When practitioners think of genetic disease, they think of purebred disease. However, we see genetic disease daily in our mixed breed and purebred patients. The most common genetic diseases we see in practice have to do with evolutionarily ancient genes that preceded the separation of breeds, and are dispersed in the domestic dog and cat genomes.

In the last century the most common diseases were due to infectious, nutritional, and environmental causes. As we have learned how to prevent and control these factors, genetic predisposition to disease becomes a more frequent disease etiology. In our purebred patients we see breed variation of the common genetic disorders. Some variation has to do with; random changes (genetic drift), the popular sire syndrome, or selection for linked traits altering the frequency of disorders between breeds. For other traits, breed variation may have to do with anatomical or conformational aspects that can alter disease liability.

The hallmark of inherited diseases is their predictability, which allows us to better diagnose, treat, and control them. As predictable triggers and modifying factors influence the expression of genetic disorders, veterinary intervention allows for improved health in our patients. It is important to recognize genetic diseases in practice because they must be treated as chronic illnesses, not episodic diseases.

**FELINE GENETIC DISORDERS**
The listed conditions are the most common genetic diseases for all cats. Ninety-five percent of feline patients are random-bred domestic cats. Random breeding propagates and disperses evolutionarily ancient disease-liability genes, causing the random development of clinical genetic disease in patients. Pedigreed breeds may have higher or lower incidence of disease, depending on the frequencies of liability genes in their gene pools.

Insurance claims and centralized hospital databases monitor the most frequent disease presentations, which helps veterinarians understand the most frequent genetic diseases. When viewing these data, one must recognize the inherent bias from each. Insurance claims cover treatment claims for disorders. Agria is the largest animal insurer in Europe.¹ VPI is the largest animal insurer in the US.² Centralized hospital databases cover diagnostic codes for conditions and symptoms that may not require treatment claims. The Banfield data report diagnostic codes at Banfield hospitals that usually do not have emergency coverage.³ The VetCompass data report diagnoses at primary care facilities in the UK.⁴ Based on weighted grading, the most common reported disorders/symptoms in cats are; cystitis, vomiting, kidney disease, obesity, dental disease, traumatic wounds, heart murmur, upper respiratory infection, conjunctivitis, colitis/diarrhea, bladder stones, hyperthyroidism, and diabetes. We recognize that many of these have environmental and infectious etiologies,

<p>| Table 1: The Most Common Feline Disorders |</p>
<table>
<thead>
<tr>
<th>Cats</th>
<th>Agria¹</th>
<th>VPI²</th>
<th>Banfield³</th>
<th>VetCompass⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Traumatic Wounds</td>
<td>Cystitis</td>
<td>Obesity</td>
<td>Dental Disease</td>
</tr>
<tr>
<td>2</td>
<td>Vomiting</td>
<td>Vomiting</td>
<td>Otitis</td>
<td>Obesity</td>
</tr>
<tr>
<td>3</td>
<td>Cystitis</td>
<td>Kidney Disease</td>
<td>URI</td>
<td>Heart Murmur</td>
</tr>
<tr>
<td>4</td>
<td>Bladder Stones</td>
<td>Diarrhea</td>
<td>Dental Disease</td>
<td>Traumatic Wound</td>
</tr>
<tr>
<td>5</td>
<td>Anorexia</td>
<td>Skin Allergy</td>
<td>Cystitis</td>
<td>Kidney Disease</td>
</tr>
<tr>
<td>6</td>
<td>Gastroenteritis</td>
<td>Diabetes</td>
<td>Conjunctivitis</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>7</td>
<td>Mammary Tumors</td>
<td>Constipation</td>
<td>Heart Murmur</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>8</td>
<td>Kidney Disease</td>
<td>Otitis</td>
<td>Malaise</td>
<td>Vomiting</td>
</tr>
<tr>
<td>9</td>
<td>Constipation</td>
<td>URI</td>
<td>Kidney Disease</td>
<td>Cystitis</td>
</tr>
<tr>
<td>10</td>
<td>Fever</td>
<td>Hyperthyroidism</td>
<td>Hyperthyroidism</td>
<td>Colitis/Diarrhea</td>
</tr>
</tbody>
</table>
but many are also caused by hereditary predisposition.

