

Reinventing serological diagnostic tests for tick-borne diseases.

Dr. Leona Gilbert
leona.gilbert@teztet.com

Teztet
www.teztet.com

TICKPLEX



Copyright Protected

Reinventing serological diagnostic tests for tick-borne diseases.



Dr. Leona Gilbert
leona.gilbert@teztad.com



TICKPLEX

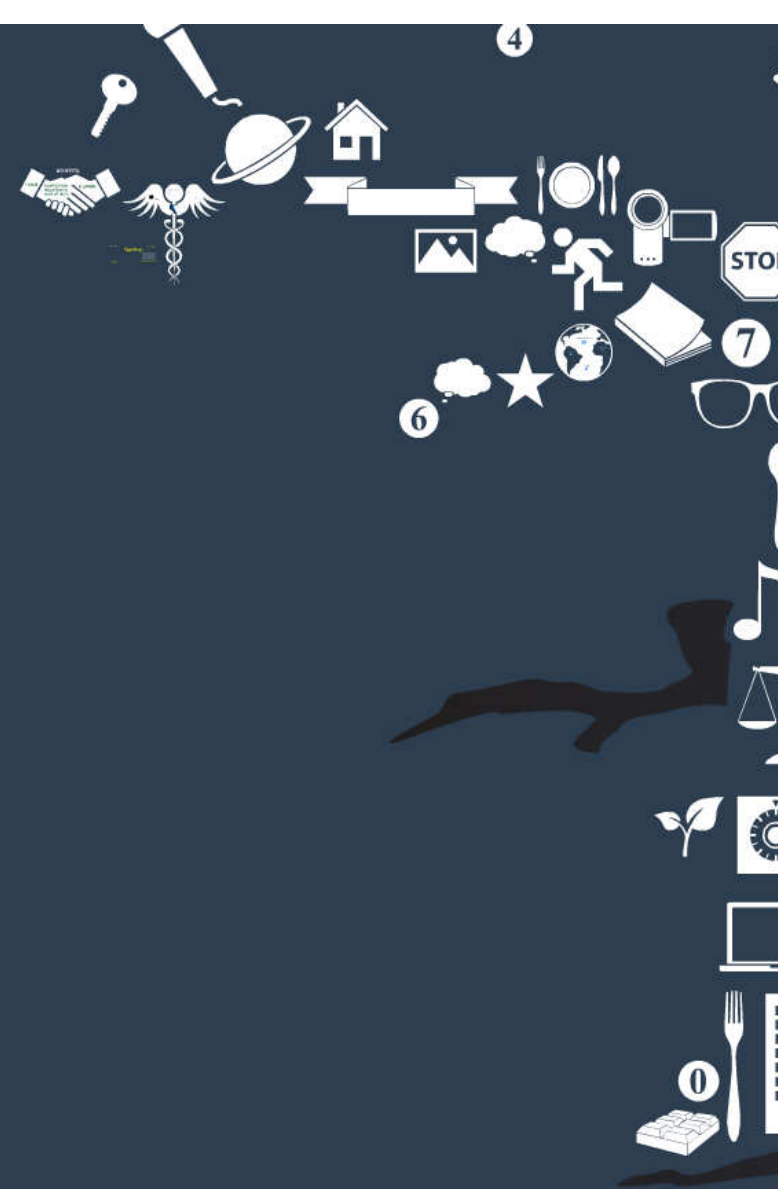
Copyright Protected

diagnostic tests for tick-borne diseases.

Dr. Leona Gilbert
leona.gilbert@teztet.com

Teztet
www.teztet.com

TICKPLEX



VISION AND MISSION

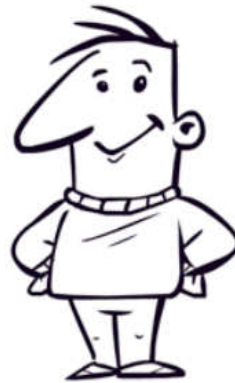
If the patient can be tested, the patient can be treated.



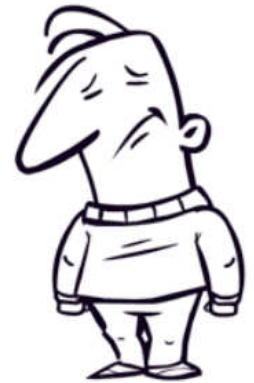
TICK-BORNE DISEASES (TBD)



