GENERAL INFORMATION SHEET

Tuberculosis due to *Mycobacterium bovis* in cats associated with feeding a commercial raw food diet

In autumn 2018 the Companion Animal TB Team, Royal (Dick) School of Veterinary Studies, became aware of cases of tuberculosis (TB) caused by *Mycobacterium bovis* in young mainly pedigree cats living in areas of the UK where this infection is not found naturally in cattle or badgers. Since the cats could not have been infected by contact with infected wildlife (which is how they are thought to be commonly infected), we looked for other potential sources of infection. The cats were not fed raw milk, or exposed to infected people. The one consistent finding was that they had all been fed (to varying degrees) the same brand of commercial raw cat-food (Natural Instinct). Further investigation found they had all eaten the wild venison version of this food.

We alerted our veterinary colleagues to this potential new risk pathway via letters to the Veterinary Record and Veterinary Times (Oct 2018), which was picked up by the Sunday Times (Oct 2018).

The description of the investigation of the first six clinical cases and seven apparently infected cohabiting cats has now been published in the Journal of Feline Medicine and Surgery. It details six cats with abdominal disease (a swollen belly), enlarged lymph nodes (sometimes draining pus), and/or lung disease (causing a cough). The cats all lived exclusively indoors in five different households across England. Five of the cats were either too sick to treat or deteriorated despite treatment, and were euthanased; TB was confirmed by a positive PCR test in four of the six sick cats, all six of which were also TB blood test (IGRA) positive. All cohabiting cats were tested by the TB blood test and found to have evidence of infection; giving a total of 13 confirmed or suspected infected cats.

Our results provide compelling circumstantial evidence of an association between a single commercial raw diet and TB in cats that ate it. Working with the Animal and Plant Health Agency (APHA) and the Food Standards Authority (FSA) we are trying to confirm the source of infection. The manufacturer voluntarily recalled the product pending further investigations (Dec 2018). However, we are concerned that some owners may have missed this information, and given the long duration to the products best before date – up to August 2019 – it is important that owners are aware of this recall.

We are trying to find all cases of this infection in cats – this is vitally important for the individual cat's health, but also because there is a low but potential risk to the cats' owners. If TB caused by *M. bovis* is confirmed in your pet, APHA will inform your local Health Protection Team so that any health risks to those in contact with the pet can be investigated.

Thank you to all veterinary surgeons who have contacted us about cases. If any vets have other potential cases, please contact us as soon as possible. We are working closely with the APHA to investigate the outbreak. Vets who suspect a cat to be infected with *M. bovis* should notify APHA.

Professor Danièlle Gunn-Moore and the Companion Animal TB Team, Royal (Dick) School of Veterinary Studies: Companion.AnimalTB@ed.ac.uk.

The study was funded by the Biotechnology and Biological Sciences Research Council.

Useful links:

VIN News Report in November 2018: https://news.vin.com/vinnews.aspx?articleId=50909

Bovine tuberculosis in domestic pets: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/596240/AG-TBYP-01e.pdf

In Practice: Mycobacterial infection in cats: An update https://inpractice.bmj.com/content/39/9/399

International Cat Care: https://icatcare.org/sites/default/files/PDF/mycobacterial-disease-in-cats-in-gb.pdf

Veterinary Nursing Journal: Mycobacterial infections in cats and dogs https://www.tandfonline.com/doi/abs/10.1080/17415349.2018.1551103

VETERINARY INFORMATION SHEET

Tuberculosis due to *Mycobacterium bovis* in cats associated with feeding a commercial raw food diet

Common questions

Q. Is raw pet food definitely the cause of this outbreak?

A. Our results give compelling circumstantial evidence of an association between a single commercial raw diet and TB in cats that ate it. However, when cats live in areas of the UK where *M. bovis* is present in cattle and badger* environmental contamination can occur, as can rodent infection, and cats can be infected when hunting. If a cat develops TB after eating this diet, but lives in one of these areas of the UK, it can be difficult to tell where the infection came from – complex molecular tests are needed to 'fingerprint' the infection. Once these 'fingerprints' become available, it is possible that some of the ongoing cases will be confirmed as locally acquired infections rather than having been caused by eating commercial food.

**M. bovis* is predominately found in cattle and badger populations in the SW of England, and parts of Wales (APHA, 2019).

