

NIHR Health Protection Research Unit in Emerging and Zoonotic Infections

UK research: plans and progress

Tim Brooks
PHE & HPRU EZI

LDA Annual Conference, 8th July 2017

NIHR Health Protection Research Unit in Emerging and Zoonotic Infections

Overview

- Scientific research in PHE; role of HPRUs
- HPRU EZI, Liverpool – introduction
- Lyme & TBD research through HPRU EZI
- Lyme & TBD research workshop, 1 June 2017
- Questions and challenges
- Government-commissioned reviews

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- a collaboration between Liverpool and Public Health England

Tom Solomon
Institute of Infection and Global Health, University of Liverpool
HPRU Director

David Brown Public Health England Colindale

Miles Carroll Public Health England Porton Down

Hilary Ranson Liverpool School of Tropical Medicine

Julian Hiscox HPRU Assistant Director

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Overarching aim: to support and strengthen PHE in its role of protecting England from emerging and zoonotic infections and threats

Novel infectious agents; inadequate diagnostics
→ Enhance **Pathogen Detection & Characterisation**

Clinical presentations poorly defined
→ Improve **Clinical Surveillance methods**

Limitations to pathogen detection and clinical surveillance
→ Optimise **Epidemiological Approaches**

To identify agents most likely to emerge
→ Strengthen **Risk Assessment of Emerging & Zoonotic Threats**

£4M (2014 – 2019) For mosquito- & tick-borne pathogens
→ Better Understanding of **Vector Biology & Climate Modelling**

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Clinical Surveillance

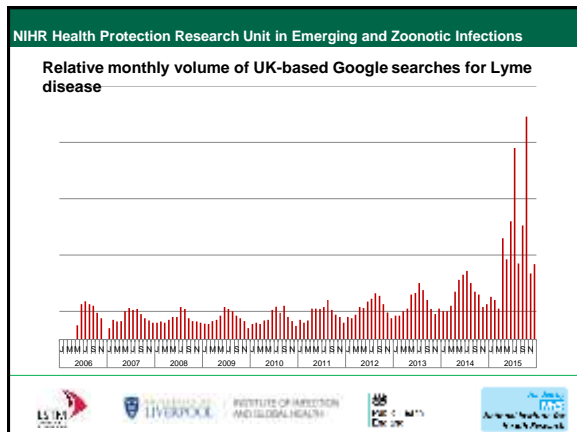
NIHR Clinical Surveillance is particularly an exciting area for research because it allows us to identify and track changes in infectious diseases in real time.

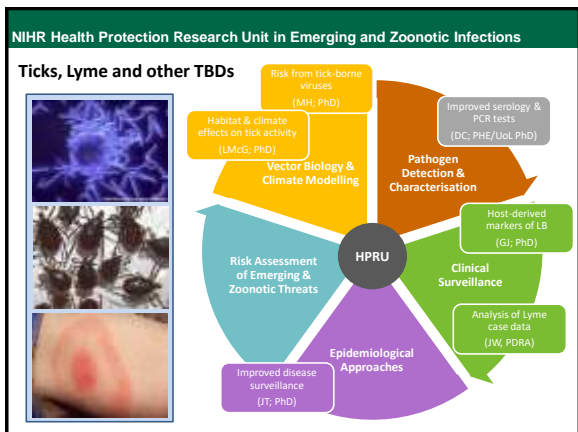
The overall aim is to improve clinical surveillance of infectious diseases to support PHE, strengthen and coordinate programmes, and to increase public engagement with disease surveillance at PHE and in academia.

Heather Leadford
NIHR Clinical Surveillance Programme Director, NIHR

Julian Hiscox
Head of the Institute of Infection and Global Health, University of Liverpool

Dr. Tim Brooks
Head of the Unit and National Pathogen Laboratory, Liverpool





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HPRU EZI Lyme and TBD Working Group

Integrates expertise in tick-borne diseases across the HPRU and provides a strategic focus to identify, co-ordinate and maximise the research output on tick-borne diseases by the HPRU EZI

'Improve our knowledge of ticks and tick-borne diseases in the UK in order to improve public health and patient outcomes'

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First meeting: **14th December 2016, Liverpool**

Top 4 actions:

- 1) Mission statement for HPRU EZI
- 2) Meet with Scottish TBD research groups
- 3) ~~Prioritise research – feasibility, fund-ability~~
- 4) Apply for pump-priming (small, doable, fast)

=>NIHR HPRU EZI STRATEGIC RESEARCH FUND CALLS 2017/18

£3K for workshop to bring together UK research groups

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Lyme & other tick-borne diseases: Present & future research in the UK

June 1st 2017, Edinburgh

A workshop funded by: the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Emerging and Zoonotic Infections at University of Liverpool in partnership with Public Health England (PHE), in collaboration with Liverpool School of Tropical Medicine. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health or Public Health England.

