Progress on Lyme Disease
July 2014

Tim Brooks, RIPL

Overview
Tests & results
Questions to consider
Guidance and information
Health Protection Research Unit
Specialist clinics
Clinical studies
Summary

Lyme service at RIPL
Started 1 June 2012
Fully automated testing
Allows paperless data transfer
Based on C6 ELISA as screen
Immunetics® IgM/IgG combination
Virastripe printed blots
Read by densitometer

Lyme C6 assay
DS2 ELISAbot
Q-pulse automated
Levy Jennings QC

Blots

Why use a printed blot?
Defined bands
Machine readable
No background
Only the bands you want
Wider testing
- Bartonella: Currently via Colindale
- Rickettsia: Euromimmun IF IgM & IgG
- Anaplasma/Ehrlichia: Via HTD
- Babesia: Other tick borne diseases
  - Q fever, tularemia, TBE complex, bunyaviruses
- Other infectious causes of symptoms

Finding the organism
- Sampling & errors
  - Skin best
  - Blood
  - CSF & synovium
- Biological limitations
  - One time “Gold Standard”
  - New techniques available
- PCR
  - Real-time PCR based on Fla gene
  - Sensitive within limits above (~50%)
  - Can be combined with culture

Reporting the result
- B. BURGDORFERI IgG/IgM (C6 EIA): POSITIVE
  - Borrelia IgM Lineblot (viralstrip) IgM to Borrelia P41 antigen: POSITIVE
  - IgM to Borrelia P39 antigen: Negative
  - IgM to Borrelia OspC antigen: Negative
  - IgM to Borrelia Vse antigen: Negative
  - Borrelia IgM Lineblot interpretation: POSITIVE
  - Composite report for early acute Lyme Disease
- Borrelia IgG Lineblot (viralstrip) IgG to Borrelia P83 antigen: Negative
  - IgG to Borrelia P43 antigen: Negative
  - IgG to Borrelia P39 antigen: Negative
  - IgG to Borrelia OspC antigen: POSITIVE
  - IgG to Borrelia p21 antigen: Negative
  - IgG to Borrelia Osp17 antigen: Negative
  - IgG to Borrelia DBPA antigen: POSITIVE
  - IgG to Borrelia P14 antigen: Negative
  - IgG to Borrelia VlsE antigen: POSITIVE
  - Borrelia IgG Lineblot interpretation: POSITIVE

Samples 2013
- Seasonal numbers of Lyme samples received: Total 12,280
- Around 10% positive by C6 & blot as new cases

Interpreting the answers: Duck Test
- Looks like a duck, Waddles, Quacks: It’s a duck!
- Looks like a duck, Waddles, No quack: Probably a duck
- Wrong look, Can’t waddle, Mute: Not a duck...

Health Protection Research Units
- In 2013, the National Institute for Health Research (NIHR) announced an open competition to fund 12 HPRUs.
- Each HPRU to be awarded to a single university working in partnership with PHE.
- HPRUs to be exclusively focussed on human disease – no animal research.
- Each HPRU to receive up to £4 million over 5 years.
- University of Liverpool (with LSTM) was awarded the HPRU in Emerging Infections (including Zoonoses)
Aims of EIZ HPRU

- Support and strengthen PHE in its role protecting England from emerging and zoonotic infections and biological threats
- Internationally leading researchers at University of Liverpool and Liverpool School of Tropical Medicine and PHE
- World class research facilities including
  - High containment labs (BSL3&4)
  - Entomology labs
  - World leading veterinary school (Liverpool)
  - Proteomics and genomics expertise
- Provide resilience to the UK in capability to deal with known and unknown biological threats through One Health approach

Theme 2: Epidemiological Approaches
Leads: Sarah O’Brien (UoL), Roberto Vivancos (PHE)

- Project One: Real time surveillance and response
  - Integrated syndromic surveillance and molecular diagnostic systems
- Project Two: Sources of newly-emerged and zoonotic infections in the UK
  - Importation of newly-emerged zoonotic pathogens into the UK
    - Using publicly available passenger travel, shipping and product importation datasets (e.g. TravelPac, Sea-web, UK trade info and other Office for National Statistics data)
  - Identifying populations at exposure risk to zoonoses
- Project Three: Social and behavioural aspects of EID and zoonoses
  - Risky behaviours, exposure to risk

