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DNA Tests for Genetic Diseases in Horses

What breeds of horses are in your Curly Horse's pedigree? What diseases exist in those bloodlines? Did you know that many breed-related diseases can be tested for by sending in a hair sample (20 to 50 mane or tail hairs including roots) for a reasonable fee?

Large scale sequencing of the complete equine genome in 2008 (Wade et al., 2009) opened up a new frontier to researchers. That has led to more and more simple hereditary diseases being isolated that can be identified with a simple genetic DNA-based test. These DNA tests are available to the public for a nominal fee, by sending in a hair sample (or an unclotted blood sample) to various labs.

There are many equine inheritable diseases for responsible breeders to be aware of. Diagnostics and testing of equine disease is a dynamic field with research development ongoing. Advancements may occur rapidly, to the great benefit of horses and owners. In this report we will examine the inheritable disorders that are easily tested for with a hair sample. Our responsibility as breeders is to determine what breeds and bloodlines influence any Curly Horse that we plan to breed, and which DNA tests are important to run on which Curly Horses. This is an important step to build responsible breeding programs. The cost of testing is small compared to the economic investment we have in our Curly Horses. We cannot gamble with the genetic health or reputation of our breed, or with our reputation as breeders. Most, if not all Curly Horses should be tested before breeding to avoid suffering, loss and heartache, and to ensure the genetic viability of our breeding stock.

What's in Your Curly Horse's Pedigree?

ACRONYM	Disease or Disorder	+ ‡	breeds associated	bloodlines associated
(GBED)	Glycogen Branching Enzyme Deficiency	R	Stockhorses	King, Zantanon
(HERDA)	Hereditary Equine Regional Dermal Asthenia	R	Stockhorses	Poco Bueno
(HYPP)	Hyperkalemic Periodic Paralysis Disease	D	Stockhorses	Impressive
(MH)	Malignant Hyperthermia	D	Stockhorses	2 undisclosed bloodlines
(PSSM1)	Polysaccharide Storage Myopathy Type 1	D	at least 20 breeds	widespread
(CSNB)	Congenital Stationary Night Blindness	R	Appaloosa, Spanish	all Lp gene horses
(LWS), (OLWS), (WFS)	Overo Lethal White Foal Syndrome	R	Stockhorses, others	frame overo bloodlines
(CA)	Cerebellar Abiotrophy	R	Arabians	Arab-derived
(LFS)	Lavender Foal Syndrome	R	Arabians	Arab-derived

(SCID)	Severe Combined Immunodeficiency	R	Arabians	Arab-derived
JEB1	Junctional Epidermolysis Bullosa Type 1	R	Belgian	Belgian-derived
JEB2	Junctional Epidermolysis Bullosa Type 2	R	American Saddlebred	Saddlebred-derived
Myotonia	Myotonia	R	New Forest ponies	New Forest-derived

GBED

Glycogen Branching Enzyme Deficiency (GBED) is a simple recessive lethal condition that disrupts glycogen metabolism. It is caused by the body's inability to properly store sugar. The affected foal is not able to store enough energy to fuel important organs, such as the heart, skeletal muscles and brain. Foals born affected by GBED suffer from a range of symptoms associated with this lack of fuel, such as low energy, weakness, difficulty rising, low body temperature, contracted muscles, seizures, and sudden death. Unfortunately, GBED is always fatal; most affected foals die before the age of 8 weeks. GBED often causes abortions; as many as 3% of aborted Quarter Horse foals were found to be homozygous for the GBED mutation. A DNA test will determine the GBED status of a horse – either affected, or a carrier of the disease. The GBED mutation may be present in 8 to 10% of all Quarter Horses and related breeds. It is very possible that this disease has existed in Quarter Horse bloodlines for many years, but went undetected.

