

Brucella Reference Unit: Frequently Asked Questions

Q. Does the Brucella Reference Unit (BRU) at Aintree deal with both sera and culture isolates?

A. No. The BRU provides a Brucella serodiagnosis service only. However, there is close collaboration with the Brucellosis Reference Laboratory of the Veterinary Laboratory Agency to whom all suspect culture isolates should be sent. For further information on referral of cultures, please contact Lorraine Perrett at lorraine.perrett@ahvla.gsi.gov.uk or on telephone number +44 (0)1932 357350 (alternative number 01932 357610).

Q. Does the BRU provide advice on the diagnosis and clinical management of Brucellosis?

A. Yes. Please contact either Dr Richard Cooke, Consultant Medical Microbiologist and Honorary Senior Clinical Lecturer in Medical Microbiology; Email: richard.cooke@aintree.nhs.uk; Telephone: 0151 931 1261; Fax: 0151 529 4918, or Dr Nick Beeching, Senior Lecturer (Clinical) in Infectious Diseases, Clinical Group, Liverpool School of Tropical Medicine; Email: nbeeching@blueyonder.co.uk; Telephone: 0151 706 3835.

Q. How likely is my patient to have brucellosis?

A. Brucellosis is a rare disease in the UK as it is a non-endemic country (except Northern Ireland). Typically, patients should have come from or have been born in a Mediterranean or Middle Eastern country. A detailed travel history is vital. Please use BRU's Serology Request Form to provide us with as much clinical details as possible.

Q. Does a negative Brucella antibody screening test exclude brucellosis?

A. The screening tests used at BRU are very sensitive (i.e. low false negatives). However, if there is a strong clinical suspicion, it is good practice to repeat the test after a 6 week period.

Q. Is serology useful in monitoring response to treatment?

A. No. Brucella antibody titres fall slowly after treatment. Follow up serology is therefore generally not recommended.

Q. How frequently are serology tests performed at BRU?

A. Weekly. However, if there is a clinical urgency, please contact our Biomedical Scientific Staff on telephone number 0151 529 4900

Q. Can BRU assist in the diagnosis of neurobrucellosis?

A. Yes, see recent report at http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1233906817853. This is a very rare condition in the UK. Negative serology should exclude the diagnosis so always send a serum sample in the first instance. Cerebrospinal fluid (CSF) will be examined for Brucella antibody only if there is evidence of Brucella sero-reactivity.

Q. What should I do if laboratory staff have been exposure to a *Brucella* isolate?

A. See the guidance document at http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1263812749489
The following steps are recommended:-

1. Notify the local occupational health department and classify exposures as high or low risk. The number of laboratory staff in each exposure category should be determined. Definitions of high and low risk exposure should follow guidance produced by the USA Centers for Disease Control (www.cdc.gov/neidod/dbmd/disease/info/brucellosis)
2. Contact BRU to ensure an 'ILOG' number is issued for the incident. All serum samples from exposed laboratory staff should have request forms sent with the 'ILOG number' included. This will allow BRU to rapidly review the serology results of exposed staff. Serum should be sent at 0, 6 and 24 weeks after exposure.
3. Post exposure prophylaxis (PEP) should be recommended for all workers with a high risk exposure to a Brucella isolate. This should be offered as soon as possible after exposure has been identified (and up to the end of the 6 month incubation period). Monotherapy with doxycycline 100mg twice daily is recommended (see BRU's review of published reports of laboratory acquired brucellosis 1950-2007). For those with a contraindication to doxycycline, trimethoprim – sulfamethoxazole (160mg/800mg) used tds for 3 weeks.

4. For pregnant laboratory workers with a high-risk *Brucella* exposure the following options should be considered:-

- A) Rifampicin 600mg once daily alone for 3 weeks
- B) Rifampicin plus co-trimoxazole and folic acid supplements for 3 weeks
- C) Observation only.

The most appropriate choice should be made in consultation with the member of staff's obstetrician.

5. A laboratory exposure to a *Brucella* isolate is reportable under RIDDOR Regulations (<http://www.hse.gov.uk/riddor/>) and should be therefore notified to the Health and Safety Executive

6. Regardless of exposure risk, all exposed individuals should be monitored for the development of symptoms for 6 months from the last exposure. Symptoms are typically non-specific and include fever, headache, low back pain, joint pain, malaise, anorexia and weight loss.

Q. How can a laboratory exposure to a *Brucella* isolate be avoided?

A. The following good practice guidelines are recommended:-

1. When Brucellosis is suspected, clinicians should note the suspicion of Brucellosis on the laboratory request form. However, clinical details are often insufficient to identify high risk specimens when received in the laboratory. Microbiology laboratories should therefore consider reviewing all blood culture request forms on receipt. Blood culture request forms indicating fever and either a significant travel history or from a patient of Middle Eastern origin should be preferably processed in a containment level 3 facility.

2. In the UK, all *Brucella* isolates over the past 5 years have been isolated only from blood culture. Hence all unusual small Gram-negative or Gram-variable rods from blood culture which are oxidase positive should be examined in a containment Level 3 facility using a Class I safety cabinet.

3. Prohibit the sniffing of opened culture plates to assist in the identification of isolates.

Q. Can routine brucella screening antibody tests exclude *Brucella canis* infection (eg following a dog bite injury)?

A. *Brucella canis* lacks surface lipopolysaccharide (LPS) and therefore will illicit only a minimal anti-LPS immunological response, hence suspected *B. canis* infection will not be identified by standard brucella antibody screening tests. Consequently, *Brucella canis* serology should be specifically requested on the request form if infection due to this species is suspected.

Q. If a *Brucella sp* is isolated from a human infection, should antimicrobial sensitivity tests be performed?

A. No, there is no evidence that antimicrobial resistance has emerged to the standard agents in the treatment of human brucellosis. However, a collaborative study between the BRU and the Veterinary Laboratories Agency is underway to confirm this point for *Brucella* isolates identified in UK patients.

Q. Is urine a risk body fluid substance for brucella exposure?

A. Patients with brucella epididymis-orchitis are typically diagnosed on the basis of positive blood cultures and serology.

It is uncommon for urine analysis to show abnormalities. Similarly, the yield from urine culture from brucella is extremely low. However, routine urine cultures should be taken in all patients to rule out other aetiologies.

Q. What is the preferred antibiotic management of brucellosis in children?

A. Management should always be overseen by a consultant paediatrician with a specialist interest in infectious diseases.

In the absence of randomised controlled trials, the guidance published by the American Academy of Paediatrics is recommended. This includes dosage guidance.

- <8 years of age - oral co-trimoxazole plus rifampicin for 4-6 weeks
- >8 years of age - oral doxycycline plus rifampicin for 6 weeks

NB For patients with osteoarticular disease, neurobrucellosis or endocarditis referral to a specialist paediatric infectious disease unit is recommended as aminoglycoside therapy is usually indicated.