

Veterinary Viewpoints

The New York State College of Veterinary Medicine at Cornell University

Vol. 3, 1984



September Morn

The bucolic scene you see above was snapped one frosty morning by veterinary student James Brown '86 as he drove by the college's Equine Annex on Snyder Hill. The effort won him the 1983 Philotherian Award. However, the calm Jim captured is misleading because just out of camera range are some of the most animated equine facilities at the college.

Our photogenic horses are grazing at the Equine Research Park Annex, where Dr. John Lowe, director of the Park, and other clinicians from the college conduct a variety of research projects. One such project examines the effectiveness of hyaluronic acid therapy in the treatment of arthritis in horses while another evaluates new equine analgesics and sedatives. In nutrition studies, acid-treated hay is under scrutiny. While artificially increasing acidity allows hay with

a higher moisture content to be harvested without subsequent mold problems in storage, researchers are studying the affect of this hay on the horse's digestion and on the nutritional content of the feed.

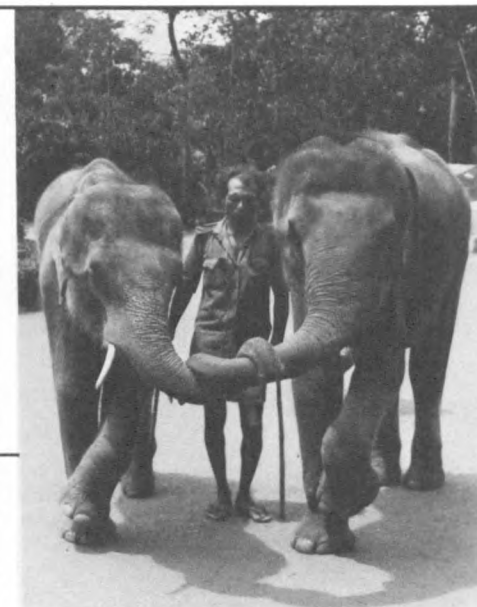
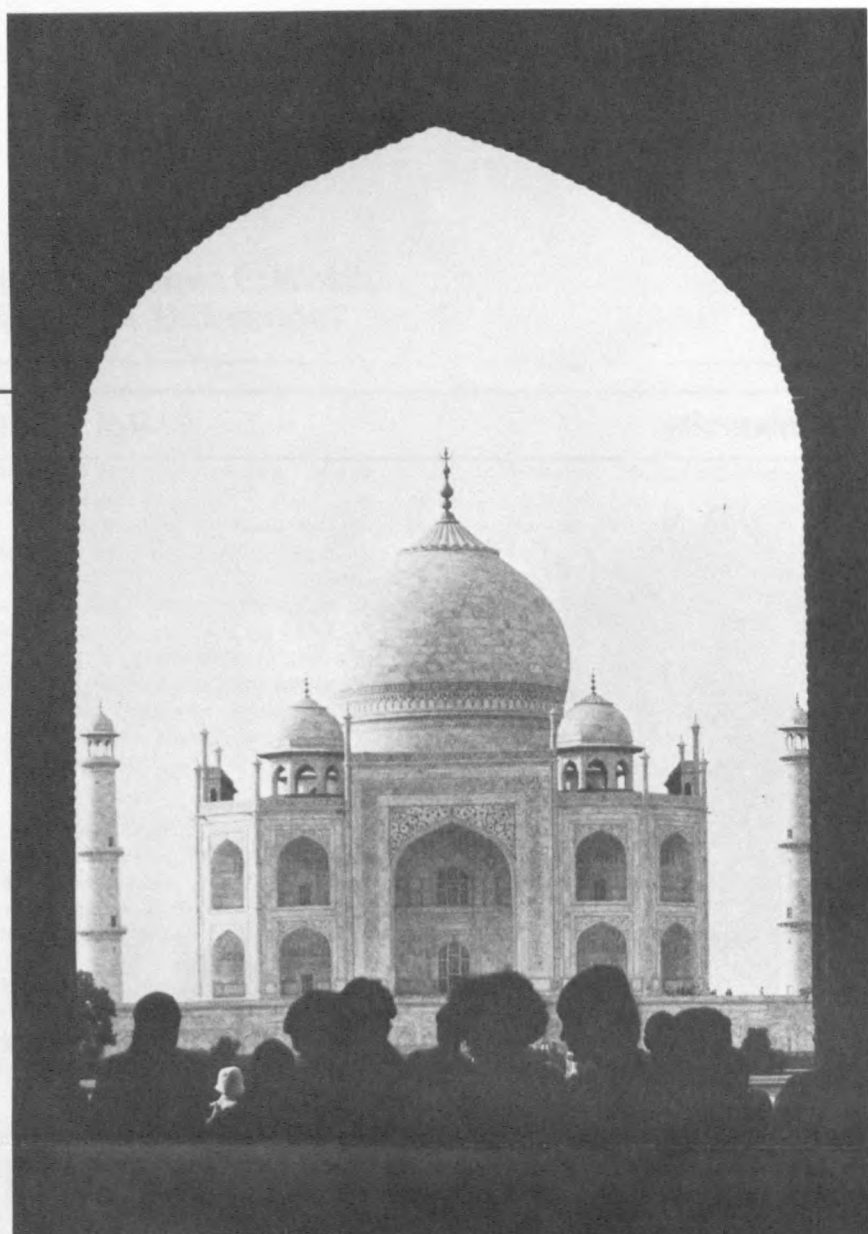
Behind the Equine Annex is the Contagious Equine Metritis (C.E.M.) Quarantine Facility remodeled with funds raised by the Travers Celebration and directed by Dr. Donald Lein. Over 200 horses have been tested here for this highly transmissible venereal disease since the facility's opening in 1982. Standardbred horses as well as warmbloods and thoroughbreds pass through the quarantine, moving on to new homes in New York, Kentucky, Florida and other eastern and mid-west states after a minimum stay of 40 days. (All breeding horses imported into the U.S. from C.E.M. affected countries must be quarantined until

they are found to be negative for the disease.) Imported mares disqualified from entering for the incomplete removal of the clitoral sinuses, the primary carrying site of this disease, can receive corrective surgery at the quarantine facility under state and federal quarantine and inspection. Only Cornell and the University of California, Davis quarantine facility on the west coast have been selected to perform these surgeries. The majority of the temporary "houseguests" at the college's facility have been mares, although the well-known Grand Prix Champion from France, the stallion Galoubet, was a recent visitor.

