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Can a Woodchuck Chuck Wood

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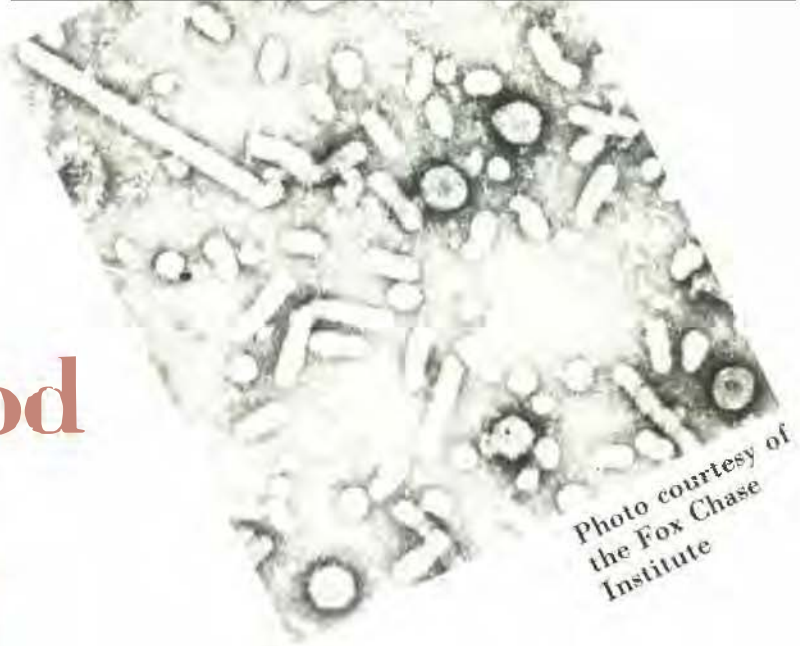

Photo courtesy of the Fox Chase Institute

Deemed a general nuisance by farmers and horse owners, the woodchuck's only claim to fame occurs once a year on Groundhog Day, when it is hailed as the official prognosticator of spring.

Now the fat, furry little rodent, whose burrowing causes damage tantamount to a Philadelphia pothole, may prove more friend than foe as it aids researchers in the hattle against cancer. As a natural carrier of the hepatitis B-like virus, experiments with the woodchuck could conceiveably lead to the prevention of primary liver cancer.

Tucked away on the wooded periphery of the New Bolton Center campus is a breeding and research colony of 100 woodchucks, established and headed by Dr. Lenore "Lenny" Southam.

"The Woodchuck Project" as it is called, was initiated in December 1979 and is run under the auspices of the Department of Clinical Investigation of the Fox Chase Institute for Cancer Research, Philadelphia. Dr. Baruch S. Blumberg, Nobel prize winner for medicine in 1976, is its director.

"Early heart-related research with woodchucks by Dr. Blumberg and colleague Dr. Robert Snyder of the Philadelphia Zoo's Penrose Laboratory revealed that the woodchuck is a natural carrier of a virus similar to the human hepititis B virus which is commonly transmitted through blood transfusions and renal dialysis," explained Dr. Southam. "Prior to this, there had been no animal model for the virus."

"Infection of the woodchuck results in acute hepatitis followed hy antibody production or, alternatively, a chronic carrier state characterized by an asymptomatic period, chronic active hepatitis and, subsequently, hepatocellular carcinoma," she continued.

Similar to the pattern of the disease in humans, as a chronic carrier of the hepatitis B virus, the woodchuck showing no signs of illness at this stage is, according to Dr. Southam, prone to liver tumor development. Noting that this form of cancer is a worldwide concern, the disease, however, is most prevalent in Africa and Asia.

"We are primarily concerned here with establishing a successful breeding colony so that we can examine the transmission and infection of artificially infected woodchuck offspring, which is one of the goals of the Project," said Dr. Southam.

Dr. Snyder had built eight woodchuck pens on the half acre site of the present colony in the early 1960's, she explained. Under a 1980 agreement between the Fox Chase Institute and the School of Veterinary Medicine, the Institute financed the construction of an office, laboratory, and animal housing areas at the vacated site. Dr. Blumberg hired Dr. Southam in 1979 to establish the woodchuck colony for his on-going hepatitis and primary liver cancer research.

