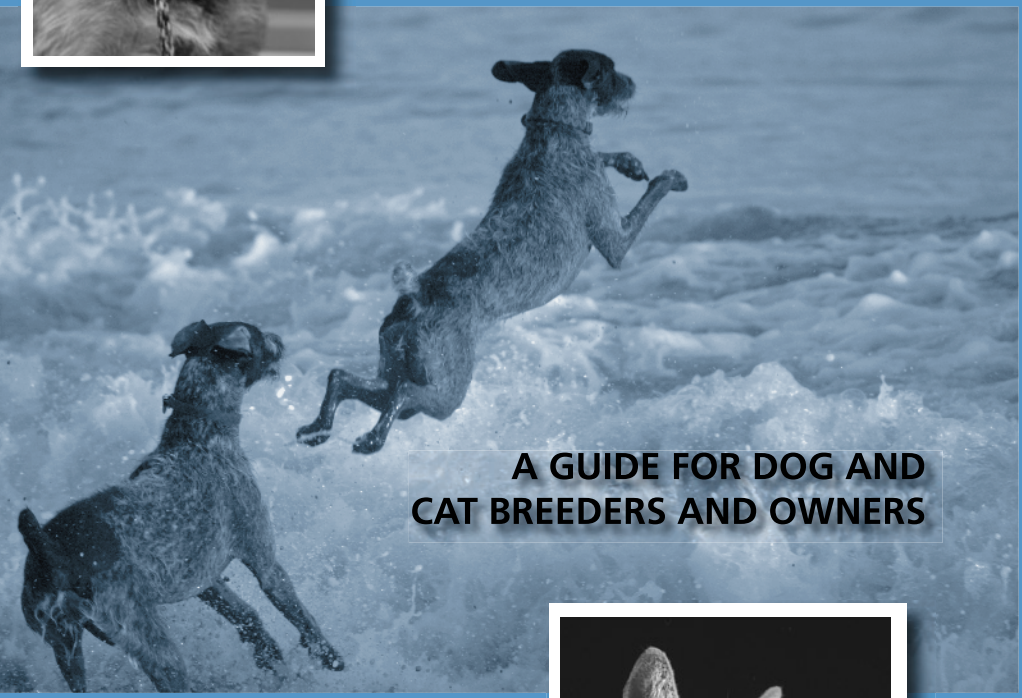
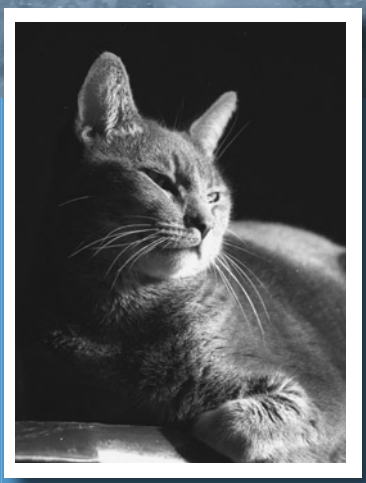
The use of health databases and selective breeding



A GUIDE FOR DOG AND CAT BREEDERS AND OWNERS



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5th edition, 2006

ORTHOPEDIC FOUNDATION FOR ANIMALS • OFA

The use of health databases and selective breeding

A GUIDE FOR DOG AND CAT BREEDERS AND OWNERS

5th edition, 2006

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IN MEMORY OF ALL OUR SPECIAL ANIMAL FRIENDS

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Introduction

Breeders have an inherent responsibility to protect the comfort and well-being of the animals they produce, yet the dog and cat owning public spends hundreds of millions of dollars each year on diagnosis and treatment of genetic diseases. These factors justify placing continued emphasis on prevention of these diseases. Responsible breeders and the more progressive breed clubs are, and have been, responding to the challenge of improving the genetic health of our companions through better breeding practices.

The Orthopedic Foundation for Animals, Inc., (OFA) is a private non-profit foundation which formed a voluntary dysplasia control database in 1966 with the following 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's voluntary databases serve all breeds of dogs and cats and have the world's largest all-breed data bank on radiographic evaluations of the hip and elbow. The testing methodology and the criteria for evaluating the test results for each database were independently established by veterinary scientists from the respective specialty areas. These standards are accepted throughout the world and the results are used to evaluate prevalence and progress in controlling the respective diseases in the breeding population. The OFA serves as a central source of information for breeders and owners based on the standards for evaluation, and as a major source of funding for studies directed at animal wellness.

The purpose of this monograph is to assist the breeder, dog owner, and veterinarian in accomplishing their goals by providing a summary of information on the OFA databases, their methodology, and a reference source for further study. Data on individual animals may be obtained at www.offa.org. This data can be useful for the breeder to determine the status of potential breeding animals and their family lines.

Genetics

Inherited traits, desirable or not, are controlled by the genetic makeup (genotype) of the individual dog or cat. The genotype is determined by the genes received from the parents, one-half from the sire and one-half from the dam. Most inherited traits in animals are polygenic. Some examples are: conformation, type, size, longevity, disease resistance, temperament, speed, milk and egg production, growth rate, maturation and sexual maturity rate, and numerous inherited diseases.

Intuitively, it is recognized that these traits do not follow inheritance patterns based on simple Mendelian genetics. Mendelian genetics usually uses one pair of genes to explain basic genetic principles. For example, assume that: 1) The color black is dominant to brown, 2) The black gene is represented by B and the brown gene by b, and 3) a homozygous black (BB) is mated with a brown (bb). All of the offspring will be black, but will have the heterozygous Bb genotype. If two heterozygous blacks (Bb) are mated, Mendelian genetics predicts the offspring are expected to be three black (1 BB and 2 Bb) and one brown (bb). The ratio of 1:2:1 for the genotypes is based on probability. If only a small number of offspring are available from this type of mating, they may not fall within the ratio, but larger numbers will produce the predicted results. In addition, the finding of one brown offspring from the mating of black parents indicates that both parents are carriers (heterozygous Bb) of the recessive brown gene. In such a case, two out of three black offspring are also carriers, but until they are bred it is uncertain which are the carriers. In the above example of simple Mendelian genetics, the probable genotype of the parents can be determined by examination of the progeny.

However, polygenic traits, such as most characteristics that breeders are concerned with, are defined as those affected by multiple gene pairs. An oversimplified example is two genes affecting the same trait. Assume the mating of two dogs with genotypes of AaBb, where the dominant alleles "A" and "B" are desirable. The expected genotypic outcome is nine different genotypes with the following frequencies:

Genotypes	AABB	AABb	Aabb	AaBB	AaBb	Aabb	aaBB	aaBb	aabb
Frequency	1/16	2/16	1/16	2/16	4/16	2/16	1/16	2/16	1/16

Only 25% of the progeny from this mating are expected to have the same genotype for the trait as the parents. Some of the remaining progeny will have a more desirable genotype (AABB, AABb, AaBB) while others will have a less desirable genotype for the trait (Aabb, AAbb, aaBB, aaBb, aabb). As the number of genes involved increases, the possible combinations soar. The problem is further magnified if each gene pair exerts a different degree of influence on a trait to produce an "additive" result. It is currently impossible to precisely predict the specific outcome of a particular mating with regard to polygenic (additive) traits and probabilities can only be generally estimated.

However, animal geneticists have developed successful breeding programs to improve milk production in cows, egg production in hens, speed in horses, growth rate in food animals, etc. They use basic genetic principles that have also been demonstrated effective in the dog. Some of the following aspects of polygenic traits considered in arriving at these principles include:

Polygenic traits have a range of manifestations from the most desirable to the least desirable characteristic under consideration.

For example, mating two dogs of ideal conformation can be expected to result in a larger number of offspring with ideal conformation when compared with offspring of a mating where one or both parents have less than ideal conformation. However, both litters will present a range of conformational characteristics.

Polygenic traits are influenced by environmental factors which may minimize or maximize genetic potential.

For example, a horse with a respiratory infection will not be able to achieve its genetic speed capability, or a cow on a starvation diet will not produce milk to its full genetic potential.

Heritability measures the phenotypic expression of multiple genes as possibly modified by environmental influences and the degree to which the resulting phenotype predicts the genotype. The equation P (phenotype) = G (genetics) + E (environment) is a starting point. This equation means the variation in phenotype presented comes about from the complex interaction of the animal's own inherited genotype with the environment to which it has been exposed. Using hip dysplasia (HD) as an example, some environmental factors include, but are not limited to, overweight, rapid growth rate, early maturation, sex of the animal, etc. The most studied environmental influence on HD is caloric intake.

It is important to understand that heritability estimates do not refer to the degree of inheritance, but rather to the degree that the additive genetic component is reflected in the phenotype. This is easier to under-

stand using a trait for which most people have a greater intuitive grasp. In dogs, wither height is a polygenic trait that may be modified by the environment. Height may be influenced by restricting calorie or vitamin intake, certain environmental effects on hormones (such as early spay/neuter), and other environmental factors. Despite those potential environmental influences, height is recognized to be an inherited trait. However, one cannot accurately predict the height of an offspring by knowing the height of parents or siblings. This is because polygenic traits have many complex genetic interactions, in addition to their interactions with the environment. Thus, when one is only able to measure the height of parents or siblings, one is measuring their phenotypes, and not able to consider their genotypes and the various possible interactions of those genes. It may be helpful to substitute "predictability" for "heritability" to further clarify this concept.

Heritability estimates are usually determined through mid-parent offspring analysis using statistical methods and express the reliability of the phenotype as a guide to the predictive breeding value of the animal. Heritability estimates are reported on a scale from 0 to 1.0 (0-100%). These are expected to vary depending on the genetic background of the studied breed population and will change over time through selective breeding.

If the heritability estimate for a given trait is 0.1, it is generally considered low and the animal's phenotype is not a good indicator of the genotype (breeding value). Genetic selection based on a single phenotype would yield poor results. Although difficult to obtain for most hobby breeders, phenotypic information on many offspring raised in different environments (progeny testing) would offer additional insight into the parent's genotype.

If it is between 0.2 and 0.3, the heritability estimate is generally considered moderate. The animal's phenotype predicts its genetic makeup to a reasonable degree, and genetic selection based on the individual animal's phenotype is expected to yield slow yet substantial results. However, more rapid results can be achieved if phenotypic information on relatives (pedigree depth and breadth) is also considered. This also increases the accuracy in predicting the animal's breeding value and aids in identifying carrier animals.

If the heritability estimate is between 0.4 and 1.0, it is generally considered high and the animal's phenotype is a good predictor of its genetic makeup. In this case, rapid results can be obtained with genetic selection based on phenotype.

Breeding based on individual phenotypes appears to be the method used by most breeders, as available information on relatives is somewhat limited. For traits considered to have moderate heritability, this approach will reduce the frequency of an undesirable trait in the progeny, but progress, while substantial, will be slow.

Information on siblings of an individual animal, plus information on the siblings of parents and grandparents, makes it possible for the breeder to apply greater selection pressure against the disease. This results in selection of animals with more ideal breeding values and provides a more rapid reduction of the undesirable trait in the breeding program.

The following breeding selection criteria have been demonstrated to more rapidly and effectively reduce the frequency of undesirable traits:

1. **Breed only normal dogs to normal dogs**—using hip dysplasia as an example, Table 1 illustrates the outcome of matings based on information extracted from the OFA database. A total of 444,451 progeny were identified where both parents had hip conformation ratings. The percentage of dysplastic progeny increased as the sire's and dam's phenotypic hip ratings decreased from excellent through dysplastic. Reed (2000) reported equal genetic contribution on progeny hip scores from the sire and dam.

Table 1: Mating probability

Based on 444,451 progeny in the OFA Hip database with known sire and dam hip scores

Sire		Dam: Excellent	Dam: Good	Dam: Fair	Dam: Dysplastic
Excellent	T =	13,694	43,240	8,077	2,255
	N =	13,177 (96%)	40,420 (93%)	7,288 (90%)	1,940 (86%)
	D =	517 (4%)	2,820 (7%)	789 (10%)	315 (14%)
Good	T =	42,045	195,696	45,874	12,724
	N =	39,465 (94%)	175,840 (90%)	39,766 (87%)	10,159 (80%)
	D =	2,580 (6%)	19,856 (10%)	7,108 (15%)	2,565 (20%)
Fair	T =	6,214	41,304	13,475	4,114
	N =	5,611 (90%)	35,407 (86%)	10,772 (80%)	2,985 (73%)
	D =	603 (10%)	5,895 (14%)	2,703 (20%)	1,129 (27%)
Dysplastic	T =	1,569	9,465	3,123	1,582
	N =	1,341 (85%)	7,651 (81%)	2,249 (72%)	1,018 (64%)
	D =	228 (15%)	1,814 (19%)	874 (28%)	564 (36%)

***T** = total number of progeny; **N** = number and percent of normal progeny; **D** = the number and percent dysplastic progeny.*

2. **Breed normal dogs that come from normal parents and grandparents**—this employs the traditional horizontal pedigree with emphasis on the most immediate three generations (50% genetic contribution from each parent, 25% from each grandparent and 12.5% from each great grandparent)
3. **Breed normal dogs that have more than 75% normal siblings**—this information is usually not available since most animals in a litter become pets and are not screened for undesirable traits. Breeders can add incentives to purchase contracts in an attempt to gather this information, such as offering reimbursement for a preliminary hip radiograph taken when the pet dog is spayed/neutered.
4. **Select a dog that has a record of producing a higher than breed average percentage of normal progeny**—if known, the comparison of production performance between individuals is an important criterion. For example, a stud dog with a track record of producing 90% normal progeny is far superior to another dog producing only 50% normal progeny.
5. **Choose replacement animals that exceed the breed average**—exert constant, consistent pressure to ensure overall breed improvement.

In summary, achieving goals in breeding program depends upon the ability to assess an animal's predictive breeding value. Important information to assist breeders in achieving their goals is available on the OFA website through the database search option (*www.offa.org*).

Hip dysplasia

Hip dysplasia (HD), literally defined as an abnormal development of the hip joint, was first reported in the dog in 1935 by Dr. G.B. Schnelle. Little to no further information was added to his report over the following decade, due primarily to limited availability of radiographic equipment and radiographic expertise within the veterinary profession.

Popularity of the working dog, particularly the German Shepherd Dog, increased greatly in the late 1940s and the importance of HD became evident to breeders, dog owners, and the veterinary profession. Unrelated, but concurrently, veterinary education underwent an explosion in numbers of veterinary colleges and in quality of specialized education. Rapid advances in the veterinary profession made it difficult for most general practicing veterinarians to remain current with expanding knowledge in animal diseases. To provide the best possible diagnosis and patient care, multiple specialty colleges were formed, including the discipline of radiology which became a recognized specialty in 1966 through the American College of Veterinary Radiology (ACVR).

Hip dysplasia has been reported in man and in most domestic species of animals. In some breeds of dogs and cats, it is the most common cause of osteoarthritis (degenerative joint disease). In recent years, interest in canine HD research has been at an all-time high, as evidenced by the number of conferences focusing on the subject and by the number of new publications in scientific journals and popular magazines.

We now know that HD is a more complex disease than what was first thought. The complexity of the problem is expected to, and has produced, research findings that appear to be contradictory. These research reports, and anecdotal writings that continually appear in the popular press, contribute to confusion and frustration in breeders and veterinarians not familiar with the scientific literature. Thus, few diseases in animals have resulted in such extreme emotional reactions, controversy, or monetary expense as HD.

While it is useful to summarize results from the scientific literature, in the final analysis more research is needed to find answers to the many unresolved questions about HD.

Hip dysplasia is currently accepted to be an inherited disease caused by the interaction of many genes (polygenic). In animals that are genetically predisposed, there are unknown complex interactions of genes with the environment that bring about the degree of phenotypic expression (mild, moderate, or severely hip dysplasia) of these genes within an individual.

At this time, selectively breeding for normal hips is the only means to reduce the genetic frequency of HD.

Radiography is currently the accepted means for evaluating the hip status and it is well documented that the frequency of HD can be significantly reduced using the standard hip extended view.

It is expected that future research studies will refine these currently accepted tenets. For example, advances in molecular genetics may bring about DNA tests to replace radiography as the primary diagnostic tool, or environmental factors such as medical or nutritional treatments may be identified that will overcome the genetic expression of HD in an individual animal.

There are many debates surrounding the myriad of possible factors that may influence or initiate one or more aspect of HD. While interesting to consider, the breeder and veterinarian can most successfully pursue their mutual goals by maintaining their focus on current knowledge without becoming mired in the debate. The responsible breeder attempts to produce the best possible representatives of the breed. The veterinarian assists the breeder in accomplishing this objective by encouraging breeder education, maintaining the general health of the dog and cat, and providing the best possible treatment when appropriate.