Just out of sight in the upper left hand corner of our cover photo is Dr. Gordon Woods' new Embryo Transfer Facility on Ellis Hollow Road. The former barn at the entrance of the Snyder Hill Research Com-

plex has been completely renovated thanks to funding from Laura Thorn and the professional guidance of Dr. C. Ben Baker. For Dr. Woods, the facility has three well-defined functions, as a center for research, as a clinical facility for the eventual commercial application of embryo transfer, and as a teaching center for junior and senior veterinary students. Several projects are already in the works at the facility including field studies on early embryonic death and the effects of stress on equine pregnancy.

Equine pregnancies are receiving a good deal of national attention at the Dorothy Havemeyer McConville Barn which lies about one mile north of the Annex. Its here that Dr. Douglas Antczak is studying immunogenetics with thoroughbred foals and their mule mothers. For more on this story, turn to pages 4 and 5.



Namaste, India*

On May 22, 1984, 8:30 p.m. Air India flight 104 departed New York with four New York State College of Veterinary Medicine students, Joanne Carter '87, Sarah Ehrenson '87, David Ashford '86 and Susan Cleary '86 and the group leader Dr. Prabin Mishra, graduate student in the College's Department of Anatomy. Some 27 hours later, they arrived in Bhubaneswar, capital of the state of Orissa in India. There to meet them, in a tumultuous welcome, were veterinary students, faculty and officials from the Orissa College of Veterinary Science & Animal Husbandry.

The journey had covered more than geography and time. Behind them were months of preparation and planning. Before leaving the U.S.A., they received tetanus, typhoid, rabies, cholera and gammagobulin shots. They carried water purification tablets in addition to a large jug of New York City's finest tap water. They'd come equipped with rain gear, first aid essentials, film, cameras, sunscreen, cups, knives, towels, sheets, travel guides and books on India, two kinds of malaria pills, insect repellent, and one jar of peanut butter. They expected to be prepared for anything and yet, as one guide book helpfully pointed out, nothing is ever quite the way you expect it to be in India.

For example, our students expected to quietly and unobtrusively take notes and observe veterinary medicine at the Orissa College of Veterinary Science & Husbandry, and to make contacts in the student community. However, as foreign visitors and especially as veterinary students, our students were the center of attention. In a way, this helped fulfill the purpose of the trip. All the students from Cornell are members of VIDA, Veterinarians Interested In Developing Areas, and were chosen for their interest in international development. This trip to Orissa, India, was their opportunity to acquire first-hand experience and exposure to some of the cultural, economic, and scientific restrictions and conditions faced here and in other foreign countries. The experience of a summer spent in a developing nation may mean a more realistic and rational approach to tropical veterinary medicine for any student contemplating a career in international development.

The differences between the two cultures' approaches to veterinary medicine were first apparent in curriculum emphasis; the Orrian veterinary students were plainly puzzled by the importance of equine programs at Cornell, while our students were surprised by the emphasis on dairy production. At Orissa, students take a greater

number of courses on ways and means to improve the production of food animals including fish, sheep, chickens, swine, and goats. A major obstacle to increasing food animal production, however, lies in the farmers' reluctance to grow feed for livestock. This may be because individual landholdings are extremely small and crops for human consumption are first priority. Instead, animals are turned out to forage for their own food. In the cities, this practice seems to be to the cattle's advantage. They look clean, and sleek, thanks to a diet that includes everything from green coconut husks to leaves and grass. But they're still rather short by our standards. It is perhaps a Western misconception that these cattle are "sacred". It's true that they have religious significance and that no devout Hindi will slaughter cattle or eat the meat. Even in the wildest traffic melees cattle may cross the street with impunity (and they seem to know it.) However, the majority of cows seen in the city or countryside are owned by individuals. Each cow keeps to a particular "range" and will return home at some point to be milked. It is also not unusual to see venders energetically driving cows away from their fruit and vegetables stalls. Reverence for life does not extend to watching a cow devour your dinner.

These cattle are also seen as patients at the Orissa Veterinary Clinic. In one visit to the clinic, the Cornell students watched as a cow was herded into the wooden stocks. The veterinarian on duty proceeded much as a vet in the U.S. would, first examining the animal and speaking with the owner, then writing out a prescription and directions for treatment. The prescription could be filled at the clinic pharmacy, but the bill is one item the client won't receive. Veterinary care in India is subsidized by the government and is free to a certain point. Vaccinations are free which may account for some degree of disease control. Rinderpest has been eliminated in cattle through this program, and a black quarter vaccine is administered in the monsoon season with the same hopes of disease control. Foot and mouth is an optional vaccination and this disease as well as tularemia and tuberculosis are still very common since control is difficult without slaughter of animals and/or massive water development and insect eradication programs.

Both the Indian government and the faculty of the Orissa University are anxious to provide villages as well as the cities with good veterinary and health services. Students are encouraged to spend occasional weekends and holidays visiting villages and, over

