

# **ANNUAL REPORT OF BRUCELLA REFERENCE UNIT FOR BRUCELLA SERO-DIAGNOSIS, 2008 – 2009.**

## **INTRODUCTION**

Brucellosis is a zoonotic disease with a high prevalence in the Mediterranean, Middle East, Latin America and Asia. Annual reports by the UK's Department of Environment Food and Rural Affairs indicate that cases of human brucellosis are rarely reported from this country. Though some cases are acute (reflecting travel to endemic areas and ingestion of infected, unpasteurized animal-milk products) and diagnosed by blood culture and / or serology, the majority are chronic infections. These cases often reflect occupational exposure to infected cattle and are usually only diagnosed serologically.

The Brucella Reference Unit (BRU) at University Hospital Aintree, Liverpool offers a Brucella sero-diagnosis service for England, Wales, Eire and Northern Ireland. Due to its protean clinical features and lack of truly diagnostic tests, brucellosis remains a difficult disease to diagnose, particularly in non-endemic countries with a low prevalent population such as the UK. BRU therefore encourages users of the service to complete a detailed clinical request form (see [www.hpa.co.uk](http://www.hpa.co.uk)). However, serological results often have to be interpreted with only minimal clinical information. As a consequence, BRU provides a panel of 5 sero-diagnostic tests to ensure that results are of high sensitivity. Specificity is less of a concern in non-endemic countries and BRU has a policy of simply requesting a follow-up serum for one-off low level positive titres (reactive samples) which are typically reported as 'non-diagnostic'.

This first annual report of the BRU outlines the work of the department from April 2008 – March 2009.

## **WORKLOAD**

BRU received 3371 serum samples for sero-diagnosis during April 2008 to March 2009. This reflects a 35% increase in workload in comparison with previous years (average annual workload 2500 samples). 3208 (95.2%) were screen negative, defined as Brucellacapt titre < 1/80, Brucella Ig G EIA < 1/20 and Brucella Ig M < 1/20. Of the 163 'reactive samples, only 11 patients (6.8%) were identified as having evidence of brucellosis at some time (see below).

BRU's sero-diagnostic services were used by 199 different hospital, veterinary or private laboratories, see Table 1

## **POSTIVE BRUCELLA SEROLOGY RESULTS**

Using a Brucellacapt titre cut off of > 1/320 with raised titres in other tests (Brucella IgM / Ig G, complement fixation and micro- agglutination) with an interpretative comment indicating a positive serological result, a total of 11 patients were identified as having significant serological results. An analysis of these patients and their serological profiles is summarised in Table 2. In all cases, BRU's interpretative comment on the serological profile indicated 'Brucella infection at some time' and a recommendation was given for a follow up serum sample to be taken in one month's time. Unfortunately, this was undertaken in only one case.

Reflecting the increased collaboration between the BRU and the Veterinary Laboratory Agency's (VLA) Brucellosis Reference Laboratory, all Brucella isolates identified by the VLA from human infections in 2008-2009 and corresponding brucella serological profiles are presented in Table 3.

## **EXTERNAL QUALITY ASSURANCE**

In the absence of a national/international external quality assurance (EQA) scheme for human Brucella serology, BRU has established a collaborative EQA scheme with the Department of Pathology and Laboratory Medicine, American University of Beirut Medical Centre, Lebanon (Departmental Head Professor George F Arag). This has been in place since December 2006. EQA results for this year has shown concordant results between the two laboratories.

## **SERVICE DEVELOPMENTS**

### **A. Management of exposure to Brucella isolates within the microbiology laboratory**

BRU has received an increased number of telephone calls from Consultant Medical Microbiologists across the UK seeking advice on the appropriate management of laboratory staff who have been inadvertently exposed to a Brucella isolate whilst performing a diagnostic procedure (See [www.cdc.gov/neidod/dbmd/diseaseinfo/brucellosis\\_g.htm](http://www.cdc.gov/neidod/dbmd/diseaseinfo/brucellosis_g.htm) ).

BRU is currently recommending actions similar to CDC US guidance but intends to produce its own written advice which will be shortly available on the HPA website.

### **B. Clinical Management of Brucella Infection**

With enhanced links with the Brucella Reference Laboratory, VLA, BRU now receives a copy report of all Brucella isolates from human cases. Once local ethical approval has been confirmed, BRU intends to contact the referring laboratory to discuss clinical management and review the containment procedures used to minimise laboratory exposure on a case by case basis.