Development of the hip joint

The embryonic hip joint and its supporting structures begin to develop from an undifferentiated mass of embryonic tissue. The differentiation of this tissue into the distinct parts of the hip joints is predetermined by a genetic code. Embryonic tissues form muscles, a specialized connective tissue that encases the joint (the joint capsule), and joint ligaments. A cartilage mold forms the unique parts of the ball and socket joint with the acetabulum functioning as the socket and the head of the femur functioning as the ball. These structures continue to grow and differentiate as the embryo matures. Ossification (bone formation) begins at approximately 49 days of pregnancy but the degree of skeletal maturity at birth appears to be breed dependent. That is, ossification in some breeds is more advanced than in others, which contributes to the continued difference in rates of skeletal growth after birth.

The surfaces of the femoral head and acetabulum are covered with smooth articular cartilage. A thin layer of fluid (synovial fluid) serves as a lubricant for the joint, carries nourishment for the articular cartilage, and separates the opposing surfaces. The head of the femur is attached to the depth of the acetabulum by a ligament (round ligament). The joint capsule encases the joint by attaching to the neck of the femur and to the rim of the acetabulum and is lined by a specialized tissue, the synovial membrane, which produces the synovial fluid. Muscles encase the entire hip structure and serve to stabilize and move the joint. The major pelvic muscles exert a forward and upward pressure on the femoral head during movement and the head of the femur is held in the acetabulum by the pelvic muscles, the joint capsule, surface tension, and the round ligament. Proper development of the joint depends upon the head of the femur being held firmly within the acetabulum.

The hip joint of the dog is reported to be normal at birth. After birth, a complex interaction of multiple genetic and environmental factors can initiate incorrect fit or function of one or more of the parts of the hip joint, although the exact pathogenesis of these interactions is not fully understood at this time. It is likely that these factors may differ between genetic lines, since HD is caused by the interaction of many genes. Currently, any attempt to define the process in an exact sequence of events is speculative.

Regardless of what the initiating interaction of factors may be, abnormal looseness (joint laxity) is generally accepted to be the most common abnormality that results in the pathologic changes of HD. However, some dogs with tight hips but shallow acetabula have also been reported to develop dysplastic changes.

Many of the early (2-14 weeks) pathologic changes are not readily detectable by clinical or radiographic examination. These include: swelling, fraying, and possible rupture of the round ligament; inflammation of the synovial membrane (synovitis) resulting in synovial fluid changes; stretching of the joint capsule; and damage to the cartilage mold of the acetabulum and femoral head. These structural alterations result in joint instability and subluxation, which are followed by erosion of the articular cartilage, changes in the bone beneath the articular cartilage, micro fractures of the dorsal acetabular rim, filling in of the acetabulum, remodeling (change in size, shape or architecture) of the femoral head, neck and acetabular rims, and production of osteophytes (bone spurs) around the joint.

Depending on the individual dog and the initiating factors of joint instability, the changes occur at varying rates and to differing degrees. Severe cases can be detected radiographically as early as 8 to 12 weeks of age, while others may not be evident until later in life (greater than two years of age).

Clinical finding of dysplasia

While most animals with HD do not exhibit clinical signs, those that do are usually first affected between three and 15 months of age. In some, the signs may not be observed until later in life. The signs vary from decreased exercise tolerance to severe crippling. They include: a reluctance or inability to go up or down stairs, difficulty in rising from a sitting or prone position, bunny-hopping gait when running, stiffness early in the morning that improves as the animal warms up, changes in disposition due to pain, lameness after exercise, a wobbly gait, a clicking sound when walking, and many others. Many animals will shift their center of gravity forward in an effort to relieve weight and pressure on the hips, thereby developing disproportionately greater muscle mass in the front limbs as compared to the rear limbs.

The hip joint is a weakened structure in dysplastic animals and is more prone to injury from normal activities such as jumping off a couch or rough housing with a playmate. Frequently, this results in an acute lameness that appears as if it might have been caused by injury, whereas the underlying dysplasia actually made the joint more susceptible to injury. Obviously, the normal hip can be injured, but radiographic examination can usually distinguish between a hip problem due to dysplasia and one due to other causes.

HD cannot be diagnosed by observing how the animal moves, acts, lies down, etc. Clinical signs may have other causes, and therefore a complete orthopedic and radiographic examination is required before arriving at the conclusion that the signs are caused by HD.

Radiographic assessment of the hip joint

Modern breeds vary widely in body size, shape and pelvic conformation. Because of these differences, OFA classifications are based on comparisons among individuals of the same breed and age. Knowledge of hip phenotype can be valuable for the breeder in selection against hip dysplasia and in estimating the potential for an active working life. It is assumed that radiographs submitted to OFA are generally screened by the veterinarian and the more obvious cases of HD are probably not submitted. Therefore, the actual frequency of HD in the general population is not known, but has been approximated by Corley (1997) and Rettenmaier (2002) to be higher than reported by OFA. **However, the main objective of the OFA is to identify phenotypically normal animals as potential breeding candidates.** Thus, the OFA reported breed frequency of HD can be used as a benchmark for breeders to gauge their breeding program's relative position.

Historically, the diagnosis of HD has been determined by radiographic examination of the hips according to the protocol established by the American Veterinary Medical Association. In this standard hip extended position (ventrodorsal view), the animal is placed on its back

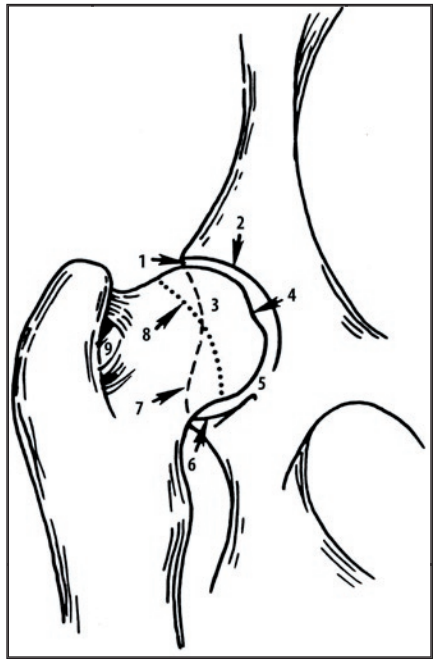
with the pelvis symmetrical, both femurs extended and parallel, and with the stifles (knees) rotated internally placing the patellas (knee caps) on the midline. The radiograph should include the last two lumbar vertebra and the stifle joints. **It is essential, particularly in marginal cases, to obtain proper position and radiographic technique.**

The radiographic criteria of subluxation, shallow acetabula, remodeling, and/or secondary degenerative joint disease are well documented. However, interpretation and application of these criteria differ between breeds, age of evaluation and veterinarians. **Figure 1** provides the nomenclature of the hip structures that are evaluated by the veterinary radiologist. The veterinary radiologist is concerned with deviations in these structures from the breed normal, and with evidence of subluxation and degenerative joint disease (also called arthritis, osteoarthritis, or osteoarthrosis).

Multiple anatomic areas of the hip are evaluated (**Fig. 1**) including:

1. **Craniolateral acetabular margin**—Area where abnormal bone spurs (osteophytes) develop as the dysplastic joint attempts to stabilize the biomechanically unstable femoral head.
2. **Cranial acetabular margin**—Area visualized in conjunction with the hip ball to assess the degree of congruity and confluence of the hip joint.
3. **Femoral head (hip ball)**—Assessed to determine its fit into the socket and degree of congruity with the cranial acetabular margin forming the joint space.
4. **Fovea capitus**—Normal flattened area on ball for attachment of the round ligament; can be mistaken for degenerative changes if there is lack of familiarity or inexperience in interpretation of hip radiographs.
5. **Acetabular notch**—Area visualized to help assess depth of socket or "degree of fit".
6. **Caudal acetabular rim**—Area where bone spurs can form.
7. **Dorsal acetabular margin**—Area visualized to assess the depth of the hip socket (acetabulum) and percent coverage of the femoral head.

Figure 1



8. **Junction of femoral head and neck**—Area visualized to assess size, shape, and architecture of the femoral head/neck. The neck of the hip ball is usually the earliest and most commonly affected area where degenerative changes occur in a dysplastic joint. In the dysplastic joint, new bone builds up at the site of attachment of the joint capsule and muscular attachments. This is a result of abnormal stress created by incongruent articulation of the ball with the acetabulum during movement.
9. **Trochanteric fossa**—Area to assess for any microtrabecular bone changes or new bone proliferation.

Unilateral hip dysplasia

Hip dysplasia may occur in only one hip (unilateral). In man, the left hip is reported to be involved more frequently than the right at a ratio of 10:1. Unilateral dysplasia in dogs follows a similar pattern, but the predominantly affected side is breed dependent. It occurs more frequently in the left hip of the Labrador Retriever, Newfoundland, Akita, and Golden Retriever, but more frequently in the right hip of the Rottweiler. The German Shepherd Dog does not appear to have a side (left or right) predilection. Frequency of unilateral HD is also independent of the frequency of HD in a breed.

Chase (2004) identified quantitative trait loci (QTL's) associated with hip joint laxity; one for the left hip and the other for the right hip in the Portuguese Water Dog.

The reported frequency of unilateral HD varies from 3% to more than 30% of the dysplastic dogs depending on the population studied. It appears that frequency of unilateral HD is higher in some genetic lines within a breed, than in other lines within the same breed. Furthermore, the same hip (right or left) is repeatedly involved within the line. That is, when several or influential ancestors have unilateral HD in, for example, the left hip then the progeny that are unilaterally affected will almost invariably show the abnormality in the left hip.

Hip dysplasia database

The OFA hip dysplasia control database functions as a voluntary screening service and as a database of hip status for dogs and cats of all breeds. Information intended to aid breeders in reducing the incidence of this polygenic problem is made available from this resource. The necessity for such a central repository was recognized by the Golden Retriever Club of America and the German Shepherd Dog Club of America, which provided the impetus for formation of the OFA.

The owner or agent should notify the veterinarian, before the x-ray examination, that the purpose is for OFA evaluation. This is best done at the time of making an appointment in order to ensure that application forms are available and that the required procedures are followed. The owner also should provide the animal's registration certificate (or copy of this information) and the animal's tattoo or microchip number at the time of radiography.

General procedures

Age—Only dogs and cats that are 24 months of age or older at the time of radiography can qualify for an OFA breed registry number. The hip joint status of younger animals will be evaluated, but only a preliminary consultation report will be issued.

Restraint—Obtaining a properly positioned film may require chemical restraint. The type of restraint used—physical, sedative, tranquilizer, or general anesthesia—is best determined by the veterinarian. The dog should not be fed on the day of radiography.

Positioning—Dorsal recumbency with the rear legs extended and parallel to each other and the stifles rotated internally is the prescribed position (**Fig. 2**). This standard ventrodorsal view is accepted worldwide as the basis for evaluation of hip joint status with respect to hip dysplasia. **Care should be exercised to be sure the patient is positioned correctly.**

Film size—For large and giant breeds of dogs, 14 X 17 inch film size is recommended. Smaller film sizes can be used for smaller breeds if the area between the sacrum and stifles can be included.

Film Identification—Permanent animal identification in the film emulsion is required for radiographs to be eligible for OFA registration. Lead letters, an I.D. camera, or radio opaque tape can be used to identify the film with: a) the hospital or veterinarian's name, date taken and registered name or number of the dog, or b) the

Figure 2

A standard position radiograph of the pelvis that has been appropriately positioned will have symmetrical obturator foreamen (long arrow), symmetrical wings of the ilium (arrowhead) and kneecaps that are centered over the knees (short arrow) with the legs extended parallel to one another.

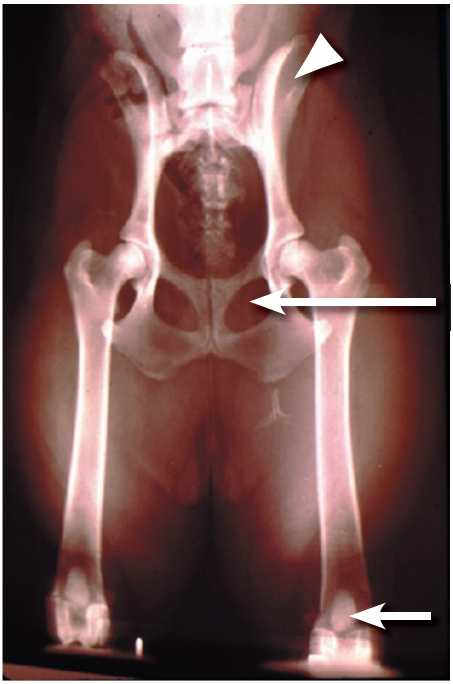
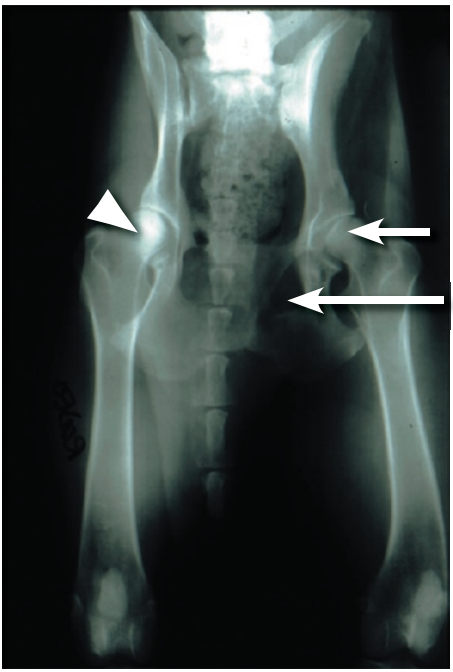


Figure 3

A standard position radiograph of the pelvis that has been inappropriately positioned will have asymmetrical obturator foreamen and asymmetrical wings of the ilium (long arrow). The distortion caused by poor positioning can inaccurately make one hip look worse than it actually is by creating a more shallow appearing hip socket (short arrow) and the opposite hip appear better than it actually is by creating more depth to the hip socket over the hip ball (arrowhead). The OFA will routinely mail poorly positioned films back to the referring veterinarian and request repeating the study.



veterinarian's or hospital's identification number or case number. In this latter case (b), the radiograph must be accompanied by a signed note from the veterinarian referring to such film by its identification number, and stating the date taken, and registered name or number of the dog as in (a) above.

If the above required information is illegible or missing, the OFA cannot accept the film for registration purposes.

Exposure—Good contrast is essential. Technique settings (low kVp and high mAs), film-screen combinations and use of grids are all considered in producing the desired contrast. Film contrast should be such that the microtrabecular pattern of the femoral head and neck are readily seen. The dorsal-lateral margin of the acetabulum must also be visible.

Radiation safety—Proper collimation and protection of attendants are the responsibility of the veterinarian. Gonadal shielding is recommended for male dogs. Radiography of females in season or pregnant should be avoided.

Application information—The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. Application forms are available on request from the OFA or can be downloaded from the OFA web site (*www.offa.org*). The radiograph, signed application form (which should include the owner's choice of open or semi-open database), and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856. All radiographic images are retained by the OFA for research and reference purposes.

Operational procedures

When a radiograph arrives at the OFA, the information on the radiograph is verified against information on the application form. The age of the dog in months is calculated and the submitted fee is recorded. The veterinary radiologist on staff at the OFA then evaluates the radiograph for diagnostic quality. If it is not of suitable diagnostic quality (the hip is tilted, too light or too dark, etc.) it is returned to the referring veterinarian with a written request that it be repeated (Figure 3). If the radiograph is accepted for evaluation, it is assigned an application number and given a "quality control" hip rating.

There is a pool of 20 to 25 board certified veterinary radiologists throughout the USA in private practice and academia that consult for the OFA. The radiographic images are forwarded to 3 radiologists. Each evaluation is independent—that is, no radiologist knows what

interpretation was given by another. The only information they have is the radiograph, application number, breed, sex, and age. The breed, age, and sex of dog are important for the radiologists to know so that normal conformational differences among and within breeds, and differences related to degree of skeletal maturity, can be taken into consideration. Each radiologist grades the hips into one of seven phenotypic hip conformation categories: excellent, good, or fair (which are normal and receive an OFA hip number); borderline; or mild, moderate, or severe (which are abnormal). When results of over 1.5 million radiographic evaluations by 35 radiologists were analyzed, it was found that all 3 radiologists agreed as to whether the dog/cat should be classified as having a normal phenotype, borderline phenotype, or HD 94.9% of the time. In addition, 73.5% of the time, all 3 radiologists agreed on the same hip phenotype (excellent, good, fair, borderline, mild, moderate, or severe).

When the final evaluation is completed, the consensus of the three evaluations is formulated. Two evaluations of the same phenotype result in a consensus of that phenotype; 3 different evaluations (i.e., excellent, good, and fair) result in a consensus of the middle phenotype. If the consensus is phenotypically normal (excellent, good, or fair) an OFA registry number is assigned. The owner of record, referring veterinarian, AKC, and appropriate breed club are notified of the evaluation results. Dysplastic results are not in the public domain unless the owner of record gives explicit direction for the release of such information by initialing the appropriate space on the application form.