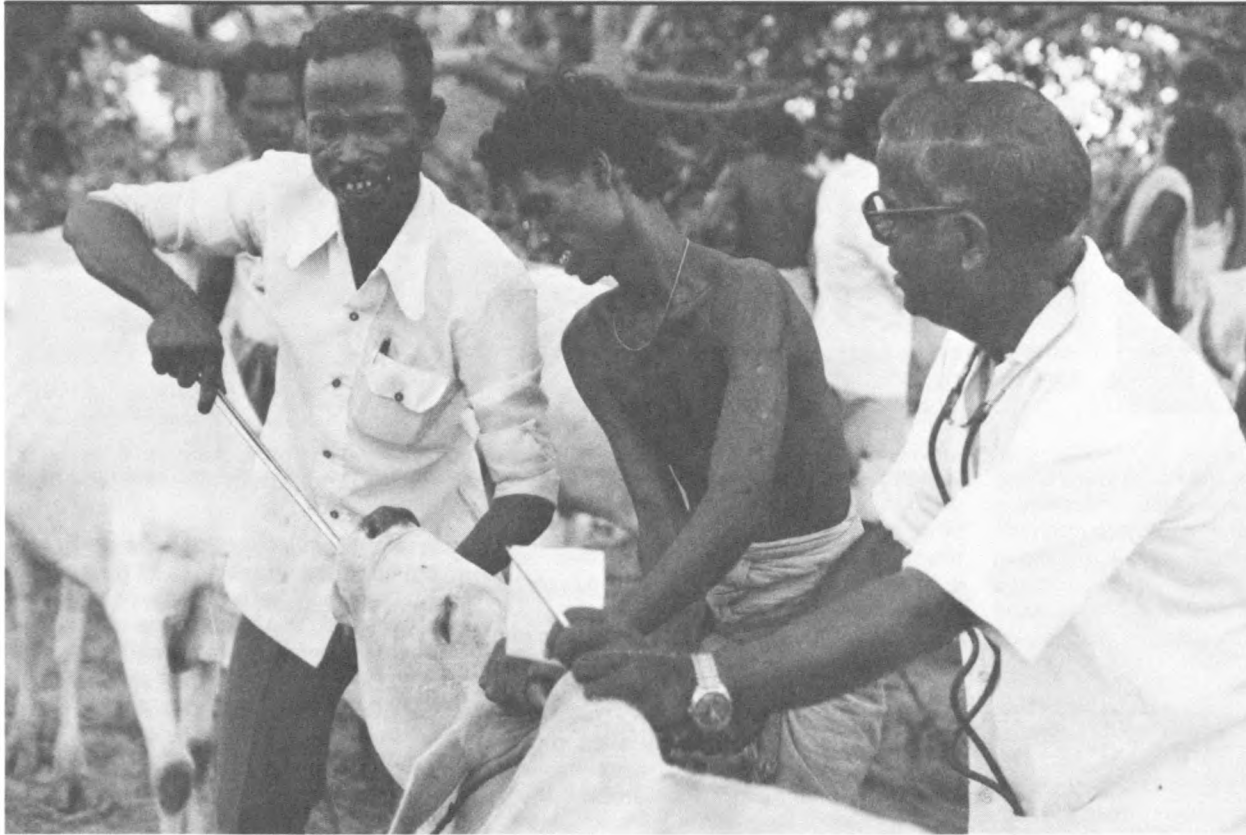
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(1) The Taj Mahal. (2) Dr. B. C. Nyak, Dean of the Orissa College of Veterinary Science & Animal Husbandry, O.U.A.T., Bhubaneswar, India. (3) The baby elephants at Nandan Kanan Biological Park in Orissa. (4) The Great Lingaraj Temple in Bhubaneswar, Orissa, India. (5) A villager and his cattle. (6) Dr. S. B. Tripathi, Head of Medicine at the Orissa College of Veterinary Science, (far right) assists in the treatment of a bullock as part of the field extension program. Dr. Tripathi received his masters degree in veterinary medicine from Cornell. (7) A client and the patient at the college's small animal clinic. (8) India's State of Orissa is bordered on the east by the Bay of Bengal, and has a land area of approximately 60,000 sq. miles. Oriyans number approximately 24 million. (9) Sheep awaiting distribution to villagers at a local farmers' market and fair.



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time, developing a rapport with the people. The Cornell veterinary students went along on one such trip that was really a combination extension and ambulatory care program that brought together specialists from the University in engineering, agronomy and veterinary medicine. The event was a farmers' market and fair and the veterinarians along on the trip expected to see 280 cases—mostly malnutrition and parasitic and skin problems.

At the village, the patients were predominantly bullocks. The work season had just begun with the start of the rains, and most of the complaints were work-related; the most common surgical procedure performed that day involved the correction of an upward fixation of the patella. The bullocks were literally standing in line for the five minute operation! Not far from the veterinary activity, government agents distributed goats to villagers in a program to help the "poorest of the poor". Begun under a project called "Lab to Land", this entails giving the very poorest families in a village a small herd of goats to raise. Ideally, the farmer will work to increase the size of his herd, selling the extra animals for meat, and thereby improving his economic condition. At the market, those goats were weighed and their general condition checked before

assignment to individuals.

The Indian government has other projects to improve economic conditions among the farmers. Such ventures involve the subsidization of farmers, providing feed allowances for cattle and supporting calf-rearing efforts. The success of the program is evident from the relatively prosperous look of the animals. Once the subsidies are discontinued however, the cattle are put back on the land to forage.

Attempts are being made to improve the quality of the domestic cattle too and at the Indo-Danish Artificial Insemination Center in Cuttack, the students were taken on a tour of the facility that raises bulls, produces its own liquid nitrogen, collects, stores and ships semen around the state, and grows feed in an experimental feed/grass project.

Veterinarians favor a mix of 50% native and 50% foreign blood in their crossbreeds because a larger percentage of the "exotics" (Jersey or Holstein) seems to produce calves with less heat resistance and a greater susceptibility to disease. Of all the breeds, Jerseys adapt the best, which leads to a great number of Indian cows resembling brown Jerseys in every way except a pronounced dewlap and an intimidating pair of horns. (Dehorning in India seems to be rare, however even the bulls seem very

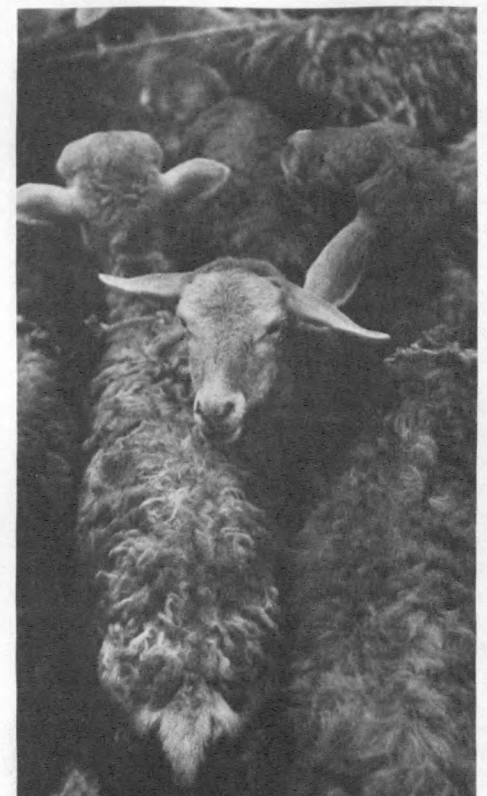
mild-mannered and perhaps the horns aren't a problem.)

