alternative Two-Tier algorithm



- CDC's Lyme Serum Repository specimens used
  - Carefully curated – clinically well defined positives
  - Common interfering conditions for "negatives" and non-endemic volunteer negatives

Pegalajar-Jurado et al. J Clin Microbiol 2018: 56(8).

Commentary Highlight

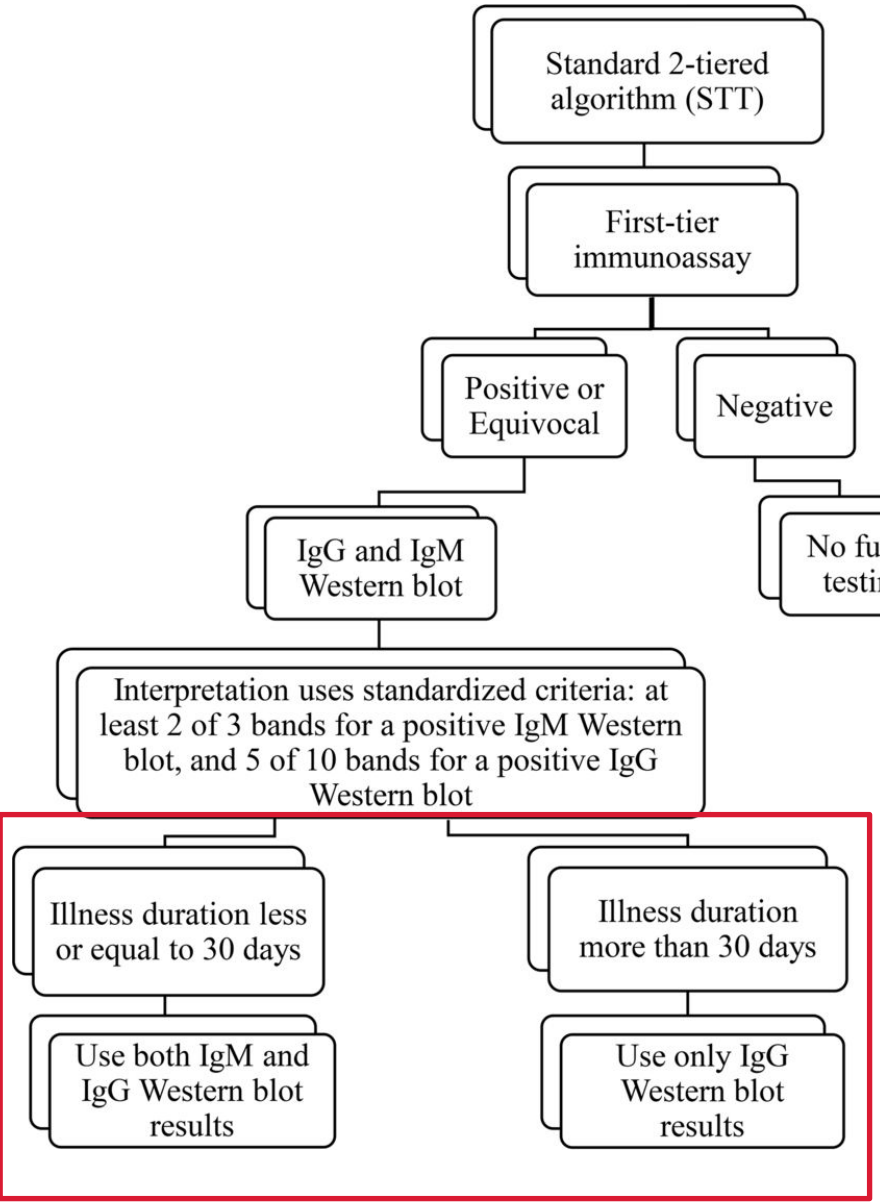
AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

Commentary

Revisiting the Lyme Disease Serodiagnostic Algorithm: the Momentum Gathers

Adriana R. Marques
Karen C. Carroll, Editor

Pegalajar-Jurado et al. J Clin Microbiol 2018: 56(8).


Standard 2-tiered algorithm (STT)
First-tier immunoassay
Positive or Equivocal
Negative
IgG and IgM Western blot
No further testing*
Interpretation uses standardized criteria: at least 2 of 3 bands for a positive IgM Western blot, and 5 of 10 bands for a positive IgG Western blot
Illness duration less or equal to 30 days
Illness duration more than 30 days
Use both IgM and IgG Western blot results
Use only IgG Western blot results

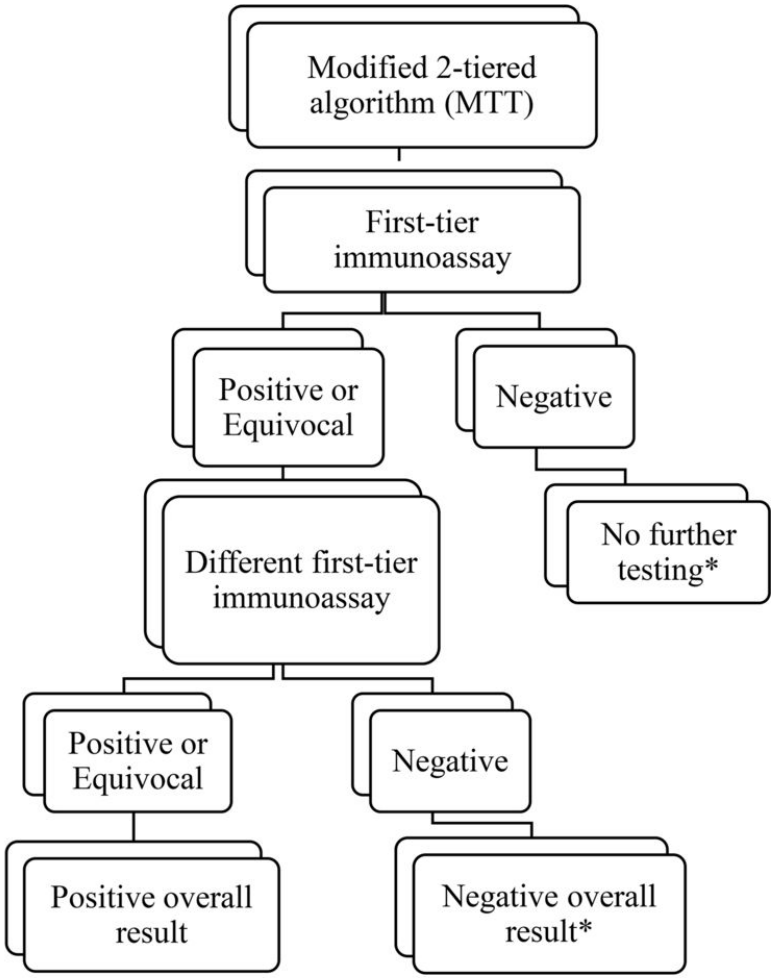

Modified 2-tiered algorithm (MTT)
First-tier immunoassay
Positive or Equivocal
Negative
No further testing*
Different first-tier immunoassay
Positive or Equivocal
Negative
Positive overall result
Negative overall result*

TABLE 1

Sensitivity of MTT algorithm versus that of the STT algorithm in acute-phase samples from patients with erythema migrans

Reference(s) (no.)	MTT algorithm[a]		STT algorithm[b]	
	Test program[c]	Acute-phase EM sensitivity (%)	Test program	Acute-phase EM sensitivity (%)
Branda et al. (16)	WCS Vidas f/b C6 EIA	52.6	WCS Vidas f/b WB	42.1
Branda et al. (27)	WCS W EIA f/b C6 EIA	38.2	C6 EIA f/b WB	36.4
	WCS W EIA f/b VlsE CLIA	36.4	VlsE CLIA f/b WB	34.5
	VlsE CLIA f/b C6 EIA	54.5	WCS W f/b WB	25.4
Molins et al. (28)[d]	WCS Vidas f/b C6 EIA	50	WCS Vidas f/b WB	47.5
Molins et al. (29)[d]	WCS Vidas f/b C6 EIA	50	LYM/G Vidas f/b WB	42.5
	LYM/LYG f/b C6 EIA	55	WCS Vidas f/b WB	47.5
Pegalajar-Jurado et al. (4)[d]	WCS Captia f/b C6 EIA	55	WCS Captia f/b WB	50
	WCS Captia f/b VlsE CLIA	57.5	VlsE CLIA f/b WB	42.5
	VlsE CLIA f/b C6 EIA	50	C6 EIA f/b WB[e]	42.5
Wormser et al. (11, 25)	WCS EIA f/b C6 EIA[f]	58.4	C6 EIA f/b WB	37.6
			WCS f/b WB	38.3

Examples of Future Areas of Investigation

- Novel/expanded antigen investigations for multiplex antibody detection
  - Bead-based detection
- Immuno-PCR (iPCR)
  - Optimize high specificity of C6 peptide with amplification of PCR
  - Reporter antibody contains DNA tag which is amplified after binding C6 specific antibodies
- Metabolomic profiling

https://www.cdc.gov/lyme/diagnosistesting/labtest/otherlab/index.html

Metabolomic profiling

- CDC study to detect early LD with better sensitivity
- Characterize low-molecular-weight (<15kDa) molecules in patients with early LD vs absence or baseline in healthy controls
- Liquid chromatography mass spectrometry
- 44 markers for early LD mainly lipids and lipophilic molecules
- More sensitive (88%) than traditional two-tier algorithm (43%) and 2-ELISA methods (48%)
- Not ready for clinical labs & will require FDA clearance

Molins et al. 2015. Clin Infect Dis **60:**1767–1775.