GBED is an autosomal recessive trait, meaning a foal will only be affected if it inherits the disease from both parents. Horses that are carriers of the GBED have 1 copy of the mutation, but do not have any symptoms associated with the disorder. This makes DNA testing important to screen for carriers and prevent this fatal condition. (Animal Genetics Inc)

HERDA

Hereditary Equine Regional Dermal Asthenia (HERDA) also known as Hyperelastosis Cutis (HC), is a rare genetic skin disease found predominately in the Quarter Horse. This disorder is recessive, which means that a horse must be homozygous positive or have two copies of the defective gene for the disease to manifest. Foals appear normal at birth, but develop skin lesions in response to mild abrasions. Areas under saddle seem to be most prone to these lesions often leaving permanent scars, soon preventing the horse from being ridden. HERDA causes a lack of adhesion within the layers of skin due to a genetic defect in the collagen that holds the skin in place. This defect causes the outer layer of skin to split or separate from the deeper layers, sometimes tearing off completely. Researchers at Mississippi State University and Cornell University believe that the origin of this genetic disorder may be the Poco Bueno's sire line. Scientists at the University of California mapped and identified the genetic mutation responsible for this disease. (UKY and Animal Genetics Inc)

HYPP

Hyperkalemic Periodic Paralysis Disease (HYPP) is caused by a dominant gene and a single copy of the gene can cause the disease. Horses with 2 copies of the gene may be more severely affected. Symptoms of HYPP may include muscle twitching, unpredictable paralysis attacks which can lead to sudden death, and respiratory noise. The severity of attacks can vary from unnoticeable to collapse to sudden death. The cause of death is usually respiratory failure and/or cardiac arrest. The gene encodes a potassium channel for cells. Cells with the mutation are unable to regulate the amount of potassium and the muscles undergo involuntary contractions. These contractions constitute exercise and the muscles become large and prominent. Bulky muscling is selected for by Quarter Horse halter horse breeders, and this disease made its appearance in a heavily used successful sire named Impressive. It is also known as the Impressive disease (or syndrome). I could not find a figure for what percent Impressive horses carry HYPP. All I know is, if your horse goes back to Impressive, test it, unless both its parents were already tested N/N. Scientists from the University of California and Pittsburgh identified this gene defect based on the occurrence of a similar defect in people. (KY Equine Research Nutrition Conference report, DVM360.com)

MH

Malignant hyperthermia (MH) is a genetic disorder that may occur in conjunction with type 1 PSSM. MH occurs in Quarter Horse bloodlines (with a high frequency in two specific lines), and horses are generally mature before exhibiting clinical signs. (nutrenaworld.com)

Malignant hyperthermia (MH) was initially recognized as a fatal syndrome in humans. It is most prevalent in swine but this syndrome has also been reported in dogs (especially Greyhounds), cats and horses. Its occurrence in swine is known as porcine stress syndrome. In horses MH is thought to be confined to Quarter Horses and members of related breeds such as Appaloosas and Paints. Less than 1% of Quarter Horses are affected, and those that are seem to trace to two specific bloodlines. The genetic disorder is apparently an autosomal dominant trait. MH is a potentially fatal disease that can be triggered by factors like exercise, stress, breeding, illnesses, anesthesia and concurrent myopathies. An additional genetic mutation in RYR1 gene (MH) influences PSSM and can increase the severity of the symptoms of PSSM in Quarter Horses and related breeds. (Animal Genetics Inc)

While researching and identifying the gene mutation responsible for PSSM1, there were 2 Quarter Horse sires consistently present in all the early findings. The 2 bloodlines were not publicly disclosed, which put researchers at odds with breeders. When simple genetic testing became available for PSSM1 in 2008, researchers discovered that PSSM1 was probably at least

1200 years old, and was widespread throughout 20 or more breeds, not just the sire lines of those 2 Quarter Horses. As I understand it, the same thing exists in the MH studies right now. The announcement of whether and which certain bloodlines carry MH is still pending more conclusive research.

PSSM1

Polysaccharide Storage Myopathy Type 1 (PSSM1). Two forms of PSSM exist in horses, Type 1 and Type 2. Type 1 PSSM is the one we include in this report, because it is the one that is easily identified by a genetic test. It is a dominant autosomal hereditary condition - a genetically caused form of tying-up with muscle damage and inability to move. PSSM (Type1) is characterized by abnormal and excessive storage of sugar (polysaccharide) in muscle cells. At least 20 breeds have been identified with Type 1 PSSM, including stockhorse breeds, Belgians, Percherons, Morgans, Mustangs, Tennessee Walking Horses, and some Warmblood breeds. The prevalence of this mutation is as high as 35-50% in Percherons and Belgians. It is rare in Clydesdales and Shires. It is present in about 8% of the Quarter Horse-related breeds and is most common in halter horse bloodlines. Several other mutations have also been identified as possibly being associated with some form of PSSM.

