

THE SQUEEZING CURE

**HOW 20 MINUTES AND A LENGTH OF ROPE CAN
SAVE THE LIFE OF A "DUMMY" FOAL**

By Christine Barakat

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UC Davis School of Veterinary Medicine professor and researcher
John Madigan inspects a maladjusted foal at Victory Rose Thorough-
breds in Vacaville, CA on January 21, 2015.

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Witnessing the start of a foal's life can be a profoundly moving experience. From lying wet and shaky in the straw, to scrambling to rise, then nickering to his dam as he nudges for his first meal, the newborn is an adorable combination of vulnerability and determination. And in an amazingly short time---as little as 30 minutes or at most an hour or two---he is ready to explore the world, even while instinctively sticking close to his dam's side. If you've ever been able to watch the transformation in those early hours, you know it can be breathtaking.

Equally powerful, in a completely different and heartbreaking way, is the sight of a foal who doesn't do well in the first hours of life. In some cases, for no clear reason, a youngster seems to get "stuck" in the earliest stages of the developmental timeline. He isn't quick to rise and gain coordination. He doesn't nurse and may not even acknowledge his dam at all. He wanders the stall, bumps into walls and seems unaware of his surroundings. He is a "dummy foal," the common term for a condition technically known as neonatal maladjustment syndrome (NMS).

Between 3 and 5 percent of foals are affected, and all will die without intensive supportive treatment. An NMS foal needs round-the-clock care, with bottle-feeding every two hours or more frequently. Severely affected foals may need critical care, including help regulating body temperature. It's an exhausting and often expensive ordeal.

When intensive care is available, most NMS foals who survive their first week of life make a dramatic, sudden improvement---literally turning around within hours---and go on to live a normal, healthy life. Those who don't improve are euthanatized. And there is no way to predict which category a dummy foal will fall into. All that could be done was wait and hope---until now.

John Madigan, DVM, has been treating foals with NMS since he started the University of California---Davis' neonatal intensive care unit in 1986.

"For a long time, everyone's best guess was some type of hypoxic injury from a traumatic birth," he says. "That would be a case of the foal not having enough oxygen at birth. But in foals so severely affected to be staggering around their stalls, you'd expect some neural cell death and that they would be

By Elizabeth Sharp

I volunteered to write this article two months ago, but decided that the EQUUS® article from last year did a wonderful job of covering the technique and especially all the scientific background, so we elected to share their article with our readers. I would however like to add my personal experience with this technique, having had it done by Dr John Madigan on one of my colts the year before last, with excellent success.

Since I live less than an hour from UC Davis, and my vet trained there, it is our go-to place for things we can't handle at home. When Prins had issues with nursing and seeming detached in general, my vet Dr. Susan Gillen, called Dr. Madigan, and we loaded him up with his mom and headed down. Dr. Madigan explained his theory, and we applied the rope, and gently laid him down. His mother had no issues with this procedure at all. During the sleep period, Dr. Madigan explained the theory, what had been done to prove the theory, and how it may be used in other species. In about 25 minutes, when pressure was released, he popped up, and willingly nursed on his own for the first time. It was amazing to witness, and when you think of the dire possible consequences of not being able to do this, it is truly a miracle.

At the AGM in Texas we had occasion to recommend it again, to Gerben Steenbeek's son, with a colt having problems. It took two tries, but the pictures of him with this article validate the procedure again. Prins's experience was recorded and shown at the AAEP convention in Las Vegas, in December 2014, when Dr. Madigan gave a presentation. I have the link to that presentation here. Dr. Madigan, who also is heavily involved in large animal rescue efforts, cannot be praised enough for the creative innovative research he does, and for continuing to teach upcoming veterinarians at UC Davis.