Examples of Unapproved Testing for Diagnosis

- Urine antigen detection
- Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- “Reverse Western blots”
- In-house criteria for interpretation of immunoblots
- IgM or IgG tests without a previous screening test

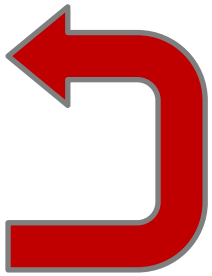
https://www.cdc.gov/lyme/diagnosistesting/labtest/otherlab/index.html

LD in Summary

- LD is a complicated infection to diagnose
  - Symptoms and exposure history can be difficult to accurately ascertain
- Emotionally and politically charged
- Technological advancements have been slow to materialize
  - New avenues of testing show promise but require more clinical validation

Case of the Chills

- 56 yo male returned from fishing vacation in southeastern California mountains 7 days prior to symptom onset
  - Stayed in upscale resort rental cabins
  - Did not recall any insect bites, no documented ticks seen
  - Spring 2012
- Fevers >104°F, 3x over ~2 d
  - Drenching sweats followed by intense chills
  - Symptoms resolved for a week then returned
- No other recent travel history



Tick Born Relapsing Fever (TBRF) and beyond

Tick Borne Relapsing Fever (TBRF)

- Causative organism in the USA…
  - *Borrelia hermsii*
  - *Borrelia parkeri*
  - *Borrelia turicatae*

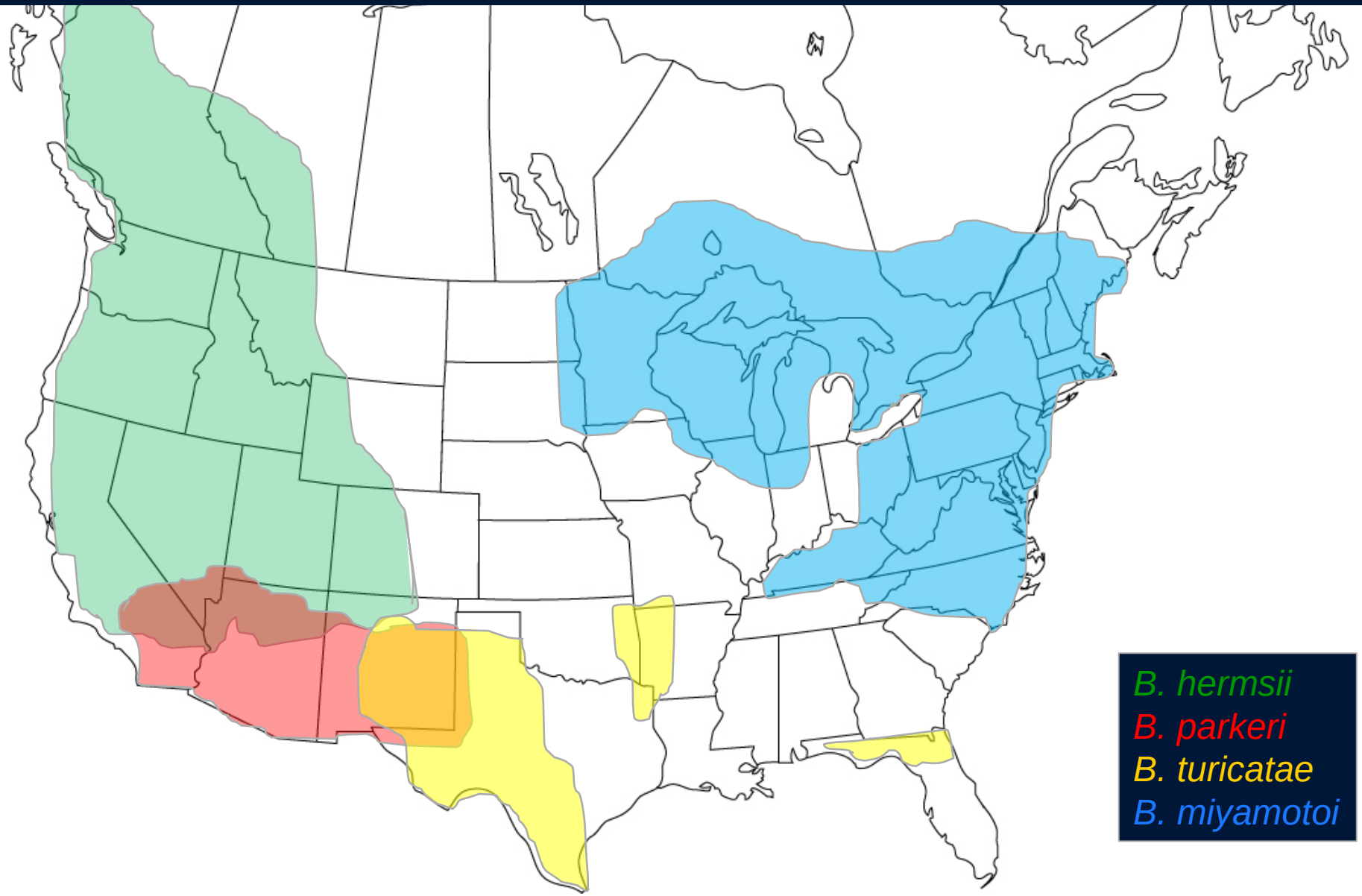
  Vector →

  - *Ornithodorus hermsi*
  - *Ornithodorus parkeri*
  - *Ornithodorus turicata*

  - ******Borrelia miyamotoi* Vector →
    - *Ixodes scapularis*

******TBRF genetic group, but clinically not TBRF

Approximate Geographic Distribution



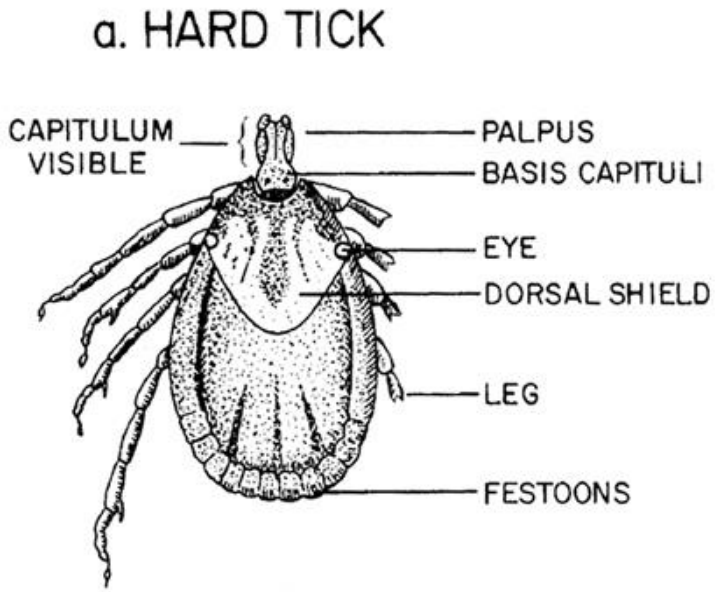
Case Distribution

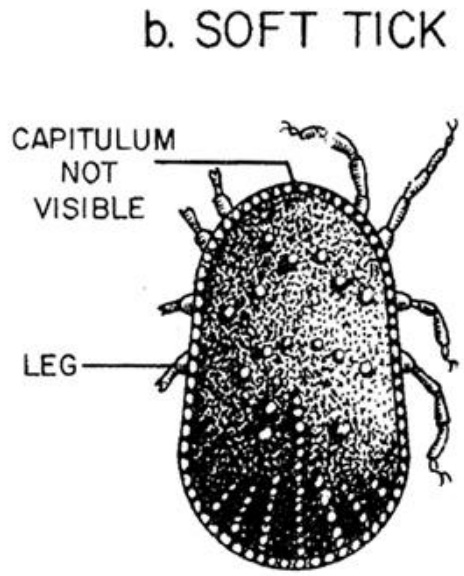
Each dot, placed randomly within the county of exposure (where known), represents one case.

Each dot, placed randomly within the county of residence, represents one case.

https://www.cdc.gov/relapsing-fever/distribution/index.html

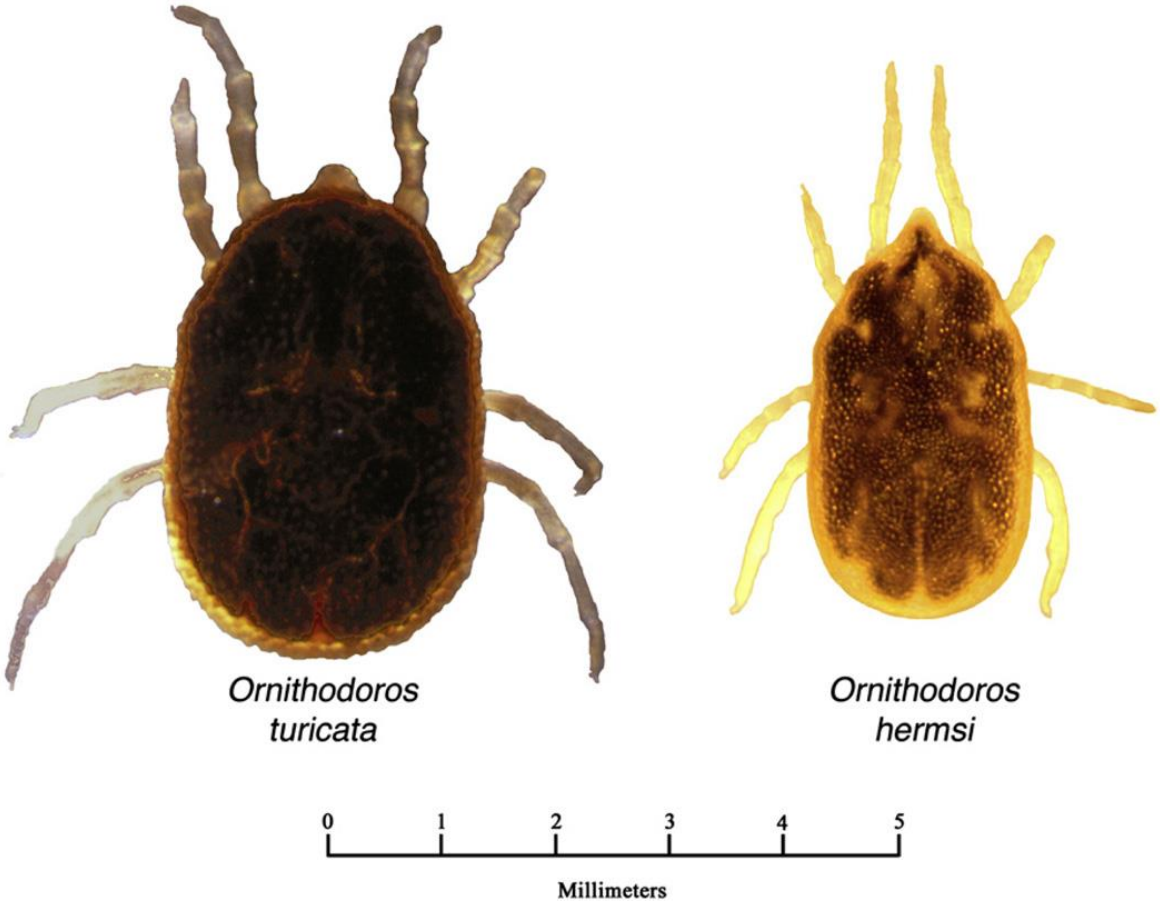
Hard Shell Tick (Ixodid) vs Soft Shell (Agasid)