Symptoms usually begin by 2 to 3 years of age. Some horses that test positive for the mutations will exhibit only minor problems and some are subclinical – they may never exhibit any noticeable problems at all. Clinical signs can include skin twitching, stiffness, firm painful muscles, sweating, weakness, and reluctance to move with light exercise. Occasionally gait abnormalities, mild colic and muscle wasting may also occur. In blood tests, serum CK and AST activity is elevated (except in draft horses). An additional genetic mutation in RYR1 gene (MH) increases the severity of the symptoms of PSSM in Quarter Horses and related breeds. Not all cases of tying up are caused by the PSSM mutation.

Type 2 PSSM (PSSM2): Breeds affected: Quarter Horse-related breeds, a few Arabians and possibly other light breeds. Like PSSM Type 1, signs usually begin by 2 to 3 years of age but may occur in weanlings. Clinical signs are typically Rhabdomyolysis with or without exercise. (Rhabdomyolysis is the breakdown of muscle tissue that causes kidney damage. When muscle is damaged, a protein called myoglobin is released into the bloodstream which is filtered out of the body by the kidneys. Myoglobin breaks down into substances that can damage kidney cells.) Testing is not a simple DNA genetic test: It requires **muscle biopsy samples** to be evaluated for the presence of abnormal polysaccharide. (AG Inc and petalia.com)

CSNB

Appaloosa Coat Pattern / Leopard Print/ Congenital Stationary Night Blindness (CSNB). According to Animal Genetics, Inc., it has long been understood that Appaloosas are affected by both Equine Recurrent Uveitis and Congenital Stationary Night Blindness (CSNB) a condition making it difficult or even impossible to see in relatively low light. Research has now shown that CSNB is a recessive disorder that is directly linked to the leopard complex (spotted coat pattern) in Appaloosa horses. The DNA test for the LP mutation is used to confirm that an animal is a true Appaloosa horse, and to identify those animals that are homozygous (LP/LP) and will be affected by CSNB.

In 2003 researchers linked the positional candidate gene for leopard complex (LP) to the TRPM1 gene on chromosome 1. Further investigations headed by Dr. Rebecca Bellone and The Appaloosa Project (a team of researchers from Canada and the US) identified several SNPs in TRPM1 showing complete association. Soon after that, the causal mutation was also discovered. Both the SNP's and the causal mutation can be used to develop a genetic test to identify horses with leopard complex." Animal Genetics, Inc. (horsetesting.com)

OLWS/LWFS

Lethal white syndrome (LWS). Also called Overo Lethal White Syndrome (OLW/OLWS) or, less often, White Foal Syndrome (WFS) is linked to a recessive gene associated with the frame overo pattern. Horses that are heterozygous carriers of the gene do not develop the condition and are physically healthy. However, when a foal is born that is homozygous O/O for the LWS gene, it should be humanely euthanized shortly after birth, or else will die within 36 hours from complications involving an underdeveloped intestinal tract. A DNA test is available for LWS so that horses who are carriers of this gene are not bred to one another. Horses can carry the LWS gene and not visibly exhibit overo coloring; cases have appeared in the offspring of both tobiano and solid-colored parents, though all cases to date are horses that had overo ancestors. LWS can occur in any equine breed where the frame overo coat pattern is found. Scientists at the University of Minnesota, University of California, and from Australia discovered the mutation based on its similarity to a human disease (Hirschsprungs Disease). (UKY and Wiki-pedia)

CA

Cerebellar Abiotrophy (CA) is a neurological disease which occurs in Arabian and Arabian cross horses. The mutation causing this disease is recessive, and is fairly common. Foals affected with CA do not usually develop symptoms until six weeks to 4 months of age. "The disease causes the death of neurons in the cerebellum of affected foals, leading to head tremor (intention tremor) and a lack of balance equilibrium (ataxia). Affected horses may show exaggerated action of the forelegs, a wide-based stance, and be unable to rise from a reclining position. They tend to startle easily and often fall due to ataxia. The neurological problems may not be apparent to owners and are frequently thought to be a consequence of a fall rather than the cause of it. CA symptoms vary in severity. Some foals show very severe symptoms, including the exaggerated gaits and a dramatic lack of balance. Others have little more than the head tremor, which may only manifest itself during goal-directed movement. Regardless of the severity of the symptoms, CA foals are often euthanized or restricted to life as pasture pets, as they are never coordinated enough to be ridden safely. They are also a danger to themselves because the condition predisposes them to accidents and injury." (UC Davis) The mutation linked definitively to this disease was identified by the University of California at Davis.