Q. Is the outbreak still happening, and when might it stop?

A. Investigations are ongoing. We anticipate more cats are infected and continue to work on these cases.

We hope any potential contamination of the diet was short lived and that all potentially contaminated food was recalled. However, anyone who has ever bought this food should check their freezers to ensure they have none dated "best before" March 2019 until August 2019 – if they have it should be returned to the point of sale. We hope this Press Release will help remove all residual samples from the food chain.

Experimental studies have shown that cats infected with *M. bovis* by mouth typically develop illness within two to five months (Francis, J. 1958). However, we do not know a great deal about latent TB in cats. In people, only 5-10% of those infected develop clinical TB when initially infected (usually developing clinical disease – e.g. coughing, weight loss and night sweats – within two years of infection). The rest develop latent infection, with another 5-10% developing TB at some point later in their life, often associated with immunosuppression. Latency is likely to be similar in cats, with a proportion of infected cats developing clinical disease within five to six months of infection, the rest developing latent infection, with more developing TB at some point during their life. Because of this, the initial outbreak may be followed by recrudescent cases for many years to come. Vets need to be aware of this possibility, even in cats that have never lived in a 'TB area' of UK, or are 'indoor only' cats; we will all need to ask detailed feeding histories.

Q. What should people do if they are concerned their cat may have eaten the recalled cat food?

A. We have recommended that concerned owners should speak to their veterinary surgeon. Their vet can assess the cat to see if it has any signs of illness that could suggest TB. If there are any lumps or apparent wounds, the vet can take samples, e.g. to assess for TB infection by culture or PCR test (see TB testing document for availability, utility, addresses and costs). If there are no obvious signs of illness the cat can be tested by the TB blood test, or its health could simply be monitored (e.g. regular weight checks, counting the breathing rate when sleeping, etc.).

Q. What sort of cats are being infected?

A. Most of the cases in this outbreak have been young, often pedigree, cats that are not allowed outside and hence are not exposed to cattle or wildlife.

Q. What does TB look like in cats?

A. In cats, most cases of TB are caused by infected bites, so skin wounds (which are often ulcerated) and/or swollen submandibular or popliteal lymph nodes are the most common presentation. Pulmonary spread is believed to be by haematogenous spread so interstitial infiltration is seen, and dyspnoea may develop. If coughing occurs it is only very late on.

In contrast, the cases associated with this cluster present with infection in the intestines and/or lungs, causing weight loss, abdominal masses, diarrhoea and/or coughing. Some pulmonary cases have developed cavitating lung lesions with haemoptysis. The majority of cases are in older kittens and young adults. Two major differential diagnoses of the abdominal form of the infection are feline infectious peritonitis or intestinal lymphoma.

Q. How is TB diagnosed in cats?

A. TB in cats caused by *M. bovis* can be confirmed by molecular tests such as PCR or by culturing the causative organism. The latter remains the gold standard for veterinary medicine as the bacterium can then be genotyped to try to determine the source of infection.

Where neither of these are possible, the TB blood test can be used to look for evidence of a specific immune response to *M. bovis.*

Q. What can be done if a cat is found to have TB?

A. If the cat is diagnosed early and disease is limited, treatment may be considered. However, treatment is long and difficult (typically involving three drugs a day for six months), with no guarantee of success. If there is significant disease (e.g. masses in its abdomen or significant lung infection), as there has been in most cases in this outbreak, then euthanasia is recommended as treatment is unlikely to be successful and there is a potential risk to people (see below). APHA do not recommend treatment of any of these cases.

If the cat has presumed latent infection (i.e. is blood test positive with no other evidence of illness) the options include monitoring, prophylactic treatment (for three to six months with rifampicin, azithromycin and pradofloxacin) or euthanasia.

The Companion Animal TB Team at the RDSVS, are happy to discuss all cases of potential TB with veterinary surgeons, providing advice tailored for individual cases, and if treatment is considered, ongoing advice and support. We are keen to gather information on all cases, including outcomes – we want to provide the best advice possible, and cats in this new outbreak may not behave the same way as previous cases. Contact: Companion.AnimalTB@ed.ac.uk.

The suspicion of tuberculosis in a cat caused by *M bovis* should notify the APHA without delay. Public Health England, Public Health Wales and Health Protection Scotland (depending where you work) can assess the risk of potential exposure to *M. bovis* by the owner and veterinary staff.

Q. Do infected cats pose a risk to human health?

A. Over the last 150 years there have only been six reported cases of *M. bovis* being passed from cats to people, globally. When infection has occurred, the cat had significant skin lesions that were

wet with infected pus. Public Health England define the risk to people as very low; however, the risk of infection must always be considered, especially where potentially immunosuppressed people may have contact with an infected cat.