**Feline Lower Urinary Tract Disease (FLUTD)**

Sterile FLUTD, including both interstitial cystitis and feline urological syndrome (FUS), is the most frequent feline hereditary predisposition observed in practice, affecting 1-2% of all domestic cats.\(^5\),\(^6\),\(^7\) No infectious causes for FLUTD have been identified,\(^8\) and it occurs in individual cats in multi-cat households.\(^9\) Studies show that the Persian breed is at increased risk, and the Siamese breed is at a decreased risk of developing FLUTD.\(^9\) In an experimental model with common housing and husbandry; when exposed to stressors, only cats predisposed to FLUTD developed symptoms and showed mRNA responses for biomarkers versus controls.\(^7\) Similar gene expression profiles are found in interstitial cystitis/bladder pain syndrome in man,\(^10\),\(^11\) and a hereditary component has been documented.\(^12\),\(^13\) There is no established mode of inheritance, and to date no predisposing genes have been identified in cats.

Most practitioners recognize that once diagnosed and controlled, signs associated with FLUTD can reoccur years later if owners are not diligent about controlling predisposing factors. Such measures can include; minimizing environmental stress, maintaining anti-inflammatory or behavior-modifying drugs that avert bladder inflammation (NSAIDs, chondroprotectants, omega fatty acids, SSRIs), maintaining dietary control for cats predisposed to crystalluria (low Mg and acidifying diets), and increasing hydration (lowering urine specific gravity).

**Diabetes Mellitus**

Diabetes mellitus is a frequent diagnosis in feline patients.\(^14\) It is primarily seen in random-bred cats, although an increased incidence is seen in Burmese\(^15\) and possibly Siamese and Abyssinian cats.\(^16\) One study found a mutation in the melanocortin 4 receptor gene to be significantly associated with diabetes in obese domestic shorthaired cats.\(^17\) This is similar to findings with human type 2 diabetes. Obesity is a predisposing factor, and controlling obesity with dietary control is the best preventative measure. Diabetes is controlled via insulin regulation and diet.

**Lymphoplasmacytic Inflammatory Disease**

The predisposition toward lymphoplasmacytic inflammation represents a complex immunological response in affected cats involving innate, humoral, and cell-mediated immunity. Lymphoplasmacytic inflammatory disease most frequently manifests as gingivostomatitis\(^18\) or inflammatory bowel disease (IBD).\(^19\) While the histopathological descriptions of these two entities are similar, they rarely occur in the same individual.

Breed predisposition to IBD in Siamese and other Asian breeds has been found, but causal genetic mutations have not been found to date.\(^19\) Liability genes for IBD have been identified in German Shepherd Dogs\(^20\) and in man.\(^21\) Liability genes have been identified for recurrent aphthous stomatitis in man, the corollary to feline lymphoplasmacytic gingivostomatitis.\(^22\)

There are many possible environmental variables, including diet (and possibly allergic reactivity), reactivity to the local microbiome, and behavioral stress. Affected cats show a lifelong propensity to inflammatory cell infiltration that does not occur in other cats in the same household. Control of both conditions can include dietary changes, anti-inflammatory or
immunoregulatory drugs, minimizing environmental stress, and dental extraction in cats with severe gingivostomatitis.

**Polycystic Kidney Disease**
The most common single-gene feline disorder seen in practice is polycystic kidney disease (PKD), which is caused by a testable autosomal dominant gene. This defective gene is present at a high frequency (38% testing positive) in Persian, Himalayan, and Persian-derived breeds. Due to its dominant inheritance, PKD is not a rare diagnosis in Persian and Himalayan cross-bred or random-bred cats, and these will be seen periodically in clinical practice. All affected cats are heterozygous (having one copy) for the defective gene, as homozygosity is prenatally lethal.

