A GENETIC EPIDEMIOLOGICAL MODEL OF PIG DISEASE RESISTANCE

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SUMMARY

This paper discusses a genetic epidemiological model (GEM) for investigating the effect of selection against susceptibility or infectivity on the epidemiology of infectious diseases in pigs. The model serves as a tool for evaluation selection strategies against different diseases in different environments.

Keywords: Pigs, Diseases, Resistance, Genetics, Epidemiology, R_0

INTRODUCTION

Infectious diseases in pigs are many and varied. Acute diseases such as classical swine fever require herd slaughter. Chronic diseases such as transmissible gastroenteritis and pseudorabies cause high production losses. Transmissible gastroenteritis is a viral disease of pigs, widespread in pig-production areas with no effective treatment or vaccine. Birds are thought to be a vector for transmission (Saif and Wesley 1992) making prevention difficult. Genetic improvement of disease resistance may be one way of dealing with such a disease. Work in other species has shown that selection to increase disease resistance is feasible. In sheep, worm burden can be reduced by selection for resistance (Woolaston and Baker 1996). In turkeys, it is possible to improve antibody response to Newcastle disease virus and *Pasteurella multocida* by selection for improvement in antibody response to each antigen, however selection would have to be made for each antigen (Sacco *et al.* 1994). Appleyard *et al.* (1992) conducted a selection experiment for antibody avidity in Yorkshire pigs. The high response group had significantly higher secondary antibody avidity than the controls. It is clear that selection for resistance needs further investigation in pigs and may be an appropriate strategy for some diseases.

The success of selection for disease resistance may be measured in terms of the epidemiology of the disease, should an infection occur. The epidemiology of the disease depends on host susceptibility and host infectivity, which are inherited traits. The aim of this paper is to develop a class of models to quantify this phenomenon, combining genetics and epidemiology. We coin the term genetic epidemiological model (GEM) for this purpose.

MATERIALS AND METHODS

The fundamental component of the GEM is the parameter R_0, the basic reproductive ratio. R_0 gives an estimate of the expected number of infections resulting from the introduction of a single infected animal into a susceptible population. If $R_0 > 1$ the infectious case will cause an epidemic, otherwise, it will not. Functions of R_0 are the proportion of animals ever infected (I)

given by $I = 1 - \exp(-R_0 I)$ and the maximum proportion of animals infected at any time (ymax) where $ymax = 1 - (1 + \ln R_0)/R_0$ (Anderson and May 1992). When $R_0 < 1$, I and ymax are zero. The model calculates the value of R_0 for a general infection introduced into a highly structured pig farm situation with a heterogeneous population, using the algorithm of De Jong *et al.* (1994). The farm is modelled as a closed system with sows being replaced by stock reared on the farm. This algorithm can be used to model farms of any size assuming the structure can be clearly defined. Genetic improvement is then incorporated to allow reduction in susceptibility or infectivity with time.

In the model pigs are allocated to 'types' and stay that type for a fixed period of time. The type describes the physiological status of an animal, which determines how susceptible or infectious it is. The algorithm makes use of the contact between pigs, the path pigs take through the farm and their infection-independent survival probability i.e. culling and mortality. These parameters depend on the pig type. Each type has a value for 'susceptibility', g, and an 'infectivity', f. These may change as infection progresses or remain constant throughout infection, depending on the biology of the disease. For example, piglets are often more susceptible to a particular infection than adult pigs. Probability of infection may be calculated from susceptibility as $1 - \exp(-\xi g_i \Delta t)$, where ξ is the concentration of infectious material and Δt is the exposure time.

The algorithm starts by introducing an infected animal of type 1, defined as the index case. This pig is followed round the farm for the duration of the infection as it infects other pigs. A matrix, **E**, is formed containing the sum of infection shed by the index case as it makes contact with other pigs. The total amount of infection depends on the probability that the pig leaves its current type alive and the length of time since the start of the infection. Infectivity is assumed to be a function of time since infection. The procedure repeated for all types of pig. The next generation matrix (Diekmann *et al.* 1990), **M**, is given by

$$m_{ij} = g_i f_j \sum_{l=1}^{n} c_{il} e_{lj}$$

where c_{il} is the contact between type i and type l. m_{ij} is the expected number of secondary cases of type i caused when the index case is type j. The dominant eigenvalue of **M**, is R_0. Since $R_0 \leq \max f_j g_j$ it is only necessary to select against the product of susceptibility and infectivity. This algorithm can be used to model farms of any size or structure assuming the structure can be clearly defined. In this paper we model a typical UK pig unit, consider a disease with a 2-week infectivity, and assume arbitrary values for susceptibility, infectivity and genetic progress in the product susceptibility x infectivity ($g_i f_j$).

RESULTS AND DISCUSSION

Figure 1 shows the effect of genetic progress of 1% per annum, on $g_i f_j$, I and ymax, assuming constant levels of $g_i f_j$ across the whole population starting with a $g_i f_j$ level arbitrarily set to 10.0, indicating a highly infectious disease. R_0 declines linearly with $g_i f_j$ and at this level of genetic improvement it takes 96 years until R_0 is less than 1.