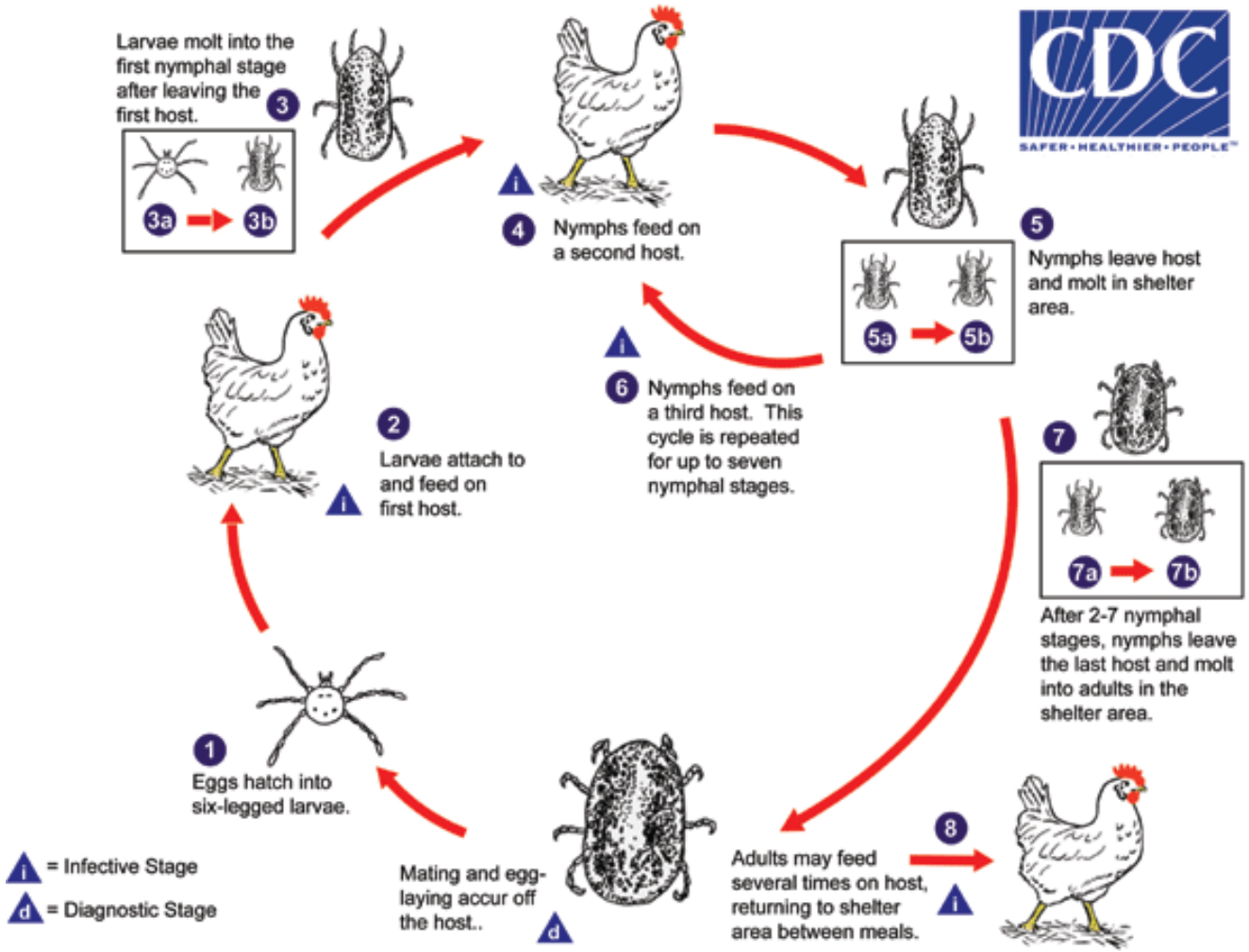
https://www.cdc.gov/dpdx/ticks/index.html

Ornithodorus spp.



Dworkin et al. Infect Dis Clin North Am. 2008 Sep; 22(3): 449–viii

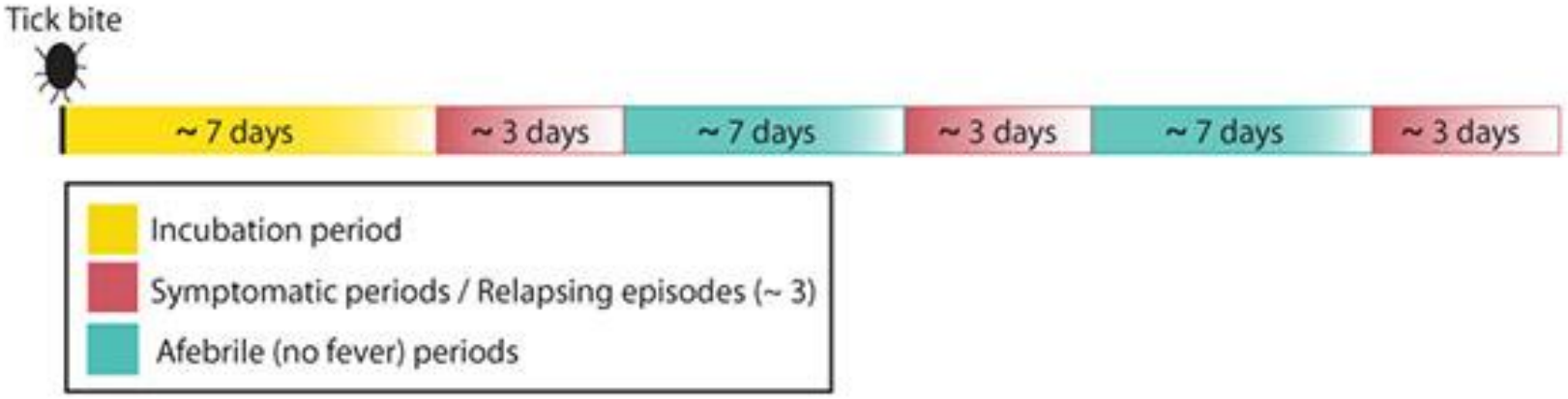
Argasidae life cycle



https://www.cdc.gov/dpdx/ticks/index.html

TBRF

- Recurring febrile episodes ~3 days, separated by afebrile period ~7 days



  - >75%: headache, myalgia, chills, nausea
  - >50%: arthralgia, vomiting
  - >25%: abdominal pain, dry cough, eye pain, diarrhea, photophobia, neck pain

https://www.cdc.gov/relapsing-fever/clinicians/index.html

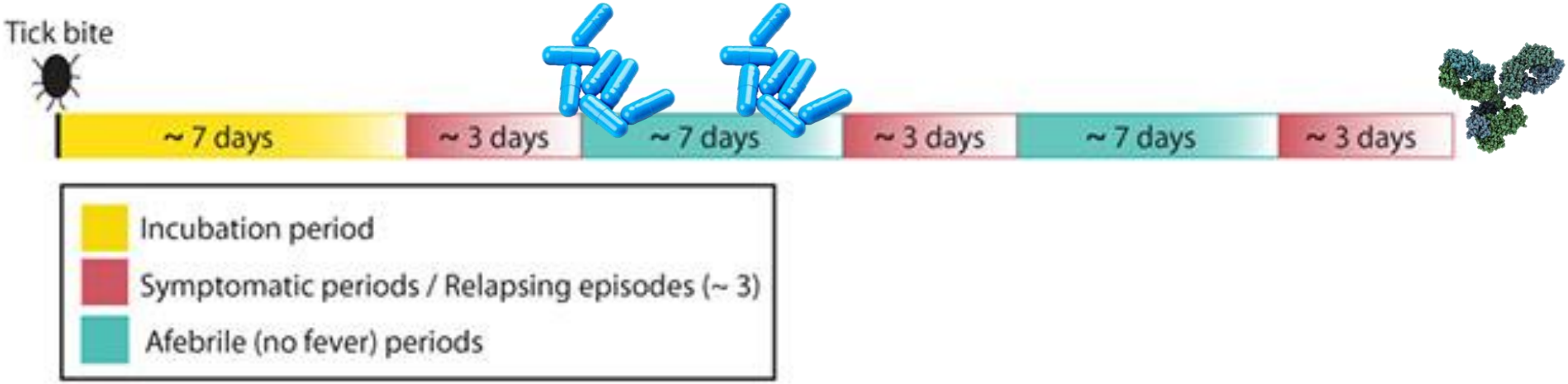
The Illness

- Fever up to 106.7°F “chill phase” (10-30 mins)
  - May become delirious, agitated, tachycardic and tachypneic
- Followed by the “flush phase”
  - Drenching sweats and a rapid decrease in body temperature.
  - Transiently hypotensive.
- Patients who are not treated will experience several episodes of fever before illness resolves.

