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

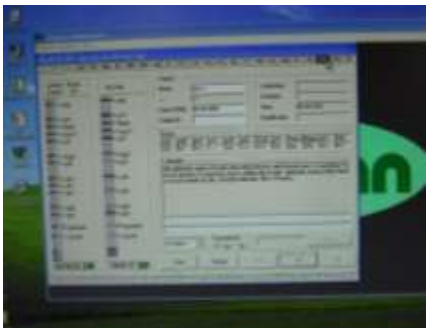
Virastripe printed blots
- Read by densitometer

Lyme C6 assay

DS2 ELISAbot

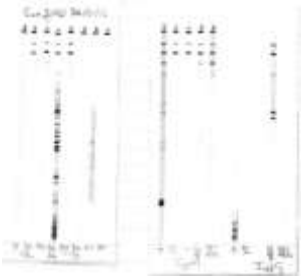
Q-pulse automated
Levy-Jennings QC

Blots



Why use a printed blot?

Defined bands
Machine readable
No background
Only the bands you want



Wider testing

Bartonella
- Currently via Colindale

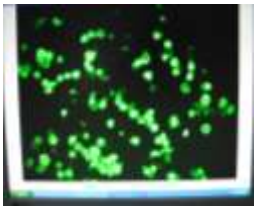
Rickettsia
- EuroImmun IF IgM & IgG

Anaplasma/Ehrlichia

Babesia
- Via HTD

Other tick borne diseases
- Q fever, tularemia,
- TBE complex, bunyaviruses

Other infectious causes of symptoms



Anaplasma phagocytophilum semi-automated immunofluorescence test

Finding the organism

Sampling & errors
- Skin best
- Blood
- CSF & synovium
- Biological limitations

Culture
- One time "Gold Standard"
- New techniques available

PCR

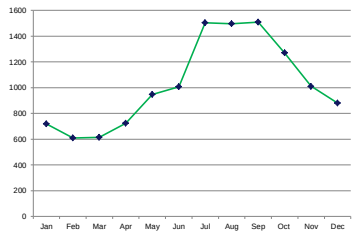
Real-time PCR based on Fla gene
- Sensitive within limits above (~50%)
- Can be combined with culture

Reporting the result

B.BURGDORFERI IgG/IgM (C6 EIA)	**POSITIVE**
Borrelia IgM Lineblot (virastripe)	
IgM to Borrelia P41 antigen	POSITIVE
IgM to Borrelia P39 antigen	Negative
IgM to Borrelia OspC antigen	POSITIVE
IgM to Borrelia Osp17 antigen	Negative
IgM to Borrelia VlsE antigen	Negative
Borrelia IgM Lineblot interpretation	**POSITIVE**
Borrelia IgG Lineblot (virastripe)	
IgG to Borrelia P83 antigen	Negative
IgG to Borrelia P58 antigen	Negative
IgG to Borrelia P43 antigen	Negative
IgG to Borrelia P39 antigen	Negative
IgG to Borrelia P30 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**

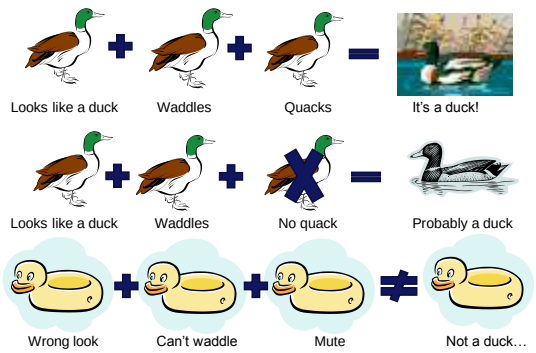
Composite report for early acute Lyme Disease

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



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)

Blood-borne and ST infections
Chemical and Radiation Threats and Hazards
Emergency Preparedness and Response
Emerging Infections (including Zoonoses)
Environmental Change and Health
Gastrointestinal Infections
Healthcare associated infections and AMR
Health impact of environmental hazards
Immunisation
Respiratory infections
Development of modelling methodology
Evaluation of interventions

HPRU in Emerging Infections (including Zoonoses) and Biological threats

Aims of EIZ HPRU

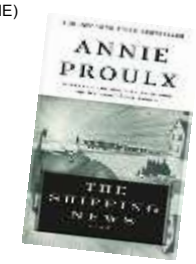
- Support and strengthen PHE in its role protecting England from emerging and zoonotic infections and biological threats
  - Internationally leading researchers at University of Liverpool and Liverpool School of Tropical Medicine and PHE
  - World class research facilities including
    - High containment 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

HPRU in Emerging Infections (including Zoonoses) and Biological threats

Theme 2: Epidemiological Approaches

Leads: Sarah O'Brien (UoL), Roberto Vivancos (PHE)

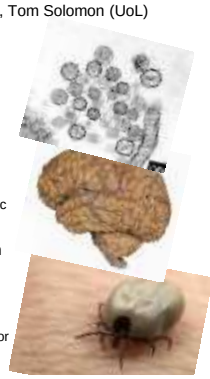
- **Project One: Real time surveillance and response**
  - Integrated syndromic surveillance and molecular diagnostic systems
- **Project Two: Sources of newly-emerged and zoonotic infections in the UK**
  - Importation of newly-emerged zoonotic pathogens into the UK
    - Using publically available 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)

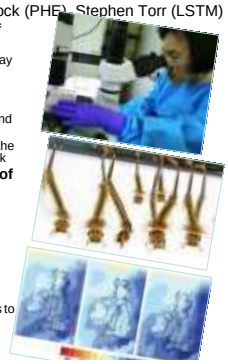
- **Project One: Improved surveillance and diagnosis of hantaviruses**
  - examine the relationship and link between hantavirus and acute kidney disease
    - a cohort study of patients acute kidney disease of unknown origin
    - prospective case-control study to examine risk factors
- **Project Two: 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.



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**
  - establish 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.



RIPL in-house research

In collaboration with Raigmore, Inverness

Organism identification

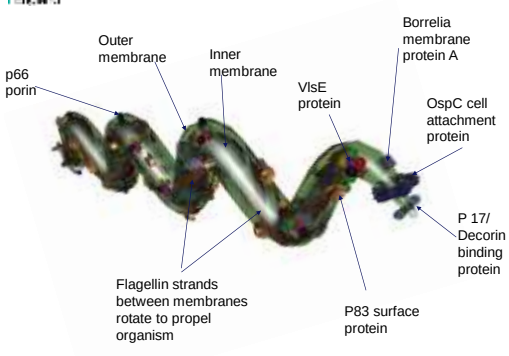
- Bespoke pan-borrelia PCR's*
- Species typing PCR*
- Wide coverage PCR's
- Large volume extraction
- Next generation sequencing (NGS)
- Cross-validation to culture

Improved serology

Data & social media mining

MiSeq NGS

Serology



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/HPAweb_C/1317141297288

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

PHE travelling tick collector

Thanks to Jackie Duggan for her EIZ slides