Ticks



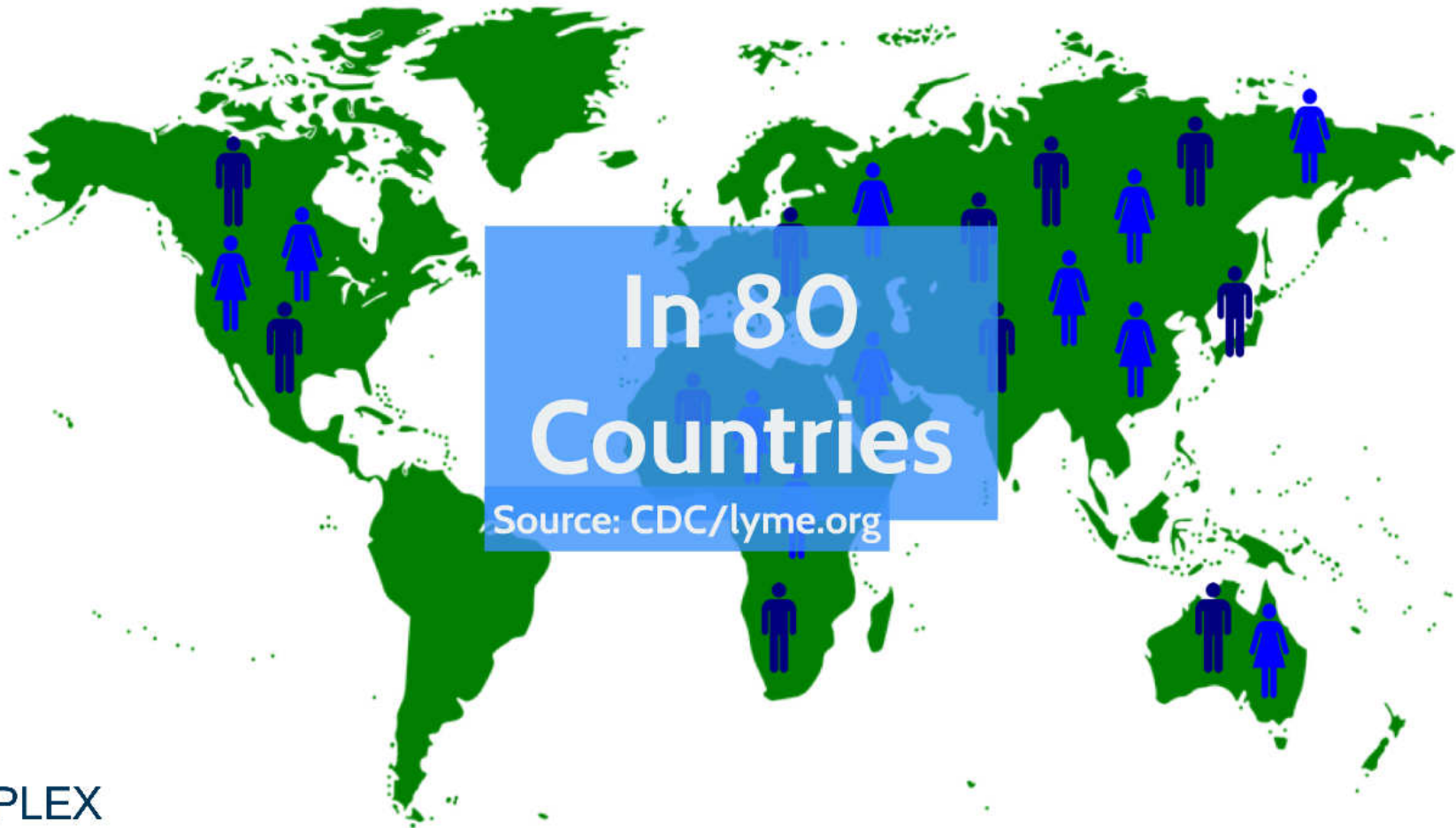
Bite
Humans



Causing
Multiple
Microbial
Infections



Tick-borne Disease Problem



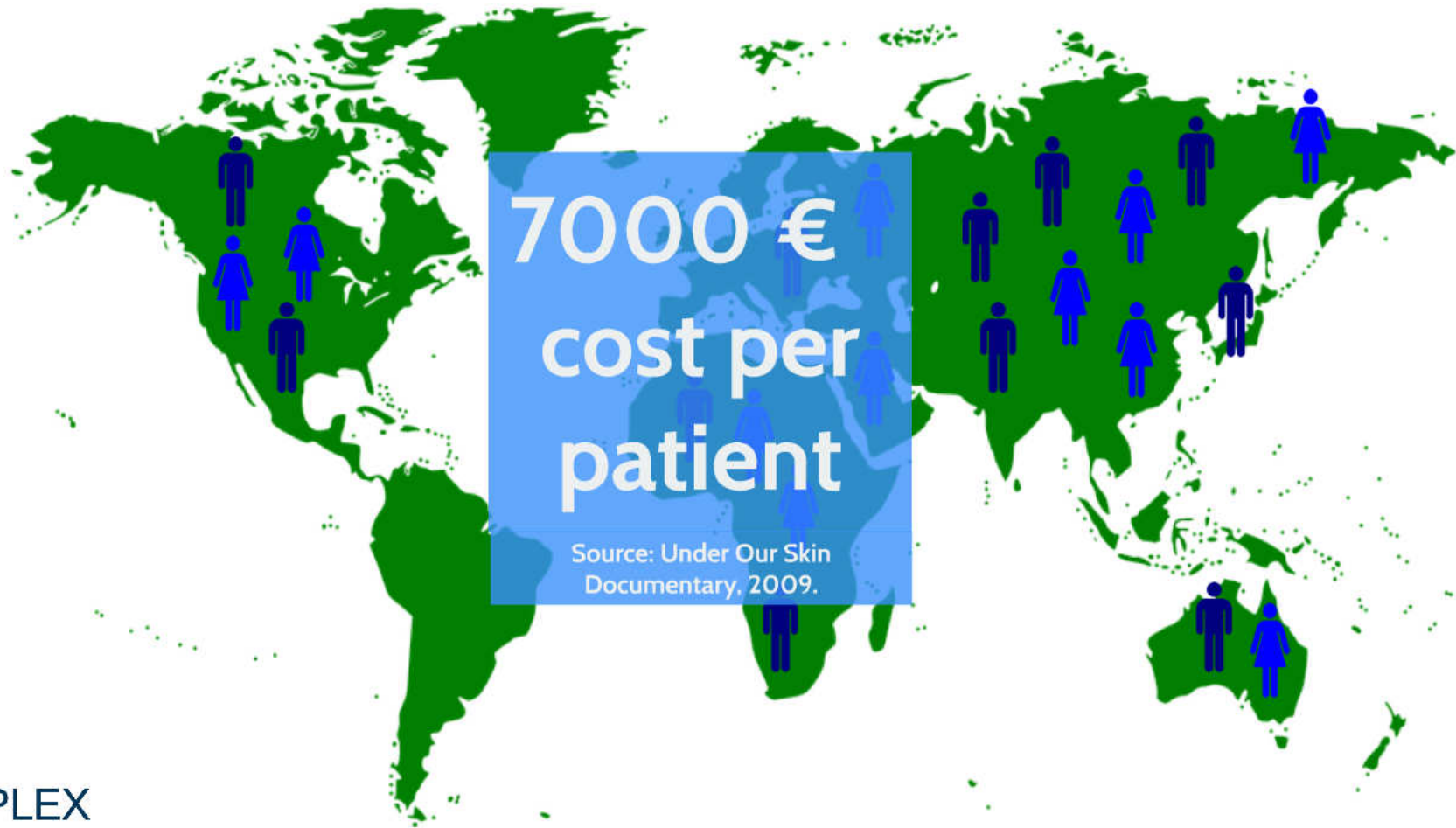
The Problem

A world map with a dark blue background and light blue landmasses. Numerous small, stylized human icons in light blue and dark blue are scattered across the map, representing people from various regions. A central white box with a dark blue border contains the text.

11
visits to a
doctor to
get a proper
diagnosis

Source: Under our skin Documentary, 2009

The Problem



The Problem with Current Diagnostics



Lyme Disease: A Multi-system Disease



Common symptoms:
Erythema migrans (50-70%), Flu-like symptoms,
Headache, Painful, Fatigue, Arthritis, Carditis, Neurological
symptoms, Gait and focalinal problems,
-of blood to diagnose

Disease can be divided to:
Acute stage (days-month)
Disseminated stage (months-year)
Chronic - autochthonous stage (years?)

New Test Testing for Lyme Disease



Two-Tier Testing Algorithm



Lyme Disease: A Multi-system Disease



Common symptoms:

Erythema migrans (50-70 %), Flu-like symptoms, Headache, Malaise, Fatigue, Arthritis, Carditis, Neuronal symptoms, Gastrointestinal problems...

· difficult to diagnose

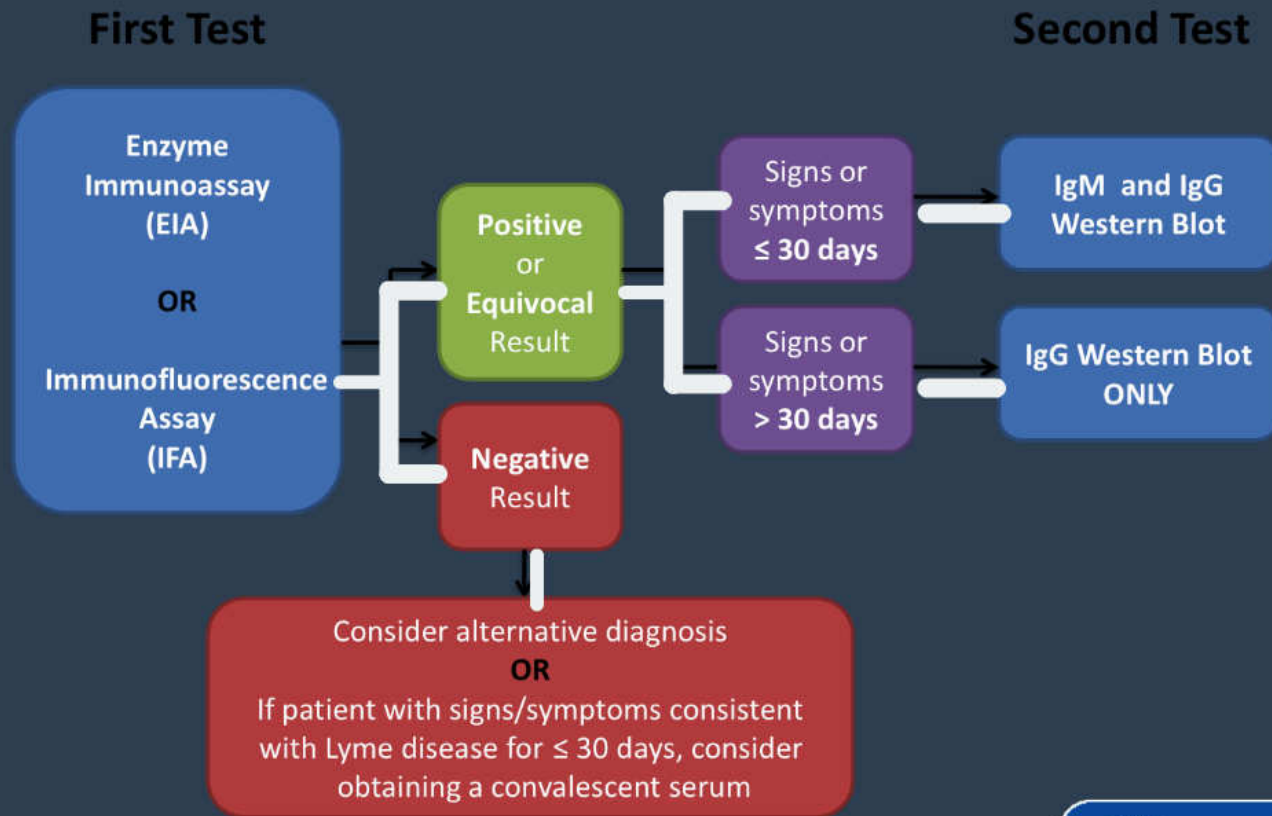
Disease can be divided to:

Acute stage (days-months)

Disseminated stage (months-years)

Chronic + autoimmune stage (years?)