The majority of affected cats develop kidney failure at an average age of 7 years (range, 4–10 years). There is variable expression of this gene where some affected cats develop a few cysts but maintain normal renal function. There is no specific treatment aside from support for renal insufficiency and failure.

Clients who want to purchase kittens of susceptible breeds should ask for the PKD test results on either both parents, or the kittens. Breeders who offer that their breeding stock is "PKD clear" on ultrasonography are using an outdated and unreliable diagnostic standard. If valid PKD test results are not available, potential buyers can collect a cheek swab from kittens for testing before purchasing. These can be sent to the UC-Davis Veterinary Genetics Lab to test for the PKD gene ($40/cat). [http://www.vgl.ucdavis.edu/services/cat/](http://www.vgl.ucdavis.edu/services/cat/)

**Hypertrophic Cardiomyopathy**
Hypertrophic cardiomyopathy (HCM) is seen as a breed-related disease in several breeds as well as in random-bred cats. A mutation (A31P) in the myosin binding protein C gene occurs in 33% of Maine coon cats, causing a highly penetrant, autosomal dominant HCM. Affected cats can present clinically with heart failure or sudden death at 6 months to 7 years of age. Cats homozygous for the mutation have a more severe and earlier-age onset than heterozygotes. The disease shows incomplete penetrance, and some heterozygous cats can remain clinically normal.

Twenty percent of the Ragdoll breed carries a different mutation in the same gene causing HCM. A genetic test is available for the specific mutation in each breed. Prospective breeding cats should be tested, or kittens should be tested before placement.

HCM occurs in individuals of the Maine coon and Ragdoll breeds that do not carry the identified breed-specific mutations. HCM is also seen in random-bred cats and individuals of other breeds. These findings support both within-breed and between-breed genetic heterogeneity for the disease. Clinical treatment for HCM involves controlling the heart failure.

The Sphynx breed has an earlier-age onset HCM, averaging 2 years of age. The Norwegian Forest cat has a cardiomyopathy with signs of both hypertrophic and restrictive disease. Causative genes have not been identified in these breeds, but pedigree studies suggest dominant inheritance with incomplete penetrance.
Polydactyly
Multiple toes is a common autosomal dominant trait with high penetrance and variable expression (numbers of toes). All cats with polydactyly usually have a similarly affected parent. Veterinarians should consider removal of extra claws that do not have an associated toe during neutering, as these tend to grow around into the paw causing pain and infection.

Deafness with blue eyes
The autosomal dominant white (W) gene can cause deafness in cats. The gene shows incomplete penetrance; where 25%-30% of homozygous (WW) cats are deaf. Not all white, blue eyed cats are due to the W gene, and therefore can have normal hearing. W affects development of structures derived from neural crest including pigment cells. Deafness is due to collapse of Rissner's membrane, atrophy of hair cells and balling up of tectorial membrane, hyalinization of stria vascularis, and collapse of the saccular macula.

Other commonly seen feline diseases with hereditary components include calcium oxalate bladder stones, allergic skin disease with or without eosinophilic granuloma complex, mammary tumors, and lymphoma. Hyperthyroidism is frequently seen in practice, but the etiology is thought to be related to environmental goitrogens and not heredity.32 There is also no published evidence for heritability of chronic geriatric kidney disease.

Many breed-specific genetic diseases are seen at a low frequency in clinical practice. The WSAVA Canine and Feline Hereditary Disease (DNA) Testing website (http://research.vet.upenn.edu/WSAVA-LabSearch) is an excellent source of information on DNA tests, susceptible breeds, and testing laboratories.33 Some of the more common breed-specific disorders include:

Burmese cranio-facial defect is a lethal autosomal recessive disease. It was unfortunately selected for by breeders preferring the wide “contemporary” facial structure associated with the heterozygous expression of the defective gene. A genetic test is available from the UC-Davis VGL: http://www.vgl.ucdavis.edu/services/cat/ Breeding carriers to only normal-testing mates, and can select towards the desired head type from normal-testing Burmese.