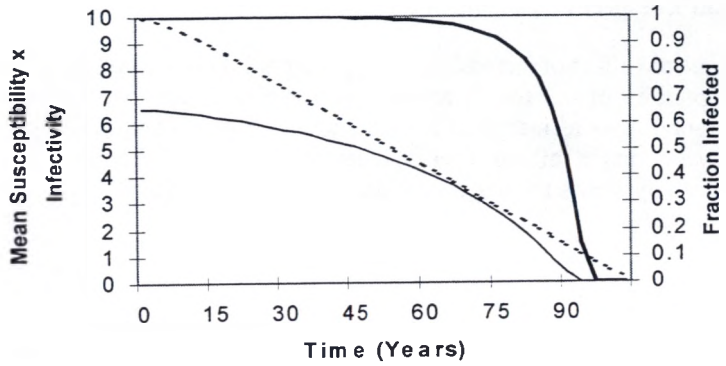

Figure 1. The effect of genetic progress on $g_i f_j$, I and ymax. Dashed line = mean herd $g_i f_i$, heavy line = I, light line = ymax.

The time taken until $R_0 < 1$ depends on the initial level of $g_i f_j$ which depends on the infection, being modelled. Figure 2 shows how I changes for different rates of genetic improvement and different initial $g_i f_j$. The populations modelled for this figure have initial mean genotypic $g_i f_j$ of 10.0 or 5.0 for all classes of animals but assume a degree of acquired immunity for animals more than 4 weeks of age. These animals have a mean phenotypic $g_i f_j$ of 0.5, until genetic progress reduces the genotypic $g_i f_j$ below this value. The rate of genetic improvement is defined as being proportional to the initial values of susceptibility and infectivity.

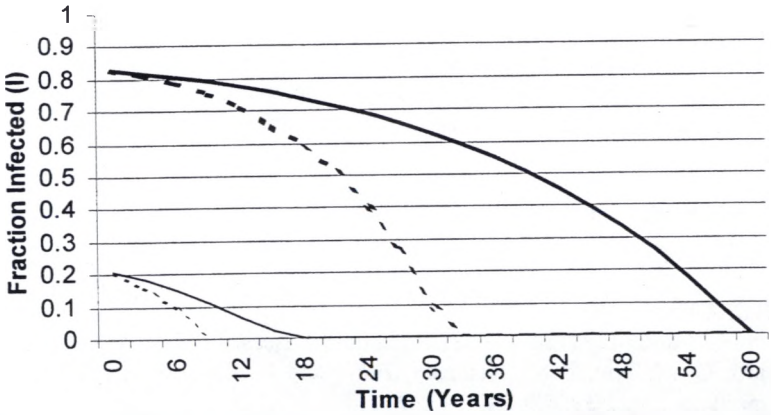

Figure 2. Effect of rate of genetic progress and initial $g_i f_j$ on I. Heavy lines initial $g_i f_j$ = 10, light lines = 5, solid lines = progress at 1%/year, dashed = 2%

For a highly contagious disease, selection will take many years to be effective, but for a disease to which the population is less susceptible selection may quickly be effective. Acquired

immunity in older animals also quickens the benefits of selection. R_0 is initially 2.1 and 1.1 for $g_i f_j$ of 10 and 5, respectively in this figure.

To investigate the effect of increasing piglet susceptibility on R_0 *per se*, the model was run with fixed susceptibility of 0.5 for all animals except piglets less than one week old. For these piglets susceptibility was increased from 0.5 to 25. Figure 3 shows that piglet susceptibility x infectivity has a major influence on whether or not a new infection will cause an epidemic. This figure clearly shows the linear relationship between $g_i f_j$ and R_0.

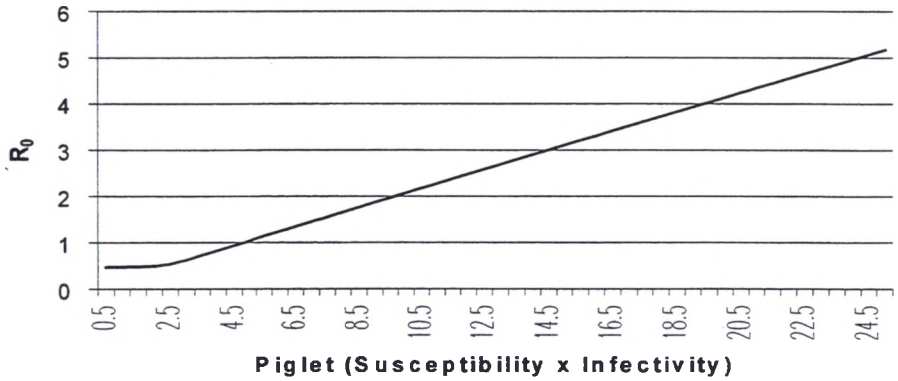

Figure 3. Effect of $g_i f_j$ on R_0

In conclusion, it has been demonstrated that selection against susceptibility or infectivity will reduce the probability of epidemics by changing the epidemiology of the disease. The likely effectiveness of selection is critically dependent on the mean values of susceptibility and infectivity for different classes of animals. The model can be used to evaluate selection strategies for different farming structures and different diseases.

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