Two Tier Testing for Lyme Disease

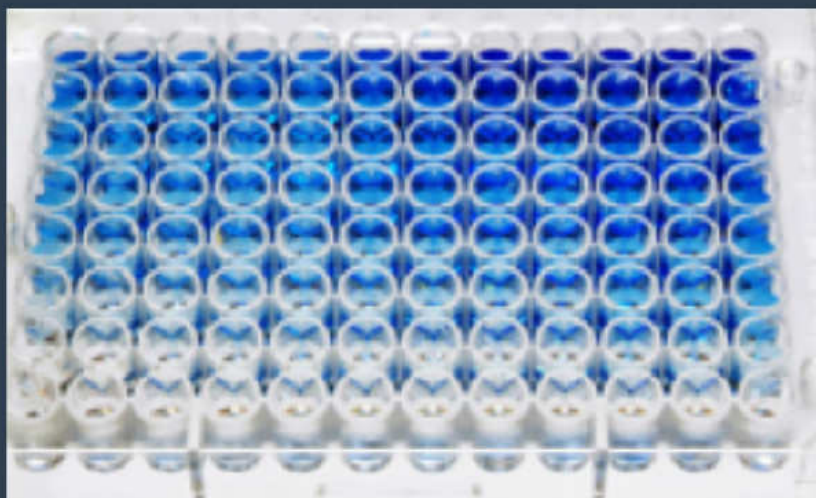


National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector Borne Diseases | Bacterial Diseases Branch



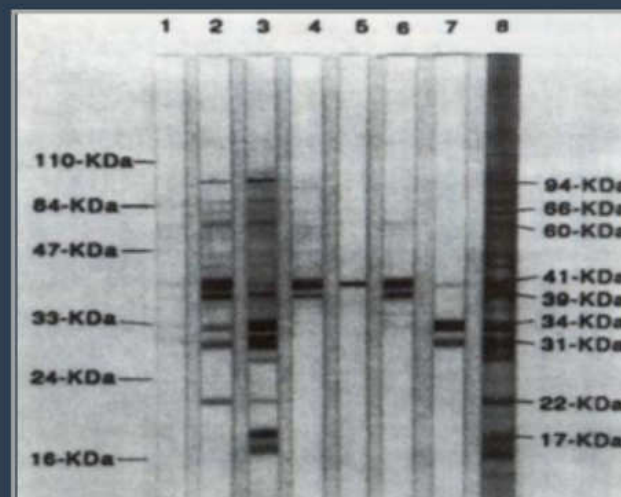
Two-Tier Testing Algorithm

ELISA



Quite sensitive
Automatable
Misses late/chronic cases

Western Blot



Specific Lacks Sensitivity
Labour intensive
Difficult to interpret
Not suitable for standardisation

Vidia anti-Borrelia recom. IgG + VlsE 95% 99 %

Vidia anti-Borrelia recomb. IgM 95% 99%

IBL International Borrelia + VlsE IgG ELISA 94% 98%

IBL International Borrelia 14kDa+OspC IgM ELISA 100% >95%

Euroimmun Anti-Borrelia-ELISA (IgM)

B. burgdorferi, B. afzelii, B. garinii IgM ELISA singlets 100% 96%

Euroimmun Anti-Borrelia-plus VlsE-ELISA (IgG)

B. burgdorferi (+VlsE), B. afzelii, B. garinii IgG ELISA singlets 100% 90 %

Novatec NovaLisa™ Borrelia burgdorferi IgG/IgM recombinant ELISA

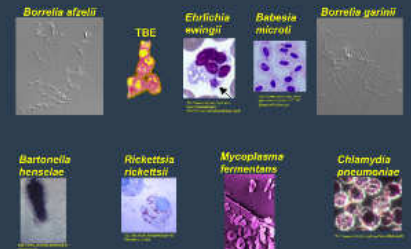
98% (IgG) 93%(IgM) 100% (IgG) 98%(IgM)

Sekisui Diagnostics Borrelia afzelii IgM ELISA Testkit - VIROTECH >99% >98%

Sekisui Diagnostics Borrelia afzelii + VlsE IgG ELISA Testkit - VIROTECH 100,0 % 100,0 %

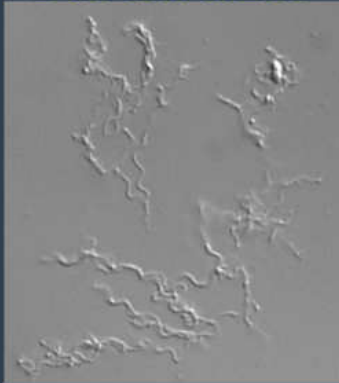


Co-infections and Secondary Infections



Co-infections and Secondary Infections

Borrelia afzelii



TBE

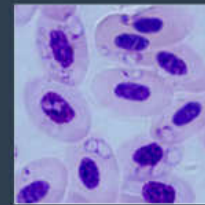


Ehrlichia ewingii



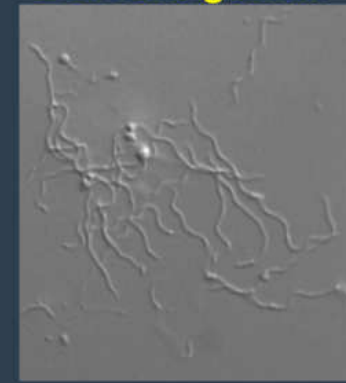
<http://www.capsvet.org/caps-recommendations/7-ehrlichia-spp-and-anaplasma-spp1/>

Babesia microti



<http://www.healthinsnet.com/wp-content/uploads/2013/01/Babesia-Picture.jpg>

Borrelia garinii

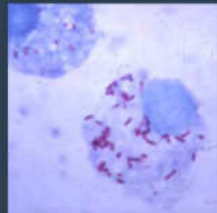


Bartonella henselae



<http://www.answers.com/search?q=barionella>

Rickettsia rickettsii

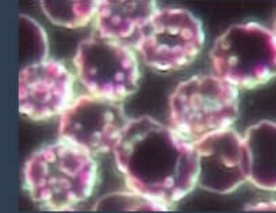


http://textbookofbacteriology.net/Rickettsia_2.html

Mycoplasma fermentans

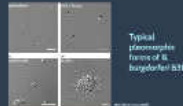
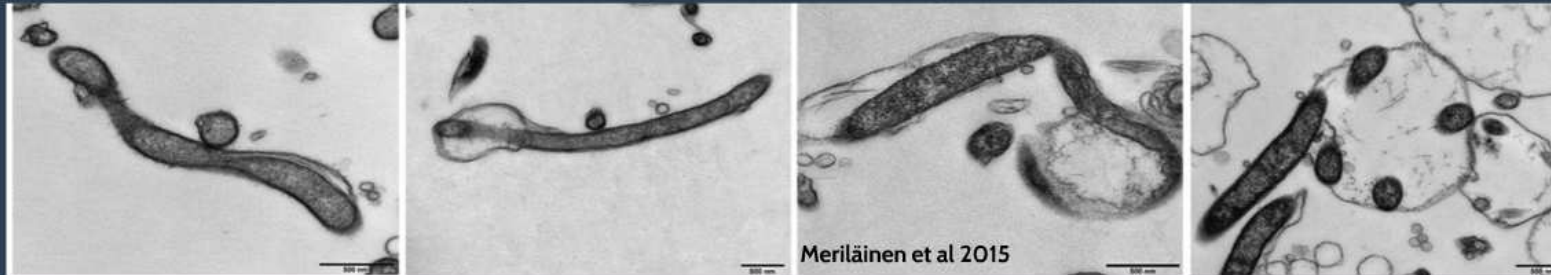