The time it takes to obtain three independent evaluations, arrive at the consensus, and type the final OFA report is dependent on a number of factors. It takes approximately a week to 10 days for the film to arrive at OFA via the mail service. Depending on the case load it takes 12 to 14 days from the time that OFA receives the film to completion of the consensus report.

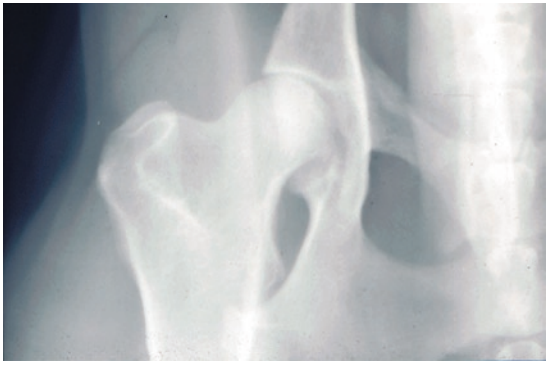
Hip joint conformation

The OFA consulting radiologists make subjective evaluations of the hip status based on criteria previously described (p.17). Although the radiologists apply the criteria subjectively, a study demonstrated good correlation between the consensus grade assigned and two objective measurements used to assess hip phenotype. These measurements are percent coverage (PC) of the femoral head within the acetabulum and Norberg angle (NA) which also estimates degree of fit. The higher the numeric value the better the degree of fit. A retrospective study of OFA hip phenotypes by Tomlinson (2000) reported a distinct difference in both percent coverage and Norberg angle values between OFA hip grades and between breeds. The following numerical values (*) for each OFA classification are averages derived from that study.

Excellent—This classification is assigned for superior hip conformation in comparison to other animals of the same age and breed. There is a deep seated ball (femoral head) which fits tightly into a well-formed socket (acetabulum) with minimal joint space width. *PC=63% NA=110

Good (Fig. 4)—The most common normal grade reported regardless of breed is slightly less than superior but a well-formed congruent hip joint is visualized. The ball fits well into the socket and good coverage is present. *PC=58% NA=108

Figure 4: Good hips



Fair—Assigned where minor irregularities in the hip joint exist. The hip joint space is wider than a good hip phenotype. This is due to the ball slipping slightly out of the socket, causing a minor degree of joint incongruency (called subluxation). There may also be slight inward deviation of the weight-bearing surface of the socket (dorsal acetabular rim) causing the socket to appear slightly shallow. This can also be a normal finding in some breeds, such as the Chinese Shar Pei, Chow Chow and Poodle. *PC=49 NA=104

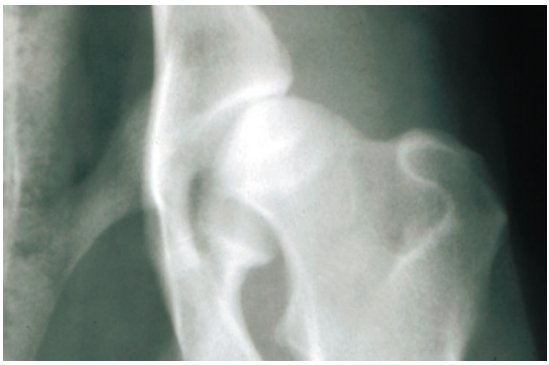
The following categories are not eligible for an OFA breed number

Borderline—There is no clear cut consensus among the radiologists to place the hip into a given category of normal or dysplastic. There is usually more incongruency present than the minor amount found in a fair, but there are no arthritic changes present that definitively diagnose the hip joint as dysplastic. There also may be bony changes present on any of the areas of the hip anatomy that cannot be accurately evaluated as either an abnormal arthritic change or a normal anatomic variant for that individual dog. To increase the accuracy of the diagnosis, it is recommended the radiographs be repeated at a later date (usually 6 months). This allows the radiologist to compare the initial film with the most recent film and assess for progressive changes that would be expected if the dog is dysplastic. Most dogs (over 50%) with this grade that show no interval change in hip conformation receive a normal hip rating upon resubmission, usually a fair hip phenotype.

Mild Hip Dysplasia—There is significant subluxation present wherein the ball is partially out of the socket, causing an incongruent and increased joint space. The socket is usually shallow, only partially covering the ball. There are usually no arthritic changes present with this classification. If the dog has other superior traits and/or a great deal of time and investment has been placed into training, there is an option to resubmit a radiograph when the dog is older so it can be reevaluated. Most dogs will remain dysplastic, showing progression of the disease with early arthritic changes. There are a few dogs however, that show improved hip conformation with increasing age. Since HD is a chronic, progressive disease, the older the dog, the more accurate the diagnosis of HD (or lack of HD). At 2 years of age, the reliability for a radiographic diagnosis of HD is 95%, and the reliability steadily increases as the dog ages. Radiographs should definitely be resubmitted if they were initially taken during times of possible detrimental environmental effects such as periods of physical inactivity, or high hormone levels related to time of a heat cycle which could lead to a "false" diagnosis of mild hip dysplasia. *PC=40% NA=97

Moderate HD (Fig.5)—There is significant subluxation present wherein the ball is barely seated into a shallow socket, causing joint incongruency. There are secondary arthritic bone changes, usually along the femoral neck and head (termed remodeling), acetabular rim changes (termed osteophytes or bone spurs), and various degrees of trabecular bone pattern changes (called sclerosis). Once arthritis is reported, there is only continued progression of arthritis over time, and the dog may or may not be lame. The onset of lameness is unpredictable and some dogs may go most of their lives without showing any signs of lameness whatsoever. *PC=30% NA=92

Figure 5: Moderate HD



Severe HD—assigned where radiographic evidence of marked dysplasia exists. There is significant subluxation present, where the ball is partially or completely out of a shallow socket. Like moderate HD, there are also large amounts of secondary arthritic bone changes along the femoral neck and head, acetabular rim changes, and large amounts of abnormal bone pattern changes. *PC=21% NA=83

In addition to assessing the dog/cat hip conformation, the veterinary radiologist reports other radiographic findings that could have familial, inherited causes, such as transitional vertebra or spondylosis. Transitional vertebra is a congenital malformation of the spine that occurs at the junctions of major divisions of the spine (usually at the thoracic and lumbar vertebral junction or the lumbar and sacral vertebral junction). Transitional vertebra take on anatomic characteristics of the two divisions of the spine between which it occurs. The most common transitional vertebra reported by OFA is in the lumbo-sacral area. Transitional vertebra are usually not associated with clinical signs and the dog/cat can be used in a breeding program, but the OFA recommends breeding to a dog/cat that does not have transitional vertebra.

Spondylosis is an incidental radiographic finding in which smooth new bone production is visualized on vertebral bodies at the intervertebral disc space margins. The new bone production can vary in extent from formation of small bone spurs to complete bridging of adjacent vertebral bodies. Spondylosis may occur secondary to spinal instability but often it is of unknown cause and clinically insignificant. A familial basis for its development has been reported. As with transitional vertebra, dogs/cats with spondylosis can be used in a breeding program.

The effect of age and the use of preliminary radiographs for early detection of hip dysplasia

Frequently, breeders want early knowledge of the hip status on puppies/kittens in a given litter. This allows early selection of animals for use as show/performance/breeding animals or animals that would be best suited for pet homes. The OFA accepts preliminary consultation radiographs on puppies and kittens as young as 4 months of age for evaluation of hip conformation. If the dog or cat is found to be dysplastic at an early age, the economic loss from cost of training, handling, showing, etc. can be minimized and the emotional loss reduced. Preliminary radiographs are read by the OFA staff veterinary radiologist and are not sent to outside radiologists as are the 24-month-old examinations. The same hip conformation grading scheme is used.

The OFA has performed a retrospective analysis of the reliability of early radiographic evaluation for canine hip dysplasia, using information in their database obtained from the standard ventrodorsal radiographic projection. Corley (1997) reported on a population of over 2,000 dogs from the four breeds with the greatest number of OFA submissions (Labrador Retrievers, Rottweilers, German Shepherds, and Golden Retrievers). The reliability of the preliminary evaluation (3 to 18 months) was determined by comparing the initial evaluation to a follow-up evaluation ($\geq$ 24 months) of the same dog. The reliability of a normal preliminary hip joint phenotype was 100% for excellent, 97.9% for good and 76.9% for fair (**Table 2**). The reliability of a preliminary

evaluation of canine hip dysplasia was 84.4% for mild, 97.4% for moderate and 100% for severe (**Table 3**). Reliability of preliminary evaluations increased significantly as age at the time of preliminary evaluation increased, regardless of whether dogs received a preliminary evaluation of normal phenotype or canine hip dysplasia (**Tables 4 & 5**).

For normal hip conformations, the reliability was 89.6% at 3-6-months, 93.8% at 7-12 months and 95.2% at 13-18 months for the four main breeds. Pooled data comparing preliminary OFA evaluations at various ages and in various breeds with final OFA evaluations at 24 months or older resulted in a similar reliability factor for preliminary evaluations of approximately 90%. The false positive rate (defined as a preliminary evaluation of HD for a dog with a follow-up evaluation of a normal phenotype) of OFA preliminary evaluations ≤ 6 months

Table 2: Reliability of normal preliminary evaluations by hip grade

	Excellent	Good	Fair	Total
Number	71	1,369	360	1,800
No Change	71	1,340	277	1,688
Norm to Dys	—	24	75	99
Norm to Boderline	—	5	8	13
Reliability	100%	97.9%	76.9%	93,8%
CI Upper	100%	98.5%	81.2%	94.8%
CI Lower	94.9%	96.9%	72.2%	92.6%

Table 3: Reliability of dysplastic preliminary evaluations by hip grade

	Mild	Moderate	Severe	Total
Number	390	38	1	429
No Change	329	37	1	367
Dys to Norm	47	1	—	48
Dys to Borderline	14	—	—	14
Reliability	84.4%	97.4%	100%	85.5%
CI Upper	87.8%	99.9%	—	88.7%
CI Lower	80.4%	86.2%	—	81.9%

Norm = Normal; Dys = Dysplastic; CI = Confidence Level

Table 4: Reliability of normal preliminary evaluations by age

	< 6 mo.	7-12 mo.	13-18 mo.	Total
Number	278	714	808	1,800
No Change	249	670	769	1,688
Norm to Dys	25	43	31	99
Norm to Boderline	4	1	8	13
Reliability	89.6%	93.8%	95.2%	93.8%
CI Upper	92.9%	95.5%	96.5	94.8%
CI Lower	85.4%	91.8%	93.5%	92.6%

Table 5: Reliability of dysplastic preliminary evaluations by age

	< 6 mo.	7-12 mo.	13-18 mo.	Total
Number	102	150	177	429
No Change	82	126	159	367
Dys to Norm	18	15	15	48
Dys to Borderline	2	9	3	14
Reliability	80.4%	84.0%	89.8%	85.5%
CI Upper	87.6%	89.5%	93.9%	88.7%
CI Lower	71.4%	77.1%	84.4%	81.9%

Norm = Normal; Dys = Dysplastic; CI = Confidence Level

of age was 18%; and the false negative rate (defined as a preliminary evaluation of normal phenotype for a dog with a follow-up evaluation of hip dysplasia) of OFA preliminary evaluation $\leq$ 6 months of age was 9%. This suggests that OFA preliminary evaluations of hip joint status in dogs are generally reliable. However, dogs that receive a preliminary evaluation of fair or mild hip joint conformation should be reevaluated at an older age (24 months).

Joint laxity

Laxity is generally considered to be one of the earliest pathologic findings in HD. The fact that joint laxity plays a role, but is not the only factor, in development of hip dysplasia and its secondary changes of degenerative joint disease has been recognized for over 30 years.

Joint laxity (looseness of the joint) is a dynamic state that may not be determined by routine radiography. The joint may appear radiographically normal, but in actual use it may be loose.

Some dogs demonstrate abnormal laxity (subluxation) radiographically, but do not develop the more definitive degenerative changes of dysplasia.

Some dogs demonstrate radiographically tight hips, but later develop the degenerative changes of dysplasia.

Recently, Chase (2005) identified quantitative trait loci (QTL's) associated with joint laxity but not osteoarthritis/degenerative joint disease and a separate QTL associated with osteoarthritis/ degenerative joint disease.

Palpation of the hips to demonstrate looseness is not generally accepted as a single diagnostic feature of HD. Stress radiography using a fulcrum or wedge (placing an object between the thighs and bringing the stifles together to force the head of the femur out of the acetabulum) has been investigated as a technique to demonstrate the degree of radiographic subluxation that is possible. Some measurement criterion such as Norberg angle, millimeters of displacement, distraction index (DI), or dorsal lateral subluxation measurement (DLS) is usually employed to calculate the amount of displacement of the femoral head when compared to a fixed anatomic structure or to a standard radiograph taken without the fulcrum or wedge. The differences in the measurements indicate the range of possible motion or joint laxity. Different devices, measurements, and positions have been developed at the University

Table 6: False-negative and false-positive results for dysplasia from 4 studies

Method	False-Negative	False-Positive
Palpation (1)	25%	33%
DI at 4 months @ .3 (2)	12%	48%
DI at 4 months @ .3 (3)	0%	45%
DI at 4 months @ .4 (3)	13%	43%
OFA Prelims @ < 6 months (4)	9%	18%

1 = Reviewed by Willis; 2 = Smith et al.; 3 = Lust et al.; 4 = Corley et al.

of Pennsylvania (PennHIP®), Cornell University and Michigan State University. Use of the fulcrum technique has demonstrated that some laxity is expected in the normal joint, but that many dogs with laxity beyond a certain amount later show the more definitive characteristic radiographic changes of dysplasia. The specific degree of laxity that is acceptable at a given age, and in various breeds of dogs and cats has not been determined and represents a major unanswered question.

Table 6 is a comparison of different early screening procedures, and with the exception of palpation, all yield similar false-negative results (initially reporting a dog as normal that is later evaluated as dysplastic). There is, however, a major difference in the comparison of false-positive results (initially reporting a dog as dysplastic that is later evaluated as normal). A later publication by Lust (2001) suggested that the strength of the hip extended view (OFA view) is its specificity. Specificity refers to the ability to correctly identify dogs without hip dysplasia and this study also noted that this is dependent on the expertise of the evaluator.

The degree of joint laxity—as demonstrated by forcing the head of the femur away from the acetabula either by palpation or by using a fulcrum/stress device—that can be normal, and what degree is abnormal (eventually leading to degenerative joint changes) is unknown.

A primary reason this is unknown is that stress radiographic techniques measure artificially forced laxity in a non-weight bearing position. Improved accuracy using laxity as the diagnostic finding might be possible with a technique that measures dynamic laxity (laxity that occurs during normal movement).

There is currently no explanation to account for adult animals with substantial joint laxity that do not develop degenerative joint disease.

There is no pathologic evidence available to determine what processes are occurring in the hips that are lax but do not develop degenerative joint disease, or in hips that are tight yet develop degenerative joint disease. Without this information, there is a deficiency of necessary data to support breeding or treatment recommendations based on laxity alone. It is obvious that dogs with "tight" hips tend to be normal and those with markedly "loose" hips tend to be abnormal. What happens between the two extremes remains unknown. Further research using carefully controlled scientific methods is needed to understand the full implication of joint laxity.

However, breeders have a phenotypic screening method (standard hip extended radiograph) readily available that is safe, accurate, of modest

cost, and effective. As an example of effectiveness, Leighton reported that while the mean DI did not change, the incidence of hip dysplasia at The Seeing Eye Inc. was dramatically reduced over five generations using the standard hip extended position and a subjective hip score similar to OFA's. That breeding program also illustrates the importance of obtaining and considering information on the hip status of siblings as well as on the dam and sire with regard to selection of potential breeding animals.

Physical restraint or chemical restraint

Chemical restraint permits easier, and as a rule, more accurate positioning and reduces potential radiation exposure risk to the patient and veterinary personnel. The types of chemical restraint, depth of general anesthesia, or use of manual restraint only are environmental variables that can affect the radiographic evaluation.

Anesthesia has been shown to influence the evaluation, as a few dogs have been found to appear normal without anesthesia and yet demonstrate subluxation with anesthesia. This probably is due to muscular relaxation. The current belief is that a dog who appears dysplastic with anesthetic and normal without, should be considered dysplastic, or at best of questionable breeding quality. However, there are some veterinarians and a few HD control programs that do not recommend anesthesia as they feel that subluxation noted under anesthesia results in a false-positive finding.

Preliminary OFA data indicates that chemical restraint does affect the radiographic appearance of the hip joints in some dogs. Current information, observations made on large numbers of dogs, and experience with follow-up studies on large numbers of dogs, supports the recommendation that chemical restraint to the point of relaxation, or general anesthesia, be used. This appears to give a truer evaluation of the hip status, but more research is needed on this controversial subject, as there is an absence of controlled scientific data.

