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How the Orthopedic Foundation for Animals (OFA) is tackling inherited disorders in the USA: Using hip and elbow dysplasia as examples

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ABSTRACT

The Orthopedic Foundation for Animals (OFA) maintains an on-line health pedigree database for inherited disorders of animals. With the American Kennel Club Canine Health Foundation, the OFA maintains the Canine Health Information Center (CHIC) for parent breed clubs to identify breed-specific required health tests. Analysis of the results of OFA evaluations in the hip and elbow registries show that selection based on phenotype improves conformation. Disorders with complex inheritance respond best to selection based on depth (ancestors) and breadth (siblings) of pedigree health test results. This information can be derived from vertical pedigrees generated on the OFA website.

Introduction

A prominent businessman in the United States, John M. Olin, was also an avid sportsman and recognized the impact of canine hip dysplasia on his Labrador retrievers. Along with the Golden Retriever Club of America, German Shepherd Club of America and the veterinary community, he organized a meeting that eventually led to the formation of the Orthopedic Foundation for Animals (OFA) in 1966. The OFA is guided by the following four specific objectives:

(1) To collate and disseminate information concerning orthopedic and genetic diseases of animals.
(2) To advise, encourage and establish control programs to lower the incidence of orthopedic and genetic diseases.
(3) To encourage and finance research in orthopedic and genetic disease in animals.
(4) To receive funds and make grants to carry out these objectives.

The OFA is governed by a voluntary Board of Directors. As a not-for-profit organization, the revenue over expenses is either held in the operating reserve or donated to support animal health-related research. Most funding is channeled through the American Kennel Club Canine Health Foundation (AKC-CHF)[1] or Morris Animal Foundation, with occasional direct funding. OFA has supported research not only in orthopedic diseases but also for cancer, cardiac, hepatic, nephritic, neurologic, ocular and thyroid disease.

While the OFA's initial focus was canine hip dysplasia, the mission has broadened to include cats and other genetic diseases, including elbow dysplasia, patella luxation, autoimmune thyroiditis, congenital heart disease, Legg–Calve–Perthes disease, osteochondrosis dissecans (shoulder osteochondrosis), sebaceous adenitis and congenital deafness. The methodology and criteria for evaluating the test results for each disorder are independently established by veterinary scientists from their respective specialty areas and the standards used are generally accepted throughout the world. Disorders present on the OFA website include those that have a defined test for normalcy. Disorders such as epilepsy, gastric dilatation/volvulus and cancers that do not have defined phenotypic or genotypic tests are not included. If genetic markers for disease liability are identified in the future, these can be added as tools for genetic disease control.

The power of the OFA genetic database lies in the compilation and integration of all health screening information in a single location. For dogs with an existing OFA record, examination results from the Canine Eye Registry Foundation (CERF) are incorporated in their OFA record. In addition, the results of genotypic tests that are either submitted by the owner or through a cooperative agreement with the parent club are also included in the OFA genetic database. Cutting-edge advancements in molecular genetics now account for over 90 DNA tests involving over 145 breeds of dogs and cats.

The collection of such data is meaningless unless the data can be disseminated to parties of interest. The OFA maintains an

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[1] See: www.akcchf.org.

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on-line database of >1 million phenotypic and genotypic test results.[2] All normal or grades of normal results in the OFA database are available on-line. Abnormal or grades of abnormal results are available on-line if released by the owner, or if the results are part of a breed club program where all (normal and abnormal) test results are published.

The Canine Health Information Center (CHIC)[3] is a program that is dually sponsored by the OFA and the AKC-CHF. The parent clubs determine the breed-specific health issues for CHIC certification and encourage breeder participation in the program. The CHIC program is not about normalcy; it is about health consciousness. Dogs receive CHIC certification if they have completed the required breed-specific health testing, regardless of the test results. Other requirements include permanent identification (tattoo or microchip) and release to the open database of abnormal results. CHIC encourages health screening to improve the overall health of breeds. There are presently over 139 parent breed clubs participating, with over 64,500 dogs achieving CHIC certification.

The acceptance of the CHIC certification program by parent breed clubs and breeders provides an avenue for the only proven method of genetic disease control: breed-specific phenotypic and genotypic screening of prospective breeding stock. The CHIC program provides a standard for breeders to practice health-conscious breeding. It also allows pet owners to screen prospective purchases for evidence of health-conscious breeding.

Another goal of the CHIC program is to collect and store canine DNA samples, along with corresponding genealogic and phenotypic information, to facilitate future research and testing aimed at reducing the incidence of inherited disease in dogs. Researchers have been hampered by the lack of appropriate DNA samples and the DNA repository addresses this need. To date, the CHIC DNA Repository contains DNA from over 12,500 dogs and has received 17 requests from researchers, resulting in the distribution of over 2,200 DNA samples with their appropriate health and pedigree information.