The overwhelming majority of veterinarians in Orissa and throughout India are employed by the government, in fact only one veterinarian is self-employed in Orissa. After graduation from the 4½ year veterinary science program, a veterinarian is assigned to a post. If the assignment is to one of the 500 dispensaries in Orissa, he may work with 3 or 4 other veterinarians with assistance from fourth year students serving six-month internships. (The use of the masculine pronoun is accurate. There is one woman in the veterinary program at Orissa and only three women have received their B.V.Sc. degrees, one of whom works as a veterinarian in the field.)

The four veterinary students, Sue, Sara, David and Joanne hope to spend time with veterinarians in dispensaries across Orissa during their stay and their impressions when they return in late August should be of interest to our own faculty and students. At the very least, they'll see their own veterinary studies in a new and different light. We'll look forward to hearing from them in our next issue of *Veterinary Viewpoints*.

*Namaste (nana-stay) means hello or goodbye in Hindi.

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The Paradox of the Pregnant Mules: An Interview with Dr. Douglas Antczak

Viewpts: Dr. Antczak, the horse and donkey offspring of the mules certainly present a striking contrast to their surrogate mothers, and there has been considerable interest in your project from horsemen around the country. Was it your object to demonstrate that female mules are capable of carrying equine fetuses to term?

Antczak: Not exactly. In fact, we never really expected the mules to have much trouble carrying horse pregnancies. And anyway, Krause and Blue Moon have put that question to rest anyway (see accompanying article). We were too enthusiastic about the immunogenetic questions which we are addressing using the mules to be concerned about technical difficulties. As it turned out, we were extremely lucky.

Viewpts: What is the relationship between immunogenetics and pregnancy, especially equine pregnancy?

Antczak: The relationship is poorly understood, but it can perhaps best be described as a paradox. With Dr. Allen, we are studying maternal immune responses to the fetus which arise as a result of genetic differences between mother and fetus at genes coding for histocompatibility, or transplantation antigens. How does the mother carry to term a fetus which expresses foreign histocompatibility antigens? The fetomaternal relationship is intimate with respect to the exchange of nutrients and proximation of blood supplies, and it is of long duration in many species, such as man, cow, and horse. The overall ability of the mother to mount immune responses against paternal transplantation antigens does not appear to be diminished during pregnancy, and yet in most pregnancies the fetus proceeds to term normally. The question of how the fetal allograft survives has puzzled immunologists and transplantation biologists for years. It is believed that an understanding of the immunoregulatory mechanisms which must operate during pregnancy will increase our knowledge not only of pregnancy, but also of other complex phenomena which involve immune regulation, such as clinical organ grafting and the tumor-host relationship.

Viewpts: Are immunological aspects of pregnancy in the mare unique in any way?

Antczak: It appears so. Pregnant mares make a range of different kinds of immune responses against their developing fetuses. These responses can be detected as early as day 50 of pregnancy, and they occur in virtually all pregnancies. This is in distinct contrast to the situation in other species, where maternal immune responses to the fetus occur much less frequently.

Viewpts: How did you and Dr. Allen begin your collaboration?

Antczak: Both Dr. Allen and I received primary training in veterinary medicine, and each of us works to some degree on prac-



tical problems in our respective fields: reproduction and immunology. However, we both have developed very basic research programs in our respective disciplines, and it is through this work that we began to collaborate.

I met Dr. Allen while I was conducting my dissertation research in Cambridge. Dr. Allen had completed his PhD there a few years earlier, working under Dr. Roger Short, the well-known mammalian reproductive physiologist and veterinarian who at that time taught at the Cambridge vet school.

Dr. Allen's main scientific interest is in the biology of the endometrial cups. The cups are small, ulcer-like structures found in the endometrium of pregnant mares during the first third of gestation. The cup cells secrete equine Chorionic Gonadotropin (eCG), which was formerly called Pregnant Mare's Serum Gonadotropin. Dr. Allen discovered that the cups are of placental, and therefore fetal, origin, and not derived from the endometrium.

The cups develop around Day 35 of gestation, and they are marked by a maternal leukocyte invasion into and surrounding the cup tissue. This maternal reaction to the cups appears very similar histologically to the cellular immune reactions of graft rejection, and Dr. Allen postulated that it represents a maternal immune response to fetal histocompatibility antigens.

At about this time, I was beginning to study histocompatibility antigens of horses. One of the first things we discovered was that the mare makes strong serum antibody responses to paternally derived histocompatibility antigens of the fetus. These responses are first detected about 2 weeks after the endometrial cups form. That is about the time it takes for many primary immune responses to develop. Therefore, for the past 4 years, an important aspect of our collaboration has been a characterization of the endometrial cup reaction.

Viewpts: Do you think there is a relationship between the endometrial cup reaction and equine abortion?

Antczak: We don't know for sure. However, about 10% of all equine pregnancies are lost during the first 100 days of gestation for causes which are never determined. This is the time when the mare is making strong immune responses to the developing conceptus. It is possible that there are some equine abortions which are due to transplantation reactions against the fetus. On the other hand, it is also possible that the immune responses of equine pregnancy are an important component of maternal recognition of the pregnant state. Pregnancy loss could be caused by failure to make an appropriate type of immune response, for example a local immunosuppressive response in the uterus. We find ourselves using the term 'regulation' more often than 'rejection' these days. The question remains open.

Viewpts: How then did the 'pregnant mule' project begin?

Antczak: It's an interesting example of how scientific research works, and how fundamental research can have unexpected practical benefits. Dr. Allen's scientific career has been marked by a series of experiments which are classic examples of de Bono's 'lateral thinking'. They do not always follow directly from his previous work, nor are they performed with a practical question in mind.

In the late 1970's Dr. Allen began to perform cross-species embryo transfer between horses and donkeys. These transfers had asymmetrical success: horse embryos transplanted to donkeys developed normally to term, while the donkey-in-horse pregnancies were abnormal and ended in abortion by day 90 in 21 of 22 cases. The remaining donkey pregnancy went to term inexplicably. The first abnormality in these pregnancies which has been detected thus far is the failure of development of the endometrial cups. There is also evidence for immune responses in these donkey-in-horse pregnancies, but the responses are different from those found in normal horse pregnancy.

