TB reactor research at APHA Weybridge

The following data demonstrate the relatively poor sensitivity of commercial post mortem inspection for confirming *M. bovis* infection in cattle, and the high sensitivity of the gamma test.

Background

Data were collated from a series of studies carried out at Weybridge and involved looking at post mortem findings of 143 field skin test reactor cattle that were supplied to the TB Research Group at APHA Weybridge between 2008 and 2017 for research purposes. It is important to bear in mind that these cattle represent a targeted sample of generally strong skin reactors, as per the request of the TB Research Group, and originated from herds with ongoing TB breakdowns.

Cattle were housed in secure research accommodation at APHA Weybridge for periods up to 12 months, after which time they were humanely slaughtered and a detailed post mortem examination carried out. During their stay at Weybridge the cattle were also sampled for gamma blood testing.

For the purposes of the studies, these post mortem examinations were much more thorough than those carried out in commercial slaughterhouses.

It is also important to note that post mortem status reported for these cattle (VL or NVL [no visible lesions]) will reflect any increases in pathology that may have accrued over the period of time spent at APHA Weybridge after the disclosing skin test.

Summary of findings

The data are summarised in the table below for these 143 skin test reactor cattle;

	Number of cattle	%	of which were severe skin test reactors[1]	%	of which were gamma-test positive	%
Visible lesion (VL)	111	77.6	9	8.1	105	94.6
Non-visible lesion (NVL)	32	22.4	14	43.8	16	50.0
Total	143	100.0	23	16.1	121	84.6

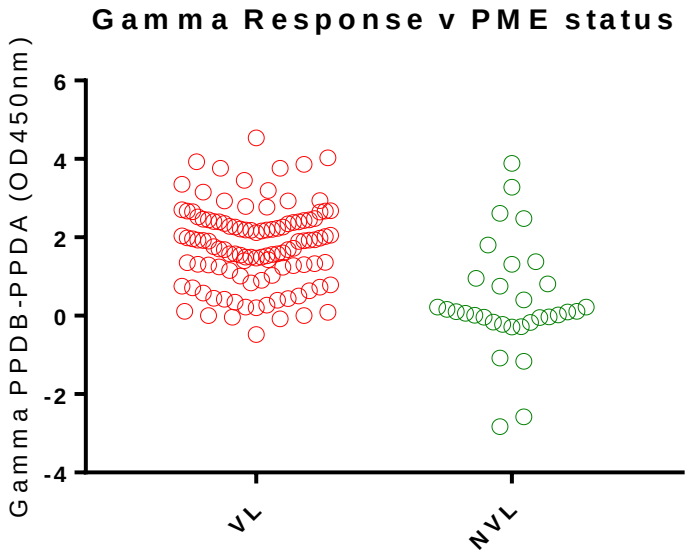
- Of the 143 skin test reactors (standard and severe combined), 77.6% were VL, of which 94.6% were gamma-positive

[1] The term 'severe' does not relate to reaction size. Instead it relates to the two possible interpretations of the skin test: 'standard' and 'severe'. Using severe interpretation increases the sensitivity of the test. For more information on skin test interpretation, visit the TB Hub https://tbhub.co.uk/dealing-with-tb-in-your-cattle-herd-in-england/what-tests-are-used-during-a-tb-breakdown/

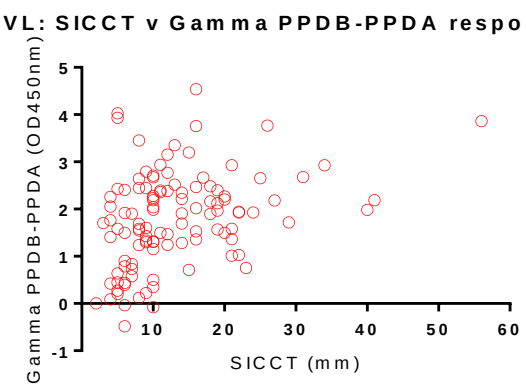
- Of the 32 NVL skin reactors (standard and severe combined) 50% were gamma-positive
- Of the 23 severe skin reactors in this study cohort, a higher proportion were NVL (61%) compared to VL (39%) – in fact severe reactors made up 43.8% of the NVL cattle group. This is not surprising as the severe interpretation of the skin test is more sensitive and so potentially detects infection before visible lesions have time to develop
- Of the 14 severe reactor NVL cattle, five (35.7%) were gamma-positive, supporting their infection status. The remaining 11 gamma-positive NVL cattle were standard skin reactors

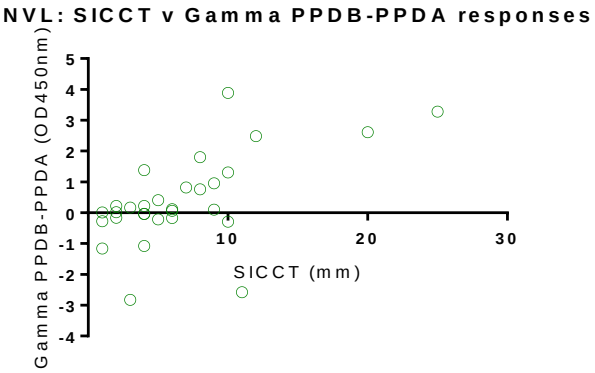
The comparative (PPDB (bovine) minus PPDA (avian)) gamma test readouts for the 111 VL and 32 NVL skin test reactor (standard and severe combined) cattle are shown on the graph below. Each dot represents the interferon-gamma response of one animal.

The data suggest proportionally higher gamma responses in VL compared to NVL cattle, but also illustrates the broad spread in the magnitude of responses from both VL and NVL cattle.



There is a positive relationship between skin and gamma test responses whether the animal is VL or NVL as illustrated by the graphs below. This relationship is not linear however, since, for example, there can be variability in skin responses between animals with a similar gamma test readout, and variability in gamma responses between animals with a similar skin reaction, as the data show.





Conclusions from the analyses

The data from this targeted cohort of skin test reactor cattle supports the following.

A high proportion of TB skin test reactors will have (or develop, given time), visible lesions resulting from infection with *M. bovis*.

The high percentage of VL findings in the skin test reactor cattle (77.6%) found by the TB Research Group at APHA Weybridge may be due to;

- a more detailed post mortem examination carried out for research purposes than would be available/required in a commercial slaughterhouse setting
- the benefit of additional life-span of the animals in the study of up to one year after the disclosing skin test, which allowed more time for the development of visible lesions (unlike most TB test reactor cattle in the field, which are removed to slaughter within ten working days of their detection)
- potentially some selection bias as animals with strong bovine PPDB reactions were purposely selected from ongoing TB breakdowns i.e. not a random sample of field reactors

A positive relationship between skin and gamma tests in infected individuals

Overall the more pathologically affected (VL) skin test reactors showed a high gamma test-positivity (94.6%) and were associated with a lower proportion of severe skin test reactors. Conversely, NVL skin test reactors showed a lower gamma test positivity (50%) compared to VL skin reactor cattle, and were associated with a higher proportion of the severe skin reactors present in this study group.

This research reinforces that most skin test reactors and gamma test positive cattle are highly likely to be infected with TB, even if they do not display lesions of TB at post-mortem inspection. This gives us a high degree of confidence in the diagnostic tests for TB in cattle and justifies the rapid removal of all TB test reactors from farms.