https://www.cdc.gov/relapsing-fever/clinicians/index.html

Recovery

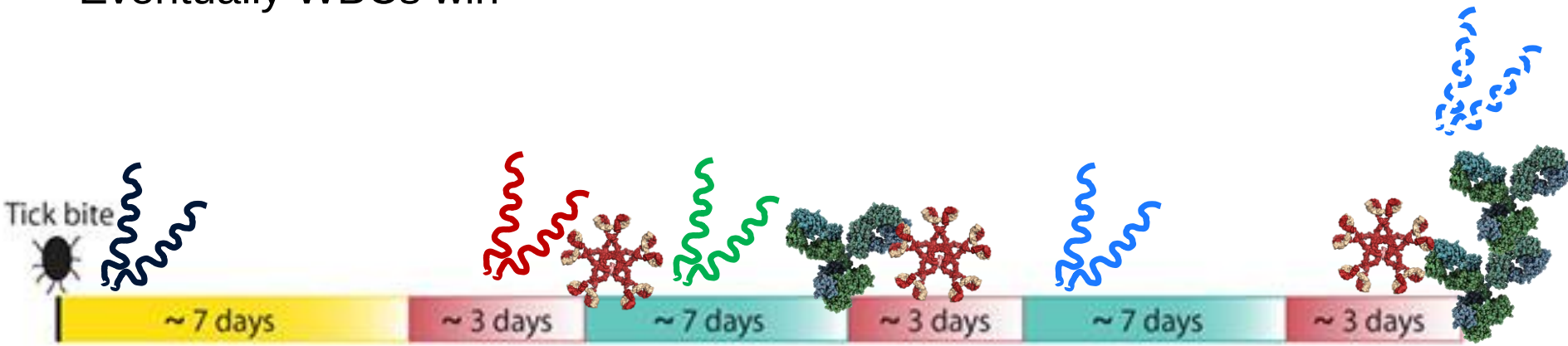
- Treatment:
  - Doxycycline – 2x daily, 7 days
- Immune control



https://www.cdc.gov/relapsing-fever/clinicians/index.html

Antigenic shift

- Genomic organization unique
- Allows shift of antigen on cell surface
  - “Hide and seek”
- Eventually WBCs win



https://www.cdc.gov/relapsing-fever/clinicians/index.html

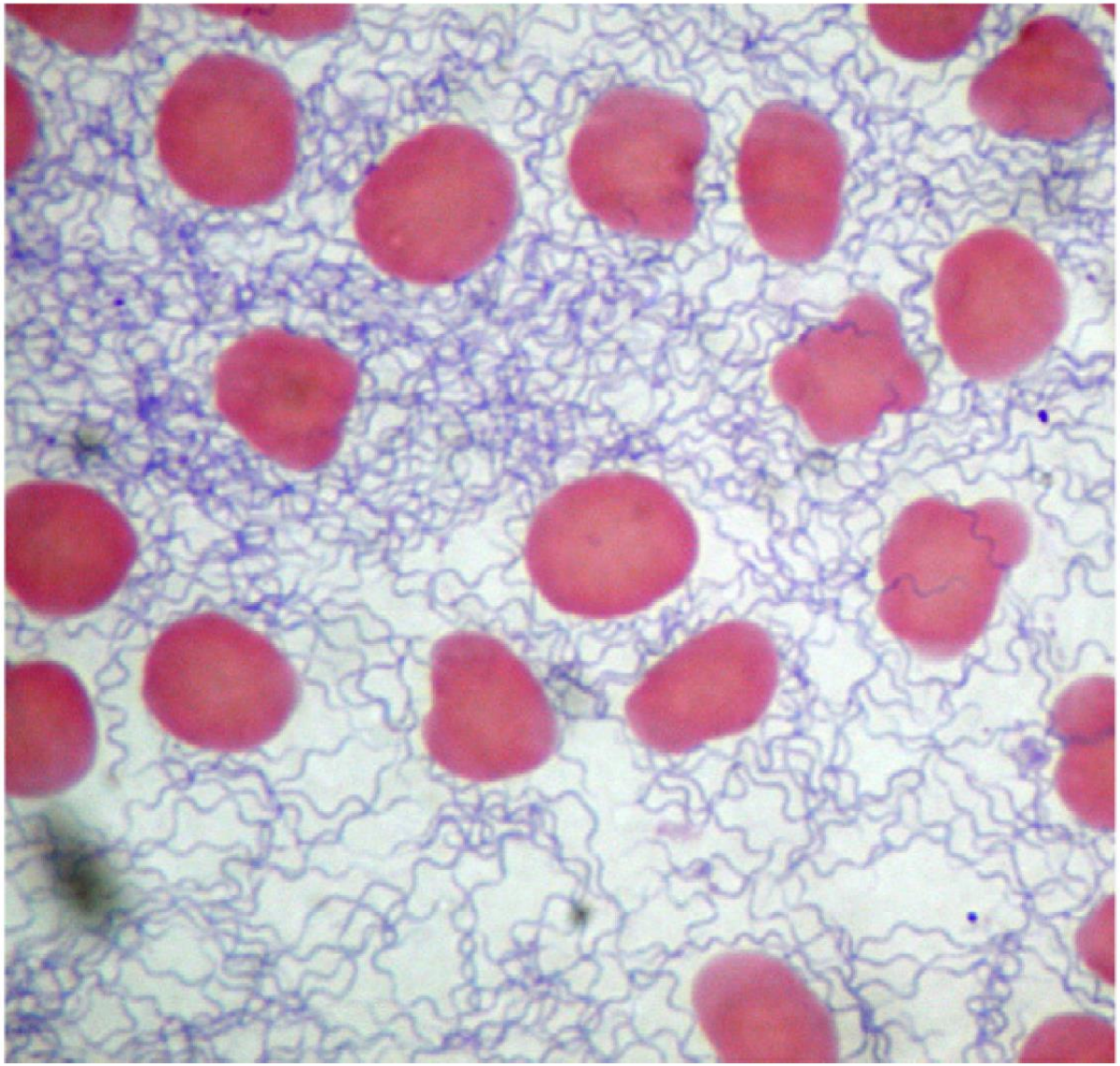
Testing

- Peripheral blood smear
- IgG serology
- Real-time PCR

Blood smear

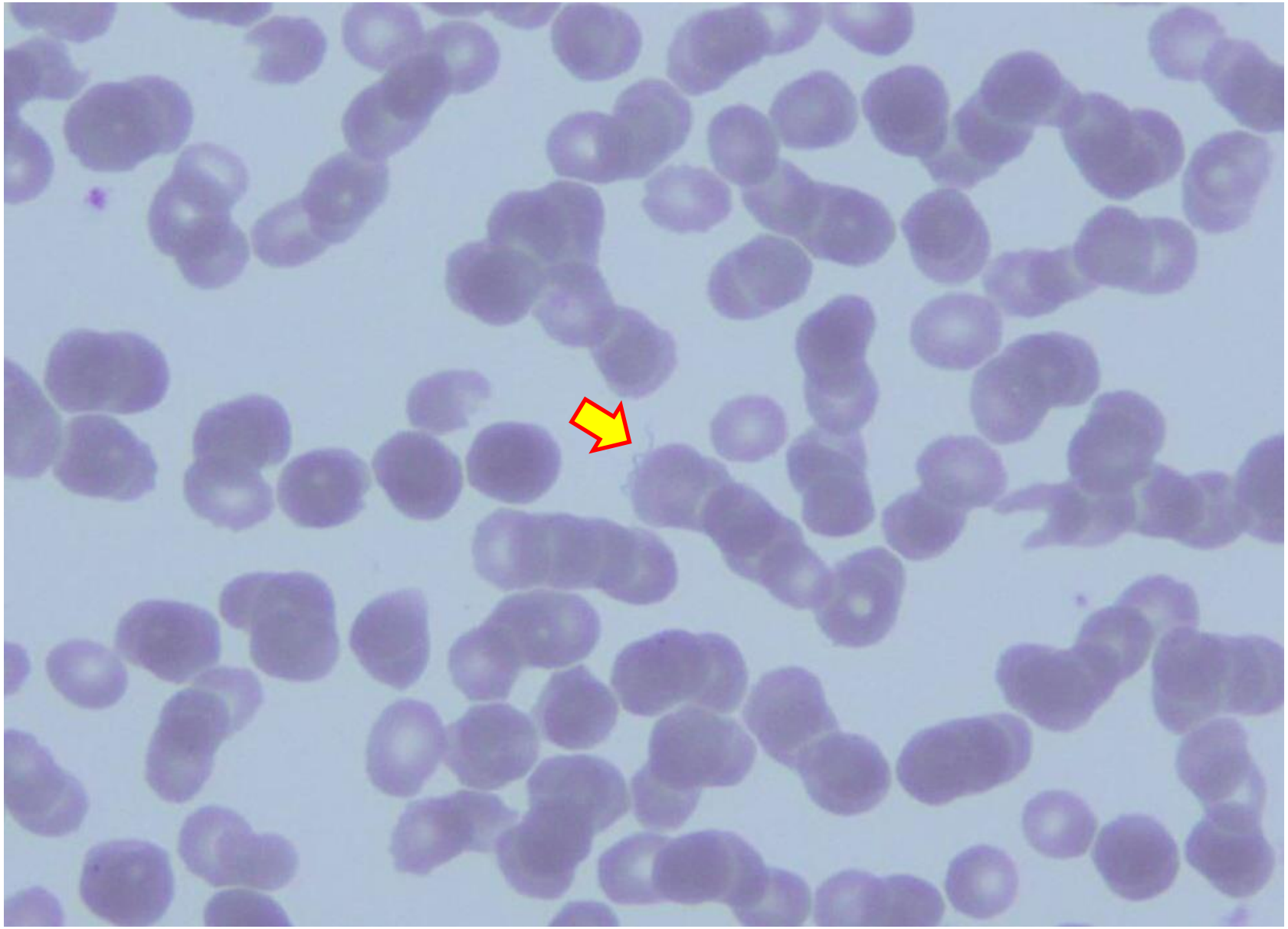
- Peripheral blood smear, performed like blood parasite screen or CBC
  - Giemsa, Wright, or Wright-Giemsa
- Good for initial diagnosis, low sensitivity
- Turn-around-time = hours
- Requires skilled readers, patience, and experience