Nutrition

Kasstrom, and later Kealy, reported that a higher than needed caloric intake during the rapid growth phase may result in earlier and more severe dysplastic changes when the genetic potential for dysplasia is present. Lower caloric intake may minimize or delay the evidence of dysplasia in the same dog, but will not change the genotype. Without genetic predisposition however, environmental influences alone will not create hip dysplasia.

There is no evidence in the scientific literature that megadoses of vitamin C (Bennett, 1987) or any other multi-vitamin/mineral supplement is beneficial in reducing the effects of, or preventing hip dysplasia.

Hormonal effects

Estrus appears to affect the reliability of diagnosis in some females. Some animals in season demonstrate a degree of subluxation (laxity) that is not present when the bitch is out of season, possibly due to the relaxation effects of estrogens on the ligaments and joint capsule. Radiography of these bitches may result in a false diagnosis of HD.

It is recommended that bitches not be examined for HD when in season and radiographs should be obtained one month prior or one month following the heat cycle. In addition, following a pregnancy the OFA recommends that the bitch's radiographs be taken at least one month after weaning the offspring.

Physical inactivity

Periods of prolonged inactivity may affect the reliability of diagnosis. A few animals exhibit subluxation after prolonged periods of inactivity due to illness, weather conditions, etc. On later examination, when the animal is in good muscular tone, the hips appear normal. Therefore, radiography is recommended when the animal is in good health and muscle tone.

Recommendations for buyers

To verify health information when considering a purchase from a particular breeder, the buyer can obtain a pedigree of the animal in question. Health information then can be verified on the sire, dam, various siblings, and other close relatives at the OFA web site, *www.offa.org*. Information in the OFA's database can be used as a tool to increase the probability for obtaining a normal dog when choosing dogs for breeding, competition, or as healthy pets. Overall, if there are a substantial number of relatives that do not have OFA numbers in the pedigree, they should be assumed to be abnormal until proven otherwise. The more animals in a pedigree with OFA numbers, and the greater the percentage of their siblings with OFA numbers, the better the genetic probability for healthy animals from a given breeding. Breedings for which 2 to 3 generations of this depth and breath of information is available and normal will usually demonstrate significantly reduced incidence of HD.

It also may be helpful to consider whether the breeding in question is a repeat breeding, a line breeding, or an outcross. With repeat breedings, there may be health information available on puppies from the previous litter resulting from the same genetic combination. In the case of line breedings, experienced, knowledgeable breeders often have extensive information about the phenotypes present in their lines, and therefore can make more informed breeding choices. Longtime health conscious breeders often have greatly reduced the incidence of disease in their breeding programs, and this will be reflected in their track re-

cord (as verifiable on the OFA web site). Outcross breedings require more diligence of the breeder to fully investigate the new lines that are brought into the pedigree, and again, information available on the OFA web site may greatly aid in this effort.

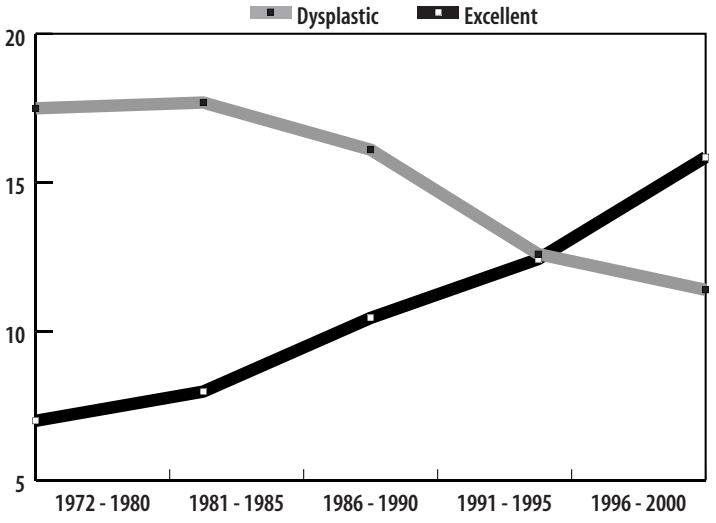
Impact of OFA hip evaluations through multiple generations of a population subset

Retrospective studies covering the period of 1972–2000 have demonstrated steady and encouraging progress as a result of the collaborative efforts of responsible breeders and the OFA. The OFA database population represents a specific subset of the general population of animals, primarily show dogs and cats, and working/hunting dogs. Accumulated data clearly illustrates the impact that the focused efforts of conscientious breeders can have on reducing the frequency of HD, and further indicates that the hip status of progeny follows that of parents (**Table 1**, p.10).

Success in reducing HD in a breed depends first on breeders recognizing that a problem exists. This must then be followed by a commitment to solve the problem and dedication to consistent use of a standard hip evaluation protocol.

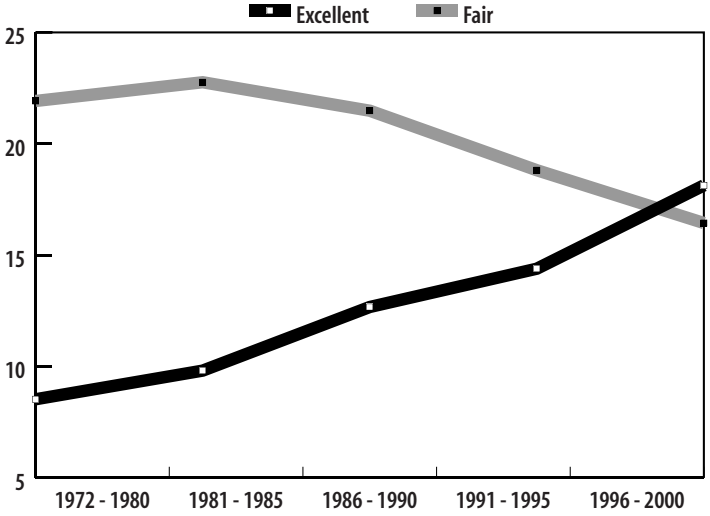
HD has been reported in all breeds of dogs and some cat breeds that have been evaluated by the OFA. The OFA database is an important tool that can provide breeders with information regarding changes in hip status of specific breeds over time. The frequency of HD in most breeds has steadily declined. Concurrently, the percentage of animals with excellent hip conformation has steadily increased (**Graph 1**) in most breeds.

Graph 1: Percent dysplastic & excellent by birth year

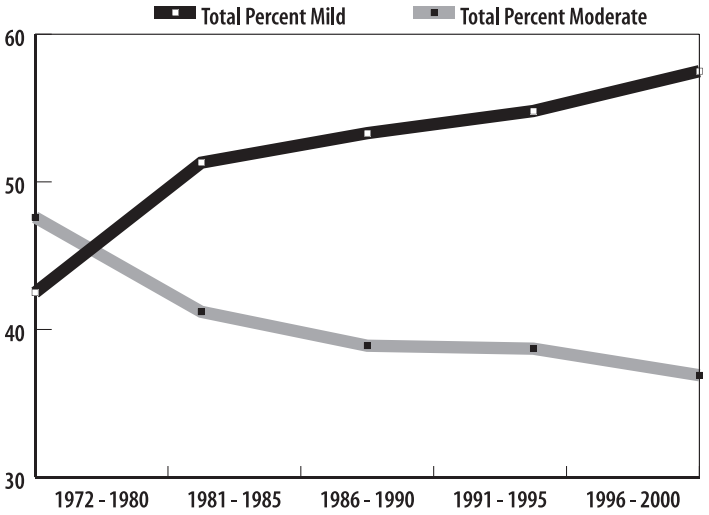


Within the OFA population of animals with normal hip conformation, there has been a steady decrease in the percentage of fair and an increase in the percentage of excellent (**Graph 2**). Within the OFA population of dysplastic animals, there has been a steady increase in the percentage of mild with a corresponding decrease in the percentage of moderate dysplasia (**Graph 3**).

Graph 2: Percent excellent vs fair by birth year



Graph 3: Percent mild vs moderate by birth year



While this may be surprising to some, it is also important to realize that some of the smaller sized breeds and mixed breeds have as high a percentage of HD as the larger breeds and purebreds. Generalizations that claim that dysplasia is limited to, or more common in, large dogs and pure breed dogs, are misleading.

HD appears to be perpetuated by breeder imposed breeding practices. However, when breeders and their breed clubs recognize HD as a problem and establish HD reduction as a priority, improvement of breed hip status can be accomplished without jeopardizing other desirable traits.

Although it is clear from the graphs that breeders have made steady progress toward reducing the frequency of hip dysplasia, some are concerned that this decline may reach a plateau. As with any polygenic disease, it is anticipated that HD will decline in an exponential manner. Therefore, after several generations, it may appear that progress has leveled out. This is to be expected when phenotypic data is used to place selection pressure against polygenic disease traits with moderate to high heritability estimates. However, Leighton has shown that rapid progress can be expected in the first 3 or 4 generations, and is followed by slower but continued progress in subsequent generations. In the future, a DNA based genetic test might overcome this, but meanwhile breeders can continue to make significant progress by committing to careful selective breeding practices.

Legg-calve-perthes database

Legg–Calve–Perthes (LCP) disease, or avascular necrosis of the femoral head, is a disorder of the hip joint(s) which occurs in both humans and dogs. LCP is an inherited disease, but in most breeds the mode of inheritance is unknown. LCP is most often seen in miniature and toy breeds between four and twelve months of age. A decrease in vascularization to the immature femoral head results in death of chondrocytes beneath the articular cartilage resulting in necrosis. Subsequent collapse of the affected area causes pain and lameness. In untreated dogs, revascularization can occur resulting in a malformed femoral head and secondary degenerative joint disease (**Fig. 6**).

OFA submission procedures are the same as for HD outlined on page 19 except for the age requirement and restraint recommendations.

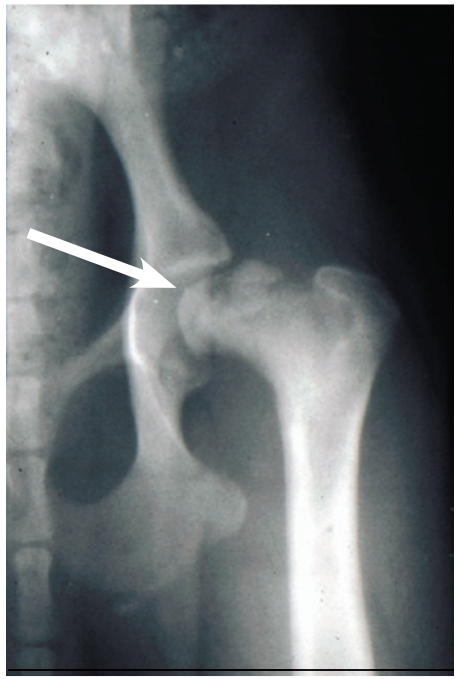
Age

Only dogs 12 months of age or older at the time of radiography can qualify for an OFA LCP breed number. The hip joint status of younger animals will be evaluated, but only a preliminary consultation report will be issued.

Restraint

Obtaining a properly positioned film may require chemical restraint, but with many small breed dogs it may be possible to obtain a well positioned image with the dog awake. The dog should not be fed on the day of radiography.

Figure 6



Note the collapse of the femoral head

Breeds at risk include:

Affenpinscher	Fox Terrier	Pug
Australian Terrier	Lakeland Terrier	Schipperke
Bichon Frise	Manchester Terrier	Scottish Terrier
Border Terrier	Miniature Pinscher	Shetland Sheepdog
Boston Terrier	Miniature Schnauzer	Silky Terrier
Cairn Terrier	Parson Russell Terrier	Welsh Terrier
Chihuahua	Pekingese	West Highland White
Cocker Spaniel	Pomeranian	Yorkshire Terrier
Dachshund	Poodle	

Application information

The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. Application forms are available on request from OFA or can be downloaded from the OFA web site (*www.offa.org*). The radiograph, signed application form (which should include the owner's choice of open or semi-open database), and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856. All radiographic images are retained by the OFA for research and reference purposes.

Elbow dysplasia database

Elbow dysplasia was originally described as a developmental disease manifested as degenerative joint disease (DJD) with or without an ununited anconeal process (UAP). Over time, two other inherited diseases, osteochondrosis (OCD) and fragmented medial coronoid process (FCP), were identified as part of the DJD complex collectively referred to as elbow dysplasia.

Etiology

Multiple theories on the cause of these abnormalities have been proposed. Olsson suggested a unitarian theory that UAP, OCD and FCP were all due to osteochondrosis. Osteochondrosis is a disturbance in endochondral ossification (the process by which bone is formed from a cartilage mold). Osteochondrosis results from a reduction in nutrients to the chondrocytes of the cartilage mold beneath articular cartilage. This loss of chondrocytes produces a weakened foundation under the articular cartilage, resulting in fracturing of the cartilage.

Wind suggested that asynchronous growth of the ulna and radius, or insufficient development of the ulnar trochlear notch, results in abnormal loading forces on the anconeal process or medial coronoid process.

Numerous studies suggest that the three diseases (UAP, OCD and FCP) are independent, inherited diseases.

Clinical presentation

The radiographic evidence of elbow dysplasia (ED), the presence of secondary degenerative joint disease (DJD), and the clinical presentation do not correlate directly. Grondalen reported on a population of 207 Rottweilers of which 141 were not lame. Yet 68% of the non-lame dogs had degenerative joint disease of the elbow. Another study by Read reported on serial radiographic and physical examination of 55 Rottweilers at 6 and 12 months of age. At 6 months of age the majority of lame dogs did not have radiographic evidence of ED; however, by 12 months of age the radiographic changes were apparent. But the majority of dogs remained sound.

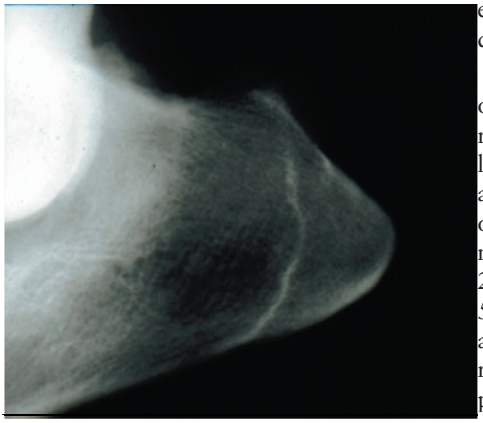
The elbow is a complex joint with overlapping osseous structures which often makes a definitive diagnosis difficult especially when dealing with pathology involving the medial coronoid process. To increase the probability of achieving an accurate diagnosis, the routine radiographic examination of the elbow (cranial-caudal and neutral medial-

lateral projections) can be supplemented with the craniolateral caudomedial oblique and an extreme flexed mediolateral projection. Even then, a definitive diagnosis can be difficult without linear tomography, computerized tomography or surgical exploration of the joint.

OFA elbow protocol

The International Elbow Working Group, (IEWG) a consortium of experts from around the world, was founded in 1989 to lower the incidence of elbow dysplasia by coordinating worldwide efforts. The OFA started its elbow database in 1990 using a modified protocol of the IEWG. The diagnosis of elbow dysplasia is based on the presence of degenerative joint disease/osteoarthrosis. Radiographically, the primary finding is sclerosis in the area of the trochlear notch and a periosteal response on the anconeal process which is best visualized on the extreme flexed mediolateral projection (**Fig. 7**). Although in and of itself, secondary degenerative joint disease is not an inherited disease, it is the end result found in dogs with elbow dysplasia.

Figure 7



Note the remodeling of the proximal surface of the anconeal process (thick arrow, top) and sclerosis in the area of the trochlear notch (thin arrow).

Therefore, OFA requires one view of each elbow clearly labeled left and right in the extreme flexed mediallateral position (**Fig. 7**). Inclusion of additional views is at the discretion of the attending veterinarian. A permanent clearance can be obtained at 24 months of age, and dogs between 5 and 24 months of age can receive a preliminary evaluation. The elbow radiographs are required to contain permanent dog identification in the emulsion. Non- grid, table top technique using high MaS and low Kvp is recommended (see p. 21).

Elbow classifications

The OFA reports elbows as normal or dysplastic. While there is no subdivision classification of normal, dysplastic elbows are graded 1 through 3, with grade 3 being the most severe. Differences between dysplastic grades are based on the severity of degenerative joint disease present.

