Available online at www.sciencedirect.com
ScienceDirect
Preventive Veterinary Medicine 78 (2007) 262–273
PREVENTIVE VETERINARY MEDICINE
www.elsevier.com/locate/prevetmed

A pedigree-analysis approach to the descriptive epidemiology of autosomal-recessive disorders

W.Y.N. Man *, F.W. Nicholas, J.W. James

Reprogen, Faculty of Veterinary Science, University of Sydney, NSW 2006, Australia

Received 22 December 2005; received in revised form 20 October 2006; accepted 23 October 2006

Abstract

We describe a pedigree-analysis approach to estimating descriptive epidemiological parameters for autosomal-recessive disorders when the ancestral source of the disorder is known. We show that the expected frequency of carriers in a cohort equals the gene contribution of the ancestral source to that cohort, which is equivalent to the direct (additive) genetic relationship of that ancestor to the cohort. Also, the expected incidence of affected foetuses ranges from $(1/2)\bar{F}^*$ to $\bar{F}^*$, where $\bar{F}^*$ is the mean partial inbreeding coefficient (due to the ancestor) of the cohort. We applied this approach to complex vertebral malformation (CVM) in Holstein–Friesians in Australia, for which the ancestral source is a USA-born bull, Carlin-M Ivanhoe Bell. The estimated frequency of carriers was 2.47% for the 1992-born and 4.44% for the 1997-born cohort of Holstein–Friesian cows in Australia. The estimated incidence of affected foetuses/calves was considerably less than one per thousand, ranging from 0.0024 to 0.0048% for the 1992-born cohort, and from 0.0288 to 0.0576% for the 1997-born cohort. These incidences correspond to expected numbers of affected female foetuses/calves ranging from 2 to 4 for the 1992-born cohort and from 28 to 56 for the 1997-born cohort. This approach is easy to implement using software that is readily available.

Keywords: Descriptive epidemiology; Pedigree analysis; Autosomal-recessive disorders; Complex vertebral malformation; CVM; Holstein–Friesians; Australia

* Corresponding author at: Scottish Agricultural College, West Mains Road, Edinburgh EH9 3JG, UK. Tel.: +44 131 5353361; fax: +44 131 5353121.
E-mail address: nicola.man@sac.ac.uk (W.Y.N. Man).

0167-5877/$ – see front matter © 2006 Published by Elsevier B.V.
doi:10.1016/j.prevetmed.2006.10.010

1. Introduction

1.1. Background

Because almost all animals carry deleterious genes (Morley, 1954), it is part of the natural process (with or without artificial insemination and other reproductive technologies) that the breeding of domesticated animals is associated with the occasional appearance of inherited disorders. Many such disorders are autosomal recessive, in which case by the time the disorder has been recognised, the deleterious allele has been in the population for some time (at least two generations). For the purpose of planning and management, it would be helpful to know the extent to which the deleterious gene has spread throughout the population, and the likely incidence of the disorder.

1.2. Objectives

Our aim was to describe how pedigree analysis can be used to provide predictions of the frequency of an autosomal-recessive deleterious gene, the frequency of carriers, and the frequency of affected offspring, when the ancestral source(s) of the gene is known.

By way of application, we illustrate this method for complex vertebral malformation (CVM; OMIA, 001340), using pedigree data that are used for routine genetic evaluation. Although a DNA test was soon developed for CVM (Anon., 2001), the method described in this paper is equally applicable to disorders that have only just been recognised and for which there is no genotyping test. The method provides population-level information that is not usually available even with a genotyping test.

Allaire et al. (1982) presented a method of estimating frequencies of recessive alleles in populations from samples of pedigrees, using a gene-counting method in ancestors with known genotypes and an adjustment for estimated gene frequencies in unknown genotypes. This adjustment was made iteratively. Hoeschele and Meinert (1990) modified this method for use with large populations rather than small samples. For the situation we consider, their estimate of gene frequency would be similar to ours. Neither of these methods provides an estimate of the frequency of affected animals.

When this work was at an advanced stage, our attention was directed to an unpublished DVM thesis by Engelhardt (1996), who applied a somewhat similar pedigree-analysis approach to the prediction of the frequency of carriers and affecteds. However, her approach was limited by using only a cohort sample of 200 animals, and she did not use software that is now readily available on the web.

2. Materials and methods

2.1. Pedigree data and ancestral source of CVM

The pedigree data used in this analysis were kindly provided by Drs. L. Jones and K. Beard from the database of the Australian Dairy Herd Improvement Scheme (ADHIS). Two cohorts of AI-bred cows with known parents were chosen for analysis: those born in