### **C. Brucella HPA Website**

This is regularly reviewed and updated as required. New developments will include 'Frequently asked questions', useful links, Annual report, publications, posters and documentation on action to take following a laboratory exposure to Brucella.

### **D. Improved reporting to the HPA's Zoonoses Surveillance Unit**

All BRU reports which suggest Brucella infection are now copied to Dr Robert Smith, Epidemiologist, HPA Zoonoses Surveillance Unit.

## **PRESENTATIONS**

18<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases, Barcelona, April 2008. Laboratory acquired brucellosis – review of published reports. Brown CE, Beeching NJ, Cooke RPD. (Poster)

<http://www.blackwellpublishing.com/eccmid18/abstract.asp?id=69750>

Brucellosis 2008 International Conference, London 2008. Laboratory acquired brucellosis – a review of published reports 1950 – 2007. Brown CE, Beeching NJ, Cooke RPD (Talk)

<http://www.blackwellpublishing.com/eccmid18/abstract.asp?id=69750>

Brucellosis 2008 International Conference, London 2008 Neurobrucellosis in the UK. Cooke RPD, Rothburn MM, Beeching NJ (Poster)

[http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6WJT-4V402DG-3&\\_user=3525477&\\_rdoc=1&\\_fmt=&\\_orig=search&\\_sort=d&\\_docanchor=&\\_view=c&\\_acct=C000052736&\\_version=1&\\_urlVersion=0&\\_userid=3525477&md5=aca0f1fd20b3e6293e6c06acf859d0ea](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WJT-4V402DG-3&_user=3525477&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&_view=c&_acct=C000052736&_version=1&_urlVersion=0&_userid=3525477&md5=aca0f1fd20b3e6293e6c06acf859d0ea)

Brucellosis 2008 International Conference, London 2008. A review of laboratory- acquired brucellosis infection and exposures amongst clinical laboratory staff in UK. Cooke RPD, Mohandas K, Perrett L, Beeching NJ (Poster)

[http://www.hpa.org.uk/web/HPAwebFile/HPAweb\\_C/1233906818744](http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1233906818744)

Federation of Infection Societies Scientific Meeting, Cardiff 2008. Neurobrucellosis in the UK. Cooke RPD, Rothburn MM, Beeching NJ (Poster PO32)

Federation of Infection Societies Scientific Meeting, CARDIFF 2008. Laboratory acquired brucellosis – a review of published reports 1950 – 2007. Brown CE, Beeching NJ, Cooke RPD (Poster, P1110)

Federation of Infection Societies Scientific Meeting, Cardiff 2008. A review of laboratory-acquired Brucella Infections and exposures amongst clinical microbiology staff in the UK. Cooke RPD, Mohandas K, Perrett L, Beeching NJ. (Poster P111)

### **PUBLICATIONS**

RPD Cooke, Beeching NJ Neurobrucellosis in the UK. J Infect 2009; 58: 88-89

[http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6WJT-4V402DG-3&\\_user=3525477&\\_rdoc=1&\\_fmt=&\\_orig=search&\\_sort=d&\\_docanchor=&\\_view=c&\\_acct=C000052736&\\_version=1&\\_urlVersion=0&\\_userid=3525477&md5=aca0f1fd20b3e6293e6c06acf859d0ea](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WJT-4V402DG-3&_user=3525477&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&_view=c&_acct=C000052736&_version=1&_urlVersion=0&_userid=3525477&md5=aca0f1fd20b3e6293e6c06acf859d0ea)

Sharma R, Chisnall C, Cooke RPD. Evaluation of in-house and commercial immunoassays for the sero-diagnosis of brucellosis in a non-endemic low prevalence population. J Infect 2008; 56: 108-113

[http://www.sciencedirect.com/science?\\_ob=ArticleListURL&\\_method=list&\\_ArticleListID=945196211&\\_sort=d&\\_view=c&\\_acct=C000052736&\\_version=1&\\_urlVersion=0&\\_userid=3525477&md5=284eb2cfb7b6143fae0d2084c52a64c1](http://www.sciencedirect.com/science?_ob=ArticleListURL&_method=list&_ArticleListID=945196211&_sort=d&_view=c&_acct=C000052736&_version=1&_urlVersion=0&_userid=3525477&md5=284eb2cfb7b6143fae0d2084c52a64c1)

### **RESEARCH PROJECTS IN PROGRESS**

1. In house study to quantify Brucella antibody levels standard international units.
2. Comparison of enzyme immunoassays for sero-diagnosis of brucellosis. Collaborative project with the Brucella Reference Laboratory, VLA.

