Small animal disease surveillance 2019: Respiratory disease, antibiotic prescription and canine infectious respiratory disease complex

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Report summary

- Presentation for investigation and/or treatment of respiratory disease comprised 0.9 per cent, 1.2 per cent and 1.2 per cent of total dog, cat and rabbit consultations respectively between 1 January 2018 and 28 February 2019.
- Coughing was the most frequently recorded respiratory disease clinical sign in dogs (68.0 per cent of cases), whereas sneezing was most common in cats (45.6 per cent of cases).
- The proportion of respiratory disease consultations which prescribed antibiotics authorised for systemic administration (including oral and injectable formulations) decreased between April 2014 and February 2019 by approximately 25 per cent.
- Between January 2016 and February 2019, 14.5 per cent of 1,602 canine and 4.9 per cent of 801 feline respiratory samples submitted to UK-based diagnostic laboratories tested positive for presence of *Bordetella bronchiseptica*.

About this report

This report is the eighth in a series by the Small Animal Veterinary Surveillance Network (SAVSNET). The other reports in the series are available from http://veterinaryrecord.bmj.com. As data are collected for longer periods, the estimates of changes in disease burden will become more refined, allowing more targeted local and perhaps national interventions. Anonymised data can be accessed for research by contacting the authors. SAVSNET also welcomes feedback on this report. More information about SAVSNET is available at www.liverpool.ac.uk/savsnet

Syndromic surveillance of respiratory disease

This report represents the third occasion the Small Animal Veterinary Surveillance Network (SAVSNET) has summarised respiratory disease in companion animals (Arsevska and others 2018a; Sánchez-Vizcaíno and others 2016). The present report considers electronic health records (EHRs) captured by the SAVSNET project from 227 voluntary veterinary practices (484 sites) over a 14-month period from 1 January 2018 to 28 February 2019. A detailed description of the methodology used by SAVSNET to capture EHRs has been previously provided (Sánchez-Vizcaíno and others 2015 and 2017). A total of 1,710,078 consultations were analysed, of which 70.2 per cent were from dogs, 26.6 per cent were from cats, 1.7 per cent were from rabbits, and the remaining 1.5 per cent were from other species, or where species was not recorded. Animals mainly presenting for investigation and/or treatment of respiratory disease according to the attending veterinary surgeon or nurse comprised 0.9 per cent, 1.2 per cent and 1.2 per cent of total dog, cat and rabbit consultations respectively.

Short questionnaires (Sánchez-Vizcaíno and others 2016) were completed by the attending practitioner after 3,937 random respiratory disease consultations (2,404 canine, 1,177 feline, 3,707 unique animals). Of these dogs, 52.2 per cent were being presented for the first time after a history of illness of up to one week (47.2 per cent). Though cats also tended to present most commonly following illness of up to one week (41.6 per cent), most were for revisits / check-ups (52.3 per cent). For both dogs and cats, the second most common duration of respiratory clinical signs was one month or longer (20.5 per cent of dogs, 32.3 per cent of cats). Whilst by far the most common presenting clinical sign in dogs was coughing, sneezing was most commonly observed in cats (Table 1). A minority of dogs (6.3 per cent) and cats (3.6 per cent) were reported as having stayed in a kennel or cattery within the preceding 10 days.

Consulting veterinary surgeons considered cases likely to be respiratory in origin in over 71.2 per cent of canine and 78.4 per cent of feline cases, with a cardiac origin being considered likely in 15.3 and 7.8 per cent of canine and feline cases respectively. Diagnostic testing was planned in 23.5 per cent of canine and 22.9 feline cases, with radiography being the most common in both dogs (6.8 per cent) and cats (7.2 per cent). Biochemistry and / or haematology were also relatively commonly planned. These findings were broadly consistent with SAVSNET's previous reports (Arsevska and others 2018a; Sánchez-Vizcaíno and others 2016).

