What causes a Shar-Pei to spike a fever and have an autoinflammatory event?

A healthy body has hyaluronan everywhere – in skin, between cells, lining the intestinal tract, filling the eye, providing viscosity to joint fluid, in the kidney where it helps control the body's hydration, in the brain's perineuronal network, lining blood vessels and countless other places where it plays critical roles in normal function including wound healing.
Healthy, native high molecular weight hyaluronan is the largest molecule in the body, both in molecular size and in the total amount present.

All Shar-Pei have a mutation that causes them over-produce hyaluronan. They may have as much as 10 times the amount of hyaluronan as a non-Shar-Pei.

A Threshold Level: Exceeding the Limit.

There is always a background level of low molecular weight hyaluronan fragments in the bloodstream, in tissue and in the lymphatics. A certain amount is okay. Hyaluronan (HA) is a dynamic molecule that is always being formed, broken down and then recycled rapidly within the body. Some HA molecules will only survive for hours or days before being broken down into tiny pieces and resynthesized where needed. It is estimated that one third of the body's total HA is turned over daily. The typical amount of HA fragments present during this continuous process is perceived as homeostasis: the background threshold level that is system normal.

Undamaged HA is a sentinel molecule of the innate immune system. Damage it and the body senses the sudden surge in HA fragments as evidence of danger and, in fact, low molecular weight HA is recognized as a Damage-Associated Molecular Pattern or DAMP that triggers inflammation. Broken bits of HA -> ALARM!!!

What can damage hyaluronan and produce these inflammation-promoting fragments?

- Injury by cold, heat, shock, trauma.
- Reactive oxidative species (ROS or free radicals).
- Infection: Hyaluronidase-secreting pathogens, e.g. some bacteria (e.g. Streptococcus) and most yeast. These pathogens secrete an enzyme that melts hyaluronan into pieces.

HA fragments both activate and prime the inflammasome.

The inflammasome is a multi-protein platform that can release a powerful chemical messenger: Interleukin-1beta (IL-1β). Tiny bits of HA activate the inflammasome. This sets the stage for inflammasome primers, which include HA fragments, to start the inflammatory cascade in motion with release of IL-1β. IL-1β is a key driver of fever and inflammation. But HA fragments can both activate and prime the inflammasome. This may be an underlying cause of some random fever events in heavily wrinkled dogs. The normal degradation process may lead to an amount of fragments that exceeds the normal homeostatic threshold. The excess degraded fragments are incorrectly perceived as evidence of damage. The activated inflammasome produces inflammatory cytokines that cause fever.

Other things can contribute to tripping that fever switch. This includes all other primers of the inflammasome, e.g. lipopolysaccharide (LPS) endotoxin from gram negative bacteria like some E.Coli and Pseudomonas aeruginosa. The inflammasome's trigger is already cocked and ready, thanks to activation by tiny bits of HA. Priming (pulling that trigger) can quickly lead to an explosion of fever.

Psychological stresses, as can occur with boarding or from household upheaval, can lead to changes in gut microflora. Overgrowth of pathogenic bacteria in bowel can lead to endotoxin release, barrier disruption, and stress diarrhea. This contributes to up-regulation of inflammation and fever may result.

Introducing a new dog into the home can sometimes lead to an "outbreak" of Shar-Pei Fever in the original pack of Pei due to these factors. I have seen numerous incidences where introduction of a rescued adult dog can bring in an intestinal tract of full of imbalanced or pathogenic bacteria to all the resident family dogs, some of which may never have fevered before, and with that altered microbiome and the stressful adjustment to a new pack dynamic, a cluster of fevers may occur in multiple dogs. It looks like all the dogs "caught" Shar-Pei Fever from the newcomer but it is more complicated than that.

Threshold Effect: Sometimes it is cumulative and not just one thing.

You have a moderately wrinkled Shar-Pei with a full meatmouth. He's got stenotic (narrow) ear canals. Seasonal plant pollen and year-round dust mite allergies plague him from time to time. He's sensitive to chicken, peanuts and soy. He's a bit itchy now and the flare-up of his allergies predisposes him to some yeast overgrowth and secondary otitis. Your son shares his veggie hot dog (soy) with the Pei at lunch without your knowledge. A groundhog bites your dog on the nose when your brave Pei confronts him in the backyard the next morning. That night, he spikes a fever of 104.8 and he's limping on his swollen right hind leg. What caused the fever event? All or some of multiple potential triggers probably contributed and he tipped over the threshold, setting off an inflammatory event and fever. Probably not one single thing but a lot of things. Can there be just one? Yes, if it's a big challenge. If a deep bite wound on his nose introduced a hyaluronidase-secreting bacteria, things could get bad real fast - but that is unusual. Most groundhogs do come out on the losing end of a tangle with a Shar-Pei.

Controlling environmental triggers helps your Shar-Pei stay healthy. (Just do the best you can.)

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Source - FB