LFS

Lavender Foal Syndrome (LFS) is an inherited lethal neurologic disorder known to affect Arabian foals and is named for its characteristic expression of a dilute coat color. LFS is a recessive genetic disorder causing newborn foals to have problems standing, often after a difficult birth. Clinical signs include seizure-like limb rigidity, hyperextension of the head, neck and spine (opisthotonus) and involuntary movement of the eyeballs (nystagmus). All affected foals are usually euthanized within days after birth. The DNA test for detecting LFS was developed by Cornell University.

SCID

Severe Combined Immunodeficiency (SCID) is a fairly common recessive gene defect in Arabian and Arabian cross breeds. The carrier frequency is at about 28% which means that one out of every three to four adult Arabian horses carries the gene for this deadly disease. Similar to the "bubble boy" condition in humans, the disease is always fatal in affected foals, which are born with no immune system, are unable to fight infections, and die within a few months. The discovery of the genetic cause of SCID in Arabian horses was made by Dr. Lance Perryman and Dr. Katherine Meek at North Carolina State University and the University of Texas in Dallas. (VetGen LLC)

JEB1, JEB2

Junctional epidermolysis bullosa (JEB1, JEB2) is an inherited disease also known as Red Foot Disease or Hairless Foal Syndrome. Two separate genetic mutations have been identified: JEB1 occurs in Belgian draft horses and related draft breeds and JEB2 which occurs in American Saddlebred horses.

This inherited disorder is caused by a mutation that inhibits the body's ability to produce certain proteins responsible for holding the skin onto the body. Affected horses are typically born alive with little symptoms, however, after 4 to 5 days of age the foal begins to develop lesions at the pressure points. These lesions quickly grow larger, creating patches all over the foal's body. Because the same protein responsible for skin adhesion is also involved in the hoof attachment, the foal also begins to slough the hoof wall, and the hoof may detach. Oral ulcers are also seen with JEB, as well as foals being born with front teeth. Foals that do not die from infections are almost always euthanized by 8 days of age for humane reasons.

JEB is inherited as a recessive trait. Horses that carry two copies of the mutated gene (homozygous recessive) will develop the disease. Animals that carry one copy of the mutated gene and one copy of the normal gene (heterozygous) are carriers of JEB. Carriers do not develop the disease and have normal epithelia. French scientists isolated the gene mutation responsible for this and developed the test for it. (UC Davis, UKY and Animal Genetics Inc)

MYOTONIA

Myotonia is another inherited neuromuscular disorder that was identified in New Forest ponies by the University of Kentucky and a Swiss researcher. It is another autosomal recessive mutation, which means a carrier is not affected, but if 2 carriers are bred together, there is 25% chance of producing an infected foal, which will be weak and exhibit gait abnormalities. (UKY)

Responsible Test Result Applications: R (recessive)

OK so you tested. One of your most valuable breeding Curlies had a positive test returned. He or she is a carrier. It will probably be a recessive mutated gene disorder, because any horse you planned to breed is not showing any signs of illness. Assuming that, now what? Does this end the future for that animal, that would have been such a valuable contribution to our rare breed? I have compiled feedback on this question from the equine scientists who work with these genetic tests and research universities.

A disease caused by an autosomal recessive trait means a foal will only be affected if it inherits the mutation for the disease from both parents. Horses that are carriers have only 1 copy of the mutation, but do not have any symptoms associated with the disorder. This makes DNA testing important to screen for carriers and prevent a miserable or fatal disorder. (Animal Genetics Inc)

If the disease your horse is positive for is an autosomal recessive disease, matings between two clear animals as well as matings between a clear and a carrier animal will NEVER produce an affected animal. By definition, carriers of genes for autosomal recessive disorders are completely free of any clinical signs of the disease. That is, carriers do not have any negative consequences to their health or performance. If two such carriers are mated, there is a 25% chance that the foal will be clear, 50% chance that it will also be a carrier and 25% chance that it will be affected, which is an unacceptable risk. Therefore, two carriers should never be bred together.

