



Summer 1983

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Recommended Citation

(1983) "Finding Out About Growth Hormone," *Bellwether Magazine*: Vol. 1 : No. 8 , Article 6.
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Finding out about Growth Hormone

A HORMONE WITH MANY COMPLEX AND INTERESTING ACTIONS.



Hormones direct, regulate, and coordinate the body systems. Since the mid 1960s they are studied intensively in small animal medicine. Researchers find that hormones have many more effects and roles than previously thought.

J. Eugen Eigenmann, D.V.M., Ph.D., assistant professor of medicine at the School of Veterinary Medicine is interested in growth hormone, a substance produced by the pituitary gland, a tiny body located at the base of the brain. "Growth hormone is unique among the hormones," he explained. "Unlike other hormones which, for instance, stimulate steroid hormone production in a specific gland, the actions of growth hormone are not confined to one main single target. Further, growth hormone stimulates the production of other hormones, somatomedins or insulin-like growth factors which are produced in the liver and other tissues and which are held responsible for growth." Growth hormone has two main activities, 1.) anabolic ones causing biochemical reactions which build up body systems and increase energy resources. This appears to be mediated by the growth factors. 2.) Catabolic

quently in elderly female dogs, is due to an overproduction of growth hormone triggered by elevated levels of progesterone. He also studied acromegaly, a condition occurring in elderly female dogs treated with progestagens or occurring spontaneously after heat. Affected animals show a sudden increase of soft tissue growth and a thickening of bone.

Diabetes melitus in dogs is not rare. A recent study concluded that the prevalence ranges from 1/100 to 1/500 in dogs brought to veterinary hospitals. The risk is lowest in young dogs and is about equal for males and females in this group. In older animals however, females are at a greater risk.

"It has been found that diabetes occurred frequently in elderly female dogs during diestrus," Dr. Eigenmann said. "It had also been found, in pharmacological studies conducted by pharmaceutical companies, that some dogs developed diabetes and acromegaly-like signs after having

been given high doses of progestagens. Thus we thought that this type of diabetes and acromegaly might be caused by progesterone-evoked growth hormone elevation."

Dr. Eigenmann used isolated canine growth hormone and developed an antibody against it for the radioimmunoassay which was needed to measure growth hormone levels in dogs. In the diabetic animals studied it was found that elderly female dogs with a mean age of 8.5 years did have elevated growth hormone levels during diestrus or after injections of medroxyprogesterone acetate (MPA), a progestagen. Diabetes occurred about four weeks after the onset of diestrus if the dog had cycled naturally. In animals which were given MPA injections, diabetes occurred also.

The dogs showed high circulating levels of growth hormone, glucose and insulin. "This is typical for growth hormone-induced diabetes," he said. "We know that growth hormone is a diabetogenic agent. It causes insulin resistance mainly

While the overproduction of growth hormone causes problems so does the underproduction of the substance. In dogs a form of dwarfism caused by low levels of growth hormone occurs.

ones where complex substances are broken down into simpler ones, this appears to be a direct effect of the growth hormone.

Dr. Eigenmann's research is concerned with these two activities of growth hormone and diseases which result when the hormone is secreted in improper quantities.

One of his studies, begun in 1979 while at the University of Utrecht, Holland, tested the hypothesis that diabetes melitus, occurring fre-



in fat tissue thus insulin cannot act normally at these sites. The dog becomes hyperglycemic and in many cases the body responds by producing more insulin. This is reflected by increased insulin levels in the blood. The dog is diabetic because insulin target tissues are resistant. This condition is reversible provided no major damage has occurred to pancreatic cells producing insulin.