Normal—No evidence of inherited pathologic change

Dysplastic

Grade 1—mild DJD – osteophytes less than 2 mm in height

Grade 2—moderate DJD – osteophytes 2 to5 mm in height

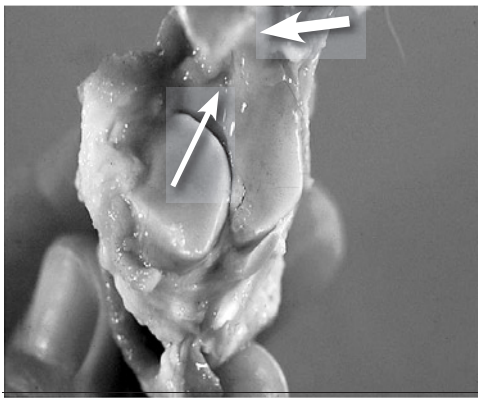
Grade 3—severe DJD—osteophytes greater than 5 mm

There can be pathology involving the medial coronoid process without a distinct fracture fragment. As seen in **Fig. 8** the malformed medial coronoid process and a fissure fracture of the articular cartilage could not be ascertained from the radiographic image, but created sufficient joint instability to produce secondary degenerative joint disease (**Fig. 7**).

Rationale for selective breeding

There are multiple studies supporting the theory that the various components of ED have a polygenic mode of inheritance. Further, it appears that environmental factors also contribute to expression of the disease. Selective breeding of phenotypically normal dogs has been shown to reduce the incidence of elbow dysplasia. In 1965, Corley reported on the inheritance of ununited anconeal process. Swenson reported on a study which included 4,515 dogs registered by the Swedish Kennel Club. As selective pressure was applied toward identifying and breeding dogs with normal elbows, there was a corresponding increase in the percentage of normal progeny.

Figure 8



Irregularly formed medial coronoid process (thin arrow) and fracture of the articular cartilage (thick arrow). These changes are difficult, if not impossible, to visualize radiographically.

There are a number of papers reporting on the inheritance of osteochondrosis and fragmented medial coronoid process. A recent report by Padgett classifies these as separate diseases that may occur alone or in combination. In this study, the initial breeding pair of Labrador Retrievers had surgically confirmed osteochondrosis and fragmented medial coronoid process in both elbows. The male dog was subsequently bred to two of his first and second generation daughters. There was a total of 31 progeny produced of which 83.9% had osteochondrosis, fragmented coronoid process or both.

Table 7 illustrates the outcome of matings based on information extracted from the OFA database. A total of 51,340 progeny were identified in which both parents had elbow dysplasia evaluations. The

Table 7: Elbow scores

Scores on 51,340 progeny from sires and dams with known elbow scores.

		Sire	
		Normal	**Dysplastic**
Dam	**Normal**	T = 40,563 D = 11.5%	T = 5,213 D = 22.8%
	Dysplastic	T = 4,527 D = 24.7%	T = 1,037 D = 43.6%

***T** = total number of progeny; **D** = the percentage of progeny with elbow dysplasia*

percentages of progeny with elbow dysplasia more than doubled if either parent had ED, and more than tripled if both parents had ED, as compared to when both parents were normal. Results of selective breeding practices indicate that elbow dysplasia should be considered in the moderate to high heritability estimate category (See page 7 for discussion on genetics).

Application information

The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. Application forms are available on request from the OFA or can be downloaded from the OFA web site (*www.offa.org*). The radiograph, signed application form (which should include the owner's choice of open or semi-open database), and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856. All radiographic images are retained by the OFA for research and reference purposes.

Osteochondrosis (OCD) of the shoulder

Etiology

While the exact mode of inheritance is unknown, osteochondrosis is considered to be an inherited disease. In affected individuals there is a disruption in ossification of the cartilage mold beneath the articular cartilage of the joint. This results in aseptic necrosis (cell death) and when the weakened area collapses, the articular cartilage fractures resulting in lameness and secondary degenerative joint disease/osteoarthritis.

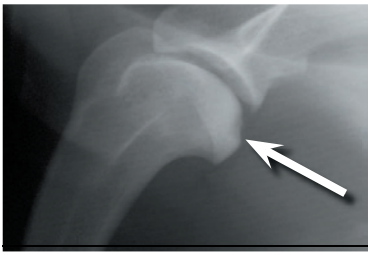
OCD has been reported to occur most often in the shoulder but can also be found in elbow, stifle, hock and spine and can be unilateral or bilateral. Most affected dogs that develop clinical sings are less than one year of age.

OCD is seen in many breeds but appears to be more common in the larger body type breeds. It is also more frequent in males than females.

Shoulder protocol

Radiographically, the primary finding is a radiolucent defect in the caudal articular surface of the humeral head. This flattening may be accompanied by sclerosis of adjacent bone and in some cases a cartilage flap may contain subchondral bone. Chronic cases may also have secondary DJD changes associated with glenoid fossa of the scapula and humeral head.

Figure 9



Note radiolucent defect in caudal articular surface of the humeral head.

OFA requires one view of each shoulder clearly labeled left and right in the neutral medial-lateral position. The radiographs are required to contain permanent dog identification in the emulsion. The shoulder interest should be pushed cranial to the thorax and the opposite shoulder pulled caudally. Inclusion of additional views is at the discretion of the attending veterinarian. A permanent clearance can be obtained at 12 months of age, and dogs between 4 and 12 months of age can receive a preliminary evaluation.

Shoulder classifications

Normal—No evidence of inherited pathologic change

Abnormal—Osteochondrosis (OCD) - radiograph changes consistent with inherited disease

Degenerative joint disease/osteoarthritis—the presence of degenerative joint disease without a definite diagnosis of, but probably due to, prior osteochondrosis.

Application Information

Application forms are available on request from the OFA or can be downloaded from the OFA web site (*www.offa.org*). The radiograph, signed application a form (which should include choice of open or semi-closed database), and the service fee should be mailed to: Orthopedic Foundation for Animals, 2300 E. Nifong Blvd., Columbia, MO 65201-3806. All radiographic images are retained by the OFA for research and reference purposes. The owner or agent should complete and sign the OFA application form and the information is best obtained from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam.

Patellar luxation database

General procedures

Purposes—To identify those dogs that are phenotypically normal prior to use in a breeding program, and to gather data on the genetic disease of patellar luxation.

Examination and classification—Each dog is to be physically examined awake and classified by an attending veterinarian according to the general information instructions.

Clearance issued—A breed registry number will be issued for all dogs found to be normal at 12 months of age or older. There is an initial OFA fee and no charge for recertification at a later age. The breed registry number will contain the age at evaluation and it is recommended that dogs be periodically reexamined as some luxations will not be evident until later in life.

Preliminary evaluation—Evaluation of dogs less than 12 months of age is encouraged if the owner desires to breed at this age. A very opportune time to gather this data is at 6-8 weeks of age, prior to the puppy's release to the new owner.

Dogs with patellar luxation—The attending veterinarian and owner are encouraged to submit all evaluations, whether normal or abnormal, to help assure accuracy of the database. There is no OFA fee for entering an abnormal evaluation of the patella in the data bank. Abnormal information will not be released into the public domain unless the owner gives permission for this release by initialing the appropriate line on the application form.

Patellar luxation classifications

Patellar luxations fall into several categories:

1. **Medial luxation in toy, miniature, and large breeds.**
2. **Lateral luxation in toy and miniature breeds.**
3. **Lateral luxation in large and giant breeds.**
4. **Luxation resulting from trauma in any breed, and of no importance to the certification process.**

Categories 1, 2 and 3 are either known to be heritable or strongly suspected to be heritable.

Classifications

A method of classifying the degree of luxation and bony deformity is useful for diagnosis, and can be applied to either medial or lateral luxations by reversing the medial-lateral directional references. The position of the patella can easily be palpated starting at the tibial tubercle and working proximal along the patellar ligament to the patella.

Grade 1

The patella easily luxates manually at full extension of the stifle joint, but returns to the trochlea when released. No crepitation is apparent. The medial, or very occasionally, lateral deviation of the tibial crest (with lateral luxation of the patella) is only minimal, and there is very slight rotation of the tibia. Flexion and extension of the stifle is in a straight line with no abduction of the hock.

Grade 2

There is frequent patellar luxation, which, in some cases, becomes more or less permanent. The limb is sometimes carried, although weight bearing routinely occurs with the stifle remaining slightly flexed.

Especially under anesthesia it is often possible to reduce the luxation by manually turning the tibia laterally, but the patella reluxates with ease when manual tension of the joint is released. As much as 30 degrees of medial tibial torsion and a slight medial deviation of the tibial crest may exist. When the patella is resting medially the hock is slightly abducted. If the condition is bilateral, more weight is thrown onto the forelimbs.

Many cases in this grade live with the condition reasonably well for many years, but the constant luxation of the patella over the medial lip of the trochlea causes erosion of the articulating surface of the patella and the proximal area of the medial lip. This results in crepitation becoming apparent when the patella is luxated manually.

Grade 3

The patella is permanently luxated with torsion of the tibia and deviation of the tibial crest of between 30 degrees and 50 degrees from the cranial/caudal plane. Although the luxation is not intermittent, many animals use the limb with the stifle held in a semi flexed position. The trochlea is very shallow or even flattened.

Grade 4

The tibia is medially twisted and the tibial crest may show further deviation medially with the result that it lies 50 degrees to 90 degrees from the cranial/caudal plane. The patella is permanently luxated. The patella lies just above the medial condyle and a space can be palpated between the patellar ligament and the distal end of the femur. The trochlea is absent or even convex. The limb is carried, or the animal moves in a crouched position with the limb partly flexed.

Medial luxation in toy, miniature, and large breeds

These luxations are often termed "congenital" because they occur early in life and are not associated with trauma. Although the luxation may not be present at birth, the anatomical deformities that cause these luxations are present at that time and are responsible for subsequent recurrent patellar luxation. Patellar luxation in these breeds should be considered an inherited disease. Medial luxation is far more common than lateral luxation in all breeds, representing 75-80% of cases, with bilateral involvement seen 20-25% of the time.

Clinical signs

Three classes of patients are identifiable

1. Neonates and older puppies often show clinical signs of abnormal hind-leg carriage and function from the time they start walking; these generally present as grades 3 and 4.
2. Young to mature animals with grade 2 to 3 luxations usually have exhibited abnormal or intermittently abnormal gaits all their lives, but are presented when the problem symptomatically worsens.
3. Older animals with grade 1 and 2 luxations may exhibit sudden signs of lameness because of further breakdown of soft tissues as result of minor trauma or because of worsening of degenerative joint disease pain.

Signs vary dramatically with the degree of luxation. In grades 1 and 2, lameness is evident only when the patella is in the luxated position. The leg is carried with the stifle joint flexed but may be touched to the ground every third or fourth step at fast gaits. Grade 3 and 4 animals exhibit a crouching, bowlegged stance (genu varum) with the feet turned inward and with most of the weight transferred to the front legs. Permanent luxation renders the quadriceps ineffective in extending the stifle. Extension of the stifle will allow reduction of the luxation in grades 1 and 2. Pain is present in some cases, especially when chondromalacia of the patella and femoral condyle is present. Most animals, however, seem to show little irritation upon palpation.

Lateral luxation in toy and miniature breeds

Lateral luxation in small breeds is most often seen late in the animal's life, from 5 to 8 years of age. The heritability is unknown. Skeletal abnormalities are relatively minor in this syndrome, which seems to represent a breakdown in soft tissue in response to obscure skeletal derangement. Thus, most lateral luxations are grades 1 and 2, and the bony changes are similar to, but opposite, those described for medial luxation. The dog has more functional disability with lateral luxation than with medial luxation.

Clinical signs

In mature animals, signs may develop rapidly and may be associated with minor trauma or strenuous activity. A knock-knee or genu valgum stance, sometimes described as seal-like, is characteristic. Sudden bilateral luxation may render the animal unable to stand and so simulate neurological disease. Physical examination is as described for medial luxation.

Lateral luxation in large and giant breeds

Also called genu valgum, this condition is usually seen in the large and giant breeds with Great Danes, St. Bernards, and Irish Wolfhounds being the most commonly affected. Components of hip dysplasia, such as coxa valga (increased angle of inclination of the femoral neck) and increased anteversion of the femoral neck, are related to lateral patellar luxation. These deformities cause internal rotation of the femur with lateral torsion and valgus deformity of the distal femur, which displaces the quadriceps mechanism and patella laterally.

Clinical signs

Bilateral involvement is most common. Animals appear to be affected by the time they are 5 to 6 months of age. The most notable finding is a knock-knee (genu valgum) stance. The patella is usually reducible, and laxity of the medial collateral ligament may be evident. The medial retinacula tissues of the stifle joint are often thickened, and the foot can often be seen to twist laterally as weight is placed on the limb.

Application information

The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. Application forms are available on request from OFA or can be downloaded from the OFA web site (*www.offa.org*). The signed application form (which should include the owner's choice of open or semi-open database), and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856.

Canine thyroid database

Autoimmune thyroiditis is the most common cause of primary hypothyroidism in dogs. The disease has variable onset, but tends to clinically manifest itself at 2 to 5 years of age. Dogs may be clinically normal for years, only to become hypothyroid at a later date. The markers for autoimmune thyroiditis, autoantibody formation (autoantibodies to thyroglobulin, T4 or T3), usually occur prior to the occurrence of clinical signs. The majority of dogs that develop autoantibodies have them by 3 to 4 years of age. Development of autoantibodies at any time in the dog's life is an indication that the dog probably has the genetic form of the disease. Using current technology only a small fraction of false positive tests occur.

As a result of the variable onset of the presence of autoantibodies, periodic testing is necessary. Dogs that are negative at 1 year of age may become positive at 6 years of age. Dogs should be tested every year or two to be certain they have not developed the condition. Since the majority of affected dogs will have autoantibodies by 4 years of age, annual testing for the first 4 years is recommended. After that, testing every other year should suffice. Unfortunately, a negative test at any one time will not guarantee that the dog will not develop thyroiditis.

This data can be used by breeders in determining which dogs are best for their breeding program. Knowing the status of the dog and the dog's lineage, breeders and genetic counselors can decide which breedings are most appropriate for reducing the incidence of autoimmune thyroiditis in the offspring. The Animal Health Diagnostic Laboratory at Michigan State University has the largest pooled database on breed prevalence of autoimmune thyroiditis (**Table 8**).

Table 8: Michigan State University thyroid statistics

Breed	Rank	No. of Evals.	% Autoimmune Thyroiditis	% Equivocal
English Setter	1	1457	31.4	7.9
Havanese	2	146	22.6	3.4
Old English Sheepdog	3	924	21.9	6.3
German Wirehaired Pointer	4	338	18.6	7.7
American Pit Bull Terrier	5	1305	18.2	6.5
Boxer	6	8910	18.0	4.5
Tibetan Terrier	7	294	17.7	9.5

Breed	Rank	No. of Evals.	% Autoimmune Thyroiditis	% Equivocal
NS Duck Tolling Retriever	8	188	17.6	9.0
Maltese	9	1705	16.5	5.6
Beagle	10	7237	16.5	5.6
Dalmatian	11	3194	16.3	6.4
Pointer	12	132	15.9	9.8
Cocker Spaniel	13	17083	15.7	6.5
Giant Schnauzer	14	748	15.5	6.7
Rhodesian Ridgeback	15	2155	15.4	5.5
Treeing Walker Coonhound	16	112	15.2	6.3
Kuvasz	17	225	15.1	8.0
American Staffordshire Terrier	18	499	14.6	5.6
Welsh Springer Spaniel	19	187	13.9	8.0
Golden Retriever	20	40622	13.2	4.6
Chesapeake Bay Retriever	21	1322	12.9	5.4
Shetland Sheepdog	22	14110	12.7	5.8
Irish Setter	23	1791	12.6	7.0
Brittany	24	1486	12.0	4.2
Siberian Husky	25	1498	11.7	4.5
English Cocker Spaniel	26	562	11.7	4.8
Gordon Setter	27	644	11.6	8.5
Borzoi	28	729	11.5	5.3
Border Collie	29	2197	11.2	5.3
Leonberger	30	314	11.1	3.8
Alaskan Malamute	31	1510	11.1	7.3
Basenji	32	741	10.8	5.5
Great Dane	33	2391	10.1	6.7
Schipperke	34	562	10.0	3.2
Coonhound	35	254	9.8	5.9
Anatolian Shepherd	36	105	9.5	5.7
Petit Basset Griffon Vendeen	37	171	9.4	5.8
Samoyed	38	1808	9.0	6.0
Manchester Terrier	39	180	8.9	6.7
Airedale Terrier	40	1312	8.8	5.3
Mastiff	41	2267	8.7	5.5
Akita	42	2673	8.6	8.2
Cockapoo	43	977	8.6	3.8
Australian Shepherd	44	2515	8.6	4.9
Belgian Malinois	45	178	8.4	4.5
Doberman Pinscher	46	9260	8.4	5.5
German Shorthaired Pointer	47	1339	8.1	5.7
Spinoni Italiano	48	100	8.0	3.0
Neapolitan Mastiff	49	101	7.9	5.9
Vizsla	50	672	7.9	4.2

April 2006

General procedures

Purposes

To identify those dogs that are phenotypically normal for breeding programs, and to gather data on the genetic disease of autoimmune thyroiditis.