Spatial distribution of respiratory disease

The spatial distribution of the relative risk for respiratory disease was evaluated in dogs and cats in England, Scotland and Wales for each season of the surveillance period between 1 January 2018 and 28 February 2019. For consultations with a valid owner postcode the centroid of each postcode was used to indicate the approximate residence of each recorded animal. Hence, these centroids were aggregated into 20km gridded cells encompassing England, Scotland and Wales, calculating the proportion of total consultations mainly presenting with respiratory disease. Standard error (SE) for each cell was calculated to provide a measure of relative confidence in findings due to variable geographic consultation coverage, with these values being used to formulate septile bi-variate maps, where the darkest red colours indicate highest proportions of respiratory disease (greater than 1.8 per cent and 2.7 per cent for dogs and cats respectively) and lowest standard errors (Fig.1). As previously observed (Arsevska and others 2018a; Sánchez-Vizcaíno and others 2016), transient regions of increased respiratory disease incidence were distributed seemingly randomly throughout the country and in most seasons. In future, SAVSNET will need to work with others to develop robust statistical and practical methods to determine whether these transient increases in respiratory disease prevalence represent actual infectious disease outbreaks.

Respiratory disease pharmacosurveillance

For the first time in this report we also analysed pharmaceutical product prescriptions given during all respiratory consultations recorded between April 1 2014 and February 28 2019 in dogs (*n* = 46,200 respiratory consultations), cats (*n* = 23,113) and rabbits (*n* = 1,448). A semi-automated text mining methodology was utilised to identify the active substance(s) dispensed in each consultation using the 'product dispensed' field of the EHR; these active substances were summarised into a hierarchical pharmaceutical classification system as previously described (Singleton and others 2018; Singleton and others 2017). For the purposes of this report, five pharmaceutical families of particular relevance to respiratory disease were analysed, including antibiotics authorised for systemic (oral or injectable) use; anti-inflammatories authorised for systemic use; respiratory-active (R-A) products (e.g. bronchodilators); cardiovascular-active (CV-A) products (e.g. diuretics), and euthanasia.

For dogs, systemic antibiotics were prescribed in 37.4 per cent of respiratory consultations, systemic anti-inflammatories in 34.6 per cent, R-A products in 5.0 per cent, and CV-A products in 12.7 per cent. For cats, systemic antibiotics were prescribed in 48.5 per cent of respiratory consultations, systemic anti-inflammatories in 21.7 per cent, R-A products in 8.4 per cent, and

CV-A products in 7.3 per cent. For rabbits, systemic antibiotics were prescribed in 64.7 per cent of respiratory consultations, systemic anti-inflammatories in 21.7 per cent, R-A products in 4.0 per cent, and CV-A products in 0.7 per cent. Dogs were euthanised in 1.2 per cent of respiratory consultations, compared to 2.4 per cent of cat and 4.2 per cent of rabbit respiratory consultations.

Temporal trends in prescription frequency were also examined in dogs and cats (Fig.2). Over the five years analysed, an approximately 25 per cent decrease in the frequency with which systemic antibiotics were prescribed was noted in this population, with other pharmaceutical families remaining broadly static over the same time period. Systemic antibiotic and anti-inflammatory prescription frequency tended to peak in the 3rd or 4th quarter of each year for dogs suggesting a seasonality to the occurrence of perceived antibiotic responsive disease; such a trend was less discernible for cats.

Laboratory-based investigations of *Bordetella bronchiseptica* in companion animals

SAVSNET collated data from four participating UK-based veterinary diagnostic laboratories (VDL) between 1 January 2016 and 28 February 2019, with data being used to identify temporal and spatial trends in the proportion of respiratory sample submissions that tested positive (as interpreted by the VDL) for presence of *Bordetella bronchiseptica* (*B. bronchiseptica*) by quantitative polymerase chain reaction (qPCR) assay. In total there were 1,602 recorded canine and 801 recorded feline tests completed, 14.5 per cent (*n*=233) and 4.9 per cent (*n*=39) testing positive respectively.

