

# REPORT ON BREED SPECIFIC HEALTH SCREENING TESTS FOR BOXERS DOGS



Screening for hereditary conditions is an important aspect of responsible breeding. IT IS NOT OK TO CHOOSE NOT TO KNOW. Where the Boxer is concerned, it is however important to bear the following in mind:

1. Many geneticists and scientists involved in genetic research warn that health test results should be used as guidelines rather than mandates. It is imperative that health tests are done, however test results should not be over-emphasised, but should be one factor amongst many in a balanced breeding program.
2. It is also regarded as counter-productive to select against too many factors at once. It is better to identify one or two of the most prevalent and serious disorders in the breed and encourage breeders to make every attempt to reduce the incidence of those conditions. Once that has been achieved, one or two further conditions should be targeted. In this way the diversity of the gene pool is not affected adversely.
3. Not all genetic disorders found in the breed are equally prevalent in all lines or families.

Various sources list the following hereditary conditions as prevalent in Boxers:

- **SUBAORTIC, AORTIC AND PULMONIC STENOSIS (SAS, AS AND PS)**  
Amongst the most common heart defects occurring in Boxers. Stenosis is a narrowing of the aortic valve or of the aorta right below it, or of the pulmonary artery and/or valve. The resultant reduced blood flow can cause fainting and even sudden death.  
Screening tests: Auscultation for heart murmurs, colour Doppler echocardiography
- **ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC)**  
A very prevalent late onset electrical conduction disorder which causes the heart to beat erratically (to have arrhythmias) some of the time and can result in weakness, collapse or sudden death.  
Screening tests: Holter Monitor (24 hour ambulatory ECG) (not available in South Africa), DNA based genetic test (available in USA but still controversial)
- **HIP DYSPLASIA (HD)**  
An inheritable malformation of the hip joint leading to progressive osteoarthritis.  
Screening test: Radiographs
- **DEGENERATIVE MYELOPATHY (DM)**  
An inherited adult-onset, progressive spinal cord disease causing weakness in the hind limbs and eventually paraplegia. Dog owners usually elect euthanasia within a year of diagnosis. Testing done in the USA through February 2011 has shown that more than 80% of the Boxers tested carried one or two copies of the mutated gene causing DM.  
Screening test: DNA based genetic test available in USA
- **HYPOTHYROIDISM**  
An inactive thyroid gland which can be responsible for such conditions as epilepsy, alopecia (hair loss), obesity, lethargy, hyperpigmentation, pyoderma and other skin conditions. While not considered life threatening, the quality of life for a dog suffering from hypothyroidism is much reduced.  
Screening tests: Thyroid panel must include the following tests: T4, Free T4, T3 auto antibodies, T4 auto antibodies (by equilibrium dialysis), TSH level, Thyroglobulin auto antibodies. (Optional tests include T3 and Free T3).
- **CORNEAL DYSTROPHY**  
An inherited abnormality that affects one or more layers of the cornea. Both eyes are usually affected, although not necessarily symmetrically. Chronic or recurring shallow ulcers may result, depending on the corneal layers affected.  
No screening DNA based test available.

- **CANCER**  
Boxers are particularly prone to the development of cancer, including mast cell tumours, lymphoma and brain tumours.  
No DNA based screening tests available
- **JUVENILE RENAL DYSPLASIA**  
An inherited condition in which the kidneys fail to develop properly during embryogenesis in the womb. At birth immature structures consisting of undifferentiated foetal cells or tissue types are found in the kidney, which are persistent throughout the life of the animal, leading to chronic renal failure.  
Screening test: A DNA based genetic test for JDR is available in the USA, but it has not been conclusively established whether the inheritance of the disease in Boxers is the same as in other breeds. Research currently in progress at the Broad Institute (USA).
- **SPONDYLOSIS**  
A degenerative disease of the spinal column, characterized by the formation of bony spurs or, less commonly, complete bony bridges around the diseased disks. The condition is very widespread in the Boxer, worse in older dogs, but a juvenile form marked by rapid deterioration has also been identified in the Boxer. It is a hereditary condition with a very high heritability and a link with hip dysplasia has been postulated.  
Screening test: Radiographs
- **GASTRIC DILATATION-VOLVULUS**  
A life-threatening condition in which the dog's stomach becomes bloated and then twists. It might be due to an inherited predisposition.  
No DNA based screening test available.
- **CRYPTORCHIDISM**  
A polygenic inherited condition where one or both testis, which develop in the abdomen, fail to descend into the scrotum. The usually underdeveloped and non-functional testis should be removed, as it could turn cancerous later in life. More prevalent in Brachycephalic breeds such as the Boxer.  
No DNA based screening test available.
- **CLEFT PALATE/HARELIP**  
Clefts of the upper lip, which may be unilateral or bilateral, complete or incomplete and often associated with clefts of the alveolar process and palate. The defect may also involve the palate alone.  
Brachycephalic breeds (such as the Boxer) can have up to a 30% risk factor. Inheritance is thought to be multifactorial, recessive, polygenic, with partial penetration. The primary aetiology is hereditary, but maternal nutritional deficiencies, drug or chemical exposure, mechanical interferences with the foetus, and some viral infections during pregnancy have also been implicated.  
No DNA based screening test available.

