A preliminary comparison of five assays for detecting past exposure to *Coxiella burnetii* for use prior to human Q Fever vaccination

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Background

Vaccination against Q Fever *(Coxiella burnetii* infection) is performed in Australia using Q-Vax, a formalin- killed whole cell vaccine.

Adverse reactions occur in those persons with prior exposure to *C. burnetii.* To prevent this adverse reaction pre-vaccination screening is performed and persons found to be positive are excluded from vaccination.

Currently a skin test (to detect T-cell immunity) and an antibody assay (to detect B-cell immunity) are undertaken on each person prior to vaccination.

However the assay that "best" correlates with prior exposer to *C. burnetii* and thus adverse reactions to the vaccine is not known.

A new Interferon-Gamma Release Assay (IGRA), Q-Detect, has recently become available. It measures the specific T-cell reaction on in-vitro stimulation of whole blood with coxiella antigen.

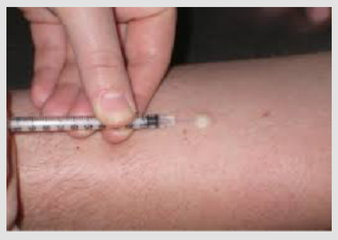
The main objectives of this study were:

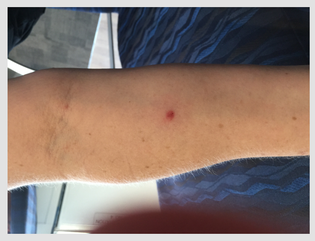
1. To compare the sensitivity and specificity of this new assay (IGRA) with intradermal skin test, IFA (Lab A & B), EIA (Lab B) and CFT (Lab B), and
2. To provide QF vaccination of the volunteers found to be negative to these assays.

Methods

A small (n=25) group of attendees from Australia, Europe and America at an Australian scientific conference were offered Q-Vax vaccination. As part of their pre-vaccination testing, five different assays were performed on them to detect their possible exposure to *C. burnetii*. These assays were:

1. Intradermal Skin Test
2. Serology by Immunofluorescence assay (IFA)
   - Lab A (Australian Rickettsial Reference Laboratory, ARRL)
   - Lab B (Sullivan Nicolaides Pathology, SNP)
3. Serology by Enzyme Immunoassay (EIA)
4. Serology by Complement Fixation Test (CFT)
5. Interferon-Gamma Release Assay (IGRA), Q-Detect





Results

Table 1: Comparative results of Intradermal skin test, Serological assays (IFA, EIA, and CFT) and Interferon gamma release assay (IGRA, Q-Detect) in persons with (A) and without (B) known exposure to *Coxiella burnetii.*