Chlamydia pneumoniae

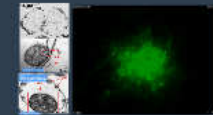


<http://www.cprhelp.org/book/export/html/408>

Pleomorphic Forms of Borrelia



Strain	Genotype	Phenotype	Location	Year
B31	Genotype B31	Genotype B31	USA	1982
B27	Genotype B27	Genotype B27	USA	1982
B4	Genotype B4	Genotype B4	USA	1982
B12	Genotype B12	Genotype B12	USA	1982
B19	Genotype B19	Genotype B19	USA	1982
B20	Genotype B20	Genotype B20	USA	1982
B21	Genotype B21	Genotype B21	USA	1982
B22	Genotype B22	Genotype B22	USA	1982
B23	Genotype B23	Genotype B23	USA	1982
B24	Genotype B24	Genotype B24	USA	1982
B25	Genotype B25	Genotype B25	USA	1982
B26	Genotype B26	Genotype B26	USA	1982
B28	Genotype B28	Genotype B28	USA	1982
B29	Genotype B29	Genotype B29	USA	1982
B30	Genotype B30	Genotype B30	USA	1982
B32	Genotype B32	Genotype B32	USA	1982
B33	Genotype B33	Genotype B33	USA	1982
B34	Genotype B34	Genotype B34	USA	1982
B35	Genotype B35	Genotype B35	USA	1982
B36	Genotype B36	Genotype B36	USA	1982
B37	Genotype B37	Genotype B37	USA	1982
B38	Genotype B38	Genotype B38	USA	1982
B39	Genotype B39	Genotype B39	USA	1982
B40	Genotype B40	Genotype B40	USA	1982
B41	Genotype B41	Genotype B41	USA	1982
B42	Genotype B42	Genotype B42	USA	1982
B43	Genotype B43	Genotype B43	USA	1982
B44	Genotype B44	Genotype B44	USA	1982
B45	Genotype B45	Genotype B45	USA	1982
B46	Genotype B46	Genotype B46	USA	1982
B47	Genotype B47	Genotype B47	USA	1982
B48	Genotype B48	Genotype B48	USA	1982
B49	Genotype B49	Genotype B49	USA	1982
B50	Genotype B50	Genotype B50	USA	1982
B51	Genotype B51	Genotype B51	USA	1982
B52	Genotype B52	Genotype B52	USA	1982
B53	Genotype B53	Genotype B53	USA	1982
B54	Genotype B54	Genotype B54	USA	1982
B55	Genotype B55	Genotype B55	USA	1982
B56	Genotype B56	Genotype B56	USA	1982
B57	Genotype B57	Genotype B57	USA	1982
B58	Genotype B58	Genotype B58	USA	1982
B59	Genotype B59	Genotype B59	USA	1982
B60	Genotype B60	Genotype B60	USA	1982
B61	Genotype B61	Genotype B61	USA	1982
B62	Genotype B62	Genotype B62	USA	1982
B63	Genotype B63	Genotype B63	USA	1982
B64	Genotype B64	Genotype B64	USA	1982
B65	Genotype B65	Genotype B65	USA	1982
B66	Genotype B66	Genotype B66	USA	1982
B67	Genotype B67	Genotype B67	USA	1982
B68	Genotype B68	Genotype B68	USA	1982
B69	Genotype B69	Genotype B69	USA	1982
B70	Genotype B70	Genotype B70	USA	1982
B71	Genotype B71	Genotype B71	USA	1982
B72	Genotype B72	Genotype B72	USA	1982
B73	Genotype B73	Genotype B73	USA	1982
B74	Genotype B74	Genotype B74	USA	1982
B75	Genotype B75	Genotype B75	USA	1982
B76	Genotype B76	Genotype B76	USA	1982
B77	Genotype B77	Genotype B77	USA	1982
B78	Genotype B78	Genotype B78	USA	1982
B79	Genotype B79	Genotype B79	USA	1982
B80	Genotype B80	Genotype B80	USA	1982
B81	Genotype B81	Genotype B81	USA	1982
B82	Genotype B82	Genotype B82	USA	1982
B83	Genotype B83	Genotype B83	USA	1982
B84	Genotype B84	Genotype B84	USA	1982
B85	Genotype B85	Genotype B85	USA	1982
B86	Genotype B86	Genotype B86	USA	1982
B87	Genotype B87	Genotype B87	USA	1982
B88	Genotype B88	Genotype B88	USA	1982
B89	Genotype B89	Genotype B89	USA	1982
B90	Genotype B90	Genotype B90	USA	1982
B91	Genotype B91	Genotype B91	USA	1982
B92	Genotype B92	Genotype B92	USA	1982
B93	Genotype B93	Genotype B93	USA	1982
B94	Genotype B94	Genotype B94	USA	1982
B95	Genotype B95	Genotype B95	USA	1982
B96	Genotype B96	Genotype B96	USA	1982
B97	Genotype B97	Genotype B97	USA	1982
B98	Genotype B98	Genotype B98	USA	1982
B99	Genotype B99	Genotype B99	USA	1982
B100	Genotype B100	Genotype B100	USA	1982



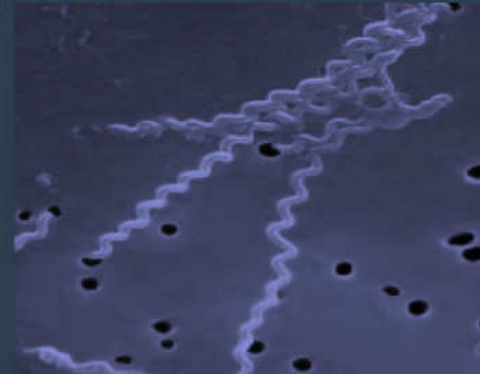
Pleomorphism



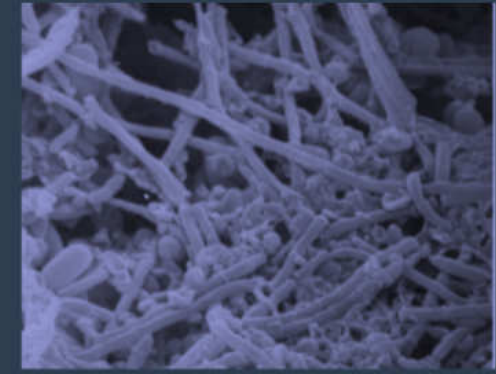
Coccoid



Rod



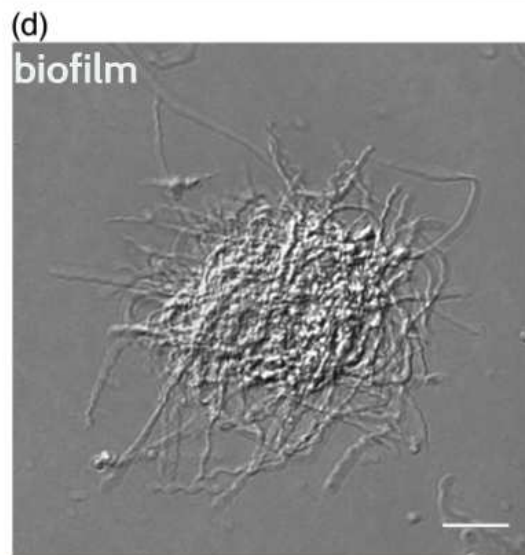
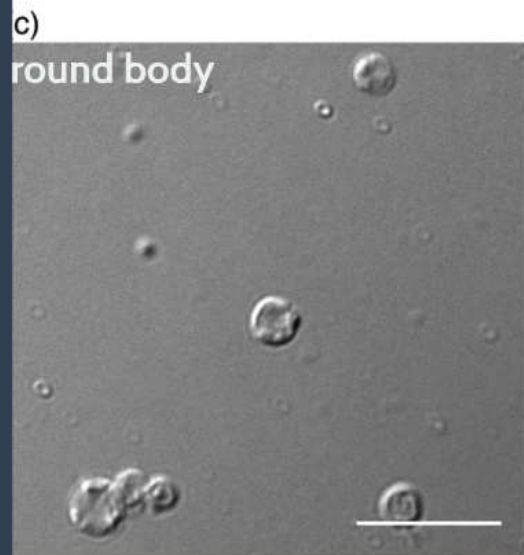
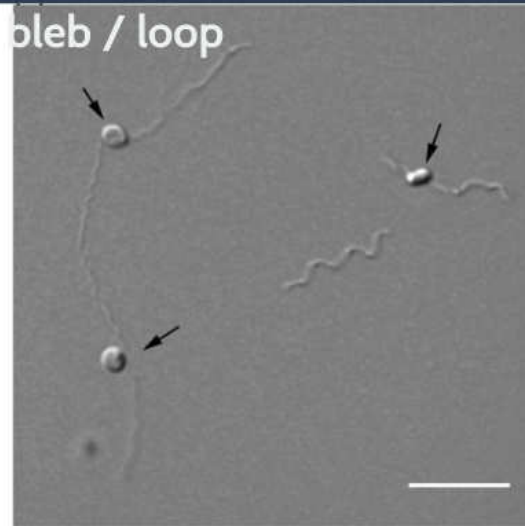
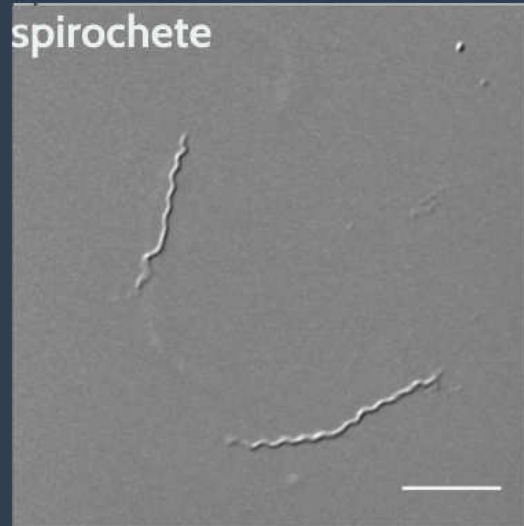
Spiral



