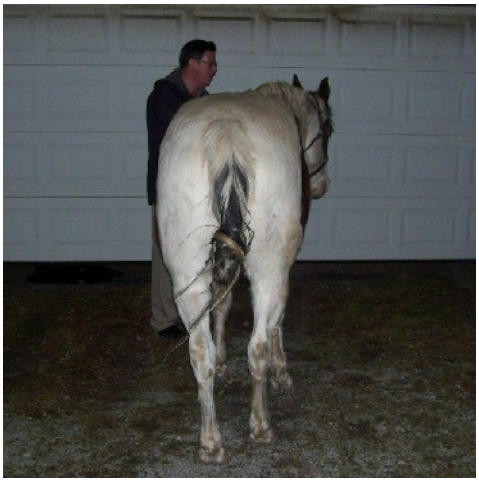
A recent post on FB questioned the possibility that their horse got EPM, equine protozoal myeloencephalitis, after he was vaccinated by their veterinarian. There were responses that led me to believe this was a repeated myth. And it is a myth. Vaccines don't cause EPM, vaccines can cause polyneuritis. We took this up in our Myth Busting series.

The relationship between vaccines and neurological signs was first on my radar when Ft. Dodge was marketing their EPM vaccine in 1999. The horses in the safety study showed clinical signs after vaccination and that concerned the vaccine developers. I didn't think of it again until one of my clients used the vaccine with negative results and was taking legal action against Ft. Dodge. I pulled in Dr. Frank Andrews a consulting veterinarian I worked with in my Bayer clinical studies. He negotiated the settlement. I didn't think much about vaccine related reactions until 2012 when we met Blue Eyed Playboy.



This story was first published in *2018 Researching EPM*. It was near Christmas 2012 when I first met Blue Eyed Playboy by email. His case was unforgettable. *The nightmare for his owner began in March of 2010. The veterinarian was summoned because "Blue" was stiff. Radiographs and vitamin E levels were normal. He didn't improve so he was radiographed again in July and had fluoroscopy performed in September. As costs for diagnostic tests increased, Blue continued to get worse. No cause for his clinical signs could be found. By March of 2011 he was admitted to Purdue's Veterinary Clinic. His clinical signs were hypermetria in his forelimbs and weakness in the rear limbs. He would fall in his field. The working diagnosis was EPM although his "EPM panel" at UC Davis came back negative. Despite the negative testing he was treated for EPM but the expensive EPM treatment he was given didn't help him.*

Over the next year he had his head, back and pelvis radiographed and injected, and he received a diagnosis of psoas injury. They were told he had Lyme disease and he was tested for PSSM. He went back to Purdue in July 2012 with a complaint of a "shifting leg" lameness. More diagnostics. More radiographs. More costs. Injections of ankles and feet didn't produce a lasting effect. The Purdue clinicians determined he was weaker, more ataxic, and the hypermetric gait persisted. He was injected in both of his stifles and both sacral-iliac joints. Blue was failing. The prognosis was poor and euthanasia was recommended.

His family couldn't let him go. In December of 2012 we tested Blue with the ELISA tests I developed based on the three serotypes of S. neurona. He was negative for S. neurona antibodies but improved to almost normal in less than two weeks using our recommendations.

He "relapsed" 3 months later and again responded to treatment. Over the next 3 years Blue's owner would call when he relapsed and we'd catch up. It was confusing, Blue responded well to treatment and get back to trail riding--only to relapse again.

Why did Blue have chronic relapsing signs that would respond so well to treatment? He didn't have *S. neurona* encephalomyelitis, EPM. He was a conundrum for his veterinarian. He was a puzzle for Purdue clinicians. He was a frustration and heartache for his family. And for us he was a challenge; we knew we could alleviate signs for 3-12 months. And we knew we'd hear from his family again. This wasn't enough, we wanted to understand more.

Section summary

A detailed investigation into a progressive equine neurological condition revealed a strong link between autoimmune responses and vaccinations in horses. This research utilized extensive data analysis and advanced testing methods to identify disease markers and improve diagnostic accuracy. The newly developed tests included the Sidewinder, an MP2/MPP ELISA.