There are two forms of Progressive Retinal Atrophy in cats where the genetic cause has been identified. An autosomal recessive (rdAc) mutation in the CEP290 gene causes late onset blindness; usually between 3-5 years in the Abyssinian, Oci Cat, Siamese, Somali, and other cat breeds. ERG changes are evident around 7 months of age. An autosomal dominant (Rdy) mutation in the CRX gene is a rarer form of PRA causing blindness around 7 weeks of age in the Abyssinian and Somali breeds. Genetic tests for both forms are available from the UC-Davis VGL.

Burmese Hypokalemia, also known as Familial Episodic Hypokalaemic Polymyopathy, is a recessive genetic defect characterized by episodes of low serum potassium levels and high CPK (creatine phosphate kinase). Clinical signs include episodes of skeletal muscle weakness which can affect the whole animal or may be restricted to certain muscles. This is most obvious in the neck muscles, but sometimes occurs in just the limbs. As a result affected cats may show problems with walking and holding their head correctly. The disease is not typically fatal and affected cats usually can be managed by adding potassium supplements to their diet.
Breeds that are at risk for this disease include; Burmese and outcrosses such as Burmilla, Bombay, Cornish Rex, Devon Rex, Singapura, Sphynx, Australian Mist, Tiffanie, and Tonkinese. A genetic test is available from the UC-Davis VGL.

CANINE GENETIC DISORDERS

Approximately half of our canine patients are purebred or designer bred, and the rest are mixed breed/random-bred dogs. Studies have shown that the most frequent canine genetic disorders seen in clinical practice are shared between purebred and mixed breed dogs. These are caused by evolutionarily ancient liability genes passed down before the separation of breeds. Some genetic mutations are so old that they occur uniformly across all dogs – purebred or mixed breed. Some mutations are more recent, and are limited to only a few breeds, or a single breed.

Studies of insurance claims and diagnostic codes from centralized hospital databases carry the same biases as stated under feline genetic disorders. Based on weighted grading, the most commonly reported disorders/symptoms in dogs are; otitis, dental disease, arthritis, skin allergy, obesity, skin tumor, diarrhea/colitis, vomiting/gastroenteritis, hypothyroidism, traumatic wounds, and heart murmur. Several of these are due to environmental influence, but several have genetic predispositions.

<table>
<thead>
<tr>
<th>Table 2: The most common canine disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>10</td>
</tr>
</tbody>
</table>

Allergic Skin Disease

According to both insurance claims and centralized hospital databases, manifestations of allergic skin disease are the most frequent disease presentation in our practices. The allergic component of chronic inflammatory otitis and hot spots are well documented. Allergic skin disease is commonly seen in mixed breed and purebred dogs. As practitioners, we see increased liability to allergies within certain breeds. In a study of atopic dermatitis in Golden and Labrador Retrievers, it showed that the heritability (percent of liability due to genetic influence) was 47%. In allergic dogs with chronic presentations we can often recognize a predictable seasonality of presentation, and should take measures to prevent pruritus before it progresses to clinical disease. Treatment can include controlling symptoms with antihistamines, omega fatty acids, steroids, cyclosporine, occlacitanib (Apoquel), shampoos and topical therapies, treating secondary infection, and also hyposensitization.

Canine Hip Dysplasia

Hip Dysplasia is the most common canine inherited musculoskeletal disorder, and occurs across all mixed breed and purebred dogs. Of all dogs with radiographs submitted to the Orthopedic Foundation for Animals (www.offa.org), 14.59% are rated as dysplastic, and this is a low estimate due to pre-screening. Small dogs with hip dysplasia usually do not show the pain and discomfort seen in larger affected dogs, demonstrating a size/weight relationship to its clinical presentation.
Hip dysplasia is controlled by having a hip radiograph taken at a minimum of 2 years of age, and submitted to the Orthopedic Foundation for Animals for evaluation prior to breeding. Another method of control is PennHIP, where compressed and distracted hip radiographs are compared, and a distraction index (DI) is formulated. This method quantifies the amount of laxity of the soft tissues of the hip joint.