A few other conditions are occasionally seen, such as ENTROPION in which the eyelid folds inward, OSTEOCHONDRITIS DISSECANS, a disorder of immature long bones, often affecting the shoulder joint, GENERALISED DEMODECTIC MANGE, a skin condition aggravated due to a compromised or weak immune system.

## **BOXER HEALTH TESTING IN VARIOUS OTHER COUNTRIES**

### **USA**

Recommendations for health screening for Boxers in breeding programs published by The American Boxer Club's Health and Research Committee at present include testing and reporting guidelines for the following conditions:

- HIP AND ELBOW DYSPLASIA
- HYPOTHYROIDISM
- AORTIC VALVE DISEASE
- AORTIC AND SUBAORTIC STENOSIS
- ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC)

A DNA based genetic test for DEGENERATIVE MYELOPATHY (DM) is now also available and used by Boxer breeders in the USA and elsewhere in the world.

In the USA the Orthopedic Foundation for Animals (OFA) collates and disseminates information concerning orthopaedic and genetic diseases, establishes control programs to lower the incidence of such diseases, encourages and finances research. OFA databases assist breeders to improve the genetic health of their breed through better breeding practices. The testing methodology and the criteria for evaluating the test results for each database are independently established by veterinary scientists from their respective specialist areas, and the standards used are generally accepted throughout the world.

#### **UNITED KINGDOM**

Boxer breeders in the UK are at present mainly concerned with heart disease and screening for both SAS/AS and ARVC is done. The UK Boxer Health Committee (a sub-committee of the UK Boxer Breed Council) provides advice and guidelines and maintains and publishes a list of Boxers that have been screened for heart disease.

#### **AUSTRALIA AND NEW ZEALAND**

A number of Boxer breeders in Australia and New Zealand test for all or most of the conditions listed above for the USA and publish the results on their websites.

The Boxer Association of Victoria has been running a Boxer Heart Murmur Control Scheme since 1993, based on the UK heart program. To date the results of more than 800 Boxers have been recorded. The Boxer Club of Western Australia also records and publishes the results of heart tested Boxers.

#### **GERMANY AND OTHER EUROPEAN COUNTRIES**

Screening for the following hereditary condition is compulsory for all Boxers used for breeding in most European countries:

- HIP DYSPLASIA

In Germany the following health tests are also compulsory (and recommended elsewhere):

- CONGENITAL HEART DEFECTS (AORTIC AND SUBAORTIC STENOSIS)
- SPONDYLOSIS

In addition, in Germany breeding partners are further selected on the basis of a system where the risk of producing offspring affected by HD and CRYPTORCHIDISM is calculated for every dog and bitch to be used for breeding, based on all available information for that animal, its parents, siblings, half sibs, as well as its progeny. The combined figure for a proposed breeding pair may not exceed a specified threshold value (105 for cryptorchidism, 100 for HD). Threshold values for SPONDYLOSIS and HEART DEFECTS will be available shortly.

#### **HEALTH TESTING IN SOUTH AFRICA**

At present screening of the following hereditary conditions affecting Boxers can be performed in South Africa:

- HIP AND ELBOW DYSPLASIA - radiographs
- SPONDYLOSIS - radiographs
- CONGENITAL HEART DEFECTS, INCLUDING SUBAORTIC, AORTIC AND PULMONIC STENOSIS - Stethoscopic screening (auscultation) for audible murmurs by qualified veterinarians. Colour Doppler echocardiography available in major cities only.
- HYPOTHYROIDISM - blood sample analysed by pathology laboratory.

