Addressing Hyaluronosis (the downside to Shar-Pei Wrinkles).

Shar-Pei have a mutation that causes them over-produce hyaluronan and they may have as much as 10 times the amount of hyaluronan as a non-Shar-Pei. It is important to keep this vital normal substance as healthy as possible in this breed. Hyaluronan is the sculpting material that supports and cushions cells, shouts "Danger" when it is injured, and assists in wound healing. Hyaluronan health is central to a healthy body. Damaged, fragmented hyaluronan promotes inflammation.

Here are Twelve Points to consider when trying to optimize the health of your Shar-Pei.

Not all of these points need to be implemented but they should be considered to see if they are appropriate for your dog's best health. Discuss your plan with your veterinarian so that you can work as a team to keep your Shar-Pei in top condition.

1. Feed a High Quality diet. There is no one single diet that is best for all Shar-Pei. They may develop individual food intolerances because of their inflamed bowel and this varies greatly from dog to dog as to what is the offending food and may change over their lifetime. Some Shar-Pei do great on commercial soy-based diets, others on nutritionally balanced raw, others on premium brand venison and sweet potato. My own dogs are on a prescription veterinary formula kibble for dogs with intestinal problems because they flourish on that nourishment and their bowel health is more consistently normal. This wide variation in what is ideal for each individual makes it difficult for owners to know what is best for their dog. I know that over-feeding cheap, grain based, over-processed junk food is a formula for making dogs (and people) unhealthy. Dogs benefit from the breakdown products of cartilage, bone and organ meat (sources of minerals, glucosamine, chondroitin sulfate, hyaluronan and vitamins). The "select cuts" of chicken breast and other muscle meats fail to provide necessary nutrients. Preparing well-balanced, nutritionally complete home-cooked meals requires advanced knowledge of dietary requirements and is highly time-consuming. If you do purchase dry kibble dog food, try to avoid purchasing more than a 2-6 week supply (depending on quality of your storage environment) to avoid the over-growth of mold, grain mites and rancidity of unsaturated fatty acids, all of which can contribute to inflammatory issues.

Some Shar-Pei with severe inflammation may need a diet low in simple carbohydrates: grain-free or containing small amounts of whole healthy fresh grains if possible. A pasture-fed meat source is preferable if money is no object (grain-fed, factory-farmed meat has a high ratio of omega-6 to omega-3 fats and is lower in antioxidants and conjugated linoleic acid). An important goal is to shift the arachidonic acid pathway away from pro-inflammatory end-products. A high dietary omega-3 to omega-6 fatty acid ratio may help reduce inflammation and result in improved overall health.

Hyperglycemia also contributes to up-regulation of hyaluronan so avoid over-feeding at any one meal to avoid blood sugar surges.

2. High dose omega-3 fatty acids from fish oil daily. Again, the goal is to shift to anti-inflammatory end-products but also for fish oil's resolvins and other inflammation-resolving

mechanisms at high doses. A high dietary omega-3 to omega-6 polyunsaturated fatty acid ratio may help reduce inflammation and result in improved overall health including decreased anxiety.

The omega-3 fatty acids, EPA & DHA, appear to decrease the production of pro-inflammatory eicosanoids, derived from arachidonic acid, as well as the cytokines IL-1β, IL-2, IL-6, interferon gamma and TNF-α. By reducing the production of these pro-inflammatory chemical messengers, omega-3 fatty acids also alter the stress response by the hypothalamic-pituitary-adrenal axis.

Purchase a high quality product that is batch-tested for rancidity, heavy metals and toxins like PCBs. Rancid fish oil is much worse than no fish oil at all!

Suggested amount for approximate 20 kg (44 lb) Shar-Pei is 800mg EPA & 400mg DHA per day with food. Store in freezer or refrigerator.

3. Lecithin: 1-2 Tbl of granules (7.5 – 15 gms) per day in food to alter the phosphatidylcholine composition of the "hyaluronasome" in plasma membrane lipid rafts; this may impact how HA fragments are internalized for further degradation.