The traditional recommendation in veterinary medicine used to be gelding of carrier stallions, to prevent other affected offspring being produced. However, this is no longer necessary and in some cases not in the best interest of the breed. Carrier animals that are breed improvers; that have all the desirable traits for which the breed is known, can now be mated to other tested animals who are clear and then never produce an affected foal. Similarly, their offspring can be tested and appropriate matings set up in the next generations without the breed ever suffering the loss of another foal to any autosomal recessive disease. In this manner, the breed still continues to benefit from all of the outstanding traits that a carrier animal may possess. Thus, the economic value of the animal should not be affected by being clear or carrier. (VetGen LLC)

UC Davis says regarding JEB, an autosomal recessive disorder: "Breeders can reliably use test results to enhance breeding strategies to avoid producing affected foals. Carriers do not need to be removed from the breeding pool. A successful breeding program can use matings of carriers (N/J) to non-carriers (N/N) without the worry of producing an affected foal."

How We Can Responsibly Use this Information:

In a perfect world, no carrier horse would ever be bred, and all diseases that we have simple tests for would be wiped out forever. Wouldn't it be great if our breed could claim no known disease genetics exist in the Curly Horse. And if you think about it, the scientists and research universities that do not discourage breeding and testing of carrier lines and individuals, will clearly reap some financial benefit of this information.

On the other hand, they definitely know what they are talking about, and are probably about as educated and impartial as any equine professional can be.

So as for breeding a recessive carrier stallion or mare, it boils down to the individual owner's personal decision. A breeder confronted with this situation will hopefully only consider breeding a carrier animal that was genuinely valuable to the genetics of the population. And the definition of a proven genetically valuable breeding horse should involve past foal crops and/or an inspection and high quality score, to avoid any possible barn blindness on the breeder's part. If a breeder follows zero-risk breeding guidelines with valuable carrier Curly Horses, they should be above reproach. If breeders are ethical, employ full disclosure, and require testing to eliminate the chance of 2 carriers ever being mated, they are breeding with the understanding that over time, with continued testing of all subsequent generations, clear horses will eventually take over a superior carrier's line, continuing only its superior genetics.

Ultimately each breeder sows his or her reputation with each decision they make. Stigma can be a concern among those who are less informed about the genetics and science of breeding. Because of that alone, some breeders may never breed a carrier animal. Any responsible informed decision is OK. The facts speak for themselves. And what the facts say are, all responsible breeders should test any potential breeding Curly Horse.

Responsible Test Result Applications: D (dominant)

Never breed: The very existence of a positive test result for a dominant mutated gene disorder, means that the horse being tested is itself affected by that genetic disease - or soon will be (other than those few that are subclinical). These diseases do not typically produce lethal foals, or they would be self-limiting and would probably have died out by now. Therefore, horses with bloodlines that are known to carry dominant gene disorders should probably be tested before raising them (if their parents are not tested) and certainly before breeding them. I believe it is safe to say that no horse with a positive dominant gene disorder should be bred.



TESTING: What, Who, Where and How Much?

Disorder	AG Inc	PMD Inc	UC Davis	VetGen	U ofMN	U ofKY
GBED (stockhorse)	\$35	\$35	\$40	\$50	-	-
HERDA (stockhorse)	\$35	\$35	\$40	-	-	-
HYPP (stockhorse)	\$30	\$35	\$40	-	-	-
MH (stockhorse)	\$35	\$35	-	-	\$65	-
PSSM1 (widespread)	\$40	\$35	-	-	\$65	-
5 panel (stockhorses)	\$95	\$85	-	-	-	-
CSNB (Lp horses)	\$40	-	-	-	-	-
OLWS (frame overo line)	\$25	\$25	\$25	-	-	-
CA (Arabian)	\$40	-	*\$40	*\$50	-	-
LFS (Arabian)	\$40	-	*\$40	*\$50	-	-
SCID (Arabian)	\$95	-	-	*\$140	-	-
3 panel (Arabian)	\$125	-	-	*\$216	-	-

JEB1 (Belgian)	\$45	-	**registry	-	-	-
JEB2 (Saddlebred)	\$45	-	**registry	-	-	\$50
Myotonia (New Forest)	-	-	-	-	-	\$50