Thus, Dr. Allen has developed a reproducible, experimental model of early equine abortion which arises from a series of defects in placental development. The system also allows us to investigate the function of the endometrial cups.

Viewpts: And the mules?

Antczak: Oh, yes, I nearly forgot. The pregnant mule project is conceptually very simple. We had hypothesized that donkey endometrial cups do not form in mares because the uterine environment is not appropriate for their development for reasons which are still undefined. We wanted to determine if the female mule, which carries both horse and donkey genes, would express the appropriate uterine environment for the development of either horse or donkey endometrial cups.

The answer seems to be 'Yes, it does', since both horse and donkey pregnancies gave rise to eCG in the mules' sera and to live foals.

Viewpts: What did you look for in your candidates for embryo transfer?

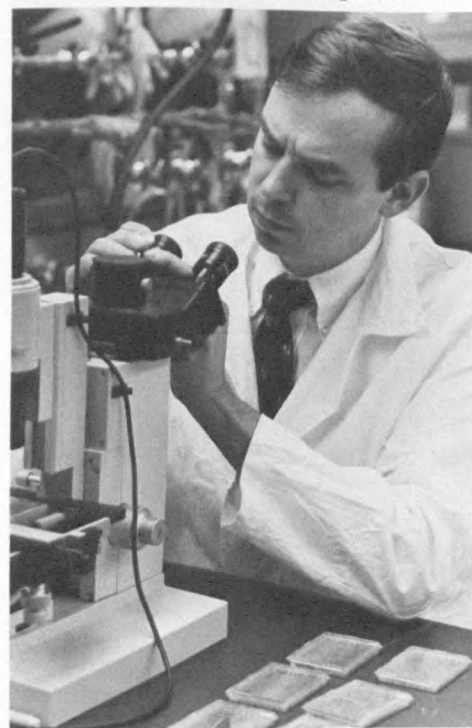
Antczak: For our purposes, female mules broke down into one of 2 categories: those which had active ovaries and went through the motions of ovulation, and those which didn't. The ones which didn't couldn't be synchronized with the donor mares and jenny donkeys, and they had no detectable levels of progesterone. Therefore, one would not expect them to carry a conceptus to term. About half of the mules we examined had active ovaries and periodic estrus cycles. However, the estrus cycles of the mules were not as regular as those of horses and donkeys.

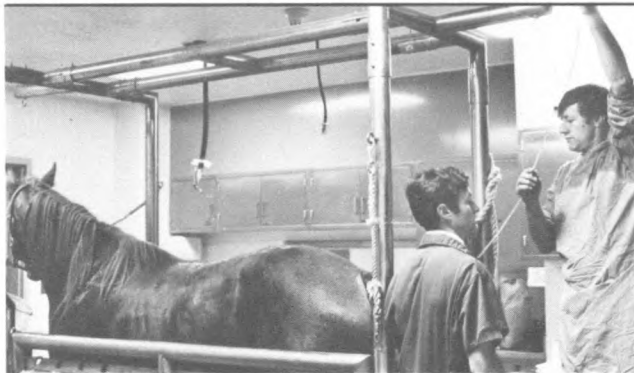
The first horses to be born at Cornell as a result of embryo transfer were foaled during the summer of 1984. They are extraordinary in several respects. Between June 5 and August 12, 2 Thoroughbreds and one donkey were born to 3 mule surrogate mothers which received transplanted embryos between June and August of 1983.

The donkey is the first to be born to a mule mother using embryo transfer techniques, while the 2 horses follow the single report in 1982 of a horse born to a mule mother in Colombia, South America, as a result of embryo transfer.

The Cornell foals are part of a collaborative research project between Dr. Douglas F. Antczak, Assistant Professor of Immunology at the James A. Baker Institute for Animal Health, and Dr. W. R. Allen, Director of the British Thoroughbred Breeders' Equine Fertility Unit in Cambridge, England.

Dr. Douglas Antczak





Flushing an embryo from the mare.



Dr. W. R. Allen examines ovum transport medium for embryo with Julia Kydd.



Embryo transfer into uterus through small puncture.

Viewpts: You mentioned luck earlier on. Did you have any problems with your transfers?

Antczak: We were very lucky. The pregnancy rate from our transfers was as high as that achieved in embryo transfers using normal horse donors and recipients. We performed a total of 11 transfers last year, using a non-surgical embryo flush on day 8 after ovulation of the donor and surgical transfer to the uterus via a midline laparotomy approach. Three of 5 cycling mules which received horse embryos became pregnant, as well as 1 of 2 cycling mules which received donkey embryos. In addition, 1 of 4 non-cycling mules which received horse embryos also became pregnant! These last 4 recipients were treated with a synthetic progesterone analog to simulate the activity of endogenous progesterone. Even so, it surprised us to get a pregnancy in that group. Most of the credit for our success must go to Dr. Allen, who organized the synchronization of donors and recipients and performed the transfer surgery.

Viewpts: Of the 5 pregnancies, only 3 went to term. What happened to the other 2?

Antczak: The mule treated with the progesterone analog aborted spontaneously at around 60 days gestation, and we performed a hysterotomy on the fifth mule at day 80 of gestation to examine the development of the placenta and endometrial cups.

Viewpts: How did the actual foalings go?

Antczak: After the first one, easier than we expected. The first Thoroughbred, which was born June 5, was carried in a mule who weighed only about 600 pounds, much smaller than the 1000 lb genetic parents of the embryo. The foal was very light at birth, only about 70 pounds. His legs were very long, however, although the normal length for a Thoroughbred foal. This was an interesting example of what may be the limit of the difference in size between embryo donor parents and recipient which will give rise to a viable foal. An embryo from a larger horse, such as a draft horse, may not have gone to term. The gestation was 12 months, which is longer than the average for horse pregnancy. However, the foal showed many signs of 'dysmaturity', such as problems with thermoregulation and orientation. He has adjusted nicely now.