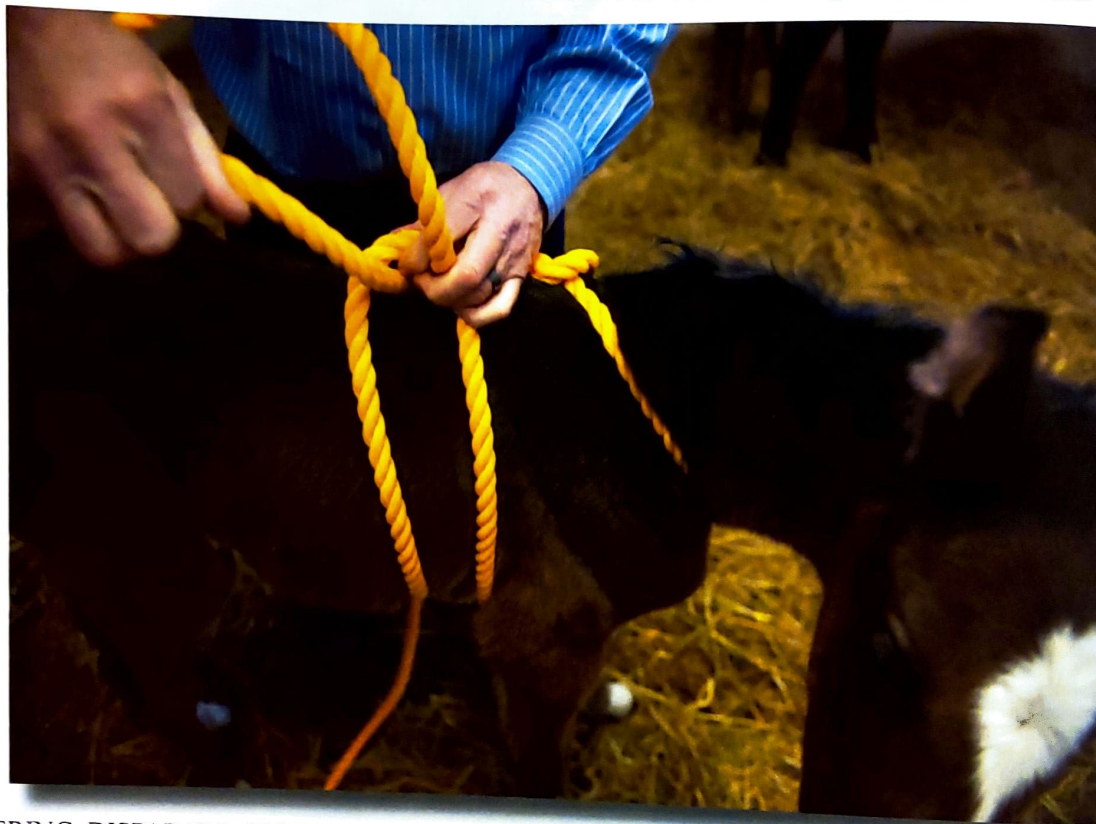
<https://youtu.be/nAqMDjuLwkc>

affected for life. Yet they aren't. They recover completely and very quickly---I'd have cases where the owners would tell me on a Saturday afternoon that they couldn't continue to keep the foal in intensive care at the clinic much longer. Then on Sunday morning, I'd call them to say the foal is bouncing around and perfectly fine. That doesn't fit the hypoxia theory, and that's always bothered me."

In the two decades since, Madigan has learned that "everyone's best guess" is far from correct.

high levels right after birth that dropped quickly, but in two maladjusted foals, those levels didn't drop. They stayed high."

Back in the lecture hall, the veterinarians continued to refer to progesterone derivatives that sedated unborn lambs. "It kept coming up in the conversation like it was a completely accepted and understood thing, which I guess it was among this group of sheep experts," says Madigan. "But I'd never heard of this before, and I was really intrigued. I remember the whole room turning to look at me when I started



GATHERING DISPARATE CLUES

Madigan began to unravel the mystery of NMS in 2005, when he crashed a scientific lecture in New Zealand while he was on sabbatical. "I was at a veterinary convention when I walked into a talk on in utero lamb conscious perception, of all things," he says.

The speakers were discussing the consciousness of unborn lambs in the context of slaughter welfare issues, which wouldn't seem to have much relevance to an equine veterinarian, but one small point caught Madigan's attention: "They were talking about progesterone derivatives acting as a sedative on the fetus, almost to an anesthetic level. These were natural hormones that kept the lamb unconscious in utero, and there was even a commercial progesterone derivative available to mimic that state," he says.