AG Inc: [Animal Genetics Inc](#), Tallahassee, Florida
PMD: [Progressive Molecular Diagnostics Inc](#), Tioga, Texas
UC Davis: [University of California, Davis](#), CA
VetGen: [Veterinary Genetic Services](#), Ann Arbor, Michigan
[University of Minnesota Equine Center](#), Neuromuscular Diagnostic Lab, St Paul MN
[University of Kentucky Gluck Equine Research Center](#), Animal Genetic Testing & Research Laboratory, Lexington KY

- * *multiple animal /test discounts when ordered together*
- ** *registry: Must these tests must be ordered through a horse breed registry?*

This report does not include every simple DNA genetic testable equine disease, but it includes all that are common enough that we need to be aware of. Interestingly, there is even a simple genetic (hair sample) test that can be done to determine a horse's aptitude for soft gaits (researched by Gus Cothran, Texas A&M, tests at UC Davis, U of KY). The advances made in equine genetic disease diagnosis are exciting, and all responsible breeders need to remain aware of any recent developments.

As you may have noticed, some labs concentrate on providing the diagnostic tests to horse owners, while some are the actual research labs. Typically the lab that discovers a new test for a disease will patent it, offer that test to the public, and sell the license to one or more other diagnostic labs. There are more labs than I have listed here, in the USA and Canada, and offshore. Other labs that I found online did not offer any more tests than those listed above, but some labs are gearing up to add more tests in the future, so this list is subject to change. I have tried to include all the current major labs and the best prices offered for comparison in this report. A current internet search will get you the most recent information.

Before testing, make sure the lab you use is "acceptable" to your horse registry. It would be unfortunate for any breed registry to hijack access to any particular breed-associated disorder (JEB)?, and hopefully that is not and will not be the trend. The danger of registries requiring and policing compliance with testing rules can also have unintended results in those registries only accepting test results from certain "approved" labs, which is not helpful to the horses, their owners, or the cause. In some cases it might have to do with pricing, when the registry poses as a retailer, or is granted a lower (wholesale) price by a particular lab. Hopefully a reciprocity policy will continue to grow between all registries and labs in the future. With equine disease identification and diagnostics advancing rapidly, registry policies may become subject to changes as well. This is a dynamic and important issue. Registries are required to serve their membership, and they are also required to protect their breed of horse. To avoid these two missions becoming at odds with each other, breeders need to step up, become proactive and take the initiative to direct their registries to legislate protection of the genetic population in their breed, with rules that will protect the breed, support responsible breeding practices, and avoid undue financial burden.

Other Diseases?

This report deals only with those disorders that can be diagnosed with simple equine genetic tests done from hair samples. Of course there are other inheritable equine diseases and disorders that are not so easily diagnosed as with these inexpensive and simple genetic DNA tests. These include such diseases as PSSM Type 2, DSLD, and unfortunately plenty more, that may be common enough to be or become a threat to the Curly Horse. As breeders we need to stay informed about *any* breed-related or genetically heritable disorders. Constant vigilance by staying informed of the latest research will be the key to helping keep the Curly Horse as free from inheritable disease as possible.

In Conclusion

The information in this report leads to a few general points for all Curly Horse breeders to consider concerning testable inheritable disorders:

- Never breed 2 untested Curly Horses together
- Any Curly Horse that is intended for breeding should be tested by any simple DNA test that is warranted by its pedigree
- The above rules can be disregarded for any offspring of 2 tested clear parents
- To that end, breeders can use [AllBreedPedigree](#) to record any known test results for each Curly Horse entered in the database
- Breeders should stay informed & aware of symptoms of *any* possible diseases or disorders common to bloodlines they breed
- Breeders must be proactive in this issue (work both with their registry and independently to promote safe responsible

breeding practices)

This report was researched and compiled by [Donna Grace Vickery](#). I will try to keep this report updated as more information comes to light. I would welcome any help you'd care to contribute to this important effort for our breed. We need to keep this information as current and accurate as possible. I am not a geneticist, so if I have committed any mis-wording of scientific genetic terms when compiling information in this report gathered from a number of sources, please send me a correction. I have tried to credit all sources I used in the area where I applied their information. Please send any updates / corrections to donna@curlyhorses.com. Thank you!

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