Over the three years, the proportion of positive results was relatively static (Fig.3). For both dogs and cats, a greater proportion of tests completed in winter were positive (dogs: 17.3 per cent; cats: 7.6 per cent), followed by summer (dogs: 14.1 per cent; cats: 4.7 per cent), autumn (dogs: 13.6 per cent; cats: 3.8 per cent) and spring (dogs: 12.9 per cent; cats: 2.8 per cent). Due to a low number of feline positive results, spatial trends were examined for dogs alone. Collating all tests from 2016 to 2019, though varied coverage should be considered, both areas of relatively high and low positive test proportions were revealed in postcode areas for which we hold relatively high volumes of data (low standard error); this suggests variable *B. bronchiseptica* infection risk in different regions of the country (Fig.4). To our knowledge it has been many years since *B. bronchiseptica* infection has been surveyed in companion animals in the UK, though a 2005 European-wide survey of cats in catteries found a comparative (5 per

cent) *B. bronchiseptica* prevalence in cats suffering from upper respiratory tract disease (Helps and others 2005).

Update on main presenting complaint temporal trends in companion animals

An observed prevalence time series for three key main presenting complaints (pruritus, gastroenteric and respiratory) from February 2017 to February 2019 is shown in Figure 5, together with a seasonal trend line (dark grey line). The trend line was calculated using a Bayesian binomial generalised linear model trained on weekly prevalence between 2014 and 2019, as fully described previously (Arsevska and others 2018b). Extreme prevalence observations describing weekly prevalence exceeding 99 per cent credible intervals, and moderate prevalence observations describing weekly prevalence exceeding 95 per cent credible intervals are displayed in red and orange respectively.

These results show continued seasonal prevalence fluctuations in both species, particularly apparent for pruritus in both dogs and cats, and respiratory disease in dogs. In dogs and cats, this seasonal pattern for pruritus appeared generally stable, though both species reported a few extreme case increase weeks in January 2019. Respiratory disease was less stable, suggesting an extreme increase above expected levels in respiratory cases in dogs and cats at the beginning of 2019. It is currently unknown whether these findings represent a true increase in disease prevalence, or reflect the changing nature of participation in the SAVSNET project.

Global perspective

Aujeszky’s disease in a dog

An 18-month-old Munsterlander was killed by Aujeszky's disease virus after a hunt in Moselle in February. The disease, caused by an alphaherpesvirus, can be transmitted from wild boars to domestic carnivores. The UK was declared disease free in 2012, but the virus persists in some wild populations of pigs in parts of mainland Europe. In dogs and cats, clinical signs include frantic and traumatic scratching, followed by paralysis and death; their similarity to those of rabies leading to the disease’s other name – pseudorabies. In dogs, disease is rare and most likely in hunting dogs. However, Aujeszky’s disease is notifiable, and although unlikely, this case serves to remind us of the potential of this disease in dogs (and cats) returning from places where the disease is endemic. Promed Archive Number: 20190218.6323356

Carbapenemase-producing Enterobacteriaceae in dogs

Carbapenems are considered a highest priority critical antibiotic used to treat already multidrug resistant infections in people. However, their use has led to the emergence of carbapenemase-producing Enterobacteriaceae (CPE) which represent a serious public health problem. Carbapenems are not authorised for veterinary patients in the UK. As a result, there is limited carbapenem susceptiblity testing conducted on companion animal-derived clinical isolates in veterinary diagnostic labs, nor any formal national surveillance of carbapenemase production in companion animals in the UK. Researchers have now isolated a carbapenemase-producing *E. coli* from a UK practice-derived veterinary culture collection (Reynolds and others 2019). From one isolate, originally from a skin wound in a Springer Spaniel, researchers identified a known carbapenem resistance gene ($bla_{\text{NDM-5}}$). The gene was located on the same plasmid as other genes conferring resistance to other antimicrobial classes, potentially demonstrating co-selection and maintenance of carbapenem resistance with use of other antimicrobials in companion animals. This finding highlights the perhaps growing potential of antibiotic use in pet animals to impact on human health.