Blood Smear in the Literature

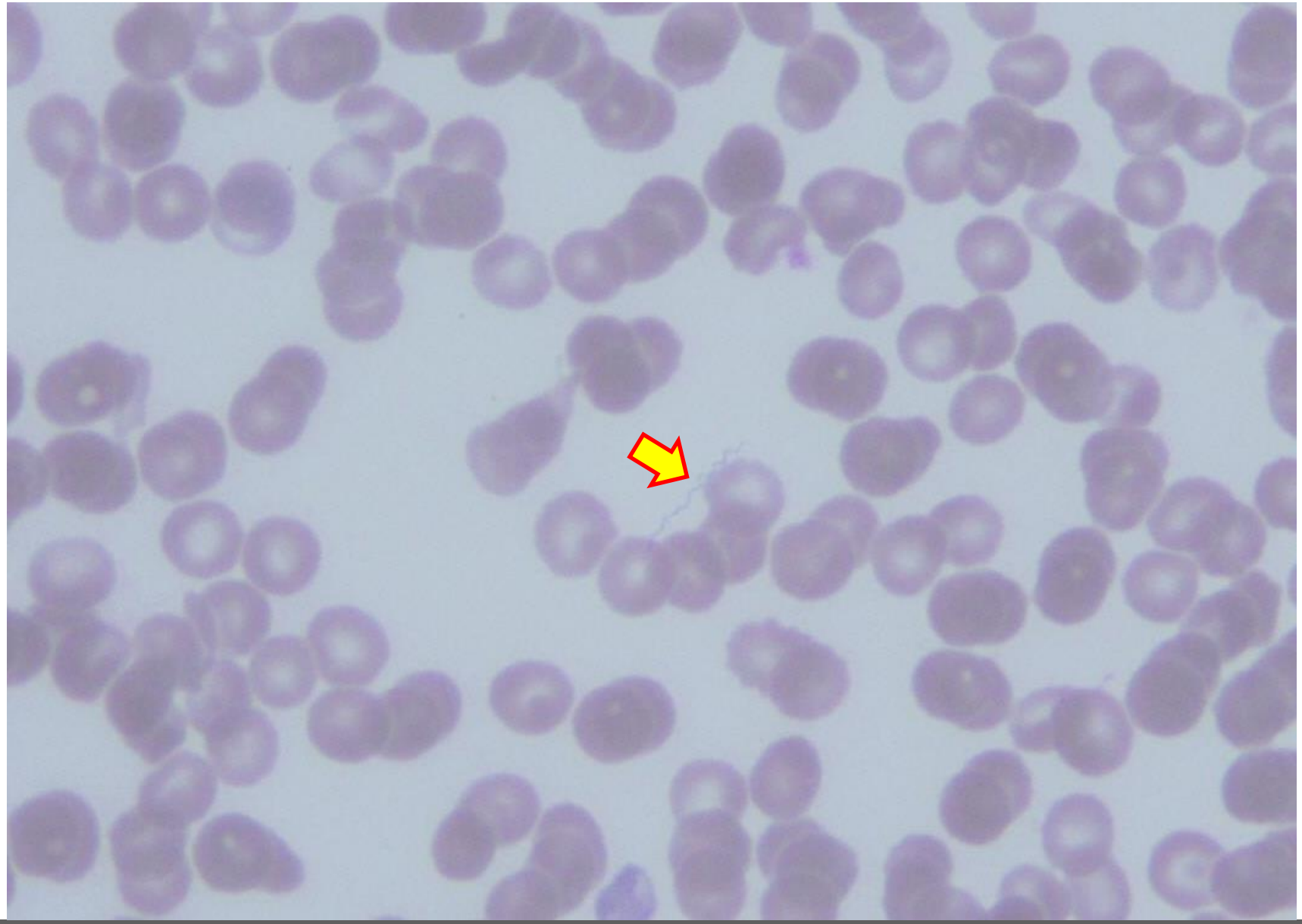


Badger MS. Wilderness Env Med J 2008. 19(4): 280-286.