A number of dogs studied recovered spontaneously from diabetes when the progesterone levels dropped at the end of diestrus or when the dogs were spayed. This was accompanied by a drop in the growth hormone level. Others recovered when the injections of MPA ceased. They too showed a decrease in the levels of progesterone and growth hormone. "Female dogs produce equally high amounts of progesterone during diestrus whether pregnant or not; also, reproductive cycles in dogs do not cease as the animal ages. It could be possible that the lifelong exposure to these high progesterone levels in some animals eventually evokes growth hormone elevation. The mechanism by which this occurs is not known, however. Yet, when ovariectomy was performed, the progesterone and growth hormone levels dropped to normal," Dr. Eigenmann explained that for elderly diabetic female dogs an ovariectomy is indicated. He recommends treating most of these dogs with insulin in order to minimize further damage to the pancreas. "In many cases, shortly after surgery, the animal returns to normal and the diabetes is gone."

This type of diabetes is likely to be seen more frequently in Europe where female dogs are rarely spayed. Instead they may be given biannual injections of MPA to prevent estrus. This may be continued throughout the dog's life unless she is bred.

Another condition associated with progestagen/progesterone-evoked growth hormone overproduction is acromegaly. In this condition the animal shows sudden increase in soft tissue growth, particularly in the head and neck area, a distended abdomen and excessive skin folds. This is found in dogs treated with MPA to prevent estrus or in animals which are allowed to cycle normally. Acromegaly can be life threatening as the extra tissue in the throat interferes with normal breathing.

Also in this disorder the level of growth hormone was found to be elevated. The animals recovered completely after an ovariectomy and/or progestagen withdrawal. The tissue shrank, the excessive skinfolds disappeared and the swelling of the abdomen ceased. "Acromegaly in the dog caused by progesterone-evoked growth hormone overproduction may provide a model for the study of the regulation of growth factors," explained Dr. Eigenmann. "It is an exciting possibility."

Growth hormone-related diabetes has also been found in a cat. Dr. Eigenmann has a donated cat which has diabetes and elevated growth hormone levels. Tests showed that the animal has a pituitary tumor which causes an excessive production of growth hormone. "Growth hormone overproduction could be the cause of diabetes in a larger number of cats," he said. "The question must be studied, though diabetes in cats is not as frequent as it is in the dog."

While the overproduction of growth hormone causes problems so does the underproduction of the substance. In dogs a form of dwarfism caused by low levels of growth hormone occurs. Dwarfism is a disorder in which the genetically determined growth potential is not reached. In order to grow the body must produce growth

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99 DOWN ONE TO GO

When it was acquired in 1952, New Bolton Center was a farm of about 220 acres, located in Chester County, about thirty-two miles southwest of Philadelphia. On the property were a manor house, a barn, and the usual implement buildings.

Dean Mark Allam and the faculty recognized that a rural campus was absolutely essential to the future existence of the Veterinary School. Mr. Harold Stassen, then president of the University, was of another opinion; he saw little future for this piece of land. Fortunately, the newly appointed dean was able to convince the University trustees of the vital need for this property and before long the rural campus had begun to take shape.

Money was scarce, so the beginning was modest, but nonetheless important. Two concrete buildings totalling about 5,000 square feet were erected initially and these served many purposes: an examination room and surgery, a diagnostic laboratory, four research laboratories, a pharmacy, and recovery stall. Clinical services, including the Field Service Unit were headquartered here, and some research was begun. In 1953, Dean Allam announced the formation of a new Department of Preventative Medicine and Hygiene (under Dr. Raymond Fagan), and the establishment of a Poultry Diagnostic Laboratory under the direction of Dr. I. George Sperling. Another early step was the appointment of Dr. Charles Hollister as director of clinics at New Bolton Center.

In 1958 a major program was undertaken to obtain funds to construct a large animal hospital and a dormitory complex. One million dollars was raised from private sources for the hospital and sufficient funds were contributed by alumni to provide a dormitory complex. The hospital was dedicated in 1964 and the dormitory in 1965. For the dormitory, an initial appeal was made to alumni, under a plan in which they would become shareholders in the complex for a three-year period. The response was swift but, after building commenced, it became apparent that the structure would not meet federal standards for residency. Additional funds were urgently needed, and a second appeal was made to alumni for more substantial gifts. The response was heartwarming; a total of \$380,000 was contributed and the structure was named Alumni House. The residency portion of the structure is known as the Joseph Vansant Dormitory in recognition of a major gift by the Vansant family in memory of Dr. Joseph Vansant, Class of 1902.