"We spent the winter and spring clearing out the pens, which had grown over with thick underbrush," said Dr. Southam. "We began by trapping wild woodchucks, using box-type cages baited with apples at the entrance to their burrows. The building wasn't completed yet. We used dog cages lined with styrofoam to keep the animals cool in summer. Some of the woodchucks were left loose in the pens for breeding.

"By the end of 1980, we had 34 woodchucks and a building complete with office, lab, and animal housing, that was ready for occupancy."

At a time when woodchucks naturally hibernate, ten animals were kept inside in cages, where they were closely observed. In the hibernation state, the woodchuck's hody temperature, metabolism and heart rates are considerably lower than normal. In the summer, care had to be exercised to shield the outside caged animals from the heat. If left in the sun, the animal would die because excessive body fat keeps heat contained," explained Dr. Southam.

More woodchucks were trapped in the spring of 1981, two litters were born in the outside pens, and in 1982 three more litters were born in the cages and others are expected. With the colony's current population, there is a sufficient number for breeding and it is no longer necessary to trap, she noted.

"The major goal of the Project is the study of transmission and infection in the perinatal period, when the chronic carrier state is usually initiated," she explained. "That, of course, depends on successful breeding and births in captivity."

Other objectives of the program include the study of various modes of B virus transmission and infection, and the prevention of hepatitis and formation of primary liver tumors. A vaccine for the woodchucks is also anticipated in the course of the research. A similar vaccine was recently approved for use in humans, noted Dr. Southam.

"The vaccine would he used purely as a research tool. On the theory that the woodchuck would develop liver tumors in two to four years, a vaccine for the animals would enable researchers to know much sooner if a vaccine would inhibit the development of cancerous tumors. Conversely, humans probably wouldn't develop liver cancer for at least 30 years," she explained.

Dr. Southam is aided in the Project's lab work by veterinary technician Francie Rubin. John Elling, a high school student, has pitched in since the colony's inception. Weekly blood samples are taken from the infected woodchucks and sent to the Institute, where assays detect surface antigens in the blood.

Artificially infected for ten months, one woodchuck appears to be clinically healthy, yet blood assays show chronic liver infection. Dr. Southam performs periodic liver biopsies on the animals, which are also sent to the Institute's labs. To date, two of the woodchucks in the colony have developed tumors.

Pleased with how well the woodchucks have adapted to their captive environment, she noted that the animals are thriving and gaining weight on their vegeterian diet of Purina rat chow. Taking the visitor on a tour of the facilities, she seems to have a natural way with the animals and even has her favorite "pets" among the bevy of beasts. One animal eagerly accepts a thick, sweet substance from the tube she offers through its cage.

Although foot lesions from cage floors have been fairly common, Dr. Southam feels that the colony's woodchucks are far healthier than their wild counterparts. The animals are tranquilized to permit routine handling, she said.

While setting up the woodchuck facilities, she put her mechanical skills to work. A surgery table was fashioned from a former dentist's chair. She also designed a board on which the woodchuck is restrained for blood work. A lot of experimentation also went into the design of the woodchuck cages, formerly used for dogs. Blocks of wood help

prevent foot lesions and nesting straw is provided for the mating pairs.

Dr. Southam noted that similar research with woodchucks is being conducted at Cornell University, and there is a small colony at the Philadelphia Zoo. Dr. Blumberg is also working with domestic Pekin ducks, a species also found to carry the B-like virus, she said.

Other principals involved with hepatitis B virus and primary liver cancer research at the Fox Chase Institute include Dr. Jesse Summers, Dr. Irving Millman and Dr. W. Thomas London, all colleagues of Dr. Blumberg, who is the Institute's associate director of clinical research.

A graduate of Grinnell College in Iowa, with a B.A. in biology, Dr. Southam, formerly of Demarest, N.J., earned her D.V.M. from the Veterinary School of the University of Mexico, Mexico City. Her choice of Mexico was, in part, based on the fact that it was especially difficult for a non-resident to get into Penn in the 1970's. She did, however, complete her intership at Penn.

Before entering the University of Mexico, Dr. Southam had worked as a reproduction physiology technician. No stranger to animal colonies, she raised a colony of rhesus monkeys when she was employed by the Population Council in New York.

"I was always interested in animal models and have raised colonies of rats, rabbits, and monkeys. In fact, the breeding aspect of the woodchuck colony is what interested me in the Project," she said.

An outdoorswoman, Dr. Southam likes nothing better than to take off for a camping or skiing trip in her 1974 Kharmanghia, which she keeps mechanically well-tuned. From her Thornton home on Brinton Lake, Delaware County, she makes occasional house calls. Long term plans call for a full-time private practice.