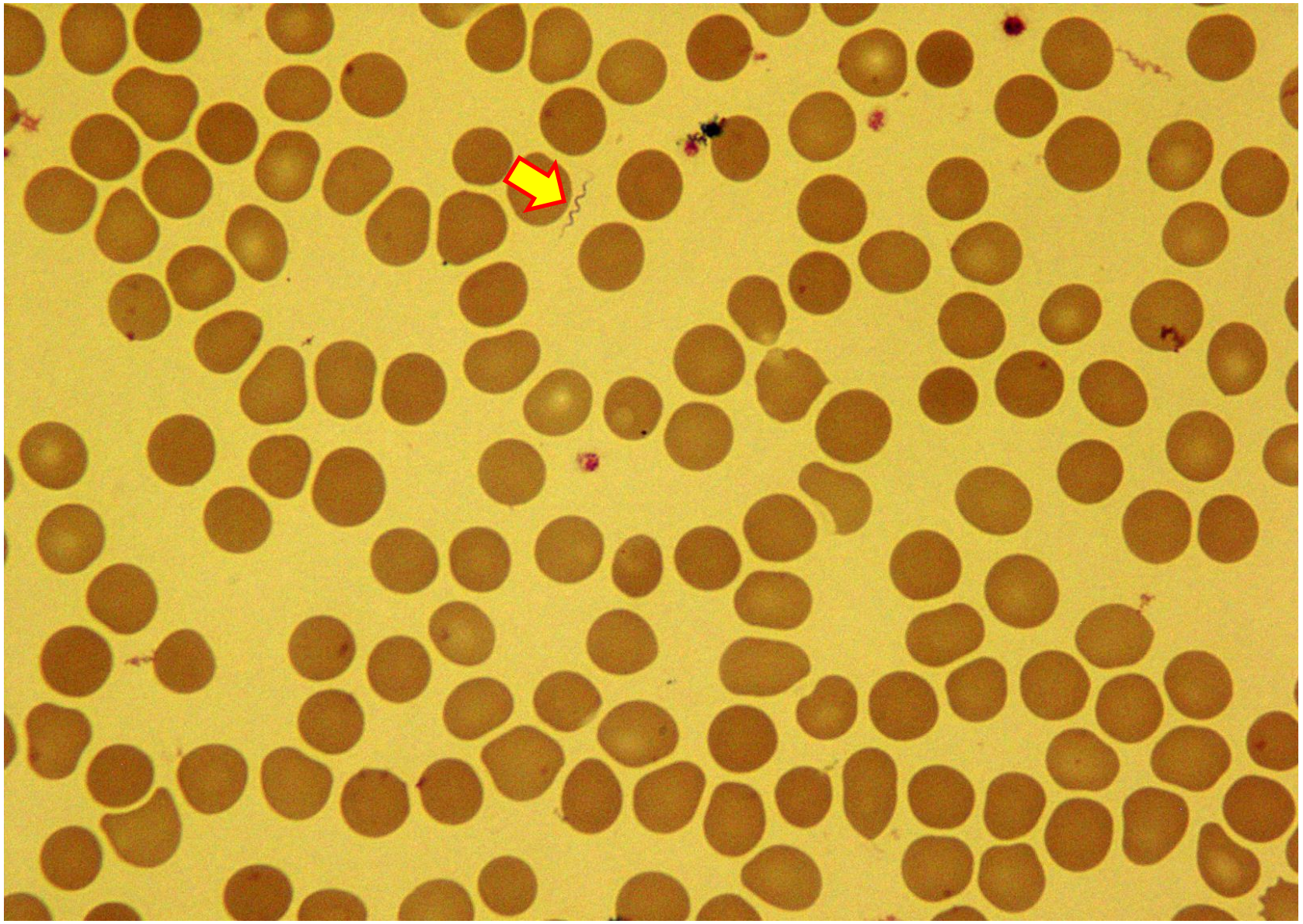
In Reality



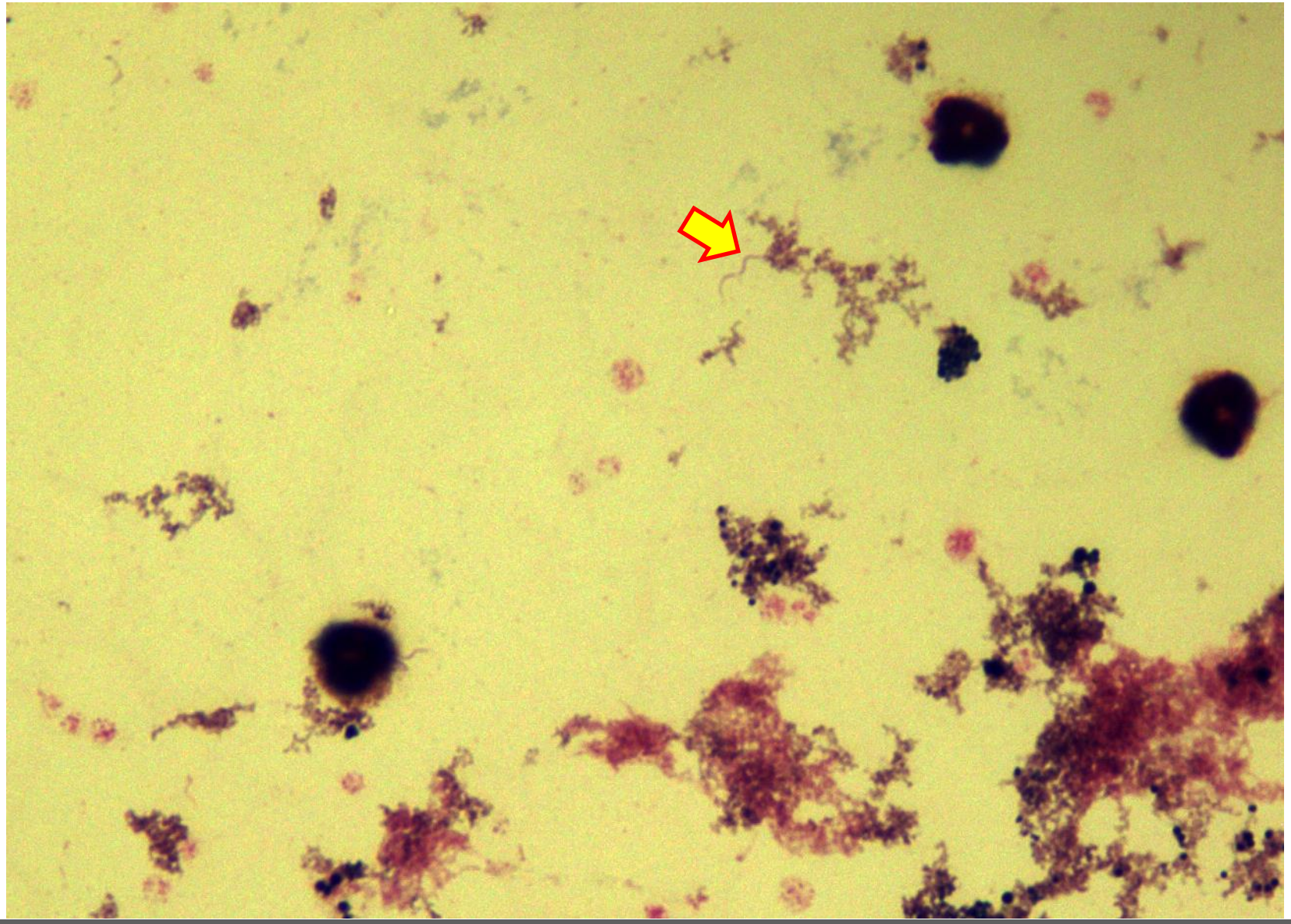
In Reality



In Reality (with Photoshop assistance)



In Reality (with Photoshop assistance)



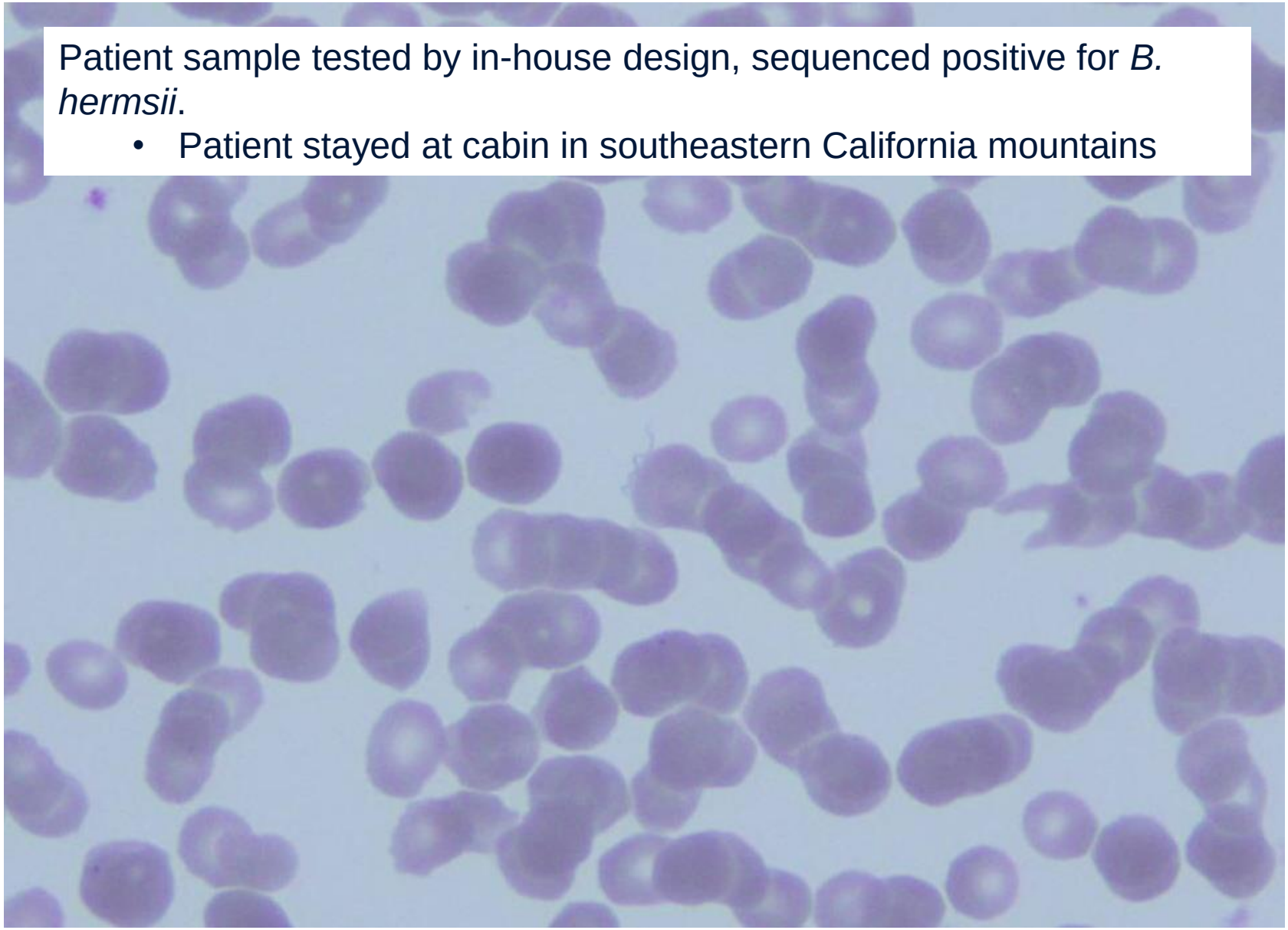
Serology

- Retrospective diagnosis or support of recent diagnosis
- Four-fold rise in IgG titer
- Cross-reactivity with Lyme
  - Lyme false-positives
- Not widely available
  - Imugen (Oxford)
  - Quest Diagnostics

PCR

- High sensitivity
- High specificity (if well designed)
- No FDA cleared assays
- Challenges
  - Detect all relevant species to N. America vs Eurasia/Africa or both
  - Do NOT detect Lyme *Borrelia* species
  - Find samples or organism to validate with

Remember this patient?



Patient sample tested by in-house design, sequenced positive for *B. hermsii*.

- Patient stayed at cabin in southeastern California mountains

PCR Development at ARUP

- Designed to detect *B. hermsii, B. parkeri, B. turicatae,* and *B. miyamotoi* (identical sequence) from blood
  - Can also detect: *B. crocidurae, B. duttoni, B. hispanica, B. recurrentis,* and *B. microti*
    - TBRF *Borrelia* spp. from Europe, Asia, Africa
    - Differ by one base pair, slightly less sensitive – can differentiate this group by melt curve analysis
    - Will not detect *B. persica* (Middle Eastern endemic)
- No cross-reactivity with Lyme *Borrelia* spp or 68 other pathogens
  - Including *Anaplasma*, *Babesia*, and multiple *Plasmodium* species

PCR Testing in Prime Time

- Available commercially at major reference labs:
  - ARUP Laboratories
  - Mayo Medical Laboratories
  - Quest Diagnostics

TBRF In Summary

- TBRF causes a textbook illness reminiscent of malaria or *Babesia* but with distinct patterning of fevers
- Caused by many species of *Borrelia*
  - Vectored by several different ticks in different regions
- Detected by multiple mechanisms, commercially available
- Likely underreported due to insensitivity of blood smear
  - PCR is significantly more sensitive

A Fatal Headache

- 5 yo boy admitted w/ right-sided headache, drowsy, fever 101ºF
  - Abnormal brain EEG, normal CSF count
- 2 days later fever 103ºF, lymphocytic predominance in CSF
  - Became unconscious and unresponsive to stimuli
- 4 days after admission, completely comatose and encephalitic
  - Patient ceased breathing in the afternoon
- 6 days later passed away

…the year was 1958…

…the town was Powassan, Ontario

…no tick bite was ever reported

McLean DM, Donahue W. Can Med Assoc J 1959; 80: 708–711.