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Lyme & other tick-borne diseases: Present & future research in the UK

June 1st 2017, Edinburgh

Aims

- To bring together the UK's leading research groups in the area of ticks and the zoonotic diseases they carry
- To review current research activities across the UK
- To identify areas of synergy between different groups
- To facilitate networking and building new partner networks
- To identify research gaps not currently being addressed
- To identify funding sources and infrastructure requirements to address research priorities around ticks and TBDs in the UK







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Participant areas of interest

Area of Interest	Count
Tick ecology, Surveillance, Risk management	15
Public health	10
Epidemiology & Disease surveillance	12
Diagnostics & Immunology	10
Behavioural science	5
Clinical management	5
Other	4

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0930	Lyme & other tick-borne diseases in the UK: a clinical perspective - Nick Beeching, UoM
0945	Session 1: Tick ecology, surveillance and risk management
0950	• Topic overview - Roman Bull, University of Glasgow
0955	• Flash presentations from participants
1000	• Discussion
1100	0955-1000
1100	Session 2: Disease epidemiology, public health and behavioural science
1105	• Topic overview - Tim Brooks, Public Health England
1110	• Flash presentations from participants
1115	• Discussion
1200	1115-1200
1200	Session 3: Diagnostics & Immunology
1205	• Topic overview - Tim Brooks, Public Health England
1210	• Flash presentations from participants
1215	• Discussion
1300	1215-1300
1300	Breakfast groups
1345	Feedback & next steps
















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Session 1: Tick ecology, surveillance and risk management

Ongoing research in both Scotland and England covering:

- Tick surveillance in environment and on hosts (e.g. dogs, deer)
- Spatial and temporal variation in:
 - tick abundance / activity
 - prevalence of *Borrelia* spp. in ticks
- Environmental factors (e.g. climate, habitat, host species, host density) affecting ticks and tick-borne diseases
 - Effects on tick abundance
 - Effects on tick activity
 - Effects on prevalence of *Borrelia* in ticks
 - Effects on prevalence of *Borrelia* genospecies in ticks
- Modelling to better predict tick activity for public health messaging
- Evidence-based habitat management to reduce tick risk to humans














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Session 1: Tick ecology, surveillance and risk management

Key unanswered questions and knowledge gaps:

- How does infection risk in ticks relate to the actual number of human LD cases?
 - Need multidisciplinary studies across different geographical areas
- What is the role of game species e.g. deer, pheasants?
 - How could altered game management change TBD risk?
- What is the effect of small mammal hosts and their density?
 - Lack of small mammal ecologists; need for animal licenses etc
- Need for long term studies (>3 yrs) with regular sampling
- Need for harmonised protocols for tick surveys and related ecological measures e.g.
 - No. sampling sites; frequency of sampling; methodology for determining number of infected ticks
- Need formal trials of management interventions with standardised outcome measures














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Session 2: Disease epidemiology, Public Health & Behavioural Science

Ongoing research/ analysis in Scotland and/or England:

- Surveillance of laboratory confirmed cases of LD in both countries
- Clinicians are encouraged to treat LD empirically if diagnosed based on EM rash
- Existing seroprevalence data for Scotland based on study of blood donors
- Scottish NLBTL works with local GPs in Highlands for enhanced surveillance
 - Regional variability in LD incidence
- PhD study looking at value of primary care and hospital episode data to better estimate LD incidence in E & W



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
Session 2: Disease epidemiology, Public Health & Behavioural Science

Key unanswered questions and knowledge gaps:

- What is the true incidence of LD (& other TBDs) in the UK?
 - Need enhanced surveillance studies
 - Access/improve primary care & secondary care data
 - Recording systems differ in England & Scotland
- Need understanding of regional variation in LD incidence to measure the response to interventions
- What is the economic burden of LD to primary & secondary care?
- Where are people actually exposed? Need better geographical data.
 - Need enhanced surveillance studies (patient postcode not sufficient)
- What public health interventions/messages are effective?
 - Need behavioural studies
- Have changes in human behaviour increased exposure to ticks & TBDs?













