Incidence and riskfactors of Actinobacillus pleuropneumoniae serotype 2 infection in the Danish SPF pig population. A grouped survival analysis

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Summary

A cohort of 2,835 Danish SPF herds, free from *Actinobacillus pleuropneumoniae* serotype 2 on the 2nd May 1996, were followed retrospectively until the 4th May 2001. The average annual risk of App2 infection was about 2.6 %. A herd-specific risk index was derived from a geographical information system (GIS), assuming that the risk contribution of a neighbouring herd was directly proportional to the herd size of the neighbour, but inversely proportional to the distance. Variations in incidence could be linked to variations in average temperature, rainfall and risk index, using a grouped survival model. The multivariate risk assessment provided evidence for the hypothesis that local transmission is a major factor responsible for App2 infection in the Danish SPF pig population.

Introduction

Respiratory diseases in pigs, such as the infection with *Actinobacillus pleuropneumoniae* serotype 2 (App2) are very prevalent in most pig populations (6). It has been estimated that about three quarters of Danish pig herds are App2 seropositive. Worldwide, App2 has been recognized as one of the most significant contributors to disease associated economic loss in pig production (5,6). Airborne transmission has commonly been regarded as one of the main routes for transmission of App2 (1,2,7). In Denmark, implementation of a specific pathogen free (SPF) programme has succeeded in controlling a number of diseases since the end of the 1960s, including *Actinobacillus Pleuropneumoniae* (7). Since the 1980's, approximately 3,500 herds have been maintained in the programme, supplying more than 80% of breeding animals. Clinical inspection is performed roughly once a month in SPF pig herds, while serological screening for App2 infection is performed once a month in the genetic SPF pig herds, and once a year in production herds. However, these herds have difficulties in maintaining their specific disease free status.
The objective of the present study was to estimate the incidence of App2 infection in the total Danish SPF herd population, and to conduct a risk factor analysis using available data on herd location and meteorological data on the national scale.

Materials and methods

The study is based on the disease status database of the Danish SPF Company, each herd being identified by its CHR-number, i.e. the central holding registration number. Extracts of the database had been collected for other purposes on a regular schedule, roughly twice a year, at the beginning of each summer and winter. The study covers the period from the 2nd May 1996 to the 4th May 2001. A total of 11 cross-sections were used, each containing the current health status of each SPF herd. A closed cohort of 2835 App2 free herds was defined at the date of entry, 2nd May

1996. Each herd was then followed, retrospectively, until the first event among the following occured: detection of App2, exit from the SPF-system or the end of study (4th May 2001). From a geographical information system (GIS) at DBMC, basic information on these herds could be obtained, including address of the farm in geo-referenced coordinates, the number of sows and slaughter pigs and geographical region defined from the post-code. Country-level, monthly averages of climatic variables during the 5-year study period where obtained from public sources at the Danish Meteorological Institute, including temperature, relative humidity, rainfall, wind speed and total number of sun hours.

Data on neighbouring herds within a 3 km radius could likewise be obtained from GIS-data, and used to derive three variants of a 'local infection potential', based on the number of heat producing units, HPU, of each neighbour (HPU=0.45*(#sows) + 0.17*(#finishing pigs)):

1. herd density = the number of neighbouring herds per square kilometre
2. pig density = $\sum_{herds}$ HPU's in neighbouring herds
3. risk index = $\sum_{herds}$ (HPU's / distance$^{\gamma}$)