RPD Cooke  
Consultant Medical Microbiologist  
And Honorary Senior Lecturer, BRU

Colin Chisnall  
Chief Biomedical Scientist, BRU

L. Perrett  
FAO/WHO/OIE Collaborating for Referencing and  
Research on Brucellosis VLA, Surrey

NJ Beeching  
Senior Lecturer,  
Liverpool School of Tropical Medicine

**TABLE 1 – LIST OF LABORATORIES REFERRING TO BRUCELLA REFERENCE UNIT**  
**2008 – 2009**

AINTRIM AREA HOSPITAL  
ALTNAGELVIN AREA HOSPITAL  
ASHWORTH HOSPITAL NORTH  
ASHWORTH HOSPITAL OCCUPATIONAL HEALTH  
BARNET GENERAL HOSPITAL  
BARTS & LONDON NHS TRUST  
BASILDON HOSPITAL  
BASSETLAW HOSPITAL  
BEAUMONT HOSPITAL  
BEDFORD GENERAL HOSPITAL  
BELFAST CITY HOSPITAL  
BELFAST LINK LABORATORIES  
BIRMINGHAM CHILDRENS HOSPITAL  
BLACKROCK CLINIC  
BOLTON GENERAL HOSPITAL  
BON SECOURS - CORK  
BON SECOURS - DUBLIN  
BON SECOURS - TRALEE  
BORDERS GENERAL HOSPITAL  
BRIGHTON & SUSSEX UNIVERSITY HOSPITAL  
CAMBRIDGE MICROBIOLOGY  
CARDIFF UNIVERSITY HOSPITAL WALES  
CAUSEWAY LABORATORY  
CHELSEA & WESTMINISTER HOSPITAL  
CHELSFIELD PARK HOSPITAL  
CHILDRENS UNIVERSITY HOSPITAL DUBLIN  
CLAYMON LABORATORIES DUBLIN  
COLCHESTER GENERAL HOSPITAL  
CONQUEST HOSPITAL  
CPL INTERNATIONAL  
CRAWLEY HOSPITAL  
CROSSHOUSE HOSPITAL  
DARENT VALLEY HOSPITAL  
DERBY CITY GENERAL HOSPITAL  
DERBY CITY GENERAL HOSPITAL  
DIANA PRINCESS OF WALES HOSPITAL  
DORSET COUNTY HOSPITAL  
DR MARY CROWLEY 74 NEWTON PARK  
DUMFIRES ROYAL INFIRMARY  
EAST KENT MICROBIOLOGY  
EASTBOURNE DISTRICT GENERAL HOSPITAL  
FIFE AREA LABORATORY  
FIFE AREA LABORATORY

FRIMLEY PARK HOSPITAL  
FURNESS GENERAL HOSPITALS TRUST  
GALWAY CLINIC DOUGHISKI  
GATESHEAD HEALTH NHS TRUST  
GOODHOPE HOSPITAL SUTTON COLDFIELD  
GREAT ORMOND STREET HOSPITAL  
GWENT HEALTHCARE NHS TRUST  
HAMMERSMITH HOSPITAL - VIROLOGY  
HARROGATE DGH  
HCA LABORATORIES  
HEREFORD MICROBIOLOGY  
HILLINGDON HOSPITAL  
HMP ALT COURSE  
HMP RISLEY  
HMP WALTON  
HOMERTON HOSPITAL  
HOPE HOSPITAL  
ISLE OF WIGHT HOSPITAL  
JAMES CONNOLLY MEMORIAL HOSPITAL  
JAMES COOK UNIV HOSPITAL MIDDLESBOROUGH  
JAMES PAGET NHS TRUST  
KETTERING GENERAL HOSPITAL  
KING GEORGE HOSPITAL  
KINGS COLLEGE HOSPITAL  
KINGS MILL HOSPITAL  
KINGSTON HOSPITAL  
LEICESTER ROAL INFIRMARY  
LEIGHTON HOSPITAL  
LETTERKENNY GENERAL HOSPITAL  
LIMERICK REGIONAL HOSPITAL  
LISTER HOSPITAL  
LIVERPOOL TROPICAL SCHOOL  
LUTON MICROBIOLOGY  
MACCLESFIELD DISTRICT GENERAL HOSPITAL  
MAIDSTONE & TUNBRIDGE MICROBIOLOGY  
MANCHESTER ROYAL INFIRMARY  
MANOR HOSPITAL  
MATER GENERAL HOSPITAL  
MATER PRIVATE HOSPITAL  
MAYDAY UNIVERSITY HOSPITAL  
MEDWAY MARITIME HOSPITAL  
MEHT MICROBIOLOGY CHELMSFORD  
MEHT MICROBIOLOGY DEPARTMENT  
MICROBIOLOGY - GIBRALTAR  
MICROBIOLOGY - ROYAL OLDHAM  
MID ESSEX HOSPITAL TRUST