Update on Canine Infectious Respiratory Disease complex and *Bordetella bronchiseptica* infection in dogs

Background

B. bronchiseptica is a gram negative, aerobic coccobacillus. It forms part of the "kennel cough" or Canine Infectious Respiratory Disease complex (CIRDc), the names given to commonly seen signs of upper respiratory tract infections in dogs. Despite its name, the syndrome is not confined to kennels and may be transmitted anywhere where dogs mix, including shows, training classes, parks and veterinary surgeries. Pathogenesis of CIRDc is thought to frequently involve initial infection with an upper respiratory tract pathogen such as canine respiratory coronavirus (CRCoV) or canine parainfluenza virus (CPiV). This then facilitates secondary infection, often with opportunistic organisms already present in the respiratory tract, such as *Mycoplasma cynos. B. bronchiseptica* may play the role of either primary pathogen or secondary invader. In some parts of world, canine influenza viruses also contribute; these are not yet thought to be regularly circulating in the UK (Sánchez-Vizcaíno and others 2016).

Clinical signs

A hacking cough is clinically typical of CIRDc, though not pathognomonic of any one pathogen. Differentials include retching, regurgitation and oropharyngeal foreign body. In addition to the cough, dogs may have submandibular lymph node enlargement and mild

pyrexia. Whilst affected animals typically remain bright and well, in severe cases or particularly susceptible individuals, bronchopneumonia can occur, with associated increased respiratory effort, pyrexia and lethargy. Deaths are relatively uncommon. Where outbreaks of severe disease occur, aspects of husbandry such as ventilation, stress and biosecurity should be assessed and alternative pathogens such as *Streptococcus equi zooepidemicus* considered.

Diagnosis

Diagnosis of CIRDc is usually made by the presence of characteristic clinical signs. Diagnostic testing is indicated in the presence of an outbreak, where the results could inform a change in policy (such as therapy or vaccination), or in individual cases where signs are severe or fail to resolve. For upper respiratory tract disease, a deep oropharyngeal swab should be taken. A number of PCR panel tests are available, and can be helpful in checking for the presence of several organisms simultaneously. Diagnostic results need to be interpreted with care since some of the components of CIRDc can be part of normal respiratory tract flora. Additionally, CIRDc may involve different pathogens at different stages of infection. Therefore, in an outbreak, sampling several dogs at different stages of infection may be helpful.

Treatment

For most dogs with CIRDc, specific antibiotic therapy is not necessary, with symptomatic treatment (avoiding pulling on collars, rest and NSAIDS if needed) being sufficient. Use of antitussives is contentious. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines suggest empirical use of antibiotics where there is a mucopurulent discharge alongside signs of lethargy, pyrexia or anorexia (Lappin and others 2017). BSAVA PROTECT ME suggests that antibiotics are only indicated if clinical signs persist for greater than 10 days and/or the dog is systemically unwell (BSAVA/SAMSoc 2018). Where necessary, both guidelines suggest doxycycline or potentiated amoxycillin as the first choice antibiotics. Where cases fail to resolve, or if the lower respiratory tract is involved, culture and sensitivity and further investigations such as broncho-alveolar lavage may be indicated.

Control

Several pathogens involved in CIRDc are part of canine core vaccines. In the UK, *Bordetella* vaccination is given intranasally, often combined with CPiV; elsewhere subcutaneous and oral vaccines exist. Mucosal immunity commences within three days. As the vaccine is live, some dogs may have a transient cough for several days afterwards. It is essential to note that

vaccination will not fully prevent clinical CIRDc due to the range of pathogens which contribute to this syndrome. Following natural infection, dogs may shed *Bordetella* at diminishing levels for up to 12 weeks, with transmission mainly via aerosol. Therefore restricting social mixing of dogs recovering from CIRDc is important in limiting spread.