Palpable hip laxity can be predictive of hip dysplasia and later osteoarthritic changes. A gentle Ortolani procedure during vaccine appointments, and palpation for hip laxity under anesthesia during neutering should be performed and the results recorded. Practitioners may be surprised as to how much hip laxity is present in our canine patients, and how it relates to clinical arthritic hip disease later in life. Dogs with severe laxity identified at an early age could benefit from interventional surgery such as triple pelvic osteotomy or juvenile pubic symphysiodesis. Otherwise, weight restriction, chondroprotectants (as a treatment, not a preventative), NSAIDs, and surgery (femoral head and neck excision in small dogs, total hip replacement in large dogs) are recommended.

Estimated breeding values (EBVs) and genotypic breeding values based on DNA marker panels are being experimentally developed to assist with selection for hip normalcy. In the meantime, breeders should select for familial breadth and depth of normalcy in vertical pedigrees on individual dog OFA webpages (www.offa.org).

**Brachycephalic Syndrome**

Brachycephalic Syndrome, or brachycephalic obstructive airway disorder (BOAD) is a disorder of breathing difficulty in short snouted dogs and the “bully” breeds. Breeds with the highest prevalence include Bulldogs, Pugs, and French Bulldogs. This disorder arises due to a mismatch in the proportions of the skull and the soft tissues held within the nose and pharynx. Clinical signs of BOAS include; dyspnea, exercise intolerance, heat intolerance, abnormal and increased respiratory noise, cyanosis, syncope, and death. In one study, 16.7% of dogs from the high risk breeds died of respiratory failure at an average of 8.6 years of age.

This is an example of a disorder that has been directly selected for by breeding for an extreme head type that does not allow normal breathing and air flow. The clinical syndrome includes tight nostrils (stenotic nares), an elongated soft palate, everted laryngeal saccules, laryngeal collapse, and/or a narrow (hypoplastic) trachea. Brachycephalic dogs can also present with facial skin fold dermatitis and corneal ulceration. With dogs experiencing significant morbidity, corrective surgery can include rhinoplasty for stenotic nares, soft palate resection, and laryngeal saccule removal.

Breeders should select for dogs that; do not show signs of BOAD, have a muzzle that is at least one-half the depth of the cranial length (from occiput to the stop), a normal diameter trachea (ratio of lumen diameter at the thoracic inlet to the width of the proximal third rib should be ≥ 2 on a lateral radiograph), and for nostrils that are ideally 33% of the width of the nose.

**Myxomatous Mitral Valvular Disease**

Myxomatous mitral valvular disease (MMVD) or mitral valvular endocardiosis is primarily seen in toy and small bodied patients. Our small dog patients tend to live longer. At what point is a heart murmur or heart disease from mitral regurgitation considered abnormal in an old dog? That said, some breeds including the Cavalier King Charles Spaniel, and Norfolk Terriers have early-onset MMVD that causes clinical heart disease at an average of 6.25 years of age.
As this is usually beyond the age of initiation of breeding, one Cavalier dog club has established a generational breeding control program where dogs are only bred at 2 years or older if both parents are currently free of a murmur or Doppler evidence of mitral regurgitation at 4 years or older. Breeding dogs and their parents have annual Doppler ECHOs to monitor for mitral regurgitation. Treatment involves controlling the heart failure.

**Anterior Cruciate Ligament Rupture**

Anterior Cruciate Ligament Rupture is a common traumatic injury in our patients that is not usually thought of as being a hereditary disease. However, studies of ACL rupture in Newfoundlands show 27% heritability, making it a moderately heritable disease. The genetic predisposing factors for rupture may include issues with ligament extracellular matrix metabolism, degeneration, or inflammation. Predisposing factors may also involve biomechanical and conformational variations including; bone length, stifle angulation, tibial plateau variation, and narrowed distal femoral intercondylar notch. There are several surgical methods for ACL repair including; synthetic ligament replacement, tibial plateau leveling osteotomy (TPLO), and tibial tuberosity advancement (TTA).