MIDLAND REGIONAL HOSPITAL TULLAMORE  
MUSGROVE PARK HOSPITAL  
NATIONAL VIRUS REFERENCE LABORATORY  
NEVILL HALL HOSPITAL  
NEW CROSS HOSPITAL  
NINEWELLS HOSPITAL DUNDEE  
NOBLES HOSPITAL ISLE OF MAN  
NORFOLK & NORWICH HOSPITAL  
NORTH DEVON DISTRICT HOSPITAL  
NORTH HAMPSHIRE HOSPITAL  
NORTH MANCHESTER GENERAL HOSPITAL  
NORTH MIDDLESEX HOSPITAL  
NORTH STAFFORDSHIRE HOSPITAL  
NORTH TYNESIDE GENERAL HOSPITAL  
NORTHAMPTON GENERAL HOSPITAL  
NORTHUMBRIA NHS TRUST  
NORTHWICK PARK HOSPITAL  
NOTTINGHAM MICROBIOLOGY  
OUR LADY OF LOURDES HOSPITAL  
OUR LADY'S HOSPITAL FOR SCIK CHILDREN  
POOLE HOSPITAL  
PORTSMOUTH MICROBIOLOGY  
PRESTON HALL HOSPITAL  
PRINCESS ALEXANDRA HOSPITAL HARLOW  
PRINCESS ROYAL UNIVERSITY HOSPITAL  
QUEEN ELIZABETH HOSPITAL BIRMINGHAM  
QUEEN ELIZABETH HOSPITAL GATESHEAD  
QUEEN ELIZABETH HOSPITAL WOOLWICH  
QUEEN MARYS HOSPITAL SIDCUP  
QUEENS UNIVERSITY HOSPITAL NOTTINGHAM  
REGIONAL VIRUS LABORATORY  
ROTHERHAM GENERAL HOSPITAL  
ROYAL BELFAST HOSPITAL FOR SICK CHILDREN  
ROYAL BERKSHIRE & BATTLE HOSPITAL  
ROYAL CORNWALL HOSPITAL  
ROYAL DEVON & EXETER HOSPITALS  
ROYAL GLAMORGAN HOSPITAL  
ROYAL GWENT HOSPITAL  
ROYAL HAMPSHIRE CITY HOSPITAL  
ROYAL HOSPITAL HASLAR GOSPORT  
ROYAL INFIRMARY EDINBURGH  
ROYAL LANCASTER HOSPITAL  
ROYAL MARSDEN NHS TRUST  
ROYAL OLDHAM HOSPITAL  
ROYAL VICTORIA EYE & EAR HOSPITAL  
ROYAL VICTORIA HOSPITAL