Madigan's interest was piqued because of a paper he had read in 1992 that documented total progesterone levels in newborn foals: "The researchers found the foals had very

asking questions. I'm not sure what they thought about the American horse doctor who wandered into their talk and wanted to know more."

These hormones, Madigan learned, keep lambs unconscious as they are born. "It made sense to me that foals might experience the same thing," he said. "You'd want a foal to be very still as it's coming through the birth canal. A sedative neurotransmitter might be at work and somehow it gets 'switched off' after the foal is born, allowing him to become fully conscious and stand. But what if it didn't switch off?" When Madigan returned to California, he asked the state racing laboratory to create a test to quantify a specific subset of progesterone levels in newborn foals. "I asked them for an assay that would measure neurosedative progesterones," he says. "We actually started calling this research 'The Search for the Switch.'"

Meanwhile, Balazs Toth, DVM, a graduate student working under Madigan, began some research of his own. "We needed



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Joe Proudman / UC Davis©
 UC Davis School of Veterinary Medicine professor and researcher John Madigan squeezes a maladjusted foal at Victory Rose Thoroughbreds in Vacaville, CA on January 21, 2015. The squeezing simulates the foal's trip through the birth canal. Madigan's research has found the squeezing to help the foal recover from Neonatal Maladjustment Syndrome, sometimes within hours.

a short-term project and decided to look into the so-called 'flop reaction' that newborn foals have," explains Madigan.

"Anyone who has restrained a neonatal foal knows that if you can get your arms around their chest and hindquarter and hold them tight, they literally drop, as if they are sleeping," he explains. "It was thought to be some form of cataplexy or narcolepsy. It happens in other animals, too, and even humans; any new parent quickly learns that swaddling a baby tightly will help put them to sleep."

To learn more about this phenomenon, Toth and Madigan wanted to measure the brainwave patterns, and sought the help of veterinary neurologist Monica Aleman, DVM, PhD, to do so. They also wanted to measure hormone levels and other physiological parameters of a newborn foal as he was being squeezed. "The problem was we couldn't hold the squeeze long enough to collect enough data," says Madigan. The solution to that problem would come from an unexpected source.

"Cattle texts dating back to the 1950s actually describe a half-hitch rope system for putting on a calf that will cause him to flop down and lie there," says Madigan. Toth's study was redesigned to apply the same rope technique to newborn foals. "It's important to understand that you aren't restraining the foal with the ropes and making it impossible to move," says Madigan. "Instead,

the pressure from the ropes induces a state where he doesn't even attempt to move---he almost seems to be asleep."

The researchers used the squeeze technique on eight one-day-old foals, carefully applying the rope, then pulling it tight. All fell to the straw in a sleepy state within minutes and remained there for 20 minutes as the gentle pressure was applied. After the squeeze was released, the foals perked up in a few minutes and rose to their feet, completely normal. Before, during and after each squeeze session, researchers monitored the foals' heart rates and brain waves and drew blood samples for analysis.

The EEG data showed that the brain waves of the squeezed foals were consistent with sleep. The team began to refer to the state as "squeeze-induced somnolence" or "SIS."

The blood tests yielded more fascinating data: "With squeezing, we saw a huge jump in foals' hormone levels," says Madigan. "Some people thought it was a stress response, because we were handling them, but I had a hard time believing that because these foals in no way looked stressed. They were literally sleeping. In the back of my mind I kept turning it over in my brain, thinking there had to be another explanation."

FLIPPING THE SWITCH

The explanation Madigan was looking for began to emerge as pieces of a larger puzzle began coming together: "I thought about what I'd learned in New Zealand---and our search for the hormonal switch that causes that sedated pre-birth state. Then I considered what we'd been observing in the squeeze studies, which was essentially a return to that state. I began to wonder, what if the squeeze was the thing flipping that hormonal switch?"