**Patellar Luxation**

Patellar Luxation is a complexly inherited disorder that causes the kneecap to pop out of its groove either medially or laterally. This causes pain, and instability of the joint. Some affected dogs can have no clinical signs from the disorder, and some can be so painful that surgical correction is required. Weight control is an important factor in decreasing morbidity. Most affected dogs will develop arthritis of the stifle joint as they get older. Patella luxation is more common in the small stature breeds, however several larger breeds also have a high incidence of the disorder.

An OFA patella evaluation requires that you palpate the patellae at a minimum of 1 year of age, and record and grade the laxity and position of the patellae. The following are grades of patella luxation: Grade 1—The patella can be luxated manually at full extension of the stifle joint, but returns to the trochlear groove when released. Grade 2—There is frequent patellar luxation, but the patella naturally returns to the trochlea. Grade 3—The patella remains in a luxated position, though it can be manually returned to the trochlea. Grade 4—The patella is permanently luxated, and cannot be returned to the trochlea. The OFA patella database reports an average of 5.55% of submitted dogs with patellar luxation, however this is an underestimation as many affected dogs are not submitted to the database. Breeders must use breadth and depth of pedigree normalcy to select against this disorder.

**Elbow Dysplasia**

Elbow Dysplasia is a complexly inherited disorder of uncoordinated growth between the radius and ulna. When their growth is not coordinated, the radius bumps into the humerus, and can cause one of several elbow joint abnormalities. These include; ununited anconeal process (UAP), fragmented medial coronoid process (FCP), osteochondritis dessicans (OCD) of the humeral condyle, and incongruity (INC) of the elbow joint. FCP is the most common presentation. The different lesions of FCP and UAP vary between breeds, as well as between familial clusters within breeds.

Of all dogs with radiographs submitted to the OFA database, 15.42% are rated with elbow dysplasia. Over 70% of these dogs have Grade I elbow dysplasia, which is a radiographic
diagnosis that will not cause clinical disease. However, whenever a dog with Grade II or Grade III elbow dysplasia is identified, several close relatives will usually be identified with Grade I elbow dysplasia. OFA data show that a parent with Grade I elbow dysplasia produces far more elbow dysplasia than matings between two normal parents. Therefore, identification of Grade I elbow dysplasia is a sentinel for the accumulation of elbow dysplasia liability genes. The OFA will certify elbows at 2 years of age, and a discount is offered when elbow and hip radiographs are submitted together on the same dog. This is a once in a lifetime examination for a prospective breeding dog. Breeders must use breadth and depth of pedigree normalcy to select against this disorder. Some affected dogs with severe persistent lameness require surgery.

Hypothyroidism
Hypothyroidism is caused by autoimmune thyroiditis. This is an inherited autoimmune disorder where the thyroid gland is destroyed by thyroglobulin autoantibodies (TgAA). A thyroid profile is a snapshot of a moving picture of the thyroid health of a dog. An affected dog will begin to produce thyroid autoantibodies usually between 1 and 4 years of age. Most affected dogs will have clinical signs of the disease by 2 to 6 years of age. A thyroid profile including autoantibodies run at 2 and 4 years of age will identify most affected dogs. Thyroid profiles with TgAA should not be run within 3-4 months of vaccinations to avoid false positive results.

Of all dogs thyroid tested by the Michigan State University endocrinology laboratory, 7.5% test positive for thyroglobulin autoantibodies. For mixed breed dogs, 10.7% test positive for thyroglobulin autoantibodies. Breeders must use breadth and depth of pedigree normalcy to select against this disorder. The breeds with the highest percentages based on testing at Michigan State University are; English Setter, Havanese, Old English Sheepdog, German Wirehaired Pointer, Pitbull, and Boxer. Treatment is with thyroxine supplementation.