Biofilm

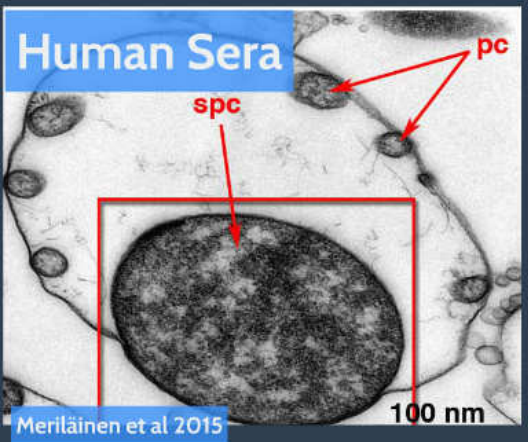
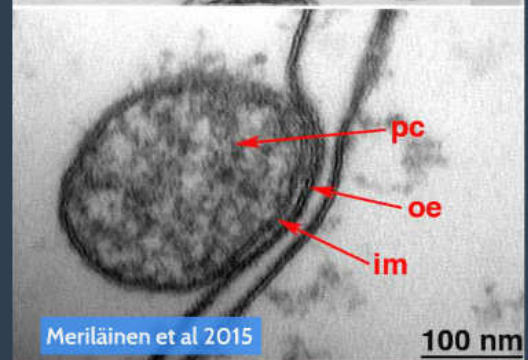
Occurrence of two or more structural forms during a life cycle

Term (Lantos et al 2015 reviewed)	Description (Allan et al 2009, Cagle 1974, Cocotl-Yanez 2011, Meriläinen et al 2015)	References for Borrelia
L-form	Phenotypic deficiency in rigid cell wall.	Allan et al 2009;
Alternative nomenclature Cell wall-deficient form L-variant L-phase L-organism	pH (Murgia & Cinco 2004); antibiotics (Barbour et al 1982, Schaller & Neubert 1994, Kersten et al 1995, Mursic et al 1996, Murgia et al 2002, Sapi et al 2011); water (Al-Robaay et al 2010, Brorson & Brorson 1998, Murgia & Cinco 2004, Meriläinen et al 2015); without sera (Brorson & Brorson 1997, Alban et al 2000); mammalian culture media (Alban et al 2000, Al-Robaay et al 2010, Dunham-Ems et al. 2012, Meriläinen et al 2015); human sera (de Taeye et al 2013, Meriläinen et al 2015).	
Subtypes Stable L-forms Unstable L-forms Spheroplast Protoplast	Permanent cell wall alterations. Cannot revert to parental form. Temporary induction of cell wall alterations by exposure to drugs and may revert back. L-form where some cell wall structure is retained. Stable or not. L-form where no cell wall structure is retained. Stable or not.	Alban et al 2000, Al-Robaay et al 2010, Brorson & Brorson 1997, 1998a & b, 1999, 2001, 2004, 2006, 2007; Dunham-Ems et al 2012; Escudero et al 1997; Feng et al 2015; Gruntar et al 2001; Kawai et al 2014; Murgia et al 2002; Mursic et al. 1996; Oliver et al 2010; Preac et al 1996; Stricker and Johnson 2011.
Cyst	Differentiated structure that is resistant to desiccation or other noxious conditions. Encystment occurs by changes in the cell wall; the cytoplasm contracts and the cell wall thickens.	
Propagule / pearls / granules	Infectious “units” of material that transmit disease.	Aberer and Duray 1991; Barbour & Hayes 1986; Escudero et al 1997; Garon et al. 1989.
Round, coccoid, globular or spherical	Descriptive morphologic terms. Not biologically defined (Lantos et al 2015).	Brorson et al 2009; Feng et al 2015; Goc et al 2015; Meriläinen et al 2015.
Bleb / Loops	An irregular membrane bulge.	Barbour & Hayes 1986; de Taeye et al 2013; Dever et al 1993; Kersten et al 1995; Kraiczky et al 2001; Meriläinen et al 2015; Whitmire & Garon 1993.
Biofilm, biofilm-like	Group of microorganisms that have adherent cells and are frequently embedded within matrix of extracellular polymeric substance. Consists of more than 10 spirochaetes/blebs/RBs.	Barbour & Hayes 1986; Feng et al 2015, 2016; Kurtti et al 1987; Goc et al 2015; Meriläinen et al 2015; Sapi et al 2012; Srivastava & de Silva 2009. Timmaraju et al. 2015.



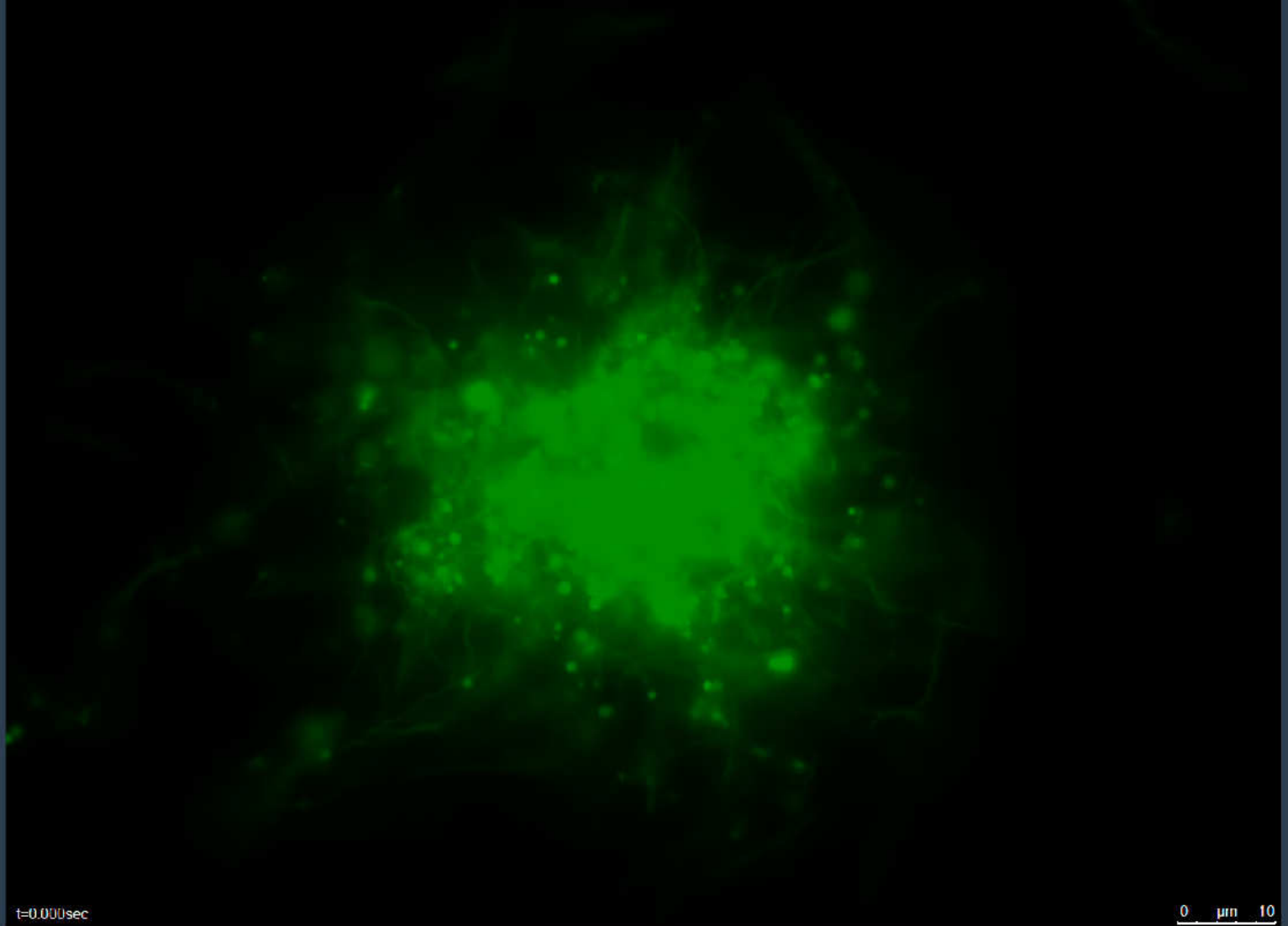
Typical
pleomorphic
forms of *B.*
burgdorferi B31

Meriläinen et al 2015



8/22/2012 9:10:20 AM

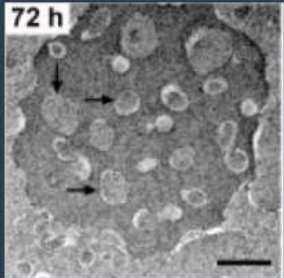
00:00:00.000



IN VIVO



Dunham-Ems et al 2012
Embers et al 2012



Lebech et al 1995

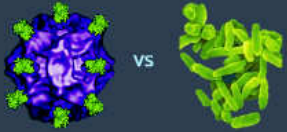


Janus et al 2014
Baneth et al 2016



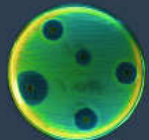
Aberer et al 1996, 1997
Brorson et al 2001
Eisendle 2007a, b, 2008
Hulinska et 1989, 1994
MacDonald 1998, 2006
MacDonald & Miranda 1987
Miklossy et al 2008
Nanagara et al 1996
Sapi et al 2016
Yoon et al 2005

Angelov et al 1996
Dietrich et al 2008
Muehlenbachs et al 2006
Phillips et al 1998
Waldo & Sidhu 1983
Zanconati et al 1994