Clearance issued

A breed registry number will be issued for all dogs found to be normal at 12 months of age or older. Age will be noted on the certificate since the classification can change as the dog ages. There is an initial OFA fee and no charge for recertification at a later date. It is recommended that reexamination occur at ages 2,3,4,6, and 8 years.

Preliminary evaluation

Dogs less than 12 months of age can be evaluated for the owner's information, however few dogs are positive at that age.

Dogs with autoimmune thyroiditis

All data, whether normal or abnormal, should be submitted to help assure accuracy of the database. There is no OFA fee for entering an abnormal evaluation of the thyroid into the data bank. Abnormal information will not be released into the public domain unless the owner gives permission for this release by initialing the appropriate line on the application form.

Thyroid abnormalities fall into several categories, and two types are defined by the registry:

a. **Autoimmune Thyroiditis**—Known or suspected to be heritable.

b. **Idiopathic Hypothyroidism**—Of unknown origin.

Dogs with laboratory results that are not definitive will be considered as equivocal. It is recommended that the test be repeated in three to six months.

Classification

Thyroid classifications are based on the most current and scientifically validated tests available.

Indices of thyroiditis

Free T4 (FT4)—This test is considered to be the "gold standard" for assessment of the thyroid's production and cellular availability of thyroxine. FT4 concentration is expected to be decreased in dogs with thyroid dysfunction due to autoimmune thyroiditis.

Canine thyroid simulating hormone (cTSH)—This test helps determine the site of the lesion in cases of hypothyroidism. In autoimmune thyroiditis, thyroid gland function is reduced, while the

pituitary gland continues to function normally. Therefore, when FT4 levels fall due to a malfunctioning thyroid gland, the pituitary produces elevated levels of cTSH in an attempt to stimulate thyroid production. Thus, the cTSH concentration is expected to be abnormally elevated in dogs with thyroid atrophy from autoimmune thyroiditis.

Thyroglobulin Autoantibodies (TgAA)—This test measures the level of thyroid autoantibodies (antibodies directed against normal body tissue). Positive levels of thyroid antibodies are an indication that an autoimmune process is damaging the dog's thyroid gland.

a. **Normal**
   FT4 within normal range
   cTSH within normal range
   TgAA is negative.

b. **Positive autoimmune thyroiditis**
   FT4 less than normal range
   cTSH greater than normal range
   TgAA is positive

c. **Positive compensative autoimmune thyroiditis**
   FT4 within normal range
   cTSH greater than or equal to normal range
   TgAA positive

d. **Idiopathically reduced thyroid function**
   FT4 less than normal range
   cTSH greater than normal range
   TgAA negative

e. **All other results are considered equivocal**

Laboratory certification

In an attempt to standardize testing methodology, laboratories are required to pass a certification process. Laboratories may apply, and if successful will be approved to perform analysis for OFA thyroid certification.

The following laboratories are approved, and should be contacted directly for the appropriate submission forms (other than the OFA application form), sample handling procedures, and laboratory service fee before collecting the sample. For the most current list of available laboratories, see the website (*www.offa.org*).

Endocrine Diagnostic Center
Diagnostic Center for Population
& Animal Health
4125 Beaumont Road, Room 122
Lansing, MI 48910-8104
517-353-0621

Texas Veterinary Medical Diagnostic Laboratory
1 Sippel Rd.
College Station, TX 77843
979-845-3414

New York State Animal Health Diagnostic Center
College of Veterinary Medicine,
Cornell University
Upper Tower Rd.
Ithaca, NY 14853
607-253-3673

Animal Health Laboratory
Laboratory Services Division
University of Guelph
Door P2 Bldg. 49, McIntosh Lane
Guelph, Ontario, N1G 2W1
CANADA
519-824-4120 ext. 54501

Veterinary Diagnostic Laboratory
Attn: OFA Special Handling
College of Veterinary Medicine
University of Minnesota
1333 Gortner Ave.
St. Paul, MN 55108
612-624-0761

University of California
Veterinary Medical Teaching Hospital
Clinical Pathology, Chemistry,
Room 1017
1 Garrod Drive
Davis, CA 95616
530-752-7380

Vita-Tech
1345 Denison St.
Markham, Ont, L3R 5V2
CANADA
1-800-667-3411

Antech Diagnostics*
1111 Marcus Ave.
Suite M28
Lake Success , NY 11042
800-872-1001

*only the Lake Success, NY location of Antech has been certified to process OFA thyroid panels

Instructions for testing

1. The veterinarian or owner must obtain the "Application for Thyroid Database" from the Orthopedic Foundation for Animals, Inc. (phone 573-442-0418), or online at *www.offa.org*.
2. The veterinarian and owner must complete their respective portions of the form.
3. Two milliliters (2 ml) of serum are needed for testing, and the serum sample must be from freshly collected blood. Use a plain "red-top" tube for blood collection. Do not use a serum separator tube with clot additives or any other type of plasma collection tube. After collection, place the blood sample in the refrigerator for 60 to 90 minutes to allow clotting. Centrifuge, collect the serum, and transfer to a plain plastic or glass tube suitable for shipping.

Clearly label the sample with the owner's name, animal's identification, date of blood collection, and "OFA Thyroid Panel." If the specimen is to be stored for more than 12 hours prior to shipping, frozen storage is recommended.

4. Ship to the approved laboratory of choice via an overnight courier service. It is recommended that all specimens be packaged properly and shipped so they are received either chilled or frozen. Serum samples arriving unchilled or at room temperature within 48 hours of the collection date will be accepted. However, samples arriving after this time must be received either chilled or frozen in order to be accepted for registry testing. Contact the laboratory for further information as necessary.
5. Female dogs should not be tested during an estrus cycle. The date of last routine vaccination should be noted.
6. Please do not submit whole blood, clotted blood, or plasma.
7. Severely lipemic or hemolyzed specimens are also unacceptable.
8. Test results will be mailed or faxed only to the submitting veterinarian and the Orthopedic Foundation for Animals, Inc.. Results will not be available from the laboratory by telephone. The OFA will send a report to the veterinarian and to the owner.

Sebaceous adenitis database

Sebaceous Adenitis (SA) is a hereditary skin disease in which the sebaceous glands become inflamed, often leading to progressive loss of hair. Diagnosing SA can be difficult as the symptoms vary by breed, the symptoms are similar to those of other diseases such as hypothyroidism or allergies, and the disease can vary greatly in its severity. Visible symptoms include excessive dandruff or scaling, hair loss, lesions, a musty odor, and even secondary skin infections. On the other hand, dogs affected with SA can be subclinical and show no outward signs of the disease. As a result, diagnosis requires microscopic examination of tissue samples. The disease is primarily seen in Standard Poodles, Akitas, and Samoyeds, although there have been reported cases in a number of other breeds and mixed breeds as well.

Two factors make SA particularly difficult for breeders to control: the possible late onset of the disease, and the subclinical state of the disease. With late onset, the dog may have already been bred long before it ever shows clinical signs of the disease. In its subclinical state, an owner may be unaware that the animal is affected since it shows no visible signs of the disease.

Sebaceous adenitis is believed to be a simple autosomal recessive in its mode of inheritance. The challenge in controlling the disorder is in identifying dogs as clear, carriers, or affecteds. DNA testing remains the "gold standard" in terms of identifying a dog's genotype, however, at present there is no DNA test to determine a dog's status with regard to SA. Today's best alternative is the phenotypic evaluation through the skin biopsy. As enough phenotypic information on families of dogs is entered into the database, breeders will be able to make educated assumptions on a dog's genotype. This will allow breeders to apply greater selective pressure in controlling and reducing the incidence of the disease.

General procedures

Purpose

To identify phenotypically normal dogs prior to breeding, and to gather data on the genetic disease of sebaceous adenitis.

Examination

Dogs are to be screened using skin biopsies examined by a dermatopathologist.

Clearance issued

A breed registry number will be issued for all dogs found to be normal at 12 months of age or older. There is an initial OFA fee and no charge for recertification at a later age. The breed registry number will contain the age at examination and it is recommended that dogs be periodically re-examined as some affected dogs may not be evident until later in life.

Dogs with sebaceous adenitis

There is no OFA fee for entering an abnormal examination into the sebaceous adenitis data bank. Abnormal information will not be released into the public domain unless the owner gives permission by initialing the appropriate line on the application form.

Sebaceous adenitis classifications

There are several classifications:

Normal—no evidence of sebaceous adenitis at the time of the examination.

Equivocal—some inflammation is present, but the cause cannot be determined.

Affected—dogs with clinical signs and histopathologic evidence of inflammatory skin disease with destruction of hair follicles, especially the sebaceous glands.

Affected without clinical signs—histopathologic evidence of sebaceous adenitis but a clinically normal appearance of skin and hair coat.

Figure 10

Sebaceous adenitis examination procedures

The attending veterinarian examines the dog for clinical symptoms of the disease and notes any findings on the application form. A minimum of two 6mm punch biopsy samples are taken from the skin of the dog's neck between the top of the head and the withers (**Fig. 10**). If there are areas of scaling and hair loss, samples should be taken from those areas. To procure the sample, a local anesthetic such as lidocaine may be used. **The area should not be scrubbed or otherwise cleaned,** however gentle clipping of the area may be necessary. The specimen should not be squeezed with the forceps while placing in a crush proof container containing 10% buffered formalin in preparation for shipment to the lab. The biopsy sites may be closed with one or two sutures.

The sample, the completed OFA application, and both the lab fee and OFA fee are shipped to one of six approved dermapathology labs for evaluation. The lab results and final diagnosis are returned to the OFA and to the owner.

Approved dermapathologists/laboratories

For the most current list of available laboratories, see the website (*www.offa.org*).

Ann M. Hargis, DVM, DACVP
DermatoDiagnostics
207 North Harkness St.
PO Box 770
Everson, WA 98247
(425) 775-6903

Maron B. Calderwood Mays, VMD, PhD, Diplomate ACVP
Florida Vet Path, Inc.
506 N. West Street
Bushnell, FL 33513
(888) 669-9693
Fax: (352) 569-9292

Brian Wilcock, DVM, PhD
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Guelph, ONT N1G 1W8
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Yager-Best
Vita-Tech
1345 Denison Street
Markham, Ontario,
Canada L3R 5V2
(416) 798-4988
(800) 667-3411 (North America Toll Free)
FAX: (905) 475-7309
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Congenital cardiac database

General procedures

Purposes

To gather data regarding congenital heart diseases in dogs, and to identify dogs which are phenotypically normal prior to use in a breeding program. For the purposes of the registry, a phenotypically normal dog is defined as:

1. **One without a cardiac murmur.**
2. **One with an innocent heart murmur that is found to be otherwise normal by virtue of an echocardiographic examination which includes Doppler studies.**

Examination and classification

Each dog is to be examined and classified by a veterinarian with expertise in the recognition of canine congenital heart disease, in accordance with procedures outlined under Identification and Classification.

Clearance issued

A breed registry number will be issued for any dog found to be normal at 12 months of age or older. There is an initial OFA fee and no charge for recertification at a later age. The breed registry number will indicate the age at evaluation and the type of examiner (C-cardiologist, S-specialist, and P-practitioner).

Preliminary evaluation

Dogs under 12 months of age can be evaluated for the owner's information. The most opportune time to gather this data is at 8–10 weeks of age, prior to the puppy's release to the new owner.

Dogs with congenital heart disease

The veterinarian and owner are encouraged to submit all evaluations, whether normal or abnormal, to help assure accuracy of the database and to assist in the analysis of patterns of inheritance in important canine congenital heart defects. There is no OFA fee for entering an abnormal cardiac evaluation into the data bank. Abnormal information will not be released into the public domain unless the owner gives permission for this release by initialing the appropriate line on the application form.

Identification and classification

General Instructions

Congenital heart disease (CHD) in dogs is a malformation of the heart or great vessels. The lesions characterizing congenital heart defects are present at birth and may develop more fully during perinatal and growth periods. Many congenital heart defects are thought to be genetically transmitted from parents to offspring; however, the exact modes of inheritance have not been precisely determined for all cardiovascular malformations.

The most common congenital cardiovascular defects can be grouped into several anatomic categories (**Table 9**, p. 63). These anatomic diagnoses include:

1. **Malformation of the atrioventricular valves.**
2. **Malformation of ventricular outflow leading to obstruction of blood flow.**
3. **Defects of the cardiac septa (shunting defects).**
4. **Abnormal development of the great vessels or other vascular structures.**
5. **Complex, multiple, or other congenital disorders of the heart, pericardium, or blood vessels.**

A careful clinical examination that emphasizes cardiac auscultation is the most expedient and cost-effective method for identifying CHD in dogs. While there are exceptions, virtually all common congenital heart defects are associated with the presence of a cardiac murmur. Consequently, it is recommended that cardiac auscultation be the primary screening method for initial identification of CHD and the initial classification of dogs.

Murmurs related to CHD may at times be difficult to distinguish from normal, innocent (also called physiologic or functional) murmurs. Innocent cardiac murmurs are believed to the related to normal blood flow in the circulation. Innocent murmurs are most common in young, growing animals. The prevalence of innocent heart murmurs in mature dogs (especially in athletic dogs) is undetermined. A common clinical problem is the distinction between innocent murmurs and murmurs arising from CHD.

Definitive diagnosis of CHD usually involves one or more of the following methods:

1. **Echocardiography with Doppler studies.**
2. **Cardiac catheterization with angiocardiography.**
3. **Post-mortem examination of the heart (necropsy).**

Other methods of cardiac evaluation, including electrocardiography and thoracic radiography, are useful in evaluating individuals with CHD, but are neither sufficiently sensitive nor specific enough to reliably identify or exclude the presence of CHD.

1. The non-invasive method of echocardiography with Doppler is the preferred method for establishing a definitive diagnosis in dogs when CHD is suspected from the clinical examination. Echocardiography is an inappropriate screening tool for the identification of congenital heart disease and should be performed only when the results of clinical examinations suggest a definite or potential cardiovascular abnormality.
2. Two-dimensional echocardiography provides an anatomic image of the heart and blood vessels. While moderate to severe cardiovascular malformations can generally be recognized by two-dimensional echocardiography, mild defects (which are often of great concern to breeders of dogs) may not be identifiable by this method alone.
3. Doppler studies, including pulsed-wave and continuous-wave spectral Doppler, and two-dimensional color Doppler, demonstrate the direction and velocity of blood flow in the heart and blood vessels. Abnormal patterns of blood flow are best recognized by Doppler studies. Results of Doppler studies can be combined with those of the two-dimensional echocardiogram in assessing the severity of CHD. Color Doppler echocardiography is used to evaluate relatively large areas of blood flow and is beneficial in the overall assessment of the dog with suspected CHD. Turbulence maps employed in color Doppler imaging are useful for identifying high velocity or disturbed blood flow but are not sufficiently specific (or uniform among manufacturers) to quantify blood velocity. It is emphasized that quantification of suspected blood flow abnormalities is essential and can only be accomplished with pulsed- or continuous-wave Doppler studies. Pulsed-wave and continuous-wave Doppler examinations provide a display of blood velocity spectra in a graphical format and are the methods of choice for assessing blood flow patterns and blood flow velocity in discrete anatomic areas.
4. Cardiac catheterization is an invasive method for identification of CHD that is considered very reliable for the diagnosis of CHD. Cardiac catheterization should be performed by a cardiologist, usually requires general anesthesia, carries a small but definite procedural risk, and is generally more costly than noninvasive studies. While cardiac catheterization with angiocardiography is considered one of the standards for the diagnosis CHD, this method has been supplanted by echocardiography with Doppler for routine evaluation of suspected CHD.

5. Necropsy examination of the heart should be done in any breeding dog that dies or is euthanized. The hearts of puppies and dogs known to have cardiac murmurs should always be examined following the death of the animal. A post mortem examination of the heart is best done by a cardiologist or pathologist with experience in evaluating CHD. While it is obvious that necropsy cannot be used as a screening method, the information provided by this examination can be useful in guiding breeders and in establishing the modes of inheritance of CHD.

Each of the methods of evaluation indicated above may be associated with false positive and false negative diagnoses. It must be recognized that some cases of CHD fall below the threshold of diagnosis. In other cases, a definitive diagnosis may not be possible with currently available technology and knowledge. These limitations can be minimized by considering the following general guidelines:

1. The results of the examinations described above are most reliable when performed by an experienced individual with advanced training and experience in cardiovascular diagnosis. Echocardiography with Doppler, cardiac catheterization, and post-mortem examination of the heart for CHD requires advanced training in cardiovascular diagnostic methods and the pathology and pathophysiology of CHD.
2. Examinations performed in mature dogs are most likely to be definitive. This is especially true when considering mild congenital heart defects. Innocent heart murmurs are less common in mature animals than in puppies and are less likely to be a source of confusion. Furthermore, the murmurs associated with some mild congenital malformations become more obvious after a dog has reached maturity. While it is quite reasonable to perform preliminary evaluations and provide provisional certification to puppies and young dogs between 8 weeks and 1 year of age, final certification prior to breeding should be obtained in mature dogs at 12 months of age or older.
3. Examination conditions must be appropriate for recognition of subtle cardiac malformations. Identification of soft cardiac murmurs is impeded by extraneous noise and by poorly restrained, anxious, or panting dogs.
4. A standardized cardiac clinical examination must be performed according to a predetermined and clearly communicated protocol. Physical examination and cardiac auscultation should be used as the initial method of cardiac evaluation. If the clinical examination is normal, no further diagnostic studies are recommended. If the clinical examination is abnormal, a tentative diagnosis may be made, but the definitive diagnosis generally requires other diagnostic studies (as indicated above).