4. HyVitality®: a formulation of my recommended vitamins, minerals, antioxidants and phytochemicals that were chosen for their hyaluronan (HA) health promoting effects. Reactive oxidative species (ROS) fragment native high molecular weight hyaluronan and the effects of ROS may be counter-acted by antioxidant therapy. Magnesium is integral to stabilizing HA in its high molecular form and magnesium deficiency is a common finding in the breed. Severe cobalamin (Vitamin B12) deficiency is also seen in Shar-Pei. I selected combinations of antioxidants, minerals, vitamins and plant-based supplements in HyVitality products to help maintain native undamaged high molecular weight, healthy hyaluronan. HyVitality supplies these key factors in amounts appropriate for dogs rather than giving over-the-counter products designed for humans. Working with a trusted manufacturer has allowed me to be assured of purity and quality: Made in U.S.A. in a certified GMP facility. *(Average Shar-Pei dose contains 50-80mg alpha lipoic acid, 60mg Coenzyme Q10, 80-160mg magnesium from dimagnesium malate), 1000 mcg methylcobalamin, 25mcg Vitamin K2 and a proprietary blend of Boswellia Serrata, Curcumin, Diosvein™ micronized diosmin & Trans-Resveratrol).* HyVitality is dosed by weight. More information at www.HyVitality.com.

Other additional health supplements that may help dogs with recurrent, refractory inflammatory episodes include 250 mg rutin/day, 500 mg bromelain/day, 250-500 mg MSM/day for most average-size adult Shar-Pei. I suggest that you try these separately for several weeks to see if they help.

Health supplements will often take 4-12 weeks of administration before improvement may be noted.

5. Vitamin C, 250mg. Shar-Pei with excess HA may need more antioxidants like Vitamin C. Also, I suspect that Shar-Pei may not synthesize adequate Vitamin C because Vitamin C and HA compete for similar biochemical synthetic pathways (both are formed by glucuronidation).

6. Ensure Adequate Vitamin D3. Active Vitamin D modulates the over-active toll like receptors (TLRs) in inflammatory disease, returning them to a more normal functionality. Hyaluronan fragments bind to TLRs to activate the pro-inflammatory cascade. Activation of the Vitamin D receptor inhibits maturation and causes death of mast cell precursors and can help inhibit allergic inflammatory responses.

A study out of Tufts' University showed that as many as 75% of dogs were insufficient or deficient in Vitamin D. Dogs on home-cooked diets had the lowest value and had the widest variation in their individual levels but dogs on commercial dog food were also very likely to have insufficient Vitamin D levels.

Supplementation may be needed if a dog is on a home-cooked diet without added dietary sources of Vitamin D, or who has severe allergies, arthritis or chronic inflammation.

Dog do not convert cholesterol into Vitamin D in the skin with sun exposure the way people do and require dietary sources. These include liver, other organ meats, fat from pastured ruminants, salmon oil, and cod liver oil.

Discuss baseline testing with your veterinarian if you are concerned that your dog may need supplementation. Maintenance need for Vitamin D3 in dogs has been estimated to be 50-475 IU per 10 lbs of body weight per day but more will be required to restore dogs insufficient or deficient to sufficient levels.

Vitamin D supplementation is best given in the morning with a fatty meal (along with some fatty meat or fish, cheese, butter or coconut oil, not a piece of bread or some plain kibble).

HyVitality contains Vitamin K2 and magnesium, necessary co-factors for proper Vitamin D3 absorption.

Excessive Vitamin D can lead to toxicity but is very uncommon unless due to rodenticide poisoning and massive overdose. Nevertheless, caution is advised when supplementing with Vitamin D.

7. Glucosamine and Chondroitin Sulfate: Hyaluronan is formed by glucuronidation of repeating units of N-acetyl-glucosamine so glucosamine is a vital ingredient in forming HA. Two recent studies have suggested that increasing the amount of intracellular UDP-N-acetylglucosamine by adding glucosamine: 1) increases the molecular weight of the hyaluronan produced (this is a very good thing) and 2) down-regulated HAS2 (hyaluronan synthase 2, the enzyme over-expressed in Shar-Pei), so less hyaluronan was made. Glucosamine also suppresses the activation of mast cells (important in many Shar-Pei disease processes). Chondroitin sulfate may interfere with the binding of low molecular weight HA to its major receptor CD44.