RUSSELLS HALL HOSPITAL  
S T BARTHOLOMEWS  
SALFORD ROYAL ACUTE NEURO (HOPE HOSPITAL)  
SALISBURY DISTRICT GENERAL HOSPITAL  
SCARBOROUGH & NE YORKSHIRE TRUST  
SHEFFIELD REGIONAL MICROBIOLOGY  
SHERWOOD FOREST HOSPITALS  
SINGLETON HOSPITAL SWANSEA  
SOUTHAMPTON MICROBIOLOGY  
SOUTHEND HOSPITAL  
SPERRIN & LAKELAND TRUST  
ST ANTHONYS HOSPITAL  
ST BARTHOLOMEWS HOSPITAL  
ST GEORGES HOSPITAL  
ST HELIER HOSPITAL  
ST JAMES HEALTH CENTRE  
ST JAMES HOSPITAL DUBLIN  
ST JOHNS HOSPITAL LIMERICK  
ST LUKES HOSPITAL - MALTA  
ST MARYS HOSPITAL LONDON  
ST MARYS HOSPITAL NEWPORT  
ST MARYS HOSPITAL PADDINGTON  
ST MARYS HOSPITAL PORTSMOUTH  
ST MICHAELS HOSPITAL  
ST PETERS HOSPITAL  
ST RICHARDS HOSPITAL  
ST THOMAS HOSPITAL OF INFECTION  
ST VINCENTS HOSPITAL  
STAFFORDSHIRE GENERAL HOSPITAL  
STEPPING HILL HOSPITAL  
STOKE MANDEVILLE HOSPITAL  
SUNDERLAND ROYAL HOSPITAL  
TAMESIDE & GLOSSOP HOSPITAL  
TAMESIDE LABORATORIES  
TAUNTON MICROBIOLOGY  
TELFORD MICROBIOLOGY  
THE DOCTORS LABORATORY  
THE ERNE HOSPITAL  
THE JOHN RADCLIFFE HOSPITAL  
THE NORTH HAMPSHIRE HOSPITAL  
THE PRIORY HOSPITAL BIRMINGHAM  
THE ROYAL BOLTON HOSPITAL  
THE ROYAL FREE HOSPITAL  
THE ROYAL LONDON HOSPITAL  
TORBAY HOSPITAL TORQUAY  
TULLAMORE GENERAL HOSPITAL

TYRONE COUNTY HOSPITAL OMAGH  
UCL HOSPITALS NHS TRUST  
UNIVERSITY COLLEGE HOSPITAL LONDON  
UNIVERSITY HOSPITAL LEWISHAM  
VETERINARY LABORATORIES AGENCY  
VIROLOGY - HAMMERSMITH HOSPITAL  
WARWICK HOSPITAL  
WATERFORD REGIONAL HOSPITAL  
WATFORD GENERAL HOSPITAL  
WEST PARK HOSPITAL  
WEST SUFFOLK HOSPITAL  
WEXHAM PARK HOSPITAL  
WHIPPS CROSS UNIVERSITY HOSPITAL  
WHITTINGTON HOSPITAL  
WORCESTERSHIRE ROYAL HOSPITAL  
WORTHING HOSPITAL  
WRIGHTINGTON HOSPITAL  
WYCOMBE HOSPITAL

**Table 2- ANALYSIS OF PATIENTS WITH SIGNIFICANT BRUCELLA SEROLOGY 2008/2009**

<u>Non- UK Nationality</u>	<u>Age (Years)</u>	<u>Sex</u>	<u>Brucellapt Titre</u>	<u>Ig G Titre</u>	<u>IgM Titre</u>	<u>MAG Titre</u>	<u>CFT Titre</u>	<u>Referring source</u>	<u>Clinical Details</u>	<u>Follow up serology</u>
YES	48	M	5120	40	<20	>2560	<4	University College London	'Brucellosis in 2007'	NO
YES	6		2560	160	<20	160	64	St Mary's Hospital London	'Post Brucellosis'	NO
YES	45	F	1280	20	<20	160	64	Leeds General Hospital	'Post Brucellosis'	NO
YES	39	M	5120	640	<20	640	256	St George's Hospital London	'Fever, Weight loss, Shoulder pain, unpasteurised cheese in Greece'	Yes
NO	45	M	640	160	<20	40	256	Private Laboratory	Nil	NO
NO	42	M	320	80	<20	80	8	Veterinary Laboratory Agency	Nil	NO
NO	19	F	1280	20	20	160	<4	Antrim, N Ireland	'Fever'	NO
NO	50	M	>5120	160	<20	320	128	Blackrock Clinic Dublin	Nil	NO
YES	67	F	2560	40	160	160	64	University College London	'Brucellosis in Turkey'	NO
YES	19	F	1280	80	<20	80	128	University College London	'Post Brucellosis'	NO
NO	40	M	320	160	<20	80	16	Private Laboratory London	'Post Brucellosis'	NO

**Table 3 - COMPARISON OF HUMAN BRUCELLA ISOLATES AND SEROLOGICAL PROFILES 2008 – 2009**

Non-UK Nationality	Age (Years)	Sex	Brucellacapt Titre	MAG Titre	IgG Titre	IgM CFT Titre	Referring Hospital	BRU Comment
YES	30	M	1/1640	<1/20	1/20	1/160	John Radcliffe, Oxford	Brucella infection at some time
YES	29	M	1/1280	1/80	<1/20	1/80	University College London	Brucella infection at some time
YES	38	F	1/5120	160	80	1/2560	Derby City	Brucella Infection at some time

\* \*All isolated from blood culture