To evaluate hip dysplasia, the OFA employs the ventrodorsal hip-extended positioning recommended by the American Veterinary Medical Association (AVMA Council on Veterinary Service, 1961). The in-house radiologist is the sole evaluator for preliminary evaluation of dogs <24 months of age. The reliability of preliminary hip evaluations for predicting of-age OFA ratings was demonstrated by Corley et al. (1997). Dogs or cats must be $\geqslant$24 months of age to receive OFA hip certification. Radiographs are independently evaluated by three board-certified veterinary radiologists out of a pool of consultants maintained by the OFA. The consensus rating of these three radiologists becomes the hip rating that is reported to the owner and referring veterinarian. There is a high degree of inter- and intra-reader correlation for conventional and digital images (Corley, 1992; Essman and Sherman, 2006).

Seven OFA hip ratings are reported: Excellent, Good, Fair, Borderline, Mild, Moderate or Severe. The first three ratings are considered to be normal, while the last three ratings are regarded as dysplastic. A Borderline rating is given when there is no clear consensus between radiologists to place the hips in a category of normal or dysplastic. It is recommended that dogs with this rating have a repeat radiograph submitted after a minimum of 6 months.

The OFA elbow dysplasia registry employs the protocol established by the International Elbow Working Group (IEWG),[4] which consists of Normal or Grades I, II or III Dysplastic based on the severity of secondary osteoarthritis/degenerative joint disease present on an extreme flexed mediolateral view (International Elbow Working Group, 2001). When a specific component of elbow dysplasia is observed, it is reported in addition to the Grade as ununited anconeal process, osteochondrosis or fragmented medical coronoid process. Elbow radiographs are subjected to the same of-age or preliminary evaluation and certification process as hip radiographs.

Diseases with complex inheritance can respond to selective pressure based on phenotype (Keller, 2006; Pirchner, 1983). In this manuscript, the OFA hip and elbow registries are used to illustrate this response.

Materials and methods

The OFA hip registry of 1,187,831 evaluations was queried for hip ratings of progeny where both parents also had known of-age hip ratings. Data were collected on progeny with of-age or preliminary hip confirmation ratings of normal (Excellent, 1; Good, 2; Fair, 3) or dysplastic (Mild, 5; Moderate, 6; Severe, 7). Progeny with Borderline (4) hip ratings were not included. The hip ratings of both parents were recorded, including all seven grades. A hip Combined Parent Score (CPS) for each mating was determined by adding together the numbers corresponding to the hip rating for each parent; for two OFA Excellent parents the CPS was 2 and for two OFA Severe parents the CPS was 14. Matings with the same CPS were combined together for analysis; e.g. Good mated to Borderline, Fair mated to Fair and Excellent mated to Mild all have a CPS of 6.

The OFA elbow registry of 260,195 evaluations was queried for elbow ratings of progeny where both parents had known of-age elbow ratings. Data were collected on progeny with preliminary or of-age elbow confirmation ratings of Normal (1) or dysplastic (Grade I, 2; Grade II, 3; Grade III, 4). An elbow CPS for each mating was determined by adding together the numbers corresponding to the elbow rating for each parent; for two OFA Normal parents the CPS was 2 and for two OFA Grade III parents the CPS was 8. Matings with the same CPS were combined together for analysis.

Pearson correlation analysis was performed to compare the CPS of matings to the observed percentages of hip dysplasia or elbow dysplasia in the progeny.

Results

Table 1 shows the hip ratings for 490,966 progeny in the OFA hip registry with known sire and dam hip ratings. The percentage of dysplastic progeny increased as the parental hip scores increased. The total number of hip radiograph submissions from parents with normal hip ratings was significantly greater than those from parents with dysplastic hip ratings ($P > 0.05$).

Fig. 1 shows the relationship between the CPS and the percentage of dysplastic progeny. Matings with the same CPS (on the diagonal of Table 1) were strongly correlated with increasing percentages of dysplastic progeny (Pearson correlation coefficient $r = 0.96$; $P > 0.05$). The single CPS that did not reflect this trend was for matings between two severely dysplastic parents, where only 18 progeny were submitted for evaluation.

Table 2 shows the elbow ratings for 67,599 progeny in the OFA elbow registry with known sire and dam elbow ratings. Matings including one normal parent had significantly lower percentages of progeny with elbow dysplasia (12.4%) than those between two parents with elbow dysplasia (45.4%) ($P > 0.05$). Matings involving a parent with Grade I elbow dysplasia produced significantly more elbow dysplasia (25.6%) than matings including a parent with normal elbows ($\chi^2 = 0.77$, 6 df, $P = 0.99$).

Fig. 2 shows the relationship between the CPS and the percentage of progeny with elbow dysplasia. The Pearson correlation coefficient between the CPS and percentage of dysplastic progeny was $r = 0.06$. The lack of correlation is due to the low percentage of dysplasia in progeny of Grade III sires bred to Grade II dams, and Grade III parents bred to each other. The total number of progeny from these matings numbered 14 and 3, respectively.

Discussion

The OFA hip data and CPS demonstrate that hip dysplasia is inherited in an additive and quantitative manner. This verifies

[2] See: www.offa.org.
[3] See: www.caninehealthinfo.org.
[4] See: www.iewg-vet.org/.