While New Bolton Center was now able to provide clinical services for farm animals and horses, hospital barns and stables were urgently needed. These became a reality through the efforts of Mr. Lawrence B. Sheppard, chairman of Hannover Shoe Farm. Mr. Sheppard had already been the major contributor to the construction of the hospital and now he once again came to the School's aid through a unique arrangement. Mr. Sheppard agreed to provide the materials and the tradesmen to construct the hospital barns and stables provided that the School would supply housing for the workers. This was done, and soon New Bolton Center was able to provide hospitalization for farm animals and horses.

Next, New Bolton Center entered a phase in which there was construction of facilities for research and special functions. The Comparative Leukemia Research Unit, under the direction of Dr. Robert M. Marshak, was established in 1963 through a grant from the National Institutes of Health. In 1969 the Georgia and Phillip Hofmann Research Center for Animal Reproduction was dedicated, followed in 1971 by the Alarik Myrin Memorial Research Building, and in 1975 by the C. Mablon Kline Orthopedic and Rehabilitation Center. In 1980, a major addition to the hospital was dedicated and the facility became known as the George D. Widener Hospital for Large Animals.

New Bolton Center is now a complete campus and makes the School of Veterinary Medicine unique among all veterinary schools in having both an urban and rural campus.

While the development of New Bolton Center was spectacular, developments on the Philadelphia campus during the period 1952 to 1973 were equally important in the renaissance of the Veterinary School. By 1952, the Small Animal Hospital was in deplorable condition and was one of the prime reasons why the Educational Council of the A.V.M.A. cited the Veterinary School as having the best faculty but the poorest physical plant of any veterinary school. In 1956 the University made \$40,000 available to the School to refurbish the reception area, business offices and examining rooms of the hospital. While this did not answer the problem of an outmoded structure it helped to improve the public image of the Hospital.

In 1959 a faculty study group developed plans for a badly needed basic science building. The Pennsylvania State General Assembly provided 2.2 million dollars for the construction of this facility and at the same time \$500,000 in federal funds were made available. This marked a turning point in the history of the School since it meant that the Commonwealth was committed to supporting and retaining a veterinary school at the University of Pennsylvania rather than establishing a school at Penn State University as had been urged in some quarters. The building was completed in 1963 and provided the School with basic science research laboratories, new classrooms and offices, a library and administrative offices. Incorporated into the building was a unique multidiscipline laboratory, arranged and equipped in such a manner as to allow for its use by a number of disciplines for laboratory instruction. When this laboratory was put in use in 1970 it allowed the School to increase its enrollment to over one hundred students per year. In 1974 the basic science facility was dedicated as the Gladys Hall Rosenthal Building in recognition of the generous, concerned support of Mr. Alfred Rosenthal. Until his death in 1979, Mr. Rosenthal remained a great friend to the Veterinary School and his wife, Gladys, continues that support.

GROWTH HORMONE

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hormone, growth factors and thyroid hormone. All three are necessary. If one is absent or deficient, normal growth will not take place.

In man hypothyroidism (low levels of thyroid hormone) is the second most frequent endocrine disorder of childhood. In the dog this juvenile hypothyroidism appears to be rare. Instead it was found that dwarfism in the dog is of pituitary origin. It is postulated that these dogs may have a cyst of the pituitary and that this interferes with growth hormone production. Another possibility is that the pituitary cells are not properly developed. At this time it is not known why growth hormone production is lessened in the affected dogs. Pedigree analysis of affected German shepherds points to the condition being transmitted by autosomal recessive inheritance.