The more Madigan thought about it, the more sense it made. "As a foal travels through the birth canal, he's being squeezed. And that's exactly the time you don't want him moving around. If the pressure in the birth canal was inducing this hormone surge, it would keep the foal quiet. Then, once he's born and the pressure is removed, the hormones would get the signal to drop and he'd wake up."

In a foal with NMS, however, Madigan postulated, the



message to "wake up" is never received. "Many of these foals are born very, very quickly. I often hear from owners that they went to the house for 10 minutes and came back to find the foal. Maybe in that rush there's a crucial moment that doesn't happen---the moment when the hormones get the signal to drop because the foal is beyond the birth canal. If you see these foals, it is almost as if they don't know they



The Healthy Friesian

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were born. They are still in that sleepy, in utero state and can't seem to snap out of it."

What if, Madigan thought, dummy foals simply never had that hormonal switch flipped? And what if squeezing the foal could flip the switch manually?

The first foal Madigan was able to test his theory on was born at Victory Rose Farm in Vacaville, California. Overseeing the birth of about 70 Thoroughbred foals a year, owner Ellen Lee Jackson had long relied on Madigan's services on referral by the farm veterinarian. She had also helped with a few of Madigan's earlier research projects and was already familiar with the squeeze technique.

"We give all of our foals hyper-immune plasma on their second day, just as a precaution," says Jackson. "And Dr. Madigan had shown us how the squeeze technique could be used to make that easier, and it really does. They just lie down quietly and let us work, so we'd been using that for a while already."

Jackson was skeptical, however, when Madigan called to tell her that he thought the squeeze technique might also be helpful for dummy foals. "I was a naysayer," she says. "Dr. Madigan is a really smart guy and a creative thinker, but this just seemed a little too out there, even for him." Madigan asked if Jackson would call him the next time a suspected dummy foal was born. She agreed, and it wasn't too long afterward when a filly was born and immediately began having trouble.

The name of the filly is lost to both Jackson and Madigan, but they remember the experience vividly. "The filly hadn't nursed on her own and was very reluctantly taking a bottle," says Madigan. "And when she wasn't down, she was just bumping around the stall with no interest in her dam or awareness of where she was." The farm veterinarian and staff had been supporting the filly as they would any foal with NMS and preparing themselves and her owner for the long, expensive and uncertain road ahead.

When Madigan arrived at the farm, a small crowd gathered. "I had come down to the barn because I just had to see him try this crazy idea myself," says Jackson. Madigan carefully fastened the rope around the filly's chest and in a half-hitch pattern along her body. As he applied pressure, she dropped to the straw as expected, in a sleep-like state.

"I held the pressure for 20 minutes," says Madigan, "which is about the time a foal is normally in the birth canal." Then he released the pressure, carefully unwound the ropes and stepped back to see what would happen.

Within minutes, the filly scrambled to her feet and nickered to her dam. "That was the first time she'd ever nickered," says Jackson. "I couldn't even speak I was so stunned." The dam answered and the filly walked over, found her way to the udder and began nursing on her own.

"It was amazing and incredible and every other adjective that doesn't seem to do it justice," says Madigan. "It was as if she'd just been born, following the typical developmental timeline, with no signs of maladjustment at all." The effects were lasting as well; the filly developed entirely normally physically and behaviorally from that morning on.

This meant that the squeeze of the birth canal could very well be what flips the hormonal switch, releasing progesterone derivatives that keep foals sedated during birth. It also suggested that if that condition isn't reversed, and the sedative hormone levels do not drop, a manual squeeze from humans could replicate the birth process enough to restore a normal, healthy state, with no long-lasting side effects.

A final clue came not much later, with a mixture of hormones based on the racing lab assay Madigan had requested when



"At the AGM in Texas we had occasion to recommend it again, to Gerben Steenbeek's son, with a colt having problems. It took two tries, but the pictures validate the procedure again." - E.Sharp. (Friesian photos not part of original article)

he returned from New Zealand. "We essentially had a syringe full of the progesterones that we suspected keep the foal sedated through birth," says Madigan. When he injected healthy foals with the hormones, they instantly went into a dummy-like state. As the hormone levels declined over the next few hours the foals returned to normal. "The fact that we could induce the state with hormones, then reverse it by allowing the injected hormones to decline suggested the hormones were the culprit for maladjustment syndrome. It wasn't just a crazy idea at that point. It seemed a valid theory, with scientific evidence to back it up, that was leading to a real breakthrough in the treatment of these foals. It doesn't get much more exciting than that."