OWNER INFORMATION SHEET

Tuberculosis due to *Mycobacterium bovis* in cats associated with feeding a commercial raw food diet

The veterinary governing body, the Royal Colleague of Veterinary Surgeons (RCVS), Code of Professional Conduct does not allow referral vets to speak to owners unless their animal has been referred to them. Without that, referral vets can only give general comments (see below). For this reason the Companion Animal TB Team here at the University of Edinburgh cannot speak to individual owners unless they been referred.

Common questions

Q. Is raw pet food definitely the cause of this outbreak?

A. Our results give compelling circumstantial evidence of an association between a single commercial raw diet and TB in cats that ate it. However, when cats live in areas of the UK where *M. bovis* is present in cattle and badger* environmental contamination can occur, as can rodent infection, and cats can be infected when hunting. If a cat develops TB after eating this diet, but lives in one of these areas of the UK, it can be difficult to tell where the infection came from – complex molecular tests are needed to 'fingerprint' the infection. Once these 'fingerprints' become available, it is possible that some of the ongoing cases will be confirmed as locally acquired infections rather than having been caused by eating commercial food.

**M. bovis* is predominately found in cattle and badger populations in the SW of England, and parts of Wales (APHA, 2019).

Q. Is the outbreak still happening, and when might it stop?

A. Investigations are ongoing. We anticipate more cats are infected and continue to work on these cases.

We hope any potential contamination of the diet was short lived and that all potentially contaminated food was recalled. However, anyone who has ever bought this food should check their freezers to ensure they have none dated "best before" March 2019 until August 2019 – if they have it should be returned to the point of sale. We hope this Press Release will help remove all residual samples from the food chain.

Experimental studies have shown that cats infected with *M. bovis* by mouth typically develop illness within two to five months (Francis, J, 1958). However, we do not know a great deal about latent TB in cats. In people, only 5-10% of those infected develop clinical TB when initially infected (usually developing clinical disease – e.g. coughing, weight loss and night sweats – within two years of infection). The rest develop latent infection, with another 5-10% developing TB at some point later in their life, often associated with immunosuppression. Latency is likely to be similar in cats, with a proportion of infected cats developing clinical disease within five to six months of infection, the rest developing latent infection, with more developing TB at some point during their life. Because of this, the initial outbreak may be followed by recrudescent cases for many years to come. Vets need to be aware of this possibility, even in cats that have never lived in a 'TB area' of UK, or are 'indoor only' cats; we will all need to ask detailed feeding histories.

Q. What should people do if they are concerned their cat may have eaten the recalled raw cat food?

A. They should speak to their veterinary surgeon. Their vet can assess the cat to see if it has any signs of illness that could suggest TB. If there are any lumps or apparent wounds, they can take samples, e.g. to assess for TB infection by culture or PCR test. If there are no obvious signs of illness the cat can be tested by the TB blood test, or its health could simply be monitored (e.g. regular weight checks, counting the breathing rate when sleeping, etc.).

Q. What sort of cats are being infected?

A. Most of the cases in this outbreak have been young, often pedigree, cats that are not allowed outside and hence are not exposed to cattle or wildlife.

Q. What does TB look like in cats?

A. In cats, most cases of TB are caused by infected bites, so we see skin wounds and/or swollen lymph nodes under the jaw or behind the knees (stifles). However, the new cases affect intestines and/or lungs, causing weight loss, abdominal masses, diarrhoea and/or coughing (which can sometimes contain blood). The diseases vets are most likely to think the cats have are feline infectious peritonitis, known as FIP, or intestinal lymphoma — a type of cancer, and/or severe pneumonia.

Q. What can be done if a cat is found to have TB?

A. If the cat is diagnosed early and disease is limited, treatment may be considered. However, treatment is long and difficult (typically involving three drugs a day for six months), with no guarantee of success. If there is significant disease (e.g. masses in its abdomen or significant lung infection), as there has been in most cases in this outbreak, then euthanasia is recommended as treatment is unlikely to be successful and there is a potential risk to people (see below). APHA do not recommend treatment of any of these cases.

If the cat has presumed latent infection (i.e. is blood test positive with no evidence of illness) the options include monitoring, preventative treatment (for three to six months with rifampicin, azithromycin and pradofloxacin) or euthanasia.

Q. Do infected cats pose a risk to human health?

A. Over the last 150 years there have only been six reported cases of *M. bovis* being passed from cats to people, globally. When infection has occurred, the cat had significant skin lesions that were wet with infected pus. Public health England (PHE) define the risk to people as very low; however, the risk of infection must always be considered, especially where potentially immunosuppressed people may have contact with an infected cat.

