

Familial Shar-Pei Fever

Familial Shar-Pei Fever (FSF) is a hereditary inflammatory disorder seen in Shar-Pei. It is inherited as an autosomal recessive condition.

Clinical signs:

Episodic fever is the most important and consistent clinical sign of this disorder. The temperature commonly is in the 105-107°F range. The fever is generally self-limiting lasting 12-36 hours. Another common clinical sign often accompanying the fever is swelling of a joint, usually the hock (tibiotarsal) joint and is known as Swollen Hock Syndrome (SHS). This painful, hot swelling can also involve the carpus (wrist) and the lips. Dogs with FSF are sick -- they are reluctant to move and when they do walk they have a characteristic "walking on eggs" gait. They often are painful in the abdomen and have a characteristic "roached" back.

Pathogenesis:

What we do know about this disease is as follows:

1. Shar-Pei with FSF have increased levels of the cytokine Interleukin-6 (IL-6). IL-6 is involved with the fever response and is an integral part of triggering the production of Acute Phase Reactant Proteins by the liver. IL-6 is also involved in the Systemic Inflammatory Response Syndrome (SIRS). Dysregulation of IL-6 is the cause of much of the disease in Shar-Pei with FSF. IL-6 also plays a major role in the body's stress response and serves to "prime" the immune system.
2. Shar-Pei with FSF are at risk from early death from systemic amyloidosis. About 25% of the FSF dogs will develop renal failure including renal amyloidosis -- a smaller percentage will develop hepatic amyloidosis. This is usually seen in Shar-Pei between the ages of 2-5 years of age. They also seem more susceptible to immune-mediated kidney disease such as membranous glomerulonephritis, protein-losing glomerulopathies, DIC, thromboembolic phenomena such as mesenteric, splenic and pulmonary embolism and Streptococcal Toxic Shock Syndrome (STSS).
3. FSF in Shar-Pei was hypothesized to be an animal model of Familial Mediterranean Fever (FMF) in humans. Recent work indicates this is not true, although FSF is very similar to FMF in man.
4. FSF is a hereditary disease with a genetic basis. It appears to be inherited as an autosomal recessive condition.

Laboratory Findings:

Unfortunately there are no blood test, etc. which are specific for FSF. During a fever episode there will often be an increased white blood cell count, an increase in liver enzyme levels and other non-specific findings. Work done by Dr. Gary Johnson at the University of Missouri College of Veterinary Medicine to develop a DNA blood test to screen for the disease was unsuccessful and the research effort will still continue.

Treatment:

It is very important to monitor the temperature in this condition. Initially, fever can be treated using aspirin. Usually a regular strength adult aspirin is given every 6 hours for the first 24 hours and then twice a day for 3-5 day thereafter. In rare cases where aspirin doesn't work or for extremely high fevers, dipyron is given. Some patients will require supportive care with intravenous fluid therapy and in extreme cases emergency treatment similar to heat stroke treatment. Antibiotics are not normally indicated in this condition.

Colchicine:

Colchicine is a drug that has been in use in people with FMF to prevent amyloidosis. It is currently being recommended in Shar-Pei with FSF for the same purpose. No studies have been completed to determine if it is useful for this purpose in the Shar-Pei or not. The clinical impression is that it does help. Those dogs on colchicine seem to have fewer FSF episodes and less severe signs while on the drug. Side-effects appear to be minimal at this time and are primarily gastrointestinal such as vomiting, diarrhea, anorexia (decreased appetite), etc.

Prevention:

Shar-Pei with FSF only show symptoms sporadically. It would appear that there are "triggers" involved in initiation of the FSF episodes. One of the major triggers appears to be stress. This may be a dog training class, a dog show, another illness, a dog in heat, excessive exercise, etc. If the owner can recognize these triggers and take steps to avoid them the number of FSF episodes can often be reduced. Diet does not appear to be helpful in prevention of FSF or kidney disease. Surely diet has a role in the management of the kidney disease once clinical signs are apparent. Low dose aspirin therapy may be useful in decreasing the incidence of FSF and its severity as well. Aspirin may also be useful as an adjunct therapy in the prevention of thromboembolism.