In addition to the size problem, the foal was also born with a cleft palate. This is a relatively rare developmental defect in horses, and there is no evidence that it is related to embryo transfer in any species. The cleft was repaired in a long surgical procedure at the Large Animal Clinic at the College, and the foal, named Goblet, is recovering well.

The other 2 mules foaled easily and without assistance, producing another Thoroughbred on July 23, and the donkey on August 12. The second horse had a 344 day gestation, while the donkey-in-mule

gestation was 356 days, a bit shorter than the 12 month pregnancy normal to donkeys.

Viewpts: What kind of mothers have the mules turned out to be?

Antczak: Excellent! All three are good milk producers and very protective of their young. Dr. Harold Hintz is studying the growth rate of the youngsters and the milk composition of their mothers, and Dr. Katherine Houpt is studying the behavior of the mule-foal pairs.

Viewpts: Have you accomplished all the objectives of the pregnant mule project?

Antczak: Yes and no. We feel we have answered the primary question about the development of donkey endometrial cups in mules, but the experiments have opened up new avenues of research using mules as well. For example, we now have a system in which we can compare the behavior of embryos of different species in a 'neutral' maternal environment. This should allow us to separate maternal and fetal components of some aspects of equine pregnancy. We have a limited amount of data of this type from the small number of pregnancies we have examined. However, it would be much better if we had larger numbers.

Viewpts: Speaking of larger numbers, this project must require many animals and a large staff.

Antczak: Not relative to the size of other major equine reproduction research centers, where herds of several hundred horses are kept. Dr. Allen maintains about 80 animals in Cambridge (roughly half of them donkeys), and we have less than 40 here in Ithaca. We do work hard at planning experiments so that our animals are not idle much of the time.

Our scientific staffs are also relatively small: 2 or 3 technicians plus perhaps a graduate student and a post-doctoral fellow. However, for the labs to operate smoothly it is necessary that everyone be an expert in at least one, and often 2 or more areas, such as tissue typing, immunohistochemistry, hormone assay, or embryo transfer. In addition, we all pitch in when muscle is needed, for example when stubborn donkeys need to be loaded onto a horse trailer. We are both very fortunate to have talented, hardworking, and dedicated people in our labs. Building staffs with such characteristics and experience takes years, and it is the most important factor in any success we may enjoy.

Finally, the academic and research environments both here and in Cambridge have been very supportive of our work. For example, we've had tremendous cooperation from the Equine Research Park, the Large Animal Clinic, and several investigators who loaned us mares to use as embryo donors.

Viewpts: It sounds as if you and Dr. Allen have developed a very satisfying and productive collaboration.

Motherhood for Mules

It's been a banner year for equine reproduction. In addition to the 3 foals born to mule mothers at Cornell as a result of embryo transfer (ET), several other equine pregnancies have made news lately.

In May, the first identical twin horses produced in the US by blastocyst splitting were born at Colorado State University. Also, a zebra was born to a Quarter Horse mare as a result of ET at the Louisville Zoo. In England in June, the first rare and endangered Przewalski Horse was born to a domestic horse mother, also a result of ET techniques. In July, in Champion, Nebraska, the now-famous molly mule Krause gave birth unexpectedly to a male mule colt, Blue Moon, as a result of a pasture mating sometime last summer to Krause's donkey sire. This is the first scientifically verified case of a truly fertile mule, one of Nature's greatest rarities. It follows only about 30 other such reports since 1500, and is the first in 50 years. Techniques such as chromosomal analysis were unavailable for verification of the previous cases.

Horses, donkeys, and zebra all belong to the genus *Equus*, one of the few mammalian genera in which interbreeding produces live offspring. With very rare exceptions, these hybrid offspring have all proved to be sterile.

The Cornell 'pregnant mule' project encompasses both the revival of interest in mules in the US (see the November 1983 cover story of 'Smithsonian' magazine) and the widespread and increasing use of embryo transfer in horses.

Antczak: We think so. The separate expertise available in our 2 labs allows us to perform experiments which neither lab alone could undertake. Dr. Allen is not only adept at the animal manipulations required for embryo transfer and other aspects of clinical reproduction, but he is a first-rate reproductive physiologist as well. This means we have a wealth of hormone assays to use as required. In addition to our experience in immunogenetic testing of horses, we also operate the Cell Fusion Center at the Baker Institute. This is a University-wide facility for the production of monoclonal antibodies which is funded by the Cornell Biotechnology Institute. Altogether, it is a truly symbiotic relationship.

Viewpts: How is your research funded?

Antczak: Both Dr. Allen and I have support from horsemen, for example, from the British Thoroughbred Breeders' Association and the Harry M. Zweig Memorial Fund for Equine Research in New York State, as well as grants from agencies which fund medical and biological research, such as the National Institutes of Health and the European Eco-

ET permits females of species such as horses and cattle, which normally have only one offspring per year, to produce many more. A valuable mare can be mated, flushed, and 're-cycled' 6 or more times in a year. In cattle, superovulation techniques can produce 10, 20, or even more embryos from a single mating. In horses, superovulation techniques are still in their infancy, so in successful uterine flushes only 1 embryo is usually recovered.

Several different techniques for synchronization of donors and recipients and for the actual transfer procedure are in use, and new methods are under development. The highest success rates thus far have come with surgical transfers, which use either a ventral midline or flank approach to the uterus. The flank approach, which is done using local anesthesia, is suitable for use in the field, while the ventral midline approach requires general anesthesia, and therefore a surgical suite. Non-surgical transfers are much less expensive to perform, but the success rate using them has been lower thus far. Embryo flushing in horses is usually carried out on day 7 or 8 after ovulations, when the embryo is just visible to the naked eye.

ET techniques will permit young performance mares to produce offspring and still continue their campaigns. In addition, it will allow offspring to be produced from valuable brood mares with extensive uterine pathology or other conditions which would not permit a pregnancy to be delivered, such as broken hips.

Our programs are quite expensive, and therefore each lab requires multiple funding sources.

Viewpts: Where do you go from here with your reproductive immunology experiments, and with the mules?