Polyneuritis equi

My clinical database became a wealth of information, and a search revealed 19 horses with histories similar to Blue. I checked up on them by calling the veterinarian and found that eighteen of the 19 horses had been euthanized for similar progressive signs and no resolution or treatments. The nineteenth horse was alive when I called but not surprisingly, succumbed in a few months after our call. And these cases led me to *polyneuritis equi*.

I compiled data from the literature, made recombinant proteins based on useful papers I read, I collected antibodies from horses as well as immunized lab animals and mapped protein epitopes on some specific proteins. These tools let us understand and modify the ELISA test that was first published by Fordyce in 1987, *Use of an ELISA in the differential diagnosis of cauda equina neuritis and other equine neuropathies*. Our data base algorithm interrogated the *thousands* of records in our database and selected a group of horses that might fit with a provisional diagnosis of PNE. A group of normal horses were also selected. I was looking for horses with hemi-paresis, a one-sided weakness, or to be more descriptive they had a "sidewinding" gait. The data set was evaluated in 2014. The Sidewinder algorithm predicted disease with uncanny accuracy.

I presented my PNE findings and discussed the progression of disease at the EPM society meeting and then published in the *International Journal of Applied Research in Veterinary*

Medicine in 2015. It was interesting that as C-reactive protein *increased* (a non-specific measure of inflammation) in these horses, the statistical probability that the sample would contain antibodies against equine myelin P2 protein increased. Not all horses with a diagnosis of EPM had anti-myelin P2 antibodies, but many did. There was an association with *S. fayeri* anti-toxin as well. We had the tools to continue to explore what was going on with Blue and we used his case to make more associations.

We last heard from Blue's folks in 2015. Life had been tough on the family and Blue's expenses hadn't helped. Our last memories of him are from a video we received. Blue's owner was astride as he ambled down a peaceful forest trail, birds were singing in the background. This was prior to his last relapse. Had we known in 2012 what we know now I have no doubt we would have a different outcome for Blue. Blue had polyneuritis equi and his disease was associated with his vaccinations.

It took a deep dive in the database to find out why. I found in 3% of the cases that had similar case histories and had anti-myelin P2 antibodies their clinical signs were associated with vaccines. I selected horses with the correct "pattern" of relapse and from those asked the owners to vaccinate their horses and let me know what happened. I was sure they would relapse and by now I knew how I could rescue the horses after vaccination. Some owners agreed to help but most didn't want to risk it, they said if I could prevent the episode that is what they would rather do.

After I got enough cases to evaluate I knew that a small number of horses reacted to the equine dermal cells used in the production of equine vaccines. After vaccination, these horses got a severe autoimmune reaction. The reaction can manifest in a short time, 2 weeks, but most often we found it took 6-8 weeks. The timing of the reaction makes it difficult for veterinarians and owners to make the association between vaccinations and signs. A complication is the reaction is dose dependent and once a horse is sensitized they produce auto-antibodies. Most horses were older (so they had numerous insults) but some were young, and almost all were over-vaccinated. We know this now but a few years ago vaccine associated reactions leading to PNE was a secret that needed to be revealed. Blue's legacy is that others benefited from his misfortune. He made a difference by helping me figure out this mystery.

In summary, the vaccines given by the veterinarian do not cause EPM. The dermal cells used to grow the vaccines released proteins that sensitized the horse to an inflammatory cytokine receptor, IL6r. This receptor increases CRP, an enzyme, that releases more IL6r into the

circulation perpetuating the inflammatory reaction. It is known that *S. fayeri* toxin stimulates host cell macrophages to increase CRP and is a second pathway to PNE. A disease model for Guillian-barre syndrome in people is PNE in horses and lab animals vaccinated with IL6r or given dermal cells succumb to autoimmune experimental encephalomyelitis.

Horses that are sensitive to vaccines don't respond to anti-protozoal drugs. They may or may not be seropositive for *Sarcocystis neurona.* They are responsive to treatment for PNE. Treating the horse prior to stimulating the autoimmune reaction can prevent clinical signs in horses.