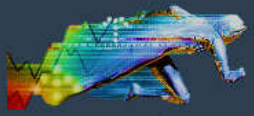
vs

what pathogen



susceptibility

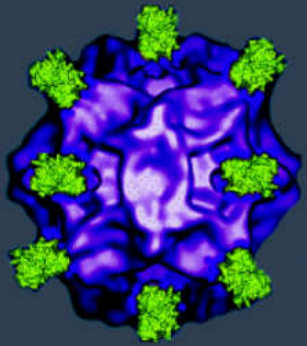
Test Must



rapid



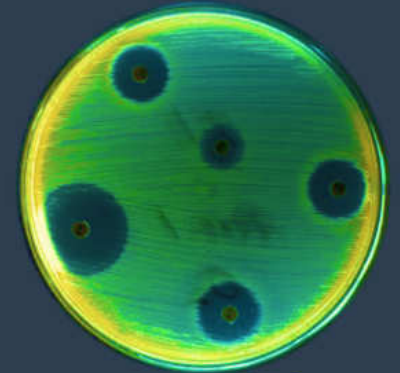
effectively communicated



vs



what pathogen



susceptibility

Test Must



rapid



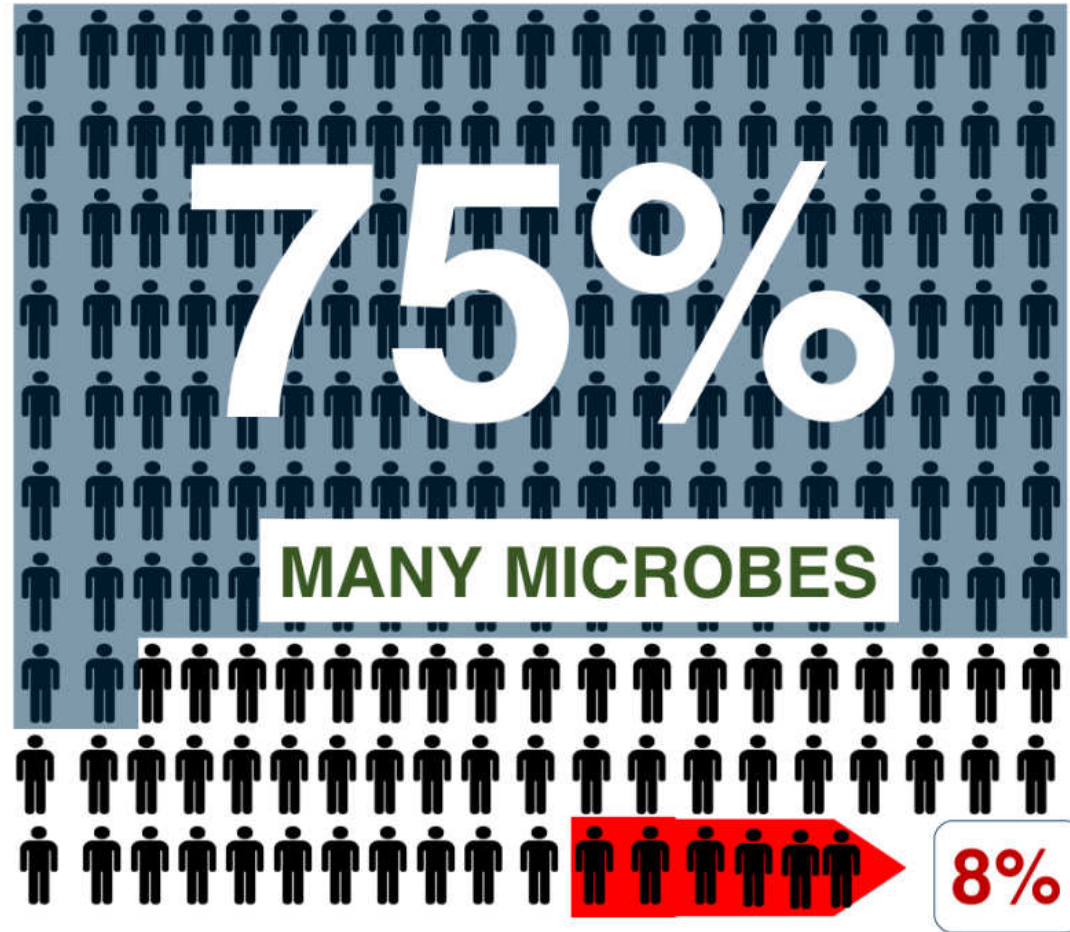
effectively communicated

Old Knowledge Challenged

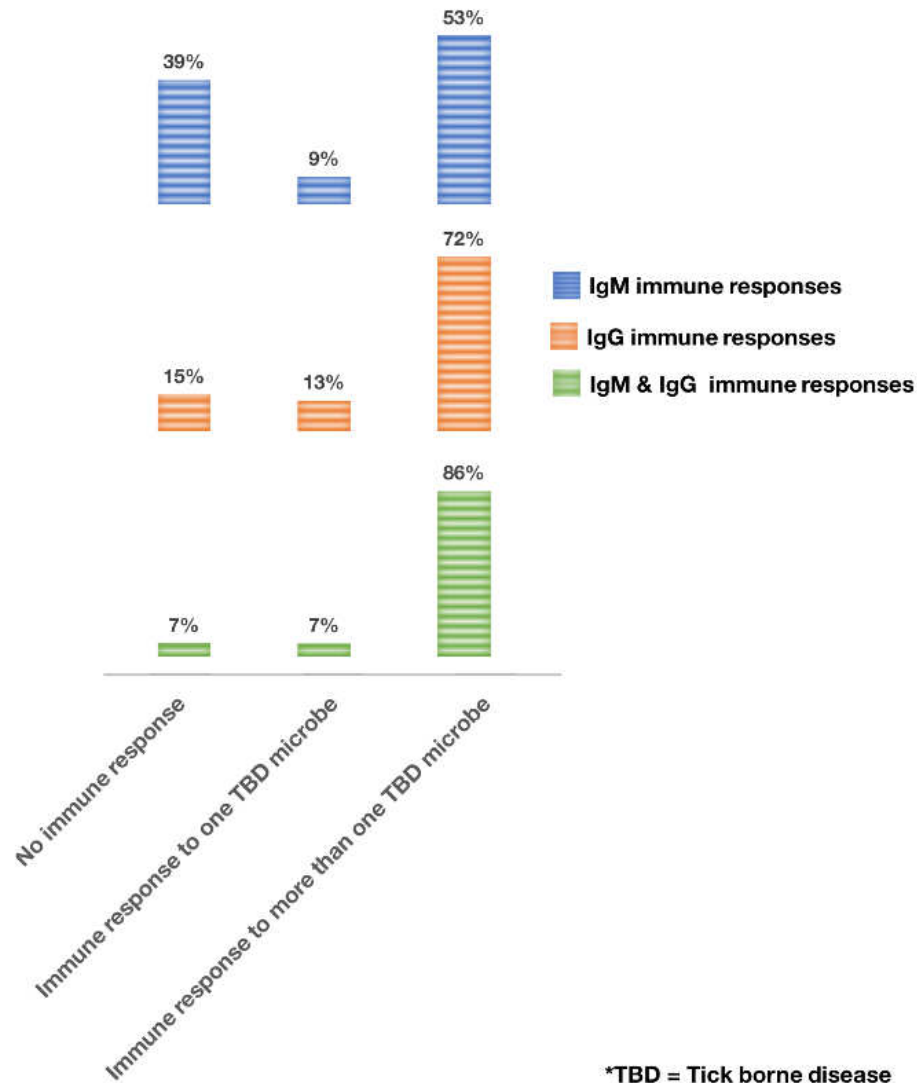
Experiment: 1100 patients were tested against 20 microbes