Monitoring:

Monitoring for the complications which often accompany FSF is one of the major goals of the owner of an FSF dog. The primary and most consistent sequela to FSF is kidney failure either due to immune-mediated kidney disease or renal amyloidosis. I currently recommend monitoring a urinalysis every 3 months. The sample should be collected first thing in the morning after the water has been taken up overnight. I primarily look at the urine specific gravity which is a measure of the concentration of the urine and the protein levels in the urine. When the kidneys begin to fail the initial indication is a loss in the ability to produce a concentrated urine. This occurs before there are blood changes related to kidney failure. Increased water consumption, increased urination are the clinical signs associated with the loss of concentrating ability, but these signs are often not recognized. I also think it is wise to do a blood panel every 6-12 months and certainly do one in the urinalysis is abnormal. Weighing your dog periodically is very important. We often don't recognize a significant weight loss because it is very subtle over a longer period of time. Water consumption and appetite are other important indicators to watch.

Complications of FSF:

We have already discussed the kidney complications in this condition. Other Complications which have been documented include thromboembolism (mesenteric, splenic, pulmonary), DIC (disseminated intravascular coagulation), SIRS (systemic inflammatory response syndrome), MODS (multiple organ dysfunction syndrome), STSS (streptococcal toxic shock syndrome), hypertension associated with renal failure. Many of the deaths following an acute FSF episode are due to these complications. No FSF episode should be treated lightly!

Diagnosis:

There is no specific diagnostic test for FSF at this time. Diagnosis is based on the clinical sign of episodic fever in a Shar-Pei. I think every Shar-Pei that dies should be autopsied to determine the cause of death, but this is even more critical in cases involving FSF. Renal amyloidosis can only be diagnosed based on kidney biopsy and staining with Congo Red stain. This stain is specific for the presence of amyloid. Amyloid has been found in other tissues in Shar-Pei as well so special staining should be requested on all tissues submitted for histopathology. Many dogs with FSF will not have amyloid in the tissues at the time the tissues were harvested -- this means the absence of amyloid in a biopsy specimen does not mean that dog will not or would not have gone on to develop amyloidosis at a later time. To further confuse the issue, not all Shar-Pei with amyloidosis have shown signs of FSF.

Future:

Research is currently underway at the University of Missouri College of Veterinary Medicine by Dr. Gary Johnson to develop a DNA blood test. The gene for human FMF was sequenced in the Fall of 1997 and with that information Dr. Johnson had hoped to sequence the FSF gene. That information was applied by Dr. Gary Johnson to FSF in a research project funded by the CSPCA Charitable Trust. That project did determine that the mutations causing FMF in man do not exist in FSF in the Shar-Pei, hence they are two distinct, although similar diseases. There are other hereditary inflammatory fever disorders in man and Dr. Kastner and the National Institutes of Health are looking at the disorder with information supplied by Dr. Tintle. Familial Hibernian Fever in man has also been ruled out as the cause of FSF by Dr. Johnson with information supplied by NIH. Work will continue to find the genetic mutation(s) responsible for FSF in Shar-Pei.

As of this writing the mutation responsible for FSF has not been found. If a test can be developed, a screening program can be established to screen breeding stock and determine normal individuals, carriers and affected dogs. With this information Shar-Pei breeders can gradually eliminate this genetic disease from the breed. One of the major obstacles to research revolves around the unpredictable phenotype of FSF. There is no consistent age range when clinical signs develop, the clinical signs can be variable, some dogs develop amyloidosis, some don't, etc. This makes it very difficult to use genetic selection methods which are based on phenotype.

Recommendations:

All Shar-Pei with FSF should be on colchicine and be regularly monitored via urine samples and blood work for development of complications. Dogs with FSF should not be

used in breeding programs and should be neutered. Dogs with a family history of FSF should be on colchicine and monitored. Dogs with FSF should be maintained as stress-free as possible.