Heart Disease
Aside from MMVD, hereditary heart disease comes in several other varieties. Congenital heart anomalies include patent ductus arteriosus (PDA), aortic stenosis, ventricular septal defect, ventricular stenosis, persistent right aortic arch, and Tetrology of Fallot. Primary heart muscle disorders include hypertrophic cardiomyopathy, dilated cardiomyopathy (liability test for Dobermans available from WSU), and taurine responsive cardiomyopathy. Primary arrhythmias include autosomal dominant Boxer arrhythmogenic right ventricular cardiomyopathy (liability test available from WSU), sick sinus syndrome in Miniature Schnauzers, and fatal arrhythmia in German Shepherd Dogs.

The most frequent malignant canine cancers are lymphoma, hemangiosarcoma, mast cell tumor, and osteosarcoma. These are seen with increased breed prevalence, familial prevalence, and in individual mixed breed and purebred dogs. Research is focusing on inherited mutations in tumor suppressor genes (that act to prevent cancer), or oncogenes (that promote cancer). As research identifies predisposing mutations, breeders will be able to select against these cancers. Common tumor signatures of gene expression and chromosomal abnormalities will allow more focused therapies for predictable and consistent remissions.

Hereditary Epilepsy represents a diverse group of recurring seizure conditions, and is considered a significant problem in over twenty breeds. Many researchers are finding that epilepsy susceptibility can be caused by recessive genes. However, the high number of cross-
bred dogs with epilepsy suggests that dominant or additive modes of inheritance are also possible. Research shows that some breeds have a male predominance of affected dogs, and others show equal sex ratios. As with human epilepsies, it is expected that there will be many different epilepsy liability genes affecting many different breeds, and even within breeds.

Several **inherited eye diseases** exist in dogs. The most common include cataracts, progressive retinal atrophies, lens luxation, and conformational eyelid abnormalities. Breeding dogs should have eye screening examinations by an ACVO ophthalmologist. As many inherited eye diseases have a later age of onset, these eye examinations should be done annually, or at least every other year on breeding dogs. There are DNA genetic tests available for many inherited eye disorders that can identify carrier and affected dogs. Some of these tests are specific for individual breeds. However, because the mutations that cause many inherited eye diseases occurred in ancestral dogs that pre-dated the separation of breeds, some mutations and genetic tests are shared between breeds.

**Drug sensitivity/Ivermectin sensitivity:** The defect causing ivermectin sensitivity in Collies and other breeds has been identified as a mutation in the MDR1 or multi-drug resistance gene. This defective gene can cause neurotoxicity with hyperthermia, ataxia, seizures, coma, and death. MDR1 metabolism also involves loperamide (Imodium), vincristine, and other drugs, through alterations in the blood brain barrier. Homozygous recessive dogs are super-sensitive to these drugs, and heterozygous carriers are only sensitive at high dosages. A DNA test is available: [www.vetmed.wsu.edu/depts-VCPL/](http://www.vetmed.wsu.edu/depts-VCPL/). The following are results of testing in several susceptible breeds (%affected/%carrier): Collie (32%/46%), Australian Shepherd (2%/30%), Old English Sheepdog (1%/9%), Shetland Sheepdog (2%/17%), Longhaired Whippet (16%/52%), English Shepherd (<1%/14%).

**Portosystemic/Liver Shunts:** Five out of every 1,000 dogs in the general population are born with an inherited portosystemic shunt (PSS). A PSS is a blood vessel that bypasses the liver, leaving waste products circulating in the blood stream. Shunting can also involve microvascular dysplasia (MVD). In affected dogs, the high level of unprocessed blood ammonia and waste products can produce hepatic encephalopathy causing; drooling, mental dullness, and seizures. Affected dogs can be stunted in size. Diagnosis is by blood tests (bile acids, blood ammonia), and abdominal ultrasound. There is no DNA test. Breeders must use breadth and depth of pedigree normalcy to select against this disorder. Yorkshire Terriers are the most frequently affected breed. Thirty-three other breeds have increased risk for PSS, including; Bernese Mountain Dog, Bichon Frise, Dandie Dinmont Terrier, Havanese, Irish Wolfhound, Maltese, Miniature Schnauzer, Old English Sheepdog, Pug, Scottish Deerhound, Shih Tzu, and Standard Schnauzer. Treatment is with dietary control and lactulose, or surgical correction of large shunts.