NEW Knowledge
Many microbes = disease

OLD Knowledge
One microbe = disease

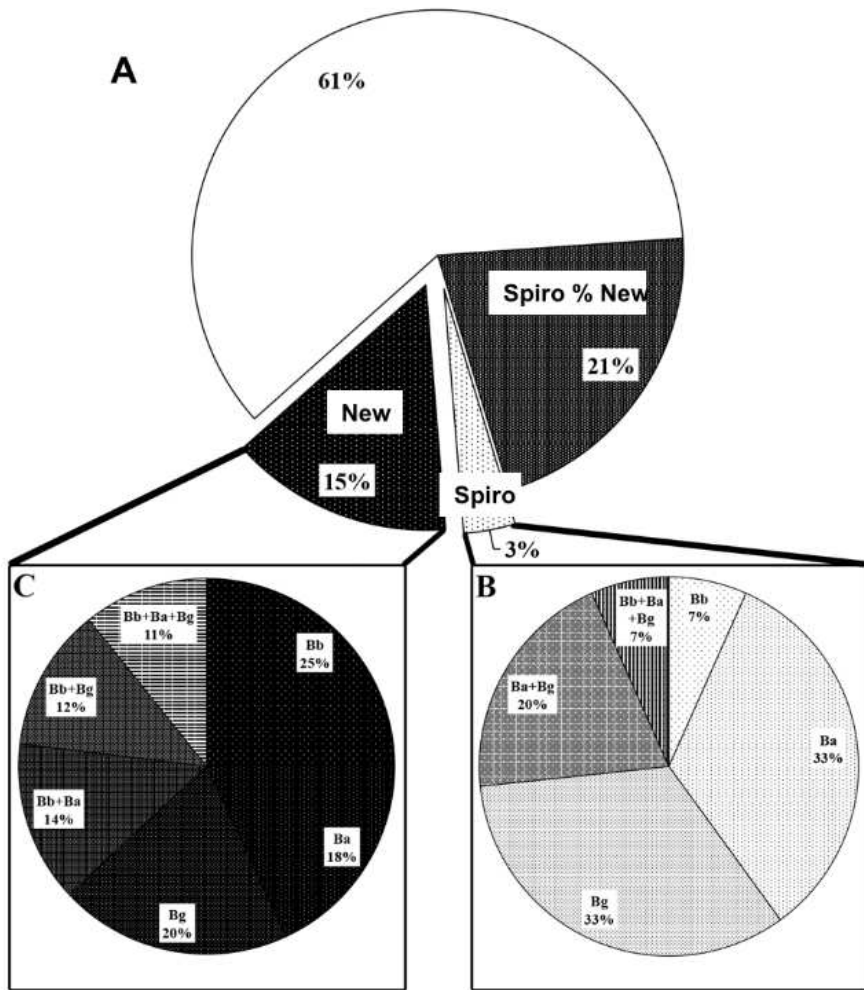


One microbe

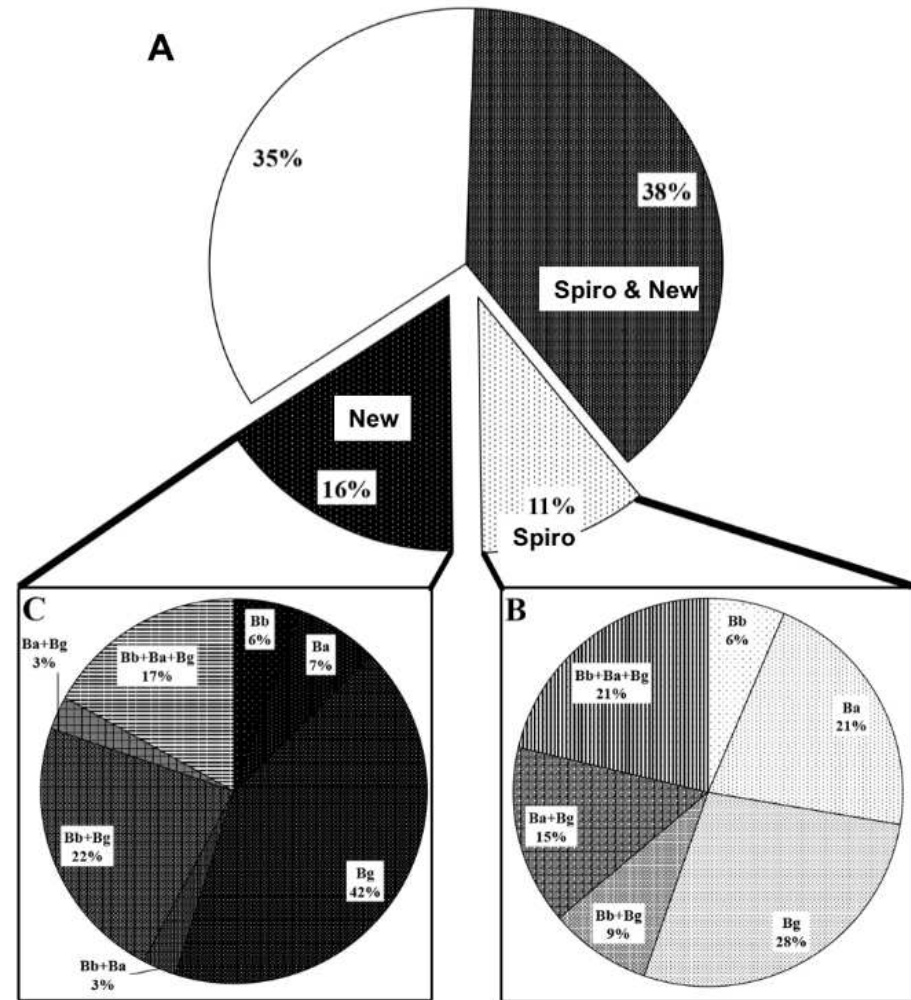


Evaluation of (A) IgM and (B) IgG immune responses against one or multiple microbial antigens.