The animals are small, they only grow for a few weeks after birth. Their skin is fragile and they do not develop an adult haircoat. Eventually the puppy coat starts to fall out and the dog becomes bald. Tests show that the animals are deficient in growth hormone and insulin-like growth factors. They can be treated with injections of growth hormone. "Treatment is quite expensive," said Dr. Eigenmann. "The growth hormone injections will cause the haircoat to grow, also the skin will lose its fragility. Treatment will have to be repeated when the hair falls out again." The injections of growth hormone do not cause the animals to grow as most are presented to Dr. Eigenmann when the growth plates have closed or are about the close.

Underproduction of growth hormone can also occur in older dogs. "This happens in some smaller breeds," Dr. Eigenmann explained. "These dogs develop normally and then at about age one to three years, begin to show signs similar to those of the dwarfs. The hair falls out and no new coat growth take place." These dogs can be treated by injections of growth hormone. It is not known why the production of growth hormone ceases. "The condition is not yet studied, though it is possibly genetic in origin," Dr. Eigenmann said.

His current work involves the study of dwarfs and the older dogs which underproduce growth hormone. He is also studying several breeds to evaluate growth hormone secretion potential and the levels of growth factors. Growth factors have only recently been identified and Dr. Eigenmann's project is designed to gather further knowledge about the importance of these factors. The dwarf dogs, the adult dogs with insufficient growth hormone levels, and dogs of different body size may provide some important answers. He is collaborating with Dr. D. F. Patterson from the Section of Medical Genetics, and Dr. E. R. Froesch, Metabolic Unit, University Hospital, Zurich, Switzerland.

Dr. Eigenmann came to the University of Pennsylvania in December 1980. He arrived here from the University of Utrecht where he received his Ph.D. in 1981. Prior to his work in Holland Dr. Eigenmann had been a visiting research fellow at the "Laboratoire Hormones," Department of Biochemistry and "Institut National de la Santé et de la Recherche Médicale," University of Paris. He received his veterinary degree from the University of Zurich in 1972 and the advanced Dr. med. vet. degree from the same institution in 1975.

ANIMAL CRACKERS

"NEW" DOG BREEDS



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The American Kennel Club recognizes 125 breeds of dogs which may compete in championship shows. Beginning January 1, 1984, three breeds will be added to the show classification. These are the Pharaoh Hound in the Hound Group, Portuguese Water Dog in the Working Group and the Tibetan Spaniel in the Non-Sporting Group.

There is a Miscellaneous Class at A.K.C. shows. These dogs are not admitted to registration in the Stud Book and are not eligible for championship points. They may compete in obedience trials and earn obedience titles. In addition to the three breeds named above, the following may compete in Miscellaneous at this time: Australian Kelpies, Border Collies, Cavalier King Charles Spaniels and Spinoni Italiani.

The Federation Cynologique Internationale which governs dog shows in 50 nations, mostly in Europe (not Great Britain), accepts 325 breeds. The latest breeds they have recognized are a long-haired Weimaraner developed in Czechoslovakia and a South Russian Sheepdog.

ANIMAL PROFILE

THE SHORT LIFE OF JUSTIN

A baby gorilla dies.

Justin, the Philadelphia Zoo's youngest gorilla, died May 20, 1983.

Since April 27, the four-month-old had been ill with shigella, a condition that resembles dysentery in human beings. According to Dr. Keith Hinshaw, Zoo veterinarian, the shigella caused a severe inflammation of the bowels. From this, the infant developed the blood poisoning (septicemia) which led to his death.

The gorilla had been removed from mother Snickers on April 27 when he was first taken ill. After intensive care by the Zoo staff and after showing signs of improvement, it was decided to place him back with Snickers on May 7 in order to allow him to nurse. He had not been feeding well for the Zoo staff. On May 18, the staff noticed that the infant had become depressed and was not nursing. The next day Justin was again taken from his mother to be given treatment, including intravenous fluids and antibiotics. Following treatment he had appeared to be improving, however, he began to lapse in and out of consciousness until he died at 6:15 am.

The Spring issue of *Bellwether* carried a story announcing the birth of the baby gorilla.



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