Zoonotic potential and cross-species transmission

B. bronchiseptica is a rare but potentially serious zoonosis (Garcia-de-la-Fuente and others 2015). Case reports of infections in cystic fibrosis and transplant patients have documented serious sequelae and even death (Brady and others 2014; Ner and others 2003). Zoonotic transmission following vaccination (including the administrator, handler and owner) is thought to be possible but extremely rare (Gisel and others 2010). Post-vaccination shedding may occur for several weeks (Iemura and others 2009). Where immunocompromised humans are in contact with dogs, the low but predictable risk of vaccination must be carefully weighed against the less predictable risk of clinical infection. Appropriate advice, including recommending at-risk owners contact their medical practitioner, should be offered.

Transmission between dogs and cats has been suggested to occur (Binns and others 1999). Additionally, cats have also been implicated in zoonotic infections (Register and others 2012).

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Tables

Table 1: Percentage of recorded clinical signs in 2,404 dog and 1,177 cat consultations presented with respiratory disease to veterinary practices in the UK (January 1, 2018 to February 28, 2019).*

Clinical sign	Number (%) of dogs	Number (%) of cats
Coughing	1631 (68.0)	333 (28.3)
Dyspnoea	328 (13.7)	246 (20.9)
Sneezing	303 (12.6)	536 (45.6)
Nasal discharge	212 (8.8)	347 (29.4)
Conjunctivitis and/or ocular discharge	42 (1.7)	170 (14.5)
Drooling	61 (2.5)	40 (3.4)
Mouth ulcers	4 (0.2)	11 (0.9)
Pyrexia	79 (3.3)	54 (4.6)
Generalised depression / lethargy	143 (5.9)	94 (8.0)
Other clinical signs	330 (13.7)	159 (13.5)

* The same animal could present with more than one sign per consultation

Figures

Figure 1: Septile bi-variate maps indicating proportion of total canine and feline consultations (1 Jan 2018 – 28 Feb 2019) presenting mainly for investigation and/or treatment of respiratory disease, summarised by 20km gridded cells encompassing England, Scotland and Wales. Proportion has been modelled against standard error to provide a measure of relative confidence in findings according to the volume of data collected in each cell. Darker red colours indicate areas of relatively high confidence and prevalence.

Figure 2: Percentage of canine and feline respiratory consultations where systemic antibiotics; systemic anti-inflammatories; respiratory- or cardiovascular-active products were prescribed, by quarter (Q2 2014 – Q1 2019). Also described are the percentage of respiratory consultations where the animal was euthanased. Shaded regions refer to 95% confidence intervals, calculated to adjust for clustering within veterinary practice site (bootstrapped estimated, *n* replicates = 5,000).

Figure 3: Percentage of canine and feline respiratory sample submissions that tested positive by PCR for *B.bronchiseptica*, summarised by quarter and year (2016-2019). Data was collated from four veterinary diagnostic laboratories situated in the UK.

Figure 4: Postcode area quintile bivariate map summary of the proportion of canine respiratory samples testing positive by PCR assay for presence of *B.bronchiseptica*, modelled against standard error to account for variable UK surveillance coverage. Samples tested between 2016 and 2019 were used, summarising data provided by four UK-based veterinary diagnostic laboratories. Postcode of the submitting veterinary practice site was used in this summary.

Fig 5: Observed prevalence for pruritus, gastroenteritis and respiratory disease in cats and dogs attending SAVSNET-participating practices from February 2017 to February 2019. Red points represent the extreme outliers (outside the 99 per cent credible interval [CI]), orange points represent the moderate outliers (outside the 95 per cent CI but within the 99 per cent CI), and green points represent the average trend (within the 95 per cent CI).

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