*TBD = Tick borne disease

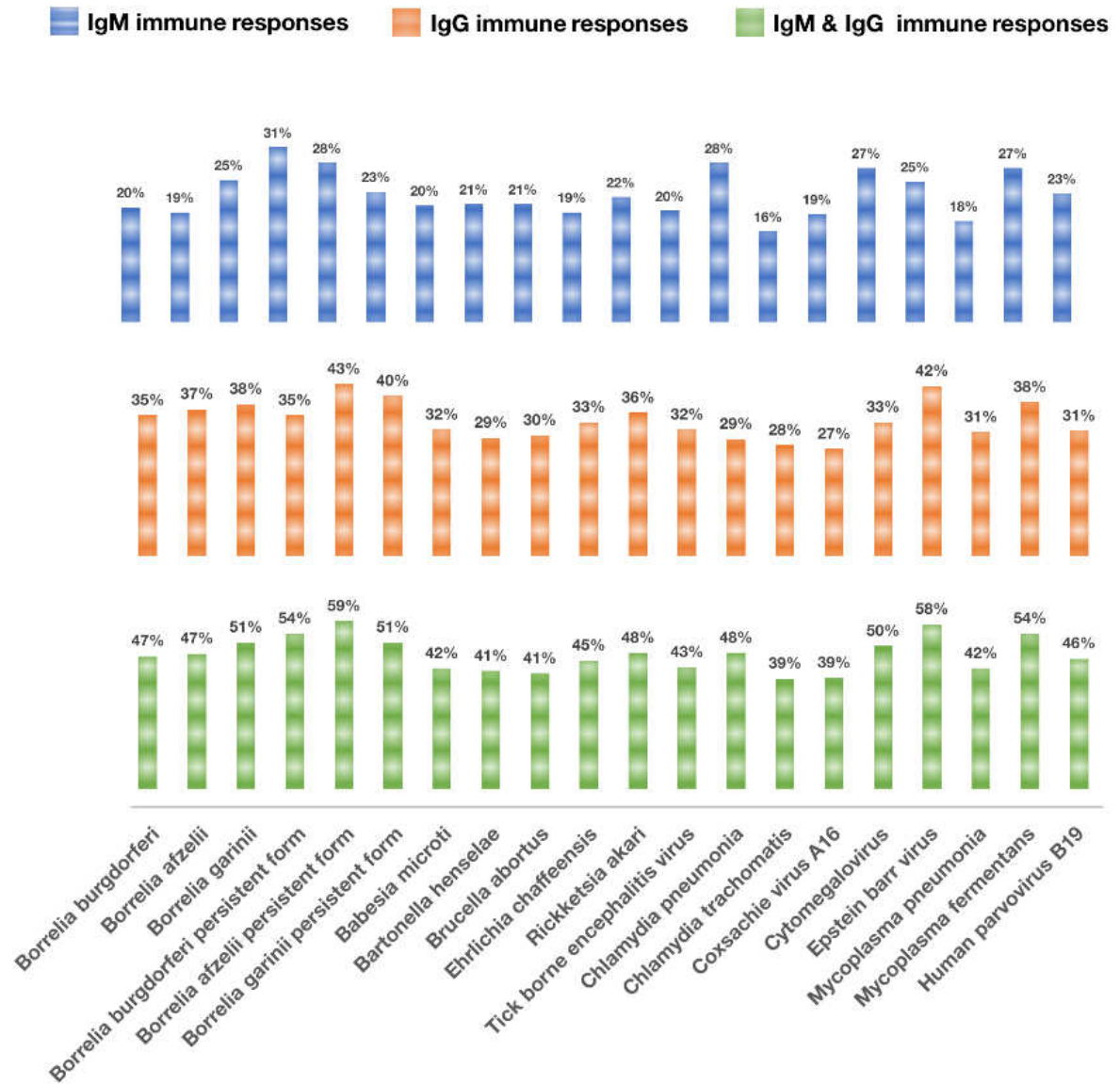


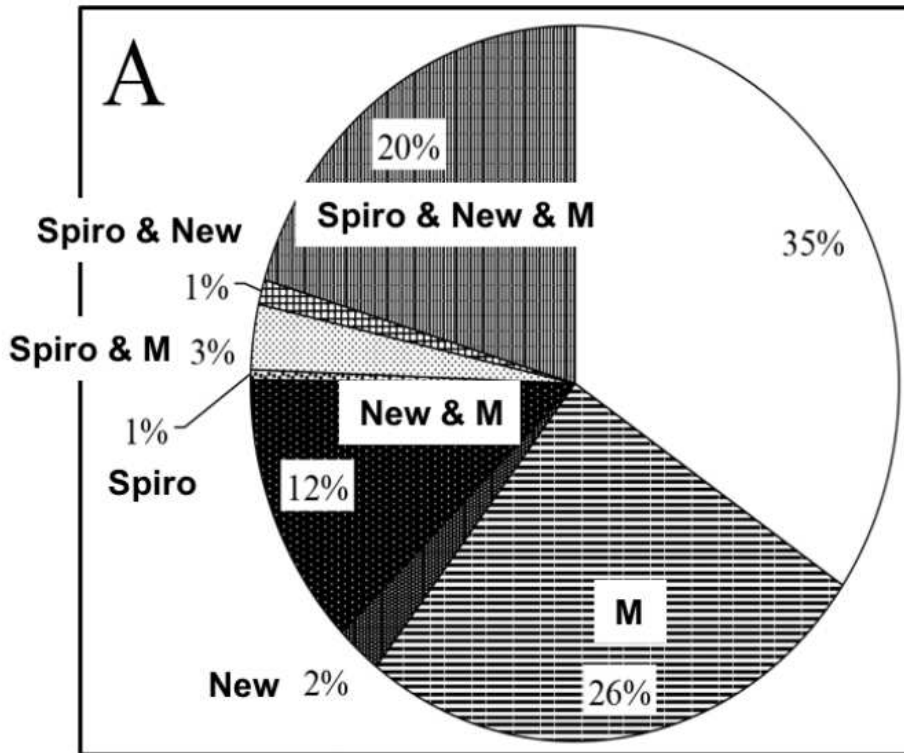
(A) Overall IgM immune responses to all *Borrelia* antigens, (B) only *Borrelia* spirochetes, and (C) only *Borrelia* new antigen.



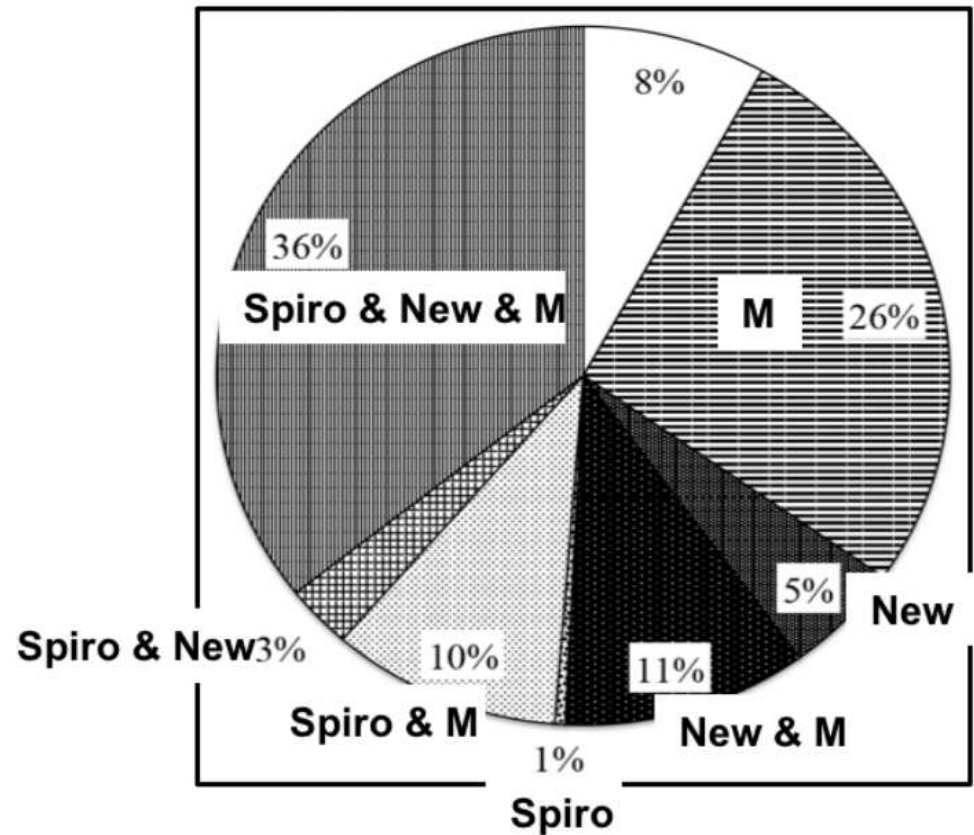
(A) Overall IgG immune responses to all *Borrelia* antigens, (B) only *Borrelia* spirochetes, and (C) only *Borrelia* new antigen.

IgM and IgG immune responses to individual microbial antigens.





Overall IgM immune response proportions by individuals to other microbes with and without *Borrelia*.



Overall IgG immune response proportions by individuals to other microbes with and without *Borrelia*.

Our Solution: A Complete Diagnostic Platform for Tick-borne Diseases

-  Tests Multiple Microbes
-  Tests Multiple Disease Stages
-  With Higher Sensitivity
-  Access Anytime and Anywhere



 3 Patents Filed & Trademark

SOLUTION

 **TICKPLEX PREMIUM** Coming Soon!

 **TICKPLEX PLUS**

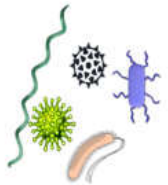
 TICKPLEX PLUS test provides a quantitative and qualitative in-vitro assay for the most common and life-threatening agents transmitted by hard-bodied ticks and the most prevalent species. The test includes per-tick analysis of the different Serogroups.

Tests for six infectious diseases: Borrelia burgdorferi (Bb), Babesia microti (Bm), Anaplasma phagocytophilum (Ap), Coxiella burnetii (Cb), Ehrlichia chaffeensis (Ec), and Ixodes ricinus (Ix).

 **TICKPLEX BASIC**

TICKPLEX BASIC test provides a qualitative and quantitative in-vitro assay for the most common and life-threatening agents transmitted by hard-bodied ticks and the most prevalent species. The test includes per-tick analysis of the different Serogroups.

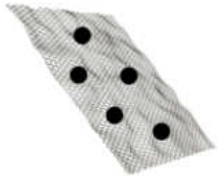
Our Solution: A Complete Diagnostic Platform for Tick-borne Diseases



Tests Multiple Microbes



Tests Multiple Disease Stages



With Higher Sensitivity



Access Anytime and Anywhere



Sensitool 100
©2018 Sensitool
Patent pending in
USA, UK,
EU, Canada
and elsewhere



3 Patents Filed & Trademark

Sensitivity: 95%

Specificity: 98%

False positive: 0.6%

False negative: 3%

PPV: 99%

NPV: 99%

95% Confidence Interval





TICKPLEX PREMIUM

Coming Soon!!



TICKPLEX PLUS

TICKPLEX® PLUS test provides a quantitative and qualitative *in vitro* assay for human IgM and IgG antibodies against *Borrelia afzelii*, *Borrelia burgdorferi*, and *Borrelia garinii* infections. The test includes persistent antigens of the different borrelia species.



Tests for co-infections (*Babesia*, *Bartonella*, *Ehrlichia*, *Rickettsia*), and opportunistic infections (Coxsackievirus, Epstein-Barr virus, Human parvovirus B19, *Mycoplasma fermentans* and *Mycoplasma pneumoniae*) associated with tick-borne diseases.



TICKPLEX BASIC

TICKPLEX® BASIC test provides a quantitative and qualitative *in vitro* assay for human IgM and IgG antibodies against *Borrelia afzelii*, *Borrelia burgdorferi*, and *Borrelia garinii* infections. The test includes persistent antigens of the different borrelia species.

BENEFITS

1 VISIT

SIGNIFICATION
REDUCTION IN
COST OF TESTS

€ SAVED







TeKes

Finnish Innovation Funding Agency

Schwartz Foundation

Reinventing serological diagnostic tests for tick-borne diseases.

Dr. Leona Gilbert
leona.gilbert@teztet.com

Teztet
www.teztet.com

TICKPLEX



Copyright Protected



Thank You!

Reinventing serological diagnostic tests for tick-borne diseases.

Dr. Leona Gilbert
leona.gilbert@teztet.com

Teztet
www.teztet.com

TICKPLEX



Copyright Protected