

Zweig

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ARIEL BULLION/UNIVERSITY PHOTOGRAPHY

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Evaluating Antibiotics
Used to Treat Lyme Disease

Equine Reproduction Bolstered by Two New Faculty

To further strengthen the research and clinical services in equine reproduction, two reproduction experts—Jonathan R. Hill BVSc, MACVS, PhD, and Dietrich H. Volkmann BVSc, MMed Vet—recently joined the faculty. Both come from overseas and bring a diverse background in theriogenology. Hill comes from Australia where he earned his veterinary degree in 1985 and worked in private practice for 10 years—most recently as a partner in a ►

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rural mixed practice and an ovine and bovine artificial breeding center. To delve further into reproductive medicine, Hill completed a residency in theriogenology at Texas A&M in 1998 and a PhD degree in reproductive physiology in 1999. While at Texas A&M, Hill was one of the first researchers to clone a calf from adult cells. He also studied whether oxytocin could improve pregnancy rates after insemination in mares (it didn't) as well as testicular degeneration in stallions.

Since joining the Cornell faculty in late 1999, Hill has been studying pregnancy losses in large animals, in vitro fertilization and embryo transfer in sheep, and ways to improve nuclear transfer (cloning) by studying the abnormalities in cloned embryos, fetuses, and calves.

"We find, for example, that most pregnancy losses are due to placenta problems, primarily a lack of vascularization in the placenta and inadequate attachment of the placenta to the uterus," says Hill. "We are trying to determine the specific mechanisms that cause these abnormalities in the first trimester."

In the future, Hill would like to study in vitro embryo production further using bovine embryos as a model. He also wants to produce cartilage precursor cells for equine joints from stem cells.

"What I'd really like to do is to make in vitro-produced and cloned embryos more viable by trying to figure out how to improve the efficiency of the techniques and the health of the offspring," he says.

Volkman grew up on a beef ranch in Namibia and was educated at the University of Pretoria in South Africa, where he worked until 2000. His most recent post was as head of the Department of Theriogenology.

"I've always been interested in reproduction, and when given an oppor-



NICOLA KOUNTIOPES/UNIVERSITY PHOTOGRAPHY

Hill studies the abnormalities in test-tube embryos, which are a major stumbling block to using cloning as a reliable means of reproduction.



CHARLES HARRINGTON/UNIVERSITY PHOTOGRAPHY

The Harry M. Zweig Memorial Fund's outstanding commitment to equine research weighed heavily in Volkman's decision to come here.



DIETRICH VOLKMAN

Immediately after its birth the foal and mare lie still for several minutes, allowing the umbilical cord to remain intact and functional. Volkmann's research aims at identifying the purpose of this arrangement.

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Jonathan Hill

tunity after vet school to do research in equine reproduction, I grabbed it and never looked back," says Volkmann.

In South Africa, veterinarians must learn about all species, so Volkmann conducted research across many veterinary species, including dogs and sheep.

"As we learn details about one species, we may or may not be able to

apply them to other species," says Volkmann, who joined the college faculty last year.

He is conducting research on epididymal sperm preservation, a process that is used when important breeding horses are castrated or put down for various reasons.

"We are exploring why sperm from the epididymis (the duct in which mature sperm are stored) are different from ejaculated sperm. We are trying to find out, for example, the role of the seminal plasma. Is the fluid of semen important for fertility or not? We assume it is not, but then what is its role?"

To date, epididymal sperm have been frozen successfully and fertility trials are in progress.

Volkmann also is testing drugs that induce ovulation in mares to give breeders more control in trying to breed their mares with frozen semen, which is viable and able to fertilize for only a very short time. Deslorelin is one drug he is looking at. This time-released implant induces ovulation. Volkmann thinks it may continue to

"Is the fluid of semen important for fertility or not? We assume it is not, but then what is its role?"

Dietrich Volkmann

be released in the body for too long, thereby inhibiting mares from coming back into heat if they fail to conceive at the induced ovulation.

Volkmann also is studying the mechanisms for the detachment of the afterbirth after foaling, as premature detachment can suffocate a fetus and delayed detachment puts the mare at extreme risk.

"We also are looking at the recent abortion syndrome in Kentucky," says Volkmann. "Last summer, hundreds of thoroughbreds lost their foals in late pregnancy and we don't know why."

At the same time, many other mares that had already conceived (a new pregnancy) in the spring were also losing their fetuses.

Volkmann is part of a research team that is analyzing blood samples from the mares that lost their pregnancies. In an early pregnancy loss, the mare loses its placenta and fetus but continues to secrete a hormone, equine chorionic gonadotropin, that prevents her from coming into heat again for up to 100 days. By that time, the breeding season is usually past and the mare will go barren. Volkmann hopes to figure out how to manipulate the hormonal environments of mares that have lost their fetuses so they will return to heat again more promptly. ■

Chang Evaluates Antibiotics Used to Treat Lyme Disease

Lyme disease persists as the most prevalent tick-borne disease afflicting horses, humans, dogs, cats, and cattle. The illness is caused by the corkscrew-shaped bacteria, *Borrelia burgdorferi*, and is characterized by nonspecific signs such as fever, stiffness, muscle pain, and swollen joints. Veterinarians often need to diagnose the disease by using a combination of medical history, clinical signs, risk of probable exposure, nondefinitive blood tests, and whether the signs respond to antibiotics.