For now, Dr. Southam enjoys her role in the Woodchuck Project and her quiet retreat in the woods. It's not uncommon for her to put in a 12-hour day, but she always finds time for a walk in the woods or a romp with her dog, who shares the premises with her along with four goats and the woodchuck pens.

Instead of grumbling about groundhog holes, it seems we owe the woodchuck a little respect in view of its sacrifice for the cause of science.

Applied Engineering in Stifle Repairs

(continued from cover)

Dr. Smith explained that it is rare when the only injured element of the joint is the anterior cruciate. In that case knee function is often regained without surgery as nature heals the injury by fibrous proliferation of the medial structure, the medial collateral ligament. This additional support compensates for the loss of the anterior cruciate. In most cases though other parts of the joint are also damaged and the natural healing process cannot overcome the pain and instability. Often the menisci are damaged and this interferes with their function as "centering devices" within the joint. Also, when the anterior cruciate ligament is torn, the "binding-like" effect ceases. The joint becomes loose and the tibia can move forward, sliding like a drawer along the joint tissue, it also can suddenly rotate. These movements irritate and erode the bone surfaces and cartilages, causing a painful inflammatory response and the development of extra bony tissue which further irritates the joint. Left untreated the condition continues to worsen and degenerative arthritis develops. As the joint thickens, movement may be impaired. To prevent these ongoing secondary changes, and to repair the initial injury, surgery can be performed.

The many surgical techniques used for the repair of a torn anterior cruciate ligament can be divided into two categories, intra articular repairs and extra articular repairs. In the first the surgeon removes the damaged ligament and replaces it with a graft, using either tissue taken from the dog or an artificial material. This procedure is quite successful and statistics show that seventy to ninety-five percent of the dogs appear to regain function of the joint. When using the extra articular technique, the surgeon stabilizes the joint by using muscles, tendons, and ligaments at the exterior of the joint and he tightens them in a manner to eliminate the joint instability. There is no attempt to replace the anterior cruciate ligament.

Dr. Smith favors the latter approach. He has developed a technique to achieve joint stability by altering the stresses and functions of two ligaments in the joint by rerouting one. He starts his procedure with the lateral collateral ligament which mainly connects the fibula with the femur, but also has a fibrous connection to the tibia. By severing this connection and moving the fibula forward onto the tibia, he changes the angle of attachment of the lateral collateral ligament, creating a resultant force which tightens the joint. This causes the medial collateral ligament, which joins the femur and the tibia on the other side of the joint, to alter its function. It now opposes and stabilizes the surgically induced forces of the lateral collateral ligament. Through this procedure, Dr. Smith creates two exterior bindings which give the joint stability and which prevent the forward and rotational movement of the tibia.

He has found that the point of surgical attachment of the lateral collateral ligament varies from dog to dog due to the stretch factor of each individual ligament and inherent anatomical variation. The object of the surgery is to obtain maximum tightening of the joint and this is assessed for each individual during surgery. Smith also found, that, contrary to earlier opinion, it is important not to remove the menisci completely but to salvage or *partially* excise them and leave them in place because they act as centering devices in the joint. In his studies, Dr. Smith found that this surgery, "fibular head transposition," provides the greatest amount of joint stability when compared to other procedures, because the fibula is moved over by the force of the altered course of the ligament. His measurements show that the drawer effect, where the tibia can be moved forward, is smaller than after other surgical techniques used to repair the injury.

Because cruciate ligament injury is so common, this is good news to dog owners. Dr. Smith explained that patients can be divided into two groups: the young athletic dog which overdoes it or uses the leg in the wrong way, and the older, often overweight dog. In the latter, it appears that the ligament weakens due to degeneration and just gives way. This problem is aggrevated by patellar luxation. Dr. Smith feels that dogs which have a luxated patella are predisposed to anterior cruciate ligament rupture and should be considered as surgical candidates for patellar relocation as a preventative measure, especially if middle aged, overweight, and unfit.

The tests Dr. Smith has conducted show that surgery, at the present time, cannot return an injured stifle to its pre-injury stability. Though he has found that by applying engineering principles to the construction and materials of the joint, a close approximation of such stability is possible for the injured dog. The studies help to determine the limits of natural and artificial materials and point the way to better surgical techniques, not only for dogs, but also for people who, like their four-footed friends, are quite prone to tearing the cruciate ligament.