5. Examiners who perform echocardiography with Doppler must use appropriate ultrasound equipment, transducers, and techniques. Such individuals should have advanced training in non-invasive cardiac diagnosis and should follow diagnostic standards established by their hospital and by the veterinary scientific community, including standards published by the American College of Veterinary Internal Medicine, Specialty of Cardiology (*J Vet Internal Med*, 1993;7:247-252).

Examination of dogs for CHD is aimed at the identification and classification of the phenotypic abnormalities. Heritable aspects of CHD cannot be addressed unless suitable genetic studies have been conducted.

Methods of examination

Clinical examination

The clinical cardiac examination should be conducted in a systematic manner. The arterial and venous pulses, mucous membranes, and precordium should be evaluated. Heart rate should be obtained. The clinical examination should be performed by an individual with advanced training in cardiac diagnosis. Board certification by the American College of Veterinary Internal Medicine, Specialty of Cardiology is considered by the Veterinary Medical Association as the benchmark of clinical proficiency for veterinarians in clinical cardiology, and examination by a Diplomate of this specialty board is recommended. Other veterinarians may be able to perform these examinations, provided they have received advanced training in the subspecialty of congenital heart disease.

Cardiac auscultation should be performed in a quiet, distraction-free environment. The animal should be standing and restrained, but sedative drugs should be avoided. Panting must be controlled and if necessary, the dog should be given time to rest and acclimate to the environment. The clinician should be able to identify the cardiac valve areas for auscultation. The examiner should gradually move the stethoscope across all valve areas and also should auscultate over the subaortic area, ascending aorta, pulmonary artery, and the left craniodorsal cardiac base. Following examination of the left precordium, the right precordium should be examined.

1. The mitral valve area is located over and immediately dorsal to the palpable left apical impulse and is identified by palpation with the tips of the fingers. The stethoscope is then placed over the mitral area and the heart sounds identified.
2. The aortic valve area is dorsal and one or two intercostal spaces cranial to the left apical impulse. The second heart sound will be most intense when the stethoscope is centered over the aortic valve area. Murmurs originating from or radiating to the subaortic area of auscultation are evident immediately caudoventral to the aortic

valve area. Murmurs originating from or radiating into the ascending aorta will be evident craniodorsal to the aortic valve and may also project to the right cranial thorax and to the carotid arteries in the neck.

3. The pulmonic valve area is ventral and one intercostal space cranial to the aortic valve area. Murmurs originating from or radiating into the main pulmonary artery will be evident dorsal to the pulmonic valve over the left hemithorax.
4. The tricuspid valve area is a relatively large area located on the right hemithorax, opposite and slightly cranial to the mitral valve
5. The clinician also should auscultate along the ventral right precordium (right sternal border) and over be right craniodorsal cardiac border.
6. Any cardiac murmurs or abnormal sounds should be noted. Murmurs should be described as indicated below.

Description of cardiac murmurs

A full description of the cardiac murmur should be made and recorded in the medical record.

- Murmurs should be designated as systolic, diastolic, or continuous.
- The point of maximal murmur intensity should be indicated as described above. When a precordial thrill is palpable, the murmur will generally be most intense over this vibration.
- Murmurs that are only detected intermittently or are variable should be so indicated.
- The radiation of the murmur should be indicated.

Grading of heart murmurs

Grade 1—A very soft murmur only detected after very careful auscultation.

Grade 2—A soft murmur that is readily evident.

Grade 3—A moderately intense murmur not associated with a palpable precordial thrill (vibration).

Grade 4—A loud murmur; a palpable precordial thrill is not present or is intermittent.

Grade 5—A loud cardiac murmur associated with a palpable precordial thrill; the murmur is not audible when the stethoscope is lifted from the thoracic body wall.

Grade 6—A loud cardiac murmur associated with a palpable precordial thrill and audible even when the stethoscope is lifted from the thoracic wall.

Other descriptive terms may be indicated at the discretion of the examiner; these include such timing descriptors as: proto- (early) systolic, ejection or crescendo-decrescendo, holo-systolic or pan-systolic, decrescendo, and tele- (late) systolic and descriptions of subjective characteristics such as: musical, vibratory, harsh, and machinery.

Effects of heart rate, heart rhythm, and exercise

Some heart murmurs become evident or louder with changes in autonomic activity, heart rate, or cardiac cycle length. Such changes may be induced by exercise or other stresses. The importance of evaluating heart murmurs after exercise is currently unresolved. It appears that some dogs with congenital subaortic stenosis or with dynamic outflow tract obstruction may have murmurs that only become evident with increased sympathetic activity or after prolonged cardiac filling periods during marked sinus arrhythmia. It also should be noted that some normal, innocent heart murmurs may increase in intensity after exercise. Furthermore, panting artifact may be a problem after exercise.

It is most likely that examining dogs after exercise will result in increased sensitivity to diagnosis of soft murmurs but probably decreased specificity as well. Auscultation of the heart following exercise is at the discretion of the examining veterinarian.

At this time the OFA does not require a post exercise examination in the assessment of heart murmurs in dogs; however, this practice may be modified should definitive information become available.

Echocardiography

The echocardiographic examination should be conducted in a systematic matter. The examiner must be able to perform two-dimensional, pulsed-wave Doppler, and continuous-wave Doppler examinations of the heart. The availability of color Doppler is valuable but not essential for most examinations. The echocardiographic examination should be performed and interpreted by individuals with advanced training in cardiac diagnosis. Board certification by the American College of Veterinary Internal Medicine, Specialty of Cardiology is considered by the American College of Veterinary Medical Association as the benchmark of clinical proficiency for veterinarians in clinical cardiology, and examination by a Diplomate of this Specialty Board is recommended. Other veterinarians may be able to perform these examinations provided they have appropriate equipment and have received advanced training in echocardiography.

The pericardial space, both atria, both ventricles, the great vessels, and the four cardiac valves should be imaged using long axis, short axis, apical, and angled image planes as necessary to perform a complete ex-

amination of the heart. Nomenclature should follow that recommended by the American College of Veterinary Internal Medicine Specialty of Cardiology. An anatomic diagnosis may be possible based on two-dimensional imaging; however, the origin of cardiac murmurs should also be evaluated using Doppler methods.

Doppler examination of all cardiac valves should be performed and recorded. Abnormal flow should be quantified using pulsed wave or continuous wave Doppler techniques. Values obtained should be compared to reference values. The depressant effects of any tranquilizers or sedative must be considered when measuring peak flow velocities. Color Doppler echocardiography should be employed if available to assess normal and abnormal blood flow patterns. Identification of abnormal flow across the cardiac septa or shunts at the level of the great vessels is best done by a combination of color and pulsed wave Doppler techniques. Typical echocardiographic features of common congenital heart defects are indicated in **Table 9**.

Special attention should be directed to the assessment of flow patterns and velocities in the left ventricular outlet and descending aorta. Optimal alignment with blood flow should be sought for accurate velocities to be reported. This may require the use of sub-xiphoid (subcostal) transducer positions as well as left apical (caudal parasternal) transducer placements. In addition to measurement of peak velocity using pulsed or color wave Doppler, the pulsed wave sample volume should be gradually advanced from the subaortic area into the ascending aorta in order to identify sudden accelerations in flow velocity, turbulence, or aortic regurgitation.

Echocardiographic studies should be reported on videotape for subsequent analysis and a written record of abnormal findings should be entered into the medical record.

Application information

The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. Application forms are available on request from OFA or can be downloaded from the OFA web site (*www.offa.org*). The signed application form (which should include the owner's choice of open or semi-open database), and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856.

Table 9: Salient auscultatory and echocardiographic findings in canine congenital heart disease

Congenital Defect	Typical Auscultatory Features*	Diagnostic Echocardiographic and Doppler Echocardiographic Features
Patent ductus arteriosus	Continuous heart murmur with maximal intensity over the left, cranial dorsal cardiac base	Continuous retrograde flow from the patent ductus arteriosus into the pulmonary artery.
Ventricular septal defect	Systolic murmur with maximal intensity over the right ventral precordium; less often maximal intensity is over the pulmonic valve area and pulmonary artery.	The septal defect can often be imaged in multiple imaging planes. Abnormal, generally high velocity, systolic flow across the septal defect is evident.
Atrial septal defect	Systolic murmur with maximal intensity over the pulmonic valve area and pulmonary artery. The second heart sound may be widely split.	The septal defect can generally be imaged in multiple imaging planes. Abnormal blood flow may be identified across the septal defect into the right atrium.
Pulmonic stenosis	Systolic murmur with maximal intensity over the pulmonic valve area and pulmonary artery.	Abnormal pulmonary valve and /or subvalvular anatomy. Sudden acceleration of blood flow in the right ventricular outlet with turbulent, high velocity systolic flow across the pulmonary valve and into the main pulmonary artery.
Valvular and subvalvular aortic stenosis	Systolic murmur with maximal intensity over the subaortic or aortic valve area and radiating into the ascending aorta. The murmur may also be prominent over the right cranial thorax.	Abnormal subvalvular or aortic valvular anatomy may be evident. Sudden acceleration of blood flow into the left ventricular outflow tract with turbulent, high velocity systolic flow across the aortic valve and into the ascending aorta. Concurrent aortic regurgitation is usually present.
Mitral valve dysplasia	Systolic murmur with maximal intensity over the left apex and mitral area.	Abnormal anatomy of the mitral valve apparatus. High velocity retrograde systolic flow across the mitral valve into the left atrium. Concurrent mitral valve stenosis may be present.

Congenital Defect	Typical Auscultatory Features*	Diagnostic Echocardiographic and Doppler Echocardiographic Features
Tricuspid valve dysplasia	Systolic murmur with maximal intensity over the tricuspid valve area.	Abnormal anatomy of the tricuspid valve apparatus. High velocity retrograde systolic flow across the tricuspid valve into the right atrium. Concurrent tricuspid valve stenosis may be present.
Right to left cardiac shunt	Variable—a systolic murmur at the left base is often detected; cyanosis is an important clinical sign.	Abnormal anatomy related to the cardiac malformations examples include: tetralogy of Fallot, patent ductus arteriosus with pulmonary hypertension, pulmonary or tricuspid valves stenosis with atrial septal defect. Right to left shunting may be documented by Doppler techniques and/or by contrast echocardiography.

**see text for description of valve and auscultation areas*

Deafness database

Genetic deafness in dogs

Printed with permission of Dr. George M. Strain, Louisiana State University—School of Veterinary Medicine, www.lsu.edu/deafness.deaf.htm

Congenital deafness in dogs (or other animals) can be acquired (caused by intrauterine infections, ototoxic drugs like gentamicin, liver disorders, or other toxic exposures before or soon after birth) or inherited. Inherited deafness can be caused by a gene defect that is autosomal dominant, recessive, sex-linked, or may involve multiple genes (more on this later). It is usually impossible to determine the cause of congenital deafness unless a clear problem has been observed in the breed, or carefully planned breedings are performed. In this article I will discuss what is currently known about the genetics of deafness in dogs so that breeders can make the best informed decisions possible when attempting to reduce or eliminate deafness.

Congenital deafness has been reported for approximately 80 breeds, with the list growing at a regular rate; it can potentially appear in any breed but especially those with white pigmentation. Deafness may have been long-established in a breed but kept hidden from outsiders to protect reputations. The disorder is usually associated with pigmentation patterns, where the presence of white in the hair coat increases the likelihood of deafness. Two pigmentation genes in particular are often associated with deafness in dogs: the merle gene (seen in the Collie, Shetland Sheepdog, Dappled Dachshund, Harlequin Great Dane, American Foxhound, Old English Sheepdog, and Norwegian Dunkerhound among others) and the piebald gene (Bull Terrier, Samoyed, Greyhound, Great Pyrenees, Sealyham Terrier, Beagle, Bulldog, Dalmatian, English Setter). However, not all breeds with these genes have been reported to be affected. The deafness, which usually develops in the first few weeks after birth while the ear canal is still closed, usually results from the degeneration of part of the blood supply to the cochlea (the stria vascularis).

Table 10

Dog Breeds with Relatively High Incidence of Reported Deafness	
Australian Cattle Dog	Dalmatian
Australian Shepherd	English Cocker Spaniel
Bull Terrier	English Setter
Catahoula Leopard Dog	

Note: dogs of any breed can have congenital deafness, from a variety of causes. Breeds with white pigmentation are most affected.

The nerve cells of the cochlea subsequently die and permanent deafness results. The cause of the vascular degeneration is not known, but appears to be associated with the absence of pigment producing cells (melanocytes) in the blood vessels. All of the function of these cells is not known, but one role is to maintain high potassium concentrations in the fluid surrounding the hair cells of the cochlea; these pigment cells are critical for survival of the stria. Deafness in the Doberman, which is also accompanied by vestibular (balance) disturbance, results from a different mechanism, where hair cell death is not the result of degeneration of the stria. Deafness may also occur later in life in dogs from other causes such as toxicities, infections, or injuries, or due to aging (presbycusis); these forms of deafness almost never have a genetic cause in animals and thus do not present a concern in breeding decisions.

The prevalence of congenital deafness in different breeds is seldom known because of the limited number of studies (see the table on Breed Specific Deafness Prevalence in Dogs at *www.lsu.edu/deafness/incidenc.htm*). In the Dalmatian, where the incidence is highest, 8% of all dogs in the U.S. are bilaterally deaf and 22% are unilaterally deaf. In the English Setter, English Cocker Spaniel, Australian Cattle Dog, and Bull Terrier, where fewer numbers of dogs have been hearing tested, the incidence appears to be about one third to one half that of Dalmatians. Unilateral or bilateral deafness is found in 75% of all white Norwegian Dunkerhounds, but the incidence in normal-color dogs is unknown. Other breeds with a high incidence are the Catahoula and Australian Shepherd. The incidence of all types of deafness in the general dog population is low, reported to be 2.56 to 6.5 cases per 10,000 dogs seen at veterinary school teaching hospitals, but these data predate the availability of hearing testing devices and so are much lower that actual values. Recognition of affected cases is often difficult, because unilaterally deaf dogs appear to hear normally unless a special test (the brainstem auditory evoked response, BAER) is performed; facilities to perform the BAER are usually only available at veterinary schools. It should be noted that a unilaterally deaf dog can be as great a genetic risk for transmission of deafness to its offspring as is a bilaterally deaf dog.

Table 11

	Dd	
Dd	DD	Dd
	Dd	dd

Theoretical outcomes of breeding of two carriers of a recessive deafness gene (d).

Table 12

	DD	
Dd	DD	DD
	Dd	Dd

Theoretical outcomes of breeding a carrier and a dog free of the recessive deafness gene.

The method of genetic transmission of deafness in dogs is usually not known. There are no recognized forms of sex-linked deafness in dogs, although this does occur in humans. The disorder has been reported to have an autosomal recessive mechanism in the Rottweiler, Bull Terrier, and Pointer, but this suggestion is not reliable because the reports were before the availability of BAER testing and the ability to detect uni-

laterally deaf dogs. References usually state that deafness transmission in most other breeds is autosomal dominant, but this is false, as will be discussed below. Pigment-associated inherited deafness is not restricted to dogs. Similar defects have been reported for mice, mink, pigs, horses, cattle, cats, and humans. Deafness in blue-eyed white cats is common and is known to be passed on as an autosomal dominant defect. Blue eyes, resulting from an absence of pigment in the iris, is common with pigment-associated deafness but is not, in and of itself, an indication of deafness or the presence of a deafness gene; however, in several breeds dogs (Dalmatian, English Setter, English Cocker Spaniel, Bull Terrier) with blue eyes are statistically more likely to be deaf. Waardenburg's syndrome, a human condition, presents with deafness, a stripe of white in the hair and beard, blue or different colored eyes (even in blacks and Asians), no pigment behind the retina, and minor structural deformities around the nose and eyes. This is an autosomal dominant disorder with incomplete penetrance, which means that individuals that inherit the disorder may not show all components of the syndrome - i.e., they may not be deaf. Incomplete penetrance of a defect greatly complicates the determination of mode of inheritance. At present there is no documentation that incomplete penetrance is a factor in any canine deafness.