8. Thyroid Function: Treat any signs of tertiary hypothyroidism with thyroid supplementation.

Low molecular weight fragments of hyaluronan, produced in the normal dynamic process of recycling hyaluronan, may give the brain a false signal that there is damage within the dog's body and that thyroid hormone production should be decreased to save the body's metabolic resources for healing and recuperation. Unfortunately in Shar-Pei, this can be situation normal due to their excess hyaluronan and yet it results in signs of clinical hypothyroidism Common signs include very sparse or missing coat, particularly along the back and inside of the thighs and hindquarters, with a generally brittle, lighter coat on the torso.

HA fragments may down-regulate TSH releasing hormone via TLR2 binding, leading to tertiary hypothyroidism characterized by low or low normal TSH and very low to low normal T3/T4 and I am looking at this in Shar-Pei now.

Response to therapy will be softer, thicker, and richer colored fur with hair re-growth, especially on hindquarters, and improved overall health and activity if the dog is functionally hypothyroid. Your veterinarian will monitor therapy as adjustments up/down are often needed to individualize therapy.

Primary hypothyroidism is often associated with myxedema, a form of hyaluronosis, and the conditions are entwined in ways that have yet to be fully described.

9. Probiotics and attention to bowel health. Skin and bowel are the immune system's biggest barriers and they are both HA rich areas. Inflammatory bowel diseases (IBD) including colitis are very common in the breed. Some flare-ups of Shar-Pei Fever and increased frequency of fever events have improved with treatment directed to eliminating over-growth of pathogenic GI bacteria in patients with IBD or stress-induced colitis. Endotoxin produced by gram negative gastrointestinal tract bacteria may trigger recurrent fever episodes and may lead to simultaneous occurrence ("outbreak") of fever episodes in multiple dogs within the same household in dogs that may share similar fecal microbiome. *(If diarrhea is frequent or persistent, discuss diagnosis and possible treatment with prescription drugs, e.g. tylosin, with your veterinarian.)*

10. Fanatical attention to skin and ear issues. Bathing by shampoo or washcloth wipe-downs as needed (microfiber dust cloths work well) - up to daily when skin is inflamed and at least every 2 weeks in a "healthy" Shar-Pei. Remove superficial yeast, bacteria (potential sources of hyaluronidases, enzymes that damage HA) and allergens like pollens, molds, and dust that may activate mast cells. At least weekly ear cleaning/flush unless the Shar-Pei has a large, open, healthy ear canal. It is important to keep the very commonly narrow vertical ear canal open and clean of wax and debris. The Zymox® product line has been very helpful in maintaining skin and ear health in many Shar-Pei as a first line of defense against opportunistic invaders. Ensure the top of the ear canal is open so that cleansing products can get down where they need to work (Zymox' instructions state that cleaning is not needed but most Shar-Pei need gentle scooping removal of some external debris at the very top of the vertical ear canal and outer folds. Always be very careful not to drive debris deeper into the ear canal as this may lead to impaction and serious problems.)

11. Very low dose aspirin: only ¼ - ½ of an 81 tablet per day in dogs with no signs of gastric upset. Platelet derived growth factor might be an important mediator in their disease

and aspirin also decreases risk of thromboembolic events. Be cautious as the breed has an increased risk for GI ulceration.

12. Detect problems early: Your veterinarian should see your Shar-Pei regularly for a complete physical examination and regular, routine monitoring of first morning urine with urinalysis (UA) as well as a CBC, blood chemistry profile and TT4. Idexx Laboratories now offers an early renal disease detection test, SDMA (symmetrical dimethylarginine), that may be useful in Shar-Pei at-risk for amyloidosis and is offered as part of their general blood chemistry profile. Discuss frequency of visits and testing with your veterinarian but at least annually in healthy Shar-Pei and more frequently in dogs with known problems or at-risk factors is recommended.

Eliminating inflammatory triggers, supporting healthy hyaluronan, reducing silent chronic inflammation wherever possible, providing good nourishment and playful daily exercise are key to Shar-Pei health.

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