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Session 3: Diagnostics & Immunology

Ongoing R&D in Scotland and/or England covering:

- Improvements to existing PCR tests to cover e.g. *B. miyamotoi*
- Using proteomics & genomics of *Borrelia* to identify antigens that may improve current serological tests
- Expression & characterisation of borrelial proteins
- Evaluation of host-derived biomarkers of early Lyme disease
- Evaluation of *Borrelia* bacteriophages as diagnostic and therapeutic tools
- Investigation of new commercial assays for improved serological diagnosis of Anaplasma
- Developing assays (veterinary) for Louping ill virus (a tick-borne encephalitis virus)



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Session 3: Diagnostics & Immunology

Key unanswered questions and knowledge gaps:

- Need diagnostic tests that have better sensitivity in early Lyme
- Need tests that can distinguish active from non-active Lyme
- What is the effect of antibiotic treatment on the evolution of the host antibody response?

⇒ To evaluate potential new diagnostic tests need:

- Well-characterised UK patient samples from longitudinal and cross-sectional studies
- Robust and harmonised case definitions
- Need better understanding of the disease course
 - What *Borrelia* spp are associated with different presentations/outcomes
 - What are the best clinical management strategies for different courses
 - Can *Borrelia* be dormant in man?

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Challenges

Funding

- Justification - need better data on true LD incidence & costs to NHS
- Multidisciplinary studies will need funding body consortia
- Sustained funding for longitudinal studies (clinical or tick surveillance)

Clinical studies

- Longitudinal studies need GP involvement
- Multiple GP practices to recruit sufficient cases
- Logistical challenge
- Lack of research-active clinical groups in UK for Lyme

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James Lind Alliance
Priority Setting Partnership

LDA
Lyme Disease Alliance

Lyme Disease Top 10

1. How effective are the current UK tests in detecting infections due to the protozoan and stages of it? Is there one which might best and/or a combination of tests perform best in diagnosing or ruling out early Lyme disease? Should stages of the disease and patient age be taken into account when developing these tests?
2. What key questions (to test) are serological tests of utility considered to help make a diagnosis of Lyme disease in children and adults in the UK and would a weighting table be useful?
3. What is the best treatment for children and adults presenting with early Lyme disease without knowledge of serological test result including maintenance and by late Lyme disease of any serological? To include consideration of health, side effects.
4. What is the optimal course of action if symptoms improve after a treatment course is finished?
5. What is the optimal course of action if symptoms persist after initial treatment - should antibiotic treatment be continued until all symptoms have resolved or should a different drug or different antibiotic be considered until all the cause of infection treatment appears to have responded?
6. What are the outcomes of cases where drug based treatment has been used?
7. How common is relapse and treatment failure and is it related to disease stage, gender, co-infections or any other factor?
8. Are there drug resistance considerations if treatment is repeated or changed?
9. Are combining symptoms allowing conventional environmental treatment due to continued infection, or an alternative response of other species?
10. Can Lyme be transmitted via other vectors - animal to human directly, translocation of by insect feeding, through human to human - through blood transfusion?

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Government initiatives (2016-2018)

NICE Guidance on the Diagnosis & Management of Lyme Disease

- Due Summer 2018

Independent systematic review of scientific evidence base

- Commissioned by DH (EPPI-Centre, UCL)
- 3 reviews
 - Prevalence & incidence
 - Diagnosis
 - Treatment
- Due autumn 2017

Outcomes: ??evidence gaps; recommendations for funding.....

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Edinburgh Workshop: Participant Feedback
(All scores out of 10)

Activity	Score (out of 10)
Overview Talks	9
Lightning presentations	9
Group discussions	9
Breakout activity	8
Opportunities to network	9
Venue/ Catering	8

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THANKS!!

Jenny Warner
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John Tulloch

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