Table 13

	Dd	
dd	Dd	dd
	Dd	dd

Theoretical outcomes of breeding a carrier and an affected dog with the recessive deafness gene.

Table 14

	DD	
dd	Dd	Dd
	Dd	Dd

Theoretical outcomes of breeding an affected dog and a dog free of the recessive gene.

In simple Mendelian genetics, each dog carries two copies of each gene, one from each parent. The possible outcomes of breedings can be demonstrated with tables showing the genotype of both parents and the possible combinations in their offspring. If deafness is carried as a theoretical simple autosomal recessive gene (d), the breeding of two hearing carriers (Dd) (**Table 11**) will result, on average, in 25% affected dogs (dd), 50% hearing carriers (Dd), and 25% free of the defect (DD). The breeding of a carrier to a dog free of the defect (**Table 12**) will result in no affected dogs but 50% carriers and 50% free. The breeding of an affected dog to a carrier (**Table 13**) will result in 50% affected, 50% carriers, and no free. Finally, the breeding of an affected dog to a dog free of the defect (**Table 14**) will result in 100% carriers and no affected or free.

If instead the deafness is carried as a simple autosomal dominant gene (D), the breeding of an affected dog (Dd) to a free dog (dd) (**Table 13**) would result on average in 50% affected and 50% free. Dogs with the genotype DD would be unlikely to occur unless two deaf dogs had been bred. All of the above assumes that incomplete penetrance is not acting. If more than one gene (recessive and/or dominant) is involved in

producing the deafness, the possible combinations become much more complicated. In humans more than 50 different autosomal recessive or dominant deafness genes or loci have been identified. The children of two deaf parents with two different recessive deafness can be unaffected but carry both genes. If deafness in dogs results from more than one recessive gene, the possible outcomes of breedings are more numerous and determination of the mechanisms of transmission will be difficult.

As stated above, deafness is often associated with the merle (dapple) gene, which produces a mingled or patchwork combination of dark and light areas. This gene (M) is dominant so that affected dogs (Mm) show the pattern, which is desirable in many breeds. However, when two dogs with merle are bred, 25% will end up with the MM genotype (i.e., **Table 11**). These dogs usually have a solid white coat and blue irises, are often deaf and/or blind, and are sterile. Breeders of these dog breeds know not to breed merle to merle. In this case the deafness is neither dominant nor recessive, but is linked to a dominant gene that disrupts pigmentation and secondarily produces deaf dogs.

Genetic transmission of deafness in dogs with the piebald (s^p) and extreme white piebald (s^w) pigment genes, such as the Dalmatian, is less clear. These genes affect the amount and distribution of white areas on the body. Deafness in Dalmatians does not appear to be autosomal dominant, since deaf puppies result from hearing parents. It does not appear to be a simple recessive disorder: we have bred pairs of deaf Dalmatians and obtained bilaterally hearing and unilaterally hearing puppies, when all should have been deaf if the disorder was recessive. These findings might be explained by a multi-gene cause, the presence of two different autosomal recessive deafness genes, or a syndrome with incomplete penetrance. Further studies (in progress) will be required to determine the mechanisms. Several candidate genes known to cause pigment-related deafness in humans or mice have been eliminated as the possible cause of pigment-associated deafness in Dalmatians. Whole-genome screens will hopefully identify the cause in this and other breeds.

Recent studies have shown that deafness in Dobermans, which do not carry the merle or piebald genes, results from direct loss of cochlear hair cells without any effects on the stria vascularis. Vestibular (balance) system signs, including head tilt and circling, are seen, and the deafness is transmitted by a simple autosomal recessive mechanism. A similar pathology has been described for the Shropshire Terrier.

So what should breeders do when deafness crops up? The most conservative approach would be to not breed the affected animal and not repeat the breeding that produced deafness. It is frequently recommended (i.e. Dalmatian Club of America) that bilaterally deaf puppies should be euthanized, since they make poor pets, are difficult to train, are prone to startle biting, frequently die from misadventure (cars), and require excessive care. There is considerable controversy on this point, and there is no question that many people have successfully raised deaf dogs. For every

story of a problem deaf dog there seems to be a story of one that was successfully raised. Unfortunately, there is no way to predict how a deaf puppy will turn out. Unilaterally deaf dogs can make good pets but should not be bred. When deafness is uncommon in a breed, affected dogs should not be bred, but this does not mean that all related dogs are a risk and must be retired from breeding. An understanding of simple autosomal recessive and dominant patterns, as explained above, can allow the breeder to make better informed decisions and likely avoid future deaf animals without sacrificing a breeding line that has been shaped over many years. However, extreme caution must be used when line breeding of dogs related to deaf dogs, whether the deafness is unilateral or bilateral. To make these decisions in an informed manner for breeds with known deafness, it is important that advantage be taken of hearing testing facilities at veterinary schools. Unilaterally deaf dogs cannot be detected by other means, and these dogs **will** pass on their deafness genes.

Application information

The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. Application forms are available on request from OFA or can be downloaded from the OFA web site (*www.offa.org*). The signed application form (which should include the owner's choice of open or semi-open database), a photocopy of the BAER tracing and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856.

DNA genetic databases

DNA testing based on identification of a specific genetic mutation is the most accurate method of identification of an animal's genotype, and knowledge of the genotypic status is the breeder's most powerful tool for elimination of a genetic disease. There are several broad categories into which DNA tests may fall. The most straightforward are tests which definitively predict whether or not a dog will manifest a certain disease, and also predict the risk to its offspring. These include tests for simple recessive genes without complex modifiers (incomplete penetrance) or environmental interaction. Most current DNA tests fall into this category. Such tests can identify affected (homozygous for the disease alleles), carrier (phenotypically normal, but heterozygous with one disease allele and one normal allele), or clear (homozygous normal) dogs, both in adults for breeding purposes, and within litters to help determine the appropriate placement of a puppy. In the case of diseases caused by recessive genes, careful and knowledgeable breeding decisions and strategies may permit the use of carrier, or rarely, affected, animals in breeding programs for a short period of time. This enables the breeder to maintain desirable breed traits within a breeding program, while being assured of producing offspring that are phenotypically normal, and making rapid progress toward the goal of producing offspring that are genotypically normal.

DNA tests can also be used to detect genes that **do** have modifiers such as incomplete penetrance or environmental influences. In the case of dominant genes with modifiers, DNA tests could definitively detect which dogs have the abnormal gene, but this would not predict with certainty whether such a dog would actually develop the disease. It would, however, give accurate information with regard to the odds of the disease gene being passed to the next generation (although once again, not with certainty whether offspring will develop the disease). Perhaps equally as important, DNA tests could be done with litter age pups. This would enable breeders to place only pups who do not carry the disease gene at all into potential breeding situations, while those who test positive could be placed into non breeding homes. Remember, however, that when a dominant gene is involved, such a pup may develop the disease and have a compromised quality of life. The ability to use DNA testing to keep pups with abnormal genes out of breeding homes should never be thought of as a way to excuse breeding a dog that is capable of producing clinical disease, and the possibility of producing

affected pups with these types of breedings must be given appropriate and compassionate weight. In the rare instance where desirable traits of an individual capable of producing disease, outweigh the undesirable genetic trait, a breeding should only be undertaken with a clear commitment to eliminate the disease gene in the next generation through diligent DNA testing.

DNA testing by linkage is not as accurate as that for identification of a specific genetic mutation, but it is still more desirable than existing tests based on phenotypic evaluations. While some minor degree of false positives and false negatives is possible, accuracy rates are usually above 95%.

The financial advantages of DNA testing and associated DNA profiling are clear. Tests are accurate, can be done at an early age, only one test is required and progeny can be cleared by parentage if DNA profiles are available for determination of parentage.

There are multiple genetic registries that utilize DNA based testing. All of these tests are more sensitive and specific for the detection of genetic disease traits than are phenotypic based tests. At this time, there are a limited number of breed-specific genetic tests. However, more and more tests will become available in the future. Call or check the OFA web site for breed specific DNA test availability.

DNA Tests, Breeds, and Laboratories

For the most current list of available tests and laboratories, see the website (*www.offa.org*). Please contact the desired laboratory for testing procedures and fees.

Disease Test Available	Breeds	Lab
Canine Leukocyte Adhesion Deficiency (CLAD)	Irish Setter, Irish Red and White Setter	Optigen
Cobalamin Malabsorption	Giant Schnauzer	PennGen
Collie Eye Anomaly	Australian Shepherd, Border Collie, Rough & Smooth Collie, Shetland Sheepdog	Optigen
Cone Degenration	German Shorthaired Pointer	Optigen
Congenital Stationary Night Blindness	Briard	Optigen
Congenital Hypothyroidism with Goiter	Toy Fox Terrier	Michigan State Univ. Lab. of Comparative Medical Diagostics
Copper Toxicosis	Bedlington Terrier	VetGen

Cystinuria	Newfoundland	PennGen, OptiGen, Vet Diagnostics Ctr, VetGen, HealthGene
Factor VII Deficiency	Beagle	PennGen
Fucosidosis	English Springer Spaniel	PennGen
Globoid Cell Leukodystrophy	Cairn Terrier, West Highland White Terrier	Dr. David Wegner
Juvenile Cataracts	Boston Terrier	Animal Health Trust, UK
MPS IIIB	Schipperke	PennGen
MPS VI	Miniature Pinscher	PennGen
MPS VII	German Shepherd	PennGen
MDR1 (multiple drug resistance gene)	Australian Shepherd, Border Collie, Collie, Shetland Sheepdog	Washington State Univ. Veterinary Diagnostic Lab
Narcolepsy	Dachshund, Doberman Pinscher, Labrador Retriever	Optigen
Neuronal Ceroid Lipofuscinosis	American Bulldog, English Setter, Dachshund	Animal Molecular Genetics Lab
Phosphofructokinase Deficiency	American Cocker Spaniel, English Springer Spaniel, Mixed Breeds	Optigen, VetGen, PennGen, HealthGene, Veterinary Diagnostic Ctr
Progressive Retinal Atrophy	Irish Setter	Optigen, VetGen, HealthGene
Progressive Retinal Atrophy	Australian Cattle Dog, Bullmastiff, Cardigan Welsh Corgi, Irish Red and White Setter, Mastiff, Miniature Poodle, Miniature Schnauzer, Toy Poodle, Samoyed, Siberian Husky, Sloughi	OptiGen
Pyruvate Kinase Deficiency	American Eskimo Dog, Basenji, Beagle, Chihuahua, Dachshund, West Highland White Terrier	Optigen, VetGen, HealthGene, Vet Diagnostics Ctr
Pyruvate Kinase Deficiency	Basenji	Animal Molecular Genetics Lab
Renal Dysplasia	Lhasa Apso, Shih Tzu, Soft Coated Wheaten Terrier	VetGen
von Willebrand's Disease	Bernese Mountain Dog, Doberman Pinscher, Kerry Blue Terrier, Manchester Terrier, Papillon, Pembroke Welsh Corgi, Poodle, Scottish Terrier, Shetland Sheepdog	VetGen

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Fax: 08700 50 24 25
E-mail: info@aht.org.uk

Animal Molecular Genetics Lab
www.CanineGeneticDiseases.net
HansenL@missouri.edu

HealthGene
1-877-371-1551
www.healthgene.com
info@healthgene.com

Michigan State University
Laboratory of Comparative
Medical Genetics
fyfe@cvm.msu.edu

OptiGen, LLC
607-257-0301
genetest@optigen.com
www.optigen.com

PennGen Laboratories
(215) 898-3375
http://w3.vet.upenn.edu/research/
centers/penngen/

VetGen
(800) 483-8436
www.vetgen.com

Veterinary Diagnostics Center
(800) 625-0874
www.vetdnacenter.com
contact@vetdnacenter.com

Washington State Univ.–
Veterinary Clinical Pharm. Lab
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VCPL/test.asp
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Application information

The OFA serves as the central repository of DNA test results from approved laboratories for purposes of monitoring the disease and as a source of information for breeders, breed clubs, owners, prospective owners, and researchers. DNA application forms can be downloaded from the OFA website (*www.offa.org*). The owner or agent should complete and sign the OFA application form, and the information is best obtained directly from the animal's certificate or registration papers. It is also important to record the animal's tattoo or microchip number, and registration numbers of the sire and dam. The signed application form (which should include the owner's choice of open or semi-open database), a photocopy of the DNA test result and the service fee should be mailed to: Orthopedic Foundation for Animals, Inc., 2300 E. Nifong Blvd., Columbia, MO 65201-3856. There is a minimal cost to enter a clear or carrier in the data bank and sibling discount rates (3 or more sibs) are available. There is no charge to enter an affected individual as it is important for scientific analysis that affected information be entered into the database.

Other OFA services

Preliminary hip and elbow evaluations

This service is offered to evaluate the hip status of an animal as young as 4 months of age. Many owners choose to breed their animals prior to 24 months or need to know the hip status of progeny produced by a particular sire and dam before using them in a repeat breeding. The evaluation is performed by one radiologist, and the response time is usually five days. Use the same application procedure as described on p. 19.

Consultation

Consultation evaluations are available on any radiographic problem (thorax, abdomen, etc.). The radiographic submission should include an appropriate clinical history. When the problem is outside the expertise of the OFA, the study will be referred to an appropriate individual for his/her evaluation.

Seminars

The OFA underwrites travel expenses to present seminars to clubs when the audience size is 100 or more. No honorarium is charged. Arrangements must be made at least 6 months in advance. Contact the OFA for more information.

Literature

Newsletters, reprints of scientific reports, etc. are periodically provided to the parent club OFA representative.

Funding of animal wellness studies

The OFA has funded nearly $3 million in research aimed at reducing the incidence and prevalence of inherited companion animal disease. The OFA funds projects through the AKC Canine Health Foundation (AKC CHF), the Morris Animal Foundation (MAF) and occasionally through direct grants. The OFA has achieved Ruby Donor status with MAF, and Millennium Founder status with the AKC CHF. OFA supported research is not limited to orthopedic disease, and has included cancers, heart disease, and thyroid disease as examples. Some research has been breed specific, some for all breeds, some for multiple species, and has been done at many of our leading universities and research institutions.

And, with the recent completion of the mapping of the canine genome, the OFA is focusing more of its research dollars towards research at the molecular level.

OFA website, www.offa.org

The primary function of the OFA website is found in the searchable disease database holding the records of every dog certified by the OFA since 1974. An indispensible tool for breeders, owners, and puppy buyers, the online database allows searches by individual dog, breed, disease, and/or result and contains over 800,000 animals. Search results list not only the animal, but sire, dam, siblings, half-siblings, and offspring either in list or pedigree format. It is cross-linked with both the Canine Health Information Center (CHIC, www.caninehealthinfo.org) certifications and CERF data. All information on the OFA website is free of charge and open to the public. In addition to the OFA disease databases, OFA website resources include:

- Information about the OFA
- Breaking health and OFA news
- Upcoming health clinics across the U.S. and Canada
- Many OFA publications (including this one) all in downloadable formats
- All OFA disease applications (which can be filled out online) plus order forms for labels, kits, etc.
- The latest disease statistics and data
- Up to date lists of genetic disease databases and DNA-linked diseases and laboratories
- Downloadable quarterly reports by breed

Canine Health Information Center (CHIC) DNA Repository

Mission Statement

The CHIC DNA Repository, co-sponsored by the OFA and the AKC/CHF, collects and stores 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.

Objectives

- Facilitate more rapid research progress by expediting the sample collection process
- Provide researchers with optimized family groups needed for research

- Allow breeders to take advantage of future DNA based disease tests as they become available
- Foster a team environment between breeders/owners and the research community improving the likelihood of genetic discovery

Submission by Blood Sample

Blood is the gold standard for genetic material; the yield of DNA is sufficient for all research methods, including technologies on the horizon. Moreover, the stability and purity of the DNA is of the highest caliber, which offers many benefits. The drawback of banking blood samples is cost — drawing, shipping, storing, and extracting DNA from blood are more expensive endeavors than the alternative.

Submission by Cheek Swab

Cheek swab-derived DNA is a viable option for DNA banking. Although the yield and purity of this DNA is inferior to that obtained from blood, the material is suitable for most genetic approaches. The swabs are inexpensive, and the samples can be taken by the owner of the dog without the necessity of a veterinary office call. Swabs are easily shipped in standard envelopes using the postal mail, and they can be stored for at least a decade at room temperature, so long as they are stored under conditions of low humidity. The success rate for obtaining DNA from a swab in the laboratory is roughly 98%, so multiple swabs should be submitted for each dog to ensure representation in the archive.

Laboratories

The CHIC DNA Repository has partnered with the Veterinary Genetics Lab at the University of California–Davis and the Animal Molecular Genetics Lab at the University of Missouri. UC Davis will receive and store all swab samples, and Missouri will receive and store all blood samples.

For health surveys, application forms, and instructions on how to participate in the DNA repository, go to www.caninehealthinfo.org/dnabank.html.

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