**Retained Testicles:** Cryptorchidism can be bilateral, or unilateral. This is a sex-limited genetic disease, where it is inherited from both parents, but only male dogs manifest the condition. In other words, female relatives of dogs with cryptorchidism can be genetically affected, and pass on a high liability for the disorder. Dogs with late descending testicles also carry liability genes for cryptorchidism. This is an important disease, as retained testicles have a high incidence of becoming cancerous in adult dogs.
**Hernias** are defects in embryonic closure of the body wall. They occur most frequently at the umbilicus or inguinal canal. These have a complex mode of inheritance. Affected dogs should not be bred (even if their hernia was surgically corrected). Closely related dogs should be considered to carry an above average genetic load of hernia liability genes. By not selecting against hernias, breeders run the risk of producing even larger hernias, or even puppies born with abdominal organs outside of the body wall.

**von Willibrand’s disease (vWD):** Autosomal recessive vWD is the most common canine hereditary bleeding disorder, and has been reported in over 50 different breeds of dogs. It is important to recognize bleeding tendencies in these breeds prior to elective or emergency surgery. The genetic testing company VetGen ([www.vetgen.com](http://www.vetgen.com)) has developed a genetic test for several breeds, which allows the diagnosis of affected, carrier, and normal dogs. VetGen lists the following frequencies of affected and carrier dogs from tested breeds (%affected/%carrier): Bernese Mountain Dog (1%/16%), Doberman (26%/49%), Manchester Terrier (4%/37%), Pembroke Welsh Corgi (6%/37%), Poodle-all varieties (1%/9%), Scottish Terrier (1%/12%), and Shetland Sheep Dog (1%/7%). VetGen also offers genetic tests for vWD in the German Pinscher, Kerry Blue Terrier, and Papillon. For breeds that do not have a genetic test, the phenotypic blood test for vWD factor should be run to identify affected dogs.

Genetic tests exist for the **progressive rod cone degeneration (prcd) form of PRA** in over 25 breeds, **Juvenile cataracts** in the Boston Terrier, French Bulldog, and Staffordshire Bull Terrier, and a susceptibility gene for **cataracts** in the Australian Shepherd. A genetic test also exists for **lens luxation** in many terrier breeds. A genetic test is available for **exercise induced collapse (EIC)** primarily in Labrador Retrievers, but also in Curly-Coated and Chesapeake Bay Retrievers, Boykin Spaniels, Old English Sheepdogs, and Pembroke Welsh Corgis. A recessive susceptibility gene for **degenerative myelopathy** is available for German Shepherd Dogs, Boxers, Corgis, Chesapeake Bay Retrievers, Rhodesian Ridgebacks, and other breeds.

**Non-struvite bladder stones, glaucoma, deafness, renal dysplasia, and Addison’s disease** are also commonly seen hereditary diseases in dogs. An excellent source of DNA tests, susceptible breeds, and testing laboratories is the WSAVA Canine and Feline Hereditary Disease (DNA) Testing website: [http://research.vet.upenn.edu/WSAVA-LabSearch](http://research.vet.upenn.edu/WSAVA-LabSearch).³³

Dogs and cats affected with genetic disorders should not be used for breeding. For complexly inherited genetic disorders, risk for carrying disease liability genes should be based on knowledge of clinical disease or normalcy in first-degree relatives of prospective breeding animals. Carriers of testable recessive disease-liability genes can be bred to normal-testing mates and replaced for breeding with a normal-testing offspring. Individuals with testable dominant disease-liability genes should be replaced for breeding with normal-testing relatives.

**REFERENCES**