When veterinarians suspect Lyme disease in a horse, they typically do prescribe an antibiotic.

"However, treatment is often prolonged, expensive, and carries some chance of toxicity," says veterinary microbiologist Yung-Fu Chang DVM, PhD.

"Although using these antibiotics is justified based on what we know about Lyme disease in other animals—such as the successful use of antibiotics for acute Lyme disease in humans—we know less about the efficacy of these medications in horses, especially those with chronic Lyme disease," he says. "Most importantly, we don't know which antibiotic would be most effective in treating the infection and its associated joint pain and swelling."

With a new grant from the Zweig fund, Chang will compare the effectiveness of two antibiotics: doxycycline and ceftiofur. To mimic infection in the wild, he will employ an equine Lyme disease model that he developed with a prior Zweig grant, which successfully infects horses with *B. burgdorferi* and causes arthritis and the other signs of a Lyme infection. First, Chang and his colleagues Thomas J. Divers DVM, Dipl ACVIM and Sean McDonough DVM, PhD will expose 10 six-month-old ponies to 40 *B. burgdorferi*-infected ticks for seven days on two separate occasions. Then

for 12 weeks, the animals will be observed for signs of illness, such as depression, fever, stiffness, and lameness. In addition, the researchers are using blood tests and skin biopsies to monitor the infection.

At the end of the 12-week observation period, during which time he will have confirmed infection in the horses, Chang will treat half of them with either doxycycline or ceftiofur. The horses will then be observed for clinical signs and monitored with blood tests, bacterial culture, and other tests. After 10 months, Chang

"Deer are not a reservoir for Lyme disease, as previously thought. Rather, deer serve as the main definitive hosts for vector ticks and provide the blood meal that adult ticks require for reproduction during the winter season."

Yung-Fu Chang

will euthanize two horses a week—one that was treated with an antibiotic and one horse that was infected but received no antibiotic—and examine and compare their tissues in detail to determine how the medications impacted the horses' condition. Chang and his colleagues will attempt to isolate the spirochetes from various tissues, such as the muscles, joints and connective tissues, nerves, brain, lymph nodes, and skin.

"This kind of information is very critical to both veterinarians and horse owners who want the most effective treatment for equine Lyme disease," says Chang, who has also worked on

vaccines for Lyme disease in both horses and dogs. He is currently evaluating the least toxic pest control products on the market for controlling ticks in home gardens. In a previous study, Chang also looked at antibiotic treatment in dogs infected with Lyme disease.

Lyme disease is the most prevalent tick-borne disease not only in the country but in the world. Most common in the Northeast, the upper Midwest, Texas, and northern California, equine Lyme disease is transmitted via infected adult deer ticks, also known as "black-legged ticks," which emerge in the fall and early spring. Ticks pick up the bacteria as larvae and nymphs when they feed on infected mice.

Signs of Lyme disease

fever

stiffness

chronic weight loss

muscle tenderness

sporadic lameness

swollen joints and limbs

panuveitis—inflammation of the uveal tract behind the eye's cornea

laminitis—inflammation of the sensitive laminae of the foot

depression

behavioral changes

loss of appetite

hyperesthesia—hypersensitivity to stimuli

head tilt and encephalitis

meningitis—inflammation of the meninges, that is the protective membrane surrounding the brain



ROBERT BARKER/UNIVERSITY PHOTOGRAPHY

Today, Lyme disease is the most prevalent tick-borne disease in the world.

"Most importantly, we don't know which antibiotic would be the most effective in treating the infection and its associated joint pain and swelling."

Yung-Fu Chang

Humans, horses, and other animals get the disease when infected tick nymphs or adult ticks feed and transmit the infection through the skin, particularly during the summer and fall.

"Deer are not a reservoir for Lyme disease, as previously thought," Chang says. "Rather, deer serve as the main definitive hosts for vector ticks and provide the blood meal that adult ticks require for reproduction during the winter season."

Until vaccines under development are approved for use in horses, owners can minimize infection by con-

trolling tick populations through daily grooming and tick removal. Ticks may also be controlled with the use of tick repellents and by keeping pastures mowed, removing brush and woodpiles, and controlling rodent populations.

"Even if we find no differences between the two antibiotic therapies or if the treatments do not eliminate the organisms, the findings still will be useful toward designing intervention protocols," says Chang. ■

The Harry M. Zweig Memorial Fund for Equine Research honors the late Dr. Harry M. Zweig, a distinguished veterinarian, and his numerous contributions to the state's equine industry. In 1979, by amendment to the pari-mutuel revenue laws, the New York State legislature created the Harry M. Zweig Memorial Fund to promote equine research at the College of Veterinary Medicine, Cornell University. The Harry M. Zweig Committee is established for the purpose of administering the fund and is composed of individuals in specified state agencies and equine industry positions and others who represent equine breeders, owners, trainers, and veterinarians.

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