Madigan is continuing his research to learn more about the physiological chain of events that leads to NMS. "We still don't know why some foals aren't making the transition from intra- to extrauterine life successfully," he says. "There are 35 different neurosteroids that could be involved and very specific areas of the brain. There's also a possibility it has to do with fetal circulation. There's still a lot left to investigate."

INTO THE FUTURE

Randomized clinical trials of the squeeze technique are in progress, but maladjusted foals can't always wait for research. Fortunately, they don't have to: Madigan has already personally used the squeeze technique on 12 NMS foals so far, and in each case, they eventually emerged from their maladjusted state. "We are choosing the foals to do this on carefully," he says. "If a foal is septic or truly has a hypoxic injury, this isn't going to help. Those foals have other issues that need to be addressed."

He adds that not all NMS foals are "fixed" after the first squeeze, either. "There have been some cases where we've had to squeeze them daily for three or four days," he says. "They get a bit better and then revert after each time. I'm not sure what is happening in those cases, but we are looking into the bloodwork to see if the hormone levels bounce back up between squeezes."

In addition to trying the technique himself, Madigan is spreading the word to other veterinarians about the potential benefits of squeezing maladjusted foals. He gave a three-hour presentation at the American Association of Equine Practitioners Convention last December and he has made information available to veterinarians that outline exactly how to apply the ropes. As a result, other practitioners have begun doing the technique with success (see "A Letter of Thanks," page 66) and sharing their experiences with each other. "One of my goals is for every equine veterinarian to know about this," he says. "And for them to feel confident

giving it a try in suspected cases of maladjustment. It has the potential to completely change how we approach these foals."

And while he is excited about the successes, Madigan is realistic about the many challenges a newborn foal might face. "Some cases that fall into the 'maladjusted foal' category can have had some degree of hypoxia and infection, which can produce very significant metabolic problems and require intensive care," he says. And in a study of foals admitted to neonatal critical care units, Madigan found that septic and other very ill youngsters have switched back to producing neurosteroids after their levels initially dropped. All of this, he says, underscores the necessity of further research.



◀ The Squeeze Cure was given to this young colt belonging to Gerben, Ria and Jordan Steenbeek, named Brent. "Now he looks very healthy, alert, and likes to play and run around." Photos courtesy of the Steenbeeks.

(Friesian photos not part of original article)



Madigan adds that there's the potential to develop a drug that would reverse the hormonal state---a medicinal way to flip the switch, as it were. "There's a neonatal maladjustment condition in giraffes," he says. "They get hypothermic and just start fading. Zoo veterinarians dealing with this have had some success with medication to change hormone levels by blocking the synthesis of specific neurosteroids." Whether or not a similar medication can be developed for horses is unclear, but for now Madigan says he is going to continue focusing on using pressure to help the foals transition to life outside the womb.

In the space of a decade, Madigan has not only unraveled many of the mysteries behind NMS but has devised a stunningly simple method for treating the condition. As a result, the future of affected foals no longer depends on physically and/or financially draining intensive care. Even as research continues, his technique for "waking up" dummy foals is saving lives. "I'm super excited for what all of this might mean and what we are going to learn," he says. "But the fact that it's working for some foals right now, even before we totally understand the mechanism, is the best news of all. Just this weekend, I received two calls from practitioners who tried this and both foals got better immediately. I love getting those calls."

The FHANA Health Committee

The FHANA Health Committee is dedicated to promoting the health of our Friesian horses and providing information to the membership. The Health Committee: Katherine Fox, DVM; Elizabeth Sharp; Ann Blakey, PhD; Monica Muehlhause-Horn; Krista Porter, DVM; Carol McCoy-Brown; Kris Fulwiler; Laurie Bell; Amy Austin.