The exponent in the definition of the risk index, γ, was taken to be 1 for a start, but is really an unknown parameter to be estimated from the data by maximum likelihood. A grouped version of the Cox proportional hazards model was used (3), which has the advantage of giving the same interpretation of fixed covariate parameters as the Cox-model. Each herd, h , characterized by a set of fixed covariates $X_h = (X_{h,1},\ldots,X_{h,k})$, is assumed to have a time dependent infection hazard, $\lambda_h(t) = \lambda_0(t)\exp(\beta X_h)$, where $\lambda_0(t)$ is the unspecified baseline hazard of the Cox-model, allowed to vary freely over calendartime. Herds are only observed at 10 common fixed points in time during the study period (excluding the start of study), $\tau_1 < \tau_2 < \ldots < \tau_{10}$, roughly spaced one half year apart. Spacing varies between 4 and 8 months: $\Delta_j = | I_j | = \tau_j - \tau_{j-1}$. In the grouped survival model the basic quantity is the conditional survival probability of a herd during time period I_j, given that the herd has escaped infection until time τ_{j-1} . The baseline hazard is assumed constant, λ_j , during period I_j . The cumulative infection risk during I_j for herd h, $p_{h,j}$, is linked to the explanatory variables by the expression:

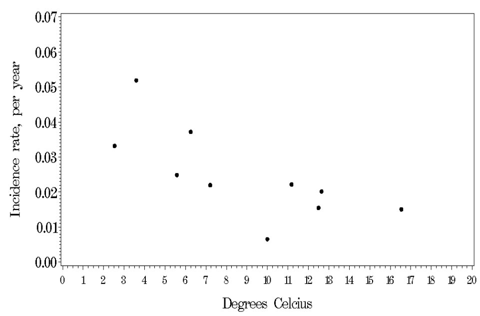
$$\log\left(-\log(1-p_{h,j})\right) = \boldsymbol{\beta}\,\mathbf{X_h} + \log\Delta_j + \log\lambda_j$$

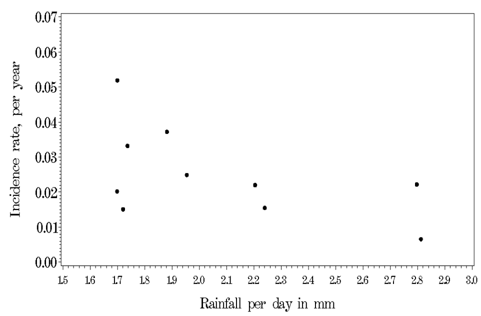
Each herd, h, contributes a binary observation for each time interval at risk: infected / not infected at the end of the interval I_j , and the probability of infection is $p_{h,j}$. The effect of climatic covariates can now be added through a model for the baseline λ_j :

$\log\lambda_j = \alpha + \beta\cdot\tau_j + \gamma\cdot Temp_j + \delta\cdot Rain_j + \ldots$ It is obvious that these meteorological covariates, in principle, could be made to depend on the location of the herd, rather than just time, but such detail was not available for the present study. Thus only country-level variables were used. Taken together, a *generalized linear model* is obtained (4), with *binary observations* and $\log\left(-\log(1-p_{h,j})\right)$ as the *link-funktion*.

Results

A total of 2835 App2 free herds were included in the present study. Of these 325 herds were infected with App2 during the 5-year study period. The average annual risk of App2 infection was about 2.6 % with no clear trend. The risk of infection was strongly associated with season, with a higher incidence during winter and spring. According to the grouped survival model, the average daily temperature and rainfall over the grouped intervals are strongly associated (negatively) with risk of App2 infection. The relative baseline risk of App2 infection decreases 8 % when the average temperature increases by 1^{o}C, or 36 % when the average rainfall per day increases by 1 mm. The risk index is associated positively with App2 infection, the risk of which increases 1.5 times if the risk index is doubled. The two plots below show the relation between the App2 incidence rate, temperature and rainfall, averaged over each of 10 observation intervals.





Discussion and conclusion

In the present study temperature and rainfall per day were associated negatively with the risk of App2 infection. The effect of rainfall is possibly due to the fact that dust concentration in the air relates negatively to the amount of rainfall in general. The presence of dust particles is a prerequisite for the formation of infective aerosols (1,2). The present study provides, we think, evidence for the hypothesis that airborne transmission of App2 is possible under field condition, since the risk index is an important predictor of infection. Unfortunately, the available data did not allow any assessment of the importance of direct import of animals into the herds.

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