Antczak: Our studies of the immune responses surrounding the endometrial cups are continuing with a molecular dissection of the equine placenta using monoclonal antibodies. In addition we are still investigating the donkey-in-horse pregnancy which we believe to be an important model for equine abortion. Finally, with respect to the mules, we hope to learn techniques for blastocyst splitting in order to create identical twins artificially. We would use these twin embryos to ask questions about non-genetic effects on development. For example, would identical twin horse embryos which developed in mare or mule mothers differ in any important physiological characteristics? We can't be sure that these experiments will give biologically significant results, but we have a certain feeling about them which makes us want to try.

Tanya

On Sunday, Tanya became a statistic—one of the thousands of dogs injured each year in traffic accidents. A few weeks later, the 9 month old black and tan doberman pinscher joined a much more exclusive statistical pool—one of a growing number of dogs who will recover from a broken back.

An unlucky encounter with a moving car left Tanya with a broken back. A vertebrae in the middle of her spinal column was fractured in the accident and radiographs would show a compression fracture of T-12. Her veterinarian guessed that when the car struck Tanya, her spinal column flexed acutely, damaging the vertebrae and breaking off a connecting rib at its base.

Throughout the following day, a Monday, her veterinarian concentrated on stabilizing Tanya's condition. He treated her for shock and gave her fluids and electrolytes intravenously. Both owners and veterinarian agreed Tanya would need surgery as soon as possible, and because of the type of surgery, and the extensive aftercare required, Tanya was referred to the Small Animal Clinic. She arrived Tuesday morning.

Her record read "HBC", hit by a car. The diagnosis: compression fracture. The prognosis: guarded to favorable. This was largely because Tanya had several points in her favor. The first was her age. Young dogs up to the age of 12 months seem to do well after this type of surgery. The reason may be that they are still growing and their bones are softer, the growth plates still open. The second, and possibly most important factor, was her response to stimuli in her hind legs. When veterinarians at the clinic lightly pinched her toes, she felt the pressure. Although Tanya wasn't using her hindlegs on admission, the pain she obviously experienced in her legs showed the spinal cord itself was still intact. Unlike muscle, bone or other living cells, spinal cord tissue does not regenerate and a dog with a severed spinal cord would never walk again.

However before surgery could be scheduled, Tanya's other physical problems had to be corrected. A routine EKG revealed a cardiac arrhythmia—an irregularity in her heart beat most likely caused by the physical trauma of the accident. Immediate treatment called for I.V. fluids and a lidocaine hydrochloride drip, a drug that has pronounced antiarrhythmic properties. Despite the temporary setback, clinicians still considered Tanya a good candidate for surgery.

On Wednesday afternoon, Dr. Dougald Gilmore and surgery resident Carol Carberry began the operation to stabilize Tanya's fracture. First, they exposed the spinal column along almost the entire length of Tanya's back. The compressed vertebrae at T12 had lost a sizeable piece of bone from its left side when the attached rib

tore free. In a procedure known as a hemilaminectomy, one half of the vertebrae, the damaged side, was drilled off.

Surgeons now had an unobstructed view of the spinal cord and it seemed undamaged although physical trauma to the spinal cord's "wrapper" of bone, the vertebrae, had caused some swelling and compression. Thanks to the newly drilled opening and the elbow room it provided, the spinal cord was decompressed and would soon return to its normal diameter.

The challenge now remained to immobilize the fractured T12 vertebrae for both sideways and up and down movement. In an active, young dog this called for considerable ingenuity. She couldn't be expected to lay or even sit still for long while she healed, therefore the immobilization method must protect the fracture against movement. Yet Tanya's activities couldn't be totally restricted. The backbone must be supported in such a way as to allow some flexure for walking, sitting and play. This required a two-part solution.

Drs. Gilmore and Carberry positioned a stainless steel ASIF plate on the left side of the backbone. To T11 and T13, the adjoining vertebrae, they securely fastened the plate with screws. A rigid support, this would stabilize the fracture against sideways movement. Across the top of the vertebrae, they placed two vinyl Lubra plates, one overlapping the other over the injured vertebrae. Lubra plates are designed with double rows of holes along their edges and can be screwed tightly to the bone. Despite their stiffness, they are relatively pliable when compared to metal. These



(Above) Tanya keeps an eye on ICU activity from her sling.

(Below) Outside, the sling does double duty as a walker.

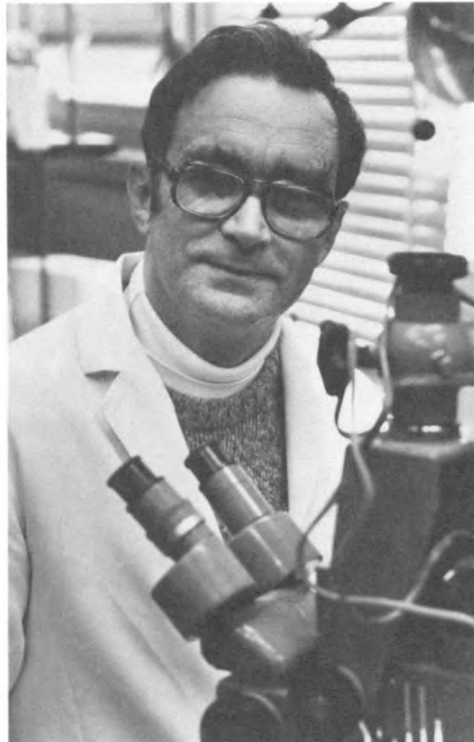


plates would stop flexion of the backbone.

Finally, with the procedure completed and the incision closed, surgeons fitted Tanya with a body wrap. This was a cumbersome looking bandage extending from Tanya's rump up to her shoulders. Inside, layers of cotton with plaster or balsa wood slabs hold the wrap rigid. Its purpose is to hold Tanya immobile while healing begins. Unfortunately, in the Intensive Care Unit following surgery, Tanya managed to wiggle free from the wrap—a good indication that she could move her hindlegs soon after surgery, but a poor way to begin a gradual convalescence. Sedation calmed her. By the Sunday following surgery, a week after the accident, Tanya was actually controlling the coordination of her hindlegs and attempting to walk.