Genetic tests:

None of these tests can currently be done in South Africa, but DNA samples can be sent by ordinary mail to the USA for processing. Payment can be made online by credit card.

- DEGENERATIVE MYELOPATHY (DM) - Orders are handled by the OFA. The cost for the test kit, including an FTA card for sample collection (cheek swabs), instructions, test order form, sterile applicator swab and address labels is \$65. College of Veterinary Medicine, University of Missouri.  
Website: <http://www.offa.org/dnatesting/dm.html>
- ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC) - swab test kits can be ordered via e-mail. Cost of test \$51. College of Veterinary Medicine, North Carolina State University.  
Website: <http://www.cvm.ncsu.edu/vhc/csds/vcgl/boxer-arvc.html>

# SABOX HEALTH SCREENING RECOMMENDATIONS

## KUSA ACCREDITED BREEDERS SCHEME

NB. All Boxers examined for any inherited disorder must be identified by means of microchip or tattoo.

After consultation with Boxer Club Gold Reef, Natal Boxer Club and Western Province Boxer Club, SABOX would like to make the following recommendations regarding the health screening of Boxers in South Africa. The recommendations will have to be revised as necessary when new diagnostic/genetic screening methods become more readily available in South Africa.

### **STUDIES HAVE SHOWN THAT CANCER AND HEART DISEASE ARE BY FAR THE MOST COMMON CAUSES OF DEATH WORLDWIDE IN THE BOXER, ACCOUNTING FOR ALMOST 50% OF ALL DEATHS.**

There is at present no genetic screening test available for cancer in dogs.

The two most serious inherited heart disorders, both of which occur in the Boxer population in South Africa, are SUBAORTIC/AORTIC STENOSIS (SAS/AS) and ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC). Some form of screening for these heart diseases is therefore desirable.

### **SCREENING FOR CONGENITAL HEART DEFECTS (CHD), INCLUDING SAS/AS:**

A congenital disorder or disease is a condition existing at birth and often before birth, or that develops immediately after birth, regardless of causation. Congenital disorders vary widely in causation and abnormalities.

Some studies suggest that Aortic Stenosis is a polygenic disease (caused by several genes), so two clear parents can produce affected offspring.

According to the Orthopedic Foundation for Animals (OFA) in the USA, while there are exceptions, virtually all common congenital heart defects are associated with the presence of a cardiac murmur. ([http://www.offa.org/cardiac\\_guidelines.html](http://www.offa.org/cardiac_guidelines.html)). Consequently, it is recommended by OFA that cardiac auscultation (i.e. stethoscopic examination) be the primary screening method for initial identification of CHD and the initial classification of dogs. Should a murmur be detected, this should then be followed by an Echo-Doppler examination. The British and Australian Heart Murmur Schemes for Boxers are similar and also based on screening by means of auscultation. (<http://www.boxerbreedcouncil.co.uk/as.htm>). Auscultation in both the USA and UK is done by specialist cardiologists. At present, although there are quite a number of veterinary specialist physicians and specialist radiologists, who diagnose and deal with cardiac disease in dogs, especially in the larger centres, there are no veterinary specialist cardiologists in South Africa.

**Colour Doppler Echocardiogram:** This is an ultrasound scan of the heart that detects abnormal flow velocities and allows for the diagnosis and quantification of the severity of Aortic Stenosis and other congenital heart defects. A clear Doppler after 12 months of age is considered conclusive (the dog does not have SAS/AS or other CHD's such as septal defects or defects of the heart valves) and will not develop it later in life.

Availability: Doppler echocardiography examinations can be carried out at the Diagnostic Imaging Section, Veterinary Science Faculty, Pretoria University and at a few other veterinary diagnostic imaging services, including Tygerberg Animal Hospital in Belville, Cape Town.