Deer Tick Virus
or Powassan virus, lineage II

Deer Tick Virus (DTV)

- DTV is one genotype of Powassan virus
  - Powassan virus lineage I = POWV = *Ixodes cookei*
  - Powassan virus lineage II = DTV = *Ixodes scapularis*
- Flavivirus closely related to tick-borne encephalitis group of viruses in Europe & Asia
- Discovered in 1958 in brain tissue
  - Fatal pediatric encephalitis in Powassan, Ontario

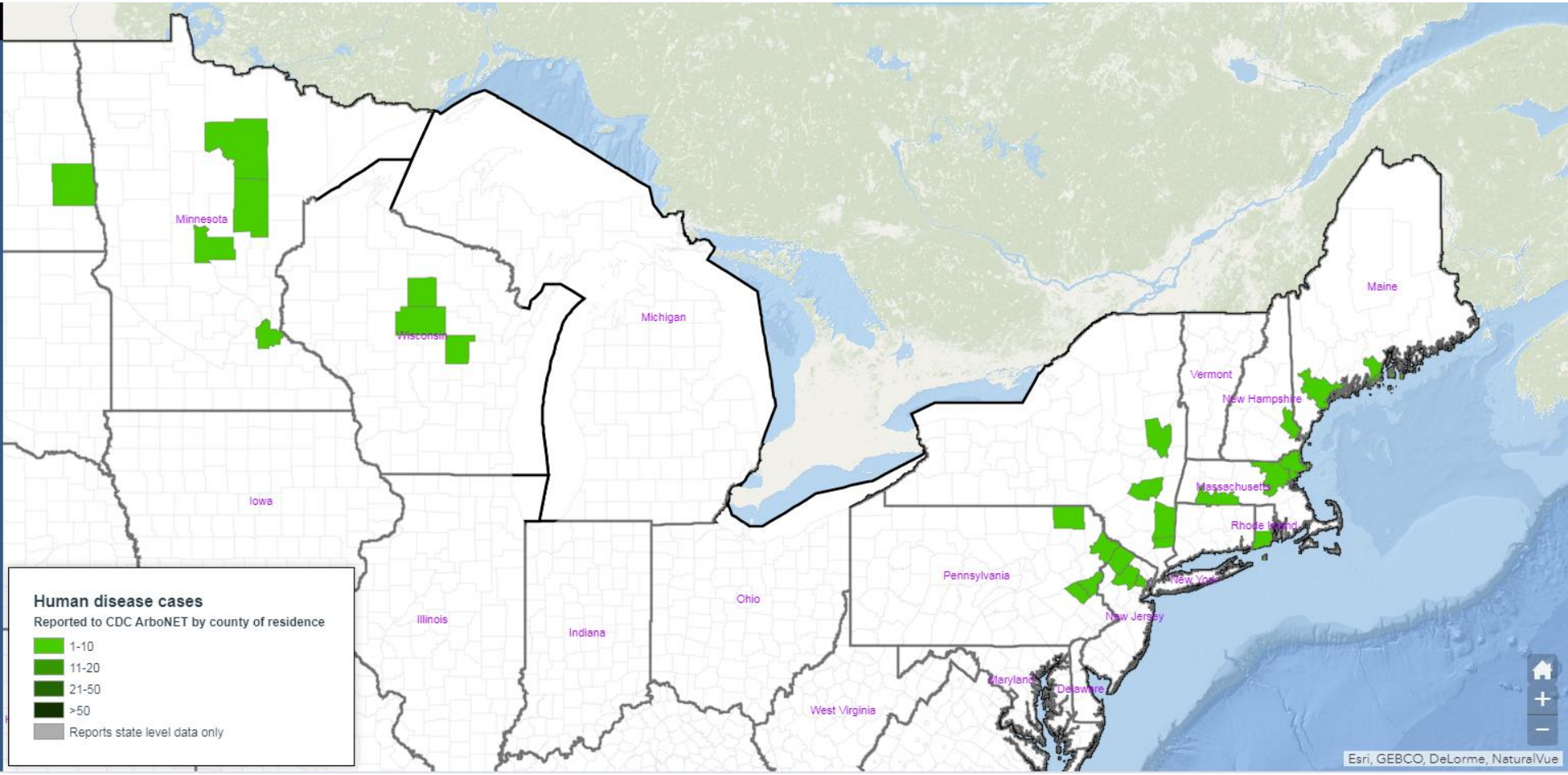
McLean DM, Donahue W. Can Med Assoc J 1959; 80: 708–711.

Case Distribution

- Likely underreported, but possibly increasing
  - 1958 – 1998 = 27 cases reported
  - 2003 – 2016 = 85 cases reported
- Cases found everywhere *Ixodes* exist
  - Colorado as rare exception
  - Incidentally found in *Dermacentor andersoni*

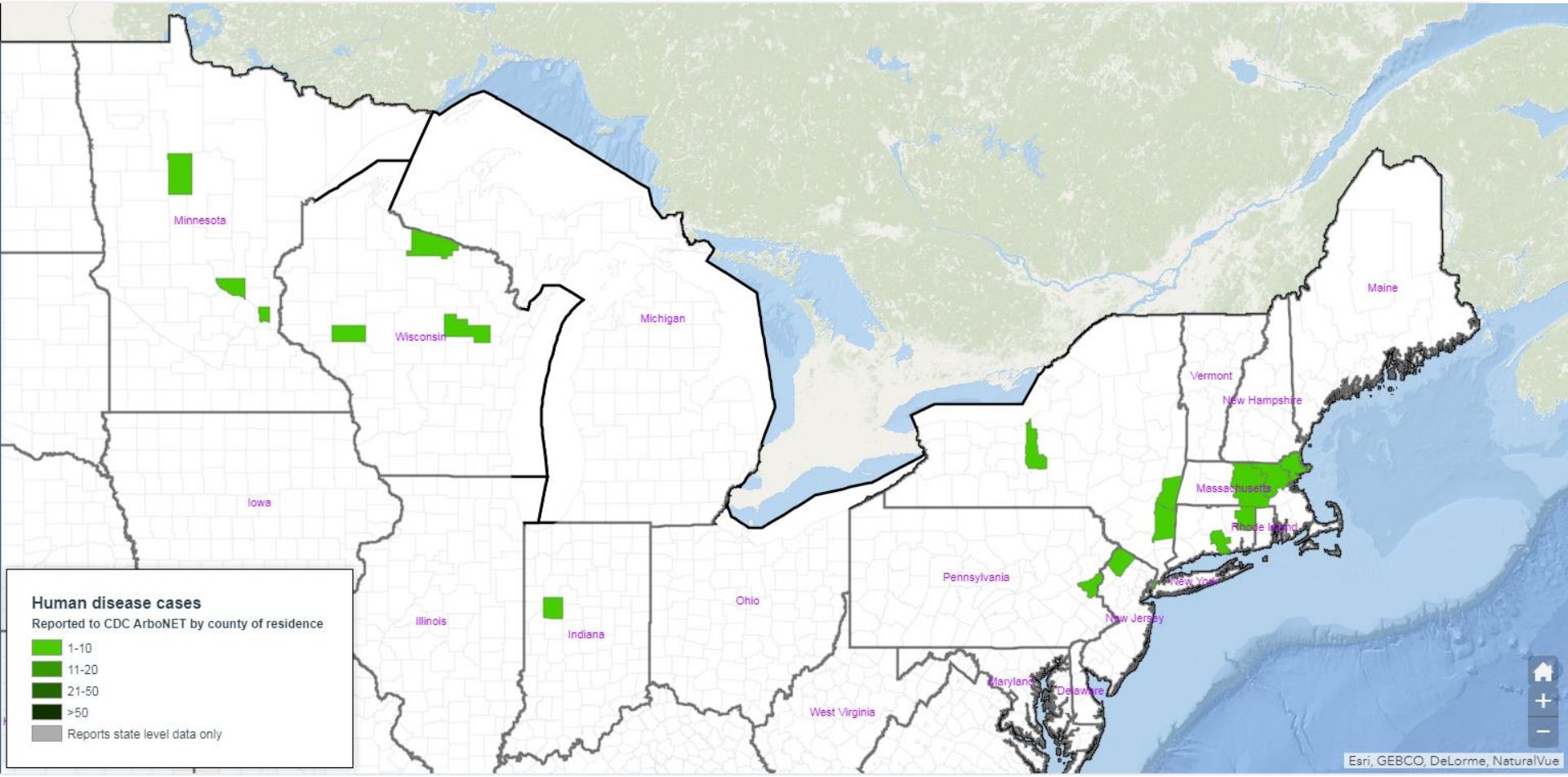
Hermance and Thangamani. 2017 Vector Borne and Zoonotic Diseases. 17(7), 453-462.