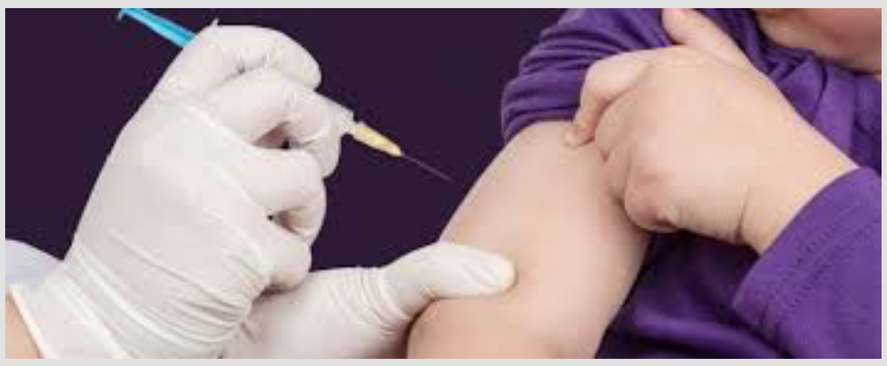
Volunteers		Intradermal Skin test	Serology				IGRA (Q-Detect)
			IFA		EIA	CFT	
ID Number	Country		Lab A	Lab B			
A. Volunteers with known *Coxiella burnetii* (Q Fever) exposure (vaccination or infection) (n=8)							
1	USA	Negative	Negative	Negative	Negative	Negative	Positive
8	Australia	Negative	Positive	Positive	Positive	Positive	Borderline
16	Australia	Negative	Positive	Negative	Negative	Negative	Borderline
17	Australia	Negative	Positive	Negative	Negative	Negative	Borderline
19	USA	Negative	Negative	Positive	Negative	Negative	Borderline
21	Australia	Positive	Negative	Positive	Negative	Negative	Positive
23	Australia	Positive	Negative	Positive	Negative	Negative	Borderline
11	Switzerland	Positive	Positive	Positive	Positive	Positive	Strong Positive
Total		**3/8**	**4/8**	**5/8**	**2/8**	**2/8**	**8/8**
B. Volunteers without Q Fever vaccination or unknown exposure *to Coxiella burnetii* (n=17)							
2	USA	Negative	Negative	Negative	Negative	Negative	Negative
3	Netherlands	Negative	Negative	Negative	Negative	Negative	Negative
4	Australia	Negative	Negative	Negative	Negative	Negative	Negative
5	Belgium	Negative	Negative	Negative	Negative	Negative	Negative
6	Australia	Negative	Negative	Negative	Negative	Negative	Borderline
7	USA	Positive	Negative	Negative	Negative	Negative	Negative
9	Germany	Negative	Negative	Negative	Negative	Negative	Borderline
10	Mexico	Positive	Negative	Negative	Negative	Positive	Negative
12	Australia	Negative	Negative	Negative	Negative	Negative	Negative
13	France	Positive	Negative	Negative	Negative	Negative	Negative
14	USA	Negative	Negative	Negative	Negative	Negative	Negative
15	Australia	Negative	Negative	Negative	Negative	Negative	Negative
18	Australia	Positive	Negative	Negative	Negative	Negative	Negative
20	Germany	Negative	Negative	Negative	Negative	Negative	Negative
22	Australia	Negative	Negative	Negative	Negative	Negative	Borderline
24	USA	Negative	Negative	Negative	Negative	Negative	Negative
25	USA	Negative	Negative	Negative	Negative	Negative	Negative
Total		**4/17**	**0/17**	**0/17**	**0/17**	**1/17**	**3/17**

Of the 25 participants in the study, 7 had known prior exposure to *C. burnetii* due to vaccination against Q Fever and 1 had prior Q Fever infection. The remaining 17 persons had no known prior exposure to *C. burnetii*.

Table 2: Comparative sensitivity and specificity of the intradermal skin test, serological assays (IFA, EIA, and CFT) and IGRA (Q-Detect) in detecting persons with prior exposure to *Coxiella burnetii*.

Assays	Sensitivity	Specificity	Comment
Intradermal Skin Test	**37%**	**76%**	**Poor assay**
Serology IFA	**62%**	**100%**	**Poor assay**
Serology EIA	**25%**	**100%**	**Poor assay**
Serology CFT	**12%**	**100%**	**Poor assay**
IGRA (Q-Detect)	**100%**	**82%**	**Good assay**

The results from 5 assays were compared in the 2 groups and presented in Table 1. The sensitivity and specificity of these assays are summarised in Table 2. The new IGRA/Q-Detect was found to be superior to the 4 currently used assays.



Volunteers negative to screening assays were vaccinated with the Australian Q Fever vaccine (Q-Vax).

Conclusions

The intradermal skin test and serology correlated poorly with known prior exposure to *C. burnetii.*

The new Interferon-Gamma Release Assay (IGRA), Q-Detect, correlates well with known prior exposure to *C. burnetii* (vaccination or likely infection). Sensitivity (100%) and specificity (82%). This assay shows promise but larger study is needed.

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The authors report no conflict of interest.

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