### **RECOMMENDATION 1: CONGENITAL HEART DEFECTS**

Colour Doppler echocardiography is the method of choice for the examination of Boxers for congenital heart defects. However, due to the fact that this can only be done at a very limited number of locations in South Africa, SABOX therefore recommends that a Heart Murmur Scheme (similar to the KUSA HD scheme) be instituted. As a minimum requirement, Boxers to be used for breeding should be examined after 12 months of age, before being bred (and annually thereafter, by means of auscultation by a qualified veterinary surgeon. An official KUSA/SABOX certificate, stating that a Boxer has been examined and found to be free of audible heart murmurs, should be signed by the veterinarian and submitted to KUSA/SABOX by the Boxer's owner. Guidelines for the veterinarian on correct auscultation procedures to be followed must be attached to the certificate. Should a murmur be detected, it is recommended that such a Boxer not be used for breeding, unless it has been examined by means of Doppler echocardiography and found to be free of congenital heart defects. (Not all murmurs are related to heart defects - sometimes harmless flow murmurs are detected during auscultation, especially in puppies).

## **SCREENING FOR ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY (ARVC)**

ARVC is a very widespread and serious hereditary cardiac disorder in Boxers. Screening for ARVC is unfortunately still very problematic, as it is an adult onset disease with clinical signs only observed for the first time between 6 and 8 years of age on average, although the initial episode could occur at any age, from much younger to much older. Because of this, it is usually not possible to conclusively diagnose the condition before dogs have been used for breeding.

None of the diagnostic/genetic screening tests used elsewhere to screen for ARVC is currently readily available in South Africa. The recommended screening tests widely used elsewhere include:

**Holter Monitor:** This is a 24-hour ambulatory electrocardiogram used to screen for ARVC. It tests for the presence of VPCs (Ventricular Premature Contractions). A zero or low number of VPCs does not indicate that the dog is free of ARVC, it only means that the dog was not exhibiting VPCs during that 24-hour period. However, consistent zero/low readings on yearly Holtering would indicate a higher possibility that the dog is not affected with ARVC. Holter testing should therefore be repeated yearly. Not available in South Africa at present.

The DNA based genetic test for the mutant gene associated with ARVC is not yet done in South Africa but samples can be sent to the USA for processing. The test is still controversial, producing many false negatives and positives. It is also suspected that there might be more than one gene involved. It is therefore usually done in conjunction with annual Holter screening.

## **RECOMMENDATION 2: ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY**

At this stage, SABOX can unfortunately only recommend that Boxers that have been diagnosed with or are suspected of suffering from ARVC (or any other serious arrhythmia) not be bred from. At this stage a witch hunt aimed at also removing all close relatives of such Boxers could have a very serious negative impact on the diversity of our already limited gene pool and could aggravate other conditions, such as cancer, for which no screening tests are available. According to Dr Kathryn Meurs (discoverer of the ARVC mutant gene), there may even be reasons for keeping in the breeding population some affected homozygous dogs (with two copies of the defective gene), if such dogs are healthy in every other way.

Breeders should however be encouraged to make use of the genetic testing available in the USA (refer p. 3), particularly before breeding a Boxer with a close relative that was diagnosed with or suspected of having ARVC or any other cardiac arrhythmia.

## **SCREENING FOR HIP DYSPLASIA (HD):**

Hip dysplasia has a polygenic and multifactorial inheritance, meaning it is caused by multiple genes and influenced by many non-genetic factors. Factors that can make the disease worse include excess weight, excess or prolonged exercise before maturity, a fast growth rate, and high-calorie or supplemented diets.

It is probably not just one disease but many diseases, which together result in degenerative effects on the hip joint. An extremely complex disorder, hip dysplasia is now thought by some to be the most noticeable manifestation of a systemic condition that can affect not only the hip joints but also those of the elbow, shoulder and even the joints between the vertebrae. It is not yet known how many, or which genes are involved. Unaffected parents could therefore produce affected offspring, and the only way to gradually reduce the incidence of hip dysplasia is by trying if possible to breed from animals that have in their pedigrees only, or as many progenitors as possible, with good (A or B) hip scores. This only becomes possible if the hip status of all the animals included in a pedigree is known and underlines the importance of screening all breeding stock.

## **RECOMMENDATION 3: HIP DYSPLASIA**

The condition is not uncommon in the local Boxer population and breeding stock should be screened for it. Boxers with hip scores worse than C2-C2 should preferably not be bred from.

**Hip radiographs:** In terms of the SAVA/KUSA Hip and Elbow Dysplasia Scheme hip & elbow radiographs (of satisfactory quality) taken after 12 months of age can be submitted for evaluation by any veterinarian to one of the certified scrutineers.