VETERINARY ASSOCIATION for WILDLIFE MANAGEMENT

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Vaccination with the Badger BCG vaccine

Dear Dr Chambers

I have now studied your detailed response to my letter of January 10, for which many thanks.

In your letter you state that the dose of *M.bovis* in the Badger BCG vaccine is 2-8 x 10^6 cfu/ml which is the high dose (HD) vaccine referred to in the Lesellier paper 2011. This comes as a surprise to me since, as you may read in my letter, I was under the impression that it was the low dose (LD) vaccine that was being used in the field. Please would you confirm that the Badger BCG vaccine is the HD vaccine. (Dr Chambers has since confirmed by e-mail (7.4.14) that the Badger BCG vaccine currently being deployed in the field is the HD vaccine)

But notwithstanding the significant protection demonstrated for the HD vaccine it remains that animals were not solidly protected and all shed *M.bovis* at some stage post challenge. This fact gives me little confidence that the vaccine will be effective in the face of the massive challenge that exists out there in the badger population. Furthermore I am mindful of the pathology of *M.bovis* in the badger and the fact that the organism, although phagocytosed by alveolar macrophages, is not killed (Gallagher & Clifton Hadley 2000, *ResVet Sci* **69**, 203-217). I suspect that this is the basis of the shortcomings of BCG to protect various species.

And I'm afraid I remain of the opinion that the difference in serological response between vaccinated and non-vaccinated badgers in the field is only indicative of just that – a different, albeit interesting, response. It cannot be regarded as direct evidence of protection as trumpeted by your co authors on BBC News on line.

Concerning the safety of the vaccine I'm afraid you have misconstrued my reference to the skin test. I entirely accept that investigation of the skin reaction of animals already infected with *M.bovis* did not reveal any significant adverse reaction but my concern is for a possible

systemic DTH response particularly a detrimental pulmonary response. And this cannot be ruled out by skin testing. I am mindful of a reference sent me by an Irish colleague, Dr Joe Cassidy, which demonstrates an increasingly severe pyogranulomatous response in the lungs of mice exposed more than once to *M.bovis* BCG (Turner and others 2000, *Infection & Immunity* **68**, 1706-1709).

Unless this can be ruled out, the possibility that the Badger BCG vaccine could actually cause harm to badgers in the field remains a real possibility.

Meanwhile time may reveal what impact the present widespread deployment of the Badger BCG vaccine may have in the field. One can only hope that your optimism prevails!

Best wishes

Dr. L.H.Thomas, secretary

Copy to: Mr Nigel Gibbens (Chief Veterinary Officer)
Dr Christianne Glossop (Chief Veterinary Officer for Wales)
Professor Glyn Hewinson (Co author)
Mr Chris House (Chairman)
Dr Joe Cassidy (UCD)

Dear Dr Chambers 10, January 2014

I have recently been studying papers from your group on the above subject and would like to make comment and raise some questions with you as the corresponding author.
In the paper:

Lesellier S, Palmer S, Gowtage-Sequiera S, Ashford R and others. *Vaccine* (2011) Protection of Eurasian badgers from tuberculosis after intra-muscular vaccination with different doses of BCG http://www.sciencedirect.com/science/article/pii/S0264410X1100380X

I am at a loss to see how, on the evidence presented, you can justify the statement in the concluding paragraph of the discussion that "IM administration of BCG was shown to confer a significant level of protection to badgers against experimental inoculation with *M.bovis*".

I accept there is notional protection demonstrated for the high dose vaccine but this is less than solid protection since all vaccinated animals shed *M.bovis* at some stage post challenge. But more significantly protection is not demonstrated for the low dose vaccine and since this is the vaccine currently being deployed in the field I suggest it is hugely misleading to claim a significant level of protection for the vaccine.

My scrutiny of your papers has been somewhat confused by what appears to be some overlap in the results from experiments reported in another paper of which you are the senior author:

Chambers M A. Rogers F, Delahay R.J., Lesellier S, Ashford R, Dalley D and others (2010) Bacillus Calmette-Guérin vaccination reduces the severity and progression of tuberculosis in badgers. http://rspb.royalsocietypublishing.org/lookup/doi/10.1098/rspb.2010.1953

Please can you confirm that the experiments VES 1 and VES 2 reported in the two papers are the same two experiments? The numbers of animals do not exactly match in VES 2 but the rogue animal in the high dose vaccine group, D313 is the same.

I should add that I am even less convinced by the claim that the difference in the serological response of vaccinated versus unvaccinated animals in the field studies reported in your paper is "evidence for a beneficial effect of BCG on *M.bovis* infection in free-living badgers". In my opinion it is simply evidence of a difference. And the claim trumpeted by BBC News on line in December 2010, apparently endorsed by two of your co-authors that the injectable Badger BCG vaccine reduces the incidence of bovine TB by 74% is in my opinion wholly unjustified. The most noteworthy finding I suggest is from the experimental studies that there is no difference in vaccinated versus unvaccinated badgers in respect of shedding *M.bovis* post challenge.

Reworking of the data in the subsequent paper (Carter and others 2012) with a range of more complex serological tests would appear to give essentially similar results to your earlier paper. It remains that this is not direct evidence of protection. Similarly the difference in response of badger cubs is interesting but cannot be regarded as "beneficial".

You also make claim in the final paragraph of the Lesellier paper that the vaccine is safe. But, having looked at the reference given (S. Lesellier, S. Palmer, D.J. Dalley, D. Davé, L. Johnson, R.G. Hewinson, M.A. Chambers, *Veterinary Immunology and Immunopathology* 2006), at: http://www.sciencedirect.com/science/article/pii/S0165242706000869
I note that post mortem examinations of vaccinated animals were not carried out. I question therefore how this claim can be fully justified since the possibility of a delayed hypersensitivity reaction cannot be ruled out without post mortem examination. We know that *M.bovis* generates a delayed type 4 hypersensitivity reaction in cattle since this is the basis of the tuberculin test. I suggest therefore that such a reaction could occur in the field in badgers already infected with *M.bovis* that are vaccinated with BCG.

I look forward to hearing your response to my comments above and apologise in advance if I have misconstrued the findings from your extensive and heroic work. I spent 32 years in large animal research!

Yours sincerely

Dr. L.H.Thomas, secretary

Copy to: Mr Nigel Gibbens (Chief Veterinary Officer)
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