From her I.C.U. cage, Tanya has moved to the sling during the day. This ungainly looking contraption, supports Tanya's body while her legs hang down through holes in the sling fabric. It operates on the same principles as an infant's walker, although Tanya is not mobile. The change in her surroundings and her nearly normal upright position seem to encourage Tanya. Lethargic in her cage, she's interested in everything that goes on around her while she's in her sling. She even feels fit enough to challenge in-coming dogs, although this is necessarily limited to verbal exchanges. Her progress so far has been remarkable and in two weeks she's expected to go home. Other dogs after similar surgery and a much slower recovery have gradually regained near normal use of their legs and it's hoped that Tanya will do as well.

Dr. Douglas McGregor



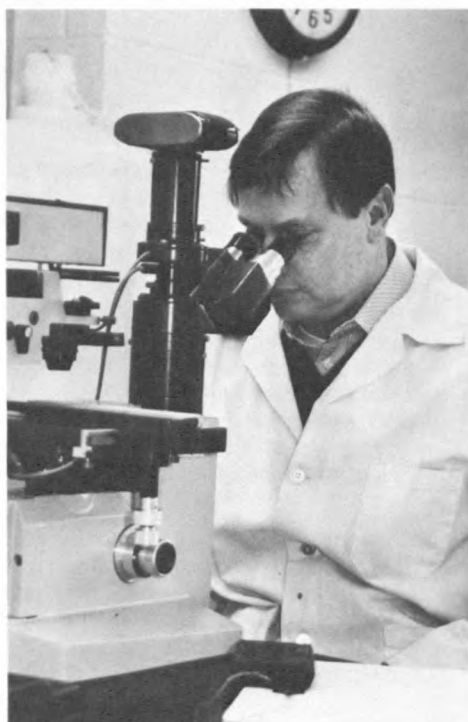
DOUGLAS D. MCGREGOR, B.A., M.D., Professor and Director of James A. Baker Institute for Animal Health, is Principal Investigator in the study "Mediator of Cellular Immunity", which was recently funded for \$83,960 by the National Institute of Allergy and Infectious Diseases. Together with Associate Investigator Dr. Douglas F. Antczak and Research Associate, Dr. Melissa C. Woan, he will continue research focusing on the T cell response to *Listeria monocytogenes* in a model system using rats. They will determine the differences and interactions, if any, between the T cells that mediate delayed-type hypersensitivity to *Listeria monocytogenes* and those that transfer sensitivity. They'll also study how T cells attach to target cells and the possible link between *Listeria* protective cells and inflamed vascular endothelium.

DREW M. NODEN, Ph.D. and Associate Professor of Veterinary Anatomy, has received a grant of \$48,203 from the National Institute of Dental Research for his study on the "Origin and Patterning of Head Muscles, Bones and Nerves." Now in the second year of a three year study, the research has already analyzed the origins of voluntary muscles and now begins the study of the origins of involuntary muscles and angiogenic tissues. Dr. Noden plans to begin analyzing the interactions that underly normal patterning of the tissues that form the wall and floor of the skull and also the face.

Grants for Research

GARY M. DUNNY Ph.D., Assistant Professor in the Department of Microbiology, has had his study "Genetic Function of a Conjugative Streptococcal R Factor" funded through July of 1985 by the National Institute of Allergy and Infectious Diseases. This is the final year in a 4 year project grant award, that this year alone will total over \$63,000. During the coming year, Dr. Dunny and his associates will attempt to produce additional mutant derivatives of a pheromone dependent plasmid, determine their genetic properties and continue to characterize the antigenic changes in the streptococcal cell surface associated with pheromone response. This work may help determine why some cells resist streptococcal infection.

WILLIAM A. HORNE, D.V.M. now in the Department of Pharmacology, has received the Physician Scientist Award from the National Institutes of Health (NIH). This award provides the opportunity for clinically trained professionals to develop independent research skills and experience in a fundamental science. Dr. Horne's study of "Regulation of Calcium Channels in Heart Cells" will receive NIH support totalling \$275,000 over a five year period. He will examine the synthesis and distribution of calcium channels, as well as the transport of calcium across the cell membrane in both normal and diseased hearts. Dr. Horne's study may show that certain diseases, such as hypertrophic cardiomyopathy are due to abnormal calcium channel function and that this may be regulated by certain cardiovascular drugs.



Dr. Donald Wassom

In addition, the National Institute of Neurologic Communicative Disorders and Stroke has renewed funding of DR. NODEN's study the "Mechanisms of Sensory Neuron and Ganglion Development". The 1984-85 award for \$50,869, continues a 6 year grant. Dr. Noden's project will define the normal development of cranial sensory ganglia, using avian embryos as models. He will then analyze the mechanisms responsible for the formation of these sensory neurons, their aggregation into discrete ganglia, and the establishment of correct peripheral and central projections by these cells. This work has necessitated the development of both neuroanatomical fiber tracing methods and antibodies that recognize transplanted nerve fibers, a combination of experimental embryology with neuroanatomy.

GEOFFREY W. G. SHARP, Ph.D., D. Sc., Professor and Chairman of the Department of Pharmacology, begins a new three year study of "Insulin Release and the Role of Calcium" with a first year grant of \$108,939 from the National Institute of Arthritis, Diabetes, Digestive & Kidney Diseases. The studies should enhance our knowledge of the way that cytosol calcium affects the rate of insulin release and the manner in which intracellular organelles help in the regulation of this critical pool of calcium. The information gained should be useful to our understanding of endocrine pancreatic function both in health and in disease states such as diabetes.

DONALD L. WASSOM, Ph.D., Assistant Professor of Parasitology and Genetics in the Department of Preventive Medicine, received a grant of \$79,732 from the National Institute of Allergy and Infectious Diseases for his continuing study "Immunogenetics of *Trichinella Spiralis* in the Mouse." the NIAID has also funded Dr. Wassom's new study on the "Genetic Control of Immunity to *Heligmosomoides Polygyrus*". This grant is for \$72,848. The research will evaluate the role played by H-2 genes in immunity to *Heligmosomoides polygyrus* infections of mice. Resistant and susceptible mice will be studied in order to identify the functional effectors of immunity against this parasite.

Dr. Gary Dunny



CALENDAR

1984

September 17 Resume deadline for students interested in job interviews, Office of Students Affairs & Admissions.

October 15 Deadline for admissions applications to the New York State College of Veterinary Medicine.

November 10-11 I love NY Horse Symposium
For more information contact:
CSHA Symposium
132 Morrison Hall,
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