TB TESTING DOCUMENT

TESTING for FELINE & CANINE MYCOBACTERIAL INFECTIONS

Useful addresses in the UK:

Danièlle Gunn-Moore,
Professor of Feline Medicine,
University of Edinburgh Small Animal Hospital, Easter Bush Veterinary Campus,
Roslin, Midlothian, Tel: +44(0)131 650 7650 or Direct 6182
Scotland, EH25 9RG Email: Companion.AnimalTB@ed.ac.uk.

Please contact the **above to discuss any case in more detail**. We are currently trying to collate all of the cases in cats in GB so that we can gain a better understanding of the presentation, causes, and treatment responses of the condition.

If a sample has been submitted for histopathology we would be grateful to receive the fixed tissue blocks from the histopathology lab, plus 1-2ml of serum and 0.5-1ml EDTA, so we can continue our studies.

To identify the Mycobacterium involved there are three options:

1. **Specialist mycobacterial culture** (fresh tissue only)
2. **PCR** to detect mycobacteria in fresh tissue, or alcohol-fixed slides or, less effectively, in fixed tissue or stained slides (but not ZN-stained slides)
3. **IGRA blood test**

For **experienced histopathology** send fixed tissue to **Finn Pathology,** marked for the attention of Dr Mel Dobromylskyj.

Suspicion of mycobacterial infection in a cat or dog carcase should be reported to the APHA without delay – APHA will review each case individually to assess its suitability for government-funded post mortem examination, histopathology and bacteriological culture. Whole carcasses, tissues and isolates cultured in another laboratory may be accepted. Pet owners are referred to GOV.UK for more information:
https://www.gov.uk/government/publications/bovine-tuberculosis-tb-in-domestic-pets.
Bacteriological culture typically takes between 8 and 16 weeks and is often negative from feline tissue. Please contact the laboratory prior to sending samples to ensure appropriate samples are submitted, and enclose case details when submitting samples on the form found at:
http://ahvla.defra.gov.uk/documents/surveillance/forms/form-ba704.pdf to:

TB Diagnosis Section (SEB2),
Animal Plant Health Agency (APHA) - Weybridge,
Wood Lane, New Haw, Addlestone,
Surrey, KT15 3NB Tel: +44(0)1932 357471

Current APHA price list for private laboratory submissions can be found at:
https://science.vla.gov.uk/Tests/PDF/CDT_PdfPriceList.pdf

PCR - There are currently two places where PCR is available; the **Leeds University Teaching Hospital** reference lab is by far the most experienced and reliable. The PCR is performed in two steps. The initial step differentiates between non-tuberculous mycobacteria (NTM) and *M. tuberculosis*-complex (MTBC) organisms; ~£120+VAT. If the sample contains NTM DNA then further sequencing of the gene product is automatically conducted at no additional cost (so this would identify

Mycobacterium avium complex [MAC] for example). However, the sequence of the gene this PCR detects is identical across all members of the MTBC so in this instance sequencing is not helpful. A further PCR and subsequent sequencing can be requested to differentiate between different MTBC organisms but this costs an additional ~£200+VAT.
Prior to submission please contact:

Dr Deborah Gascoyne-Binzi
Principal Clinical Scientist, Leeds Teaching Hospitals Trust,
Department of Microbiology, The General Infirmary, Great George Street,
Leeds LS1 3EX
Tel: 0113 392 3929 (Laboratory: 0113 392 8797)
Fax: 0113 343 5649 Email: Deborah.Gascoyne-Binzi@leedsth.nhs.uk.

The alternative PCR is a single PCR at **Liverpool Vet School**, it is cheaper, but cannot differentiate the different members of the MTBC, so is of limited use. This lab cannot handle unfixed tissue or slides.

For **IFN-γ blood testing** 2ml of heparinised blood is needed – it detects the cat's immune response to MTBC or MAC. Contact the laboratory first as the test is only run on the 1st & 3rd Thursday of the month, ~£200+VAT. Send in a well-padded envelope marked DO NOT REFRIGERATE to the address below. A canine-specific test is also available, on request – but costs £400+VAT.
Biobest Laboratories Ltd,

6 Charles Darwin House Tel: +44(0)131 440 2628
The Edinburgh Technopole Fax: +44(0)131 440 9587
Milton Bridge, Nr Penicuik, EH26 0PY www.biobest.co.uk

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