Theme 3: Clinical Surveillance
Leads: Nick Beeching (LSTM), Tim Brooks (PHE), Tom Solomon (UoL)

- Project One: Improved surveillance and diagnosis of hantaviruses
  - examine the relationship and link between hantavirus and acute kidney disease
  - a cohort study of patients acute kidney disease of unknown cause
  - prospective case-control study to examine risk factors
- Project Two: Improved diagnosis of CNS infections
  - integrated molecular approach to detecting pathogens
  - examine host response genes using transcriptomic approaches
- Project Three: Improving diagnosis and clinical management of Lyme borreliosis in the UK.
  - a clinical study investigating the link between symptoms throughout the course of disease, and the results of pathogen specific diagnostic tests
  - protein arrays for correlation between disease symptoms and antibody reactions; T-cell assays for cell-mediated immune response.

RIPL in-house research
In collaboration with Raigmore, Inverness
Organism identification
  - Bespoke pan-borrelia PCR's*
  - Species typing PCR*
  - Wide coverage PCR’s
  - Large volume extraction
  - Next generation sequencing (NGS)
  - Cross-validation to culture
Improved serology
  - Data & social media mining

Theme 5: Vector Biology & Climate Modelling
Leads: Matthew Baylis (UoL), Dr Jolyon Medlock (PHE), Stephen Torr (LSTM)

- Project One: Strategy for development of tick-arbovirus infection system
  - established colonies of UK indigenous ticks that may be important disease vectors for CCHF, TBE
- Project Two: Strategy for tick-borne borreliosis
  - tick spatial distribution modelled using historic and contemporary climate data.
  - develop a climate-driven forecasting system for the activity of Ixodes ricinus and Lyme borreliosis risk
- Project Three: Strategy for development of mosquito-borne arbovirus infection systems
  - Build on CL3 JEV system to develop DENV, and CHIK mosquito systems
- Project Four: Study of the feeding preferences of UK mosquitoes
  - quantify the behaviour of vectors
  - nationwide mosquito sampling network
  - identify factors that make important contributions to biting risk.

* p66 porin
  - Outer membrane
  - Inner membrane
  - VlsE protein
  - Flagellin strands between membranes rotate to propel organism
  - p83 surface protein
  - Borrelia membrane protein A
  - OspC cell attachment protein
  - P 17/ Decorin binding protein

Scientific illustrations by: Mike Roper

LDA Conference 2014 - Tim Brooks
Lyme clinic at Winchester
Clinic operated at Winchester from October 2013 to March
Winchester Trust closed clinic for operational reasons on 31 March
PHE provided additional resources and testing
Recommended referral pathways were published at
http://www.hpa.org.uk/webc/HPAwebFile/H
Pweb_G/1317141231268

Specialised clinics
Primary aim is to identify & treat patient's illness
Lyme is part of a differential diagnosis
Clinics should have access to supporting specialities
  Rheumatology
  Neurology
  Dermatology
  Immunology
  Radiology & Imaging
  Supportive therapies
  Standardised investigation & treatment protocols

Features of the clinic
A focus for developing standardised protocols
  For investigation
  For treatment
  For research
Research centre
  In partnership with other centres
  Clinical studies
  In collaboration with RIPL/EIZ HPRU diagnostic strategies
  With GP's etc via Clinical Research network

The dream trial
From GP presentation to neurological investigation
  Follow all processes involved
  Use all available techniques to study pathogen's progress & human response
  Compare lab confirmed disease with other presentations

Lyme Guidance
To NICE principles
Sections for each speciality
  Cover pathways for investigation & treatment
  For GPs, ID, neurology etc.
LDA will be part of committee
Will take at least 1 year to develop

The broader view
International Conference on Vector-Borne Disease
Norwegian conference on Lyme disease with US speakers
Lyme Disease discussion day
  London 6 June
  Will follow up with speakers from US.
  We have offered to collaborate with any takers from that group
Summary

PHE service at RIPL covers Lyme and related diseases

Active collaboration with Raigmore, Scotland

Initial research programme defined
  Covers pathogen identification & serology

PHE will support a clinic in S. England
  Under negotiation
  Will be a hub for clinical studies

Thanks to Jackie Duggan
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