Case Distribution – ArboNET 2017



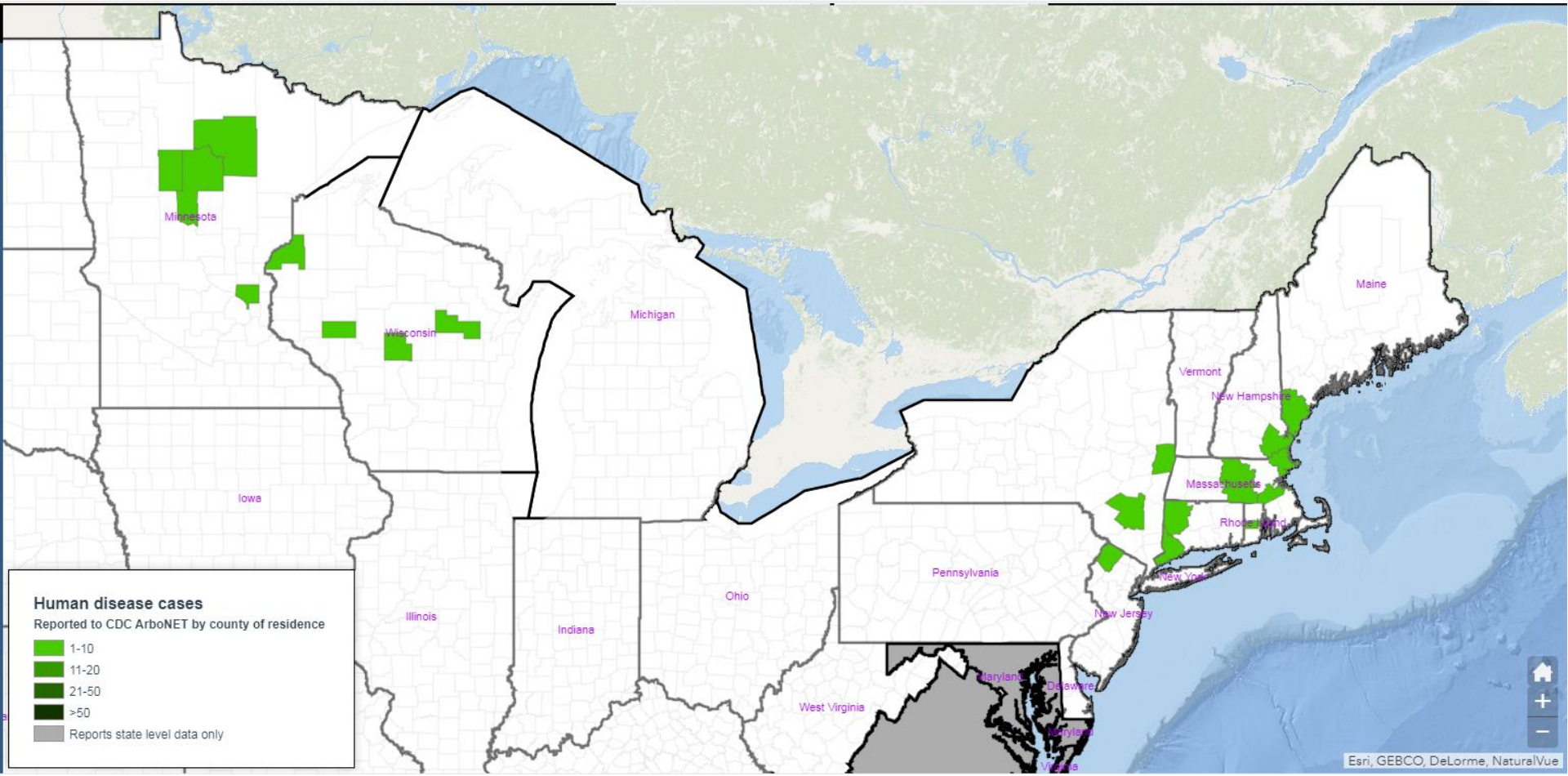
https://diseasemaps.usgs.gov/mapviewer/

Case Distribution – ArboNET 2018



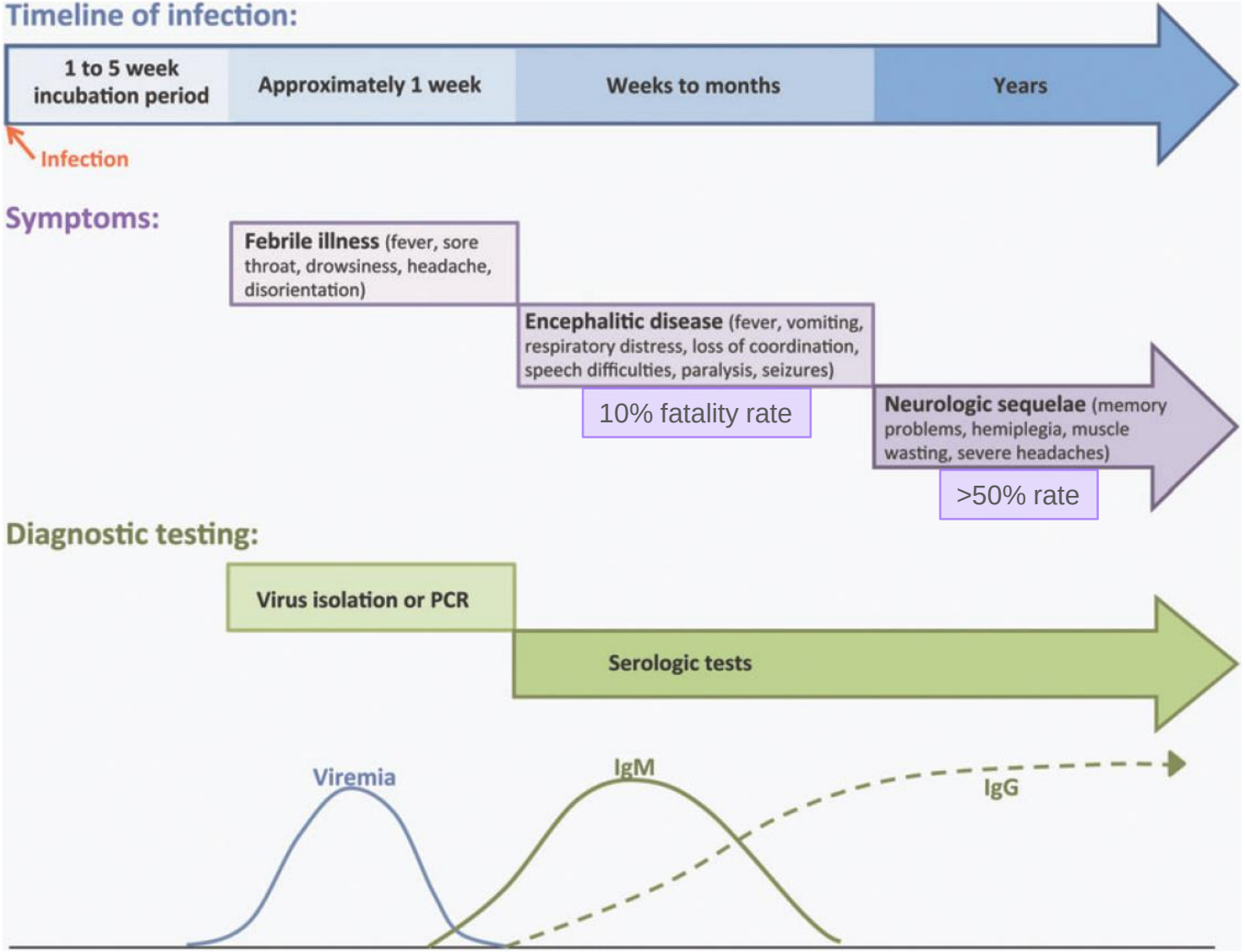
https://diseasemaps.usgs.gov/mapviewer/

Case Distribution – ArboNET 2019



https://diseasemaps.usgs.gov/mapviewer/

Symptoms



Hermance and Thangamani. 2017 Vector Borne and Zoonotic Diseases. 17(7), 453-462.

Clinical Diagnosis

Symptomatic/retrospective

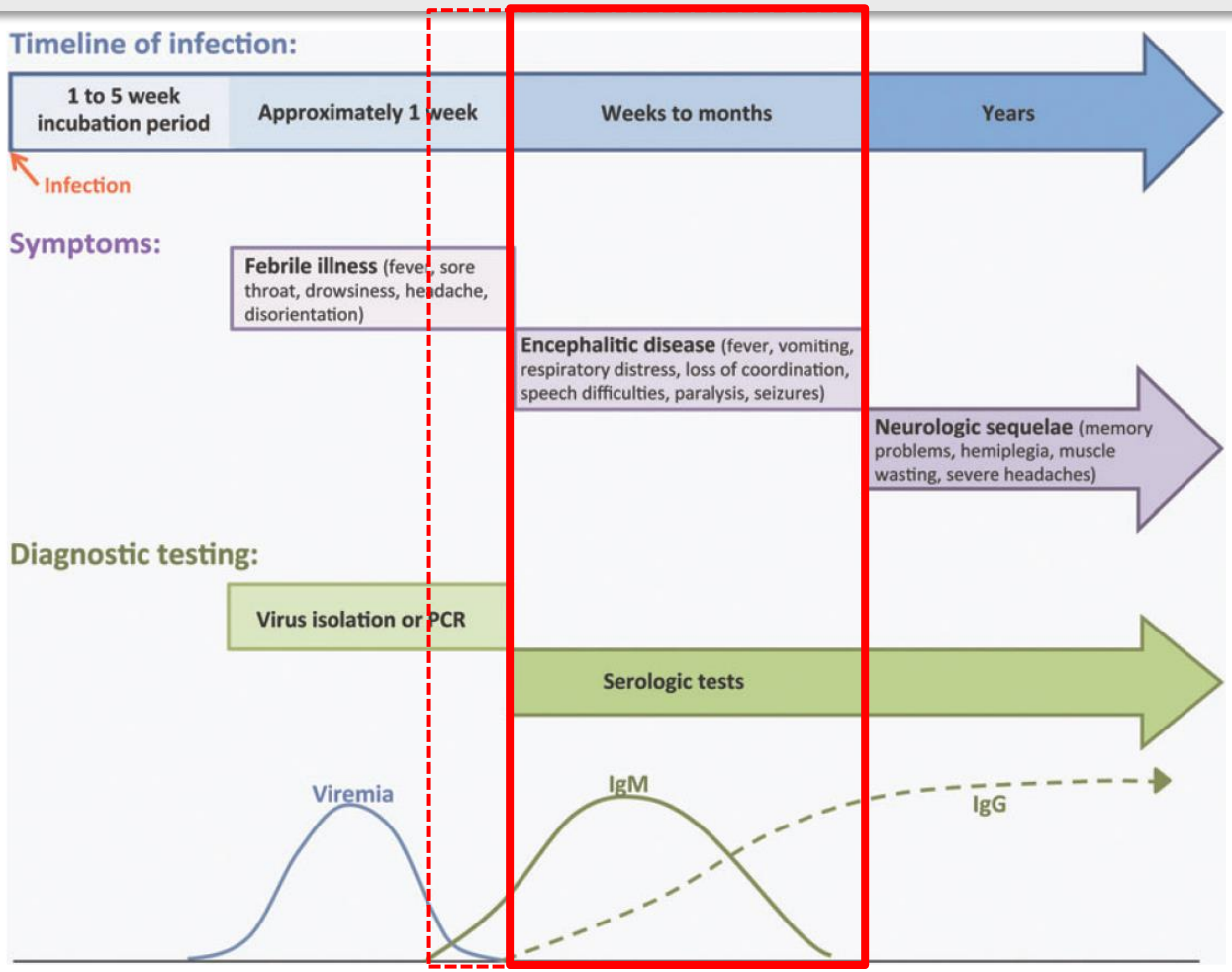
- Serology – IgM of serum or CSF

Post mortem

- Culture of virus
- PCR detection of viral RNA
- Histopathology with immunohistochemistry

None available through commercial labs – CDC or state PHL only

IgM Serology



Hermance and Thangamani. 2017 Vector Borne and Zoonotic Diseases. 17(7), 453-462.

DTV In Summary

- Emerging, life threatening tick-borne viral illness
  - Vectored by *Ixodes* tick
- Likely underreported infection
  - Very limited testing capacities
  - Should only be investigated after more common causes ruled out
- Cases with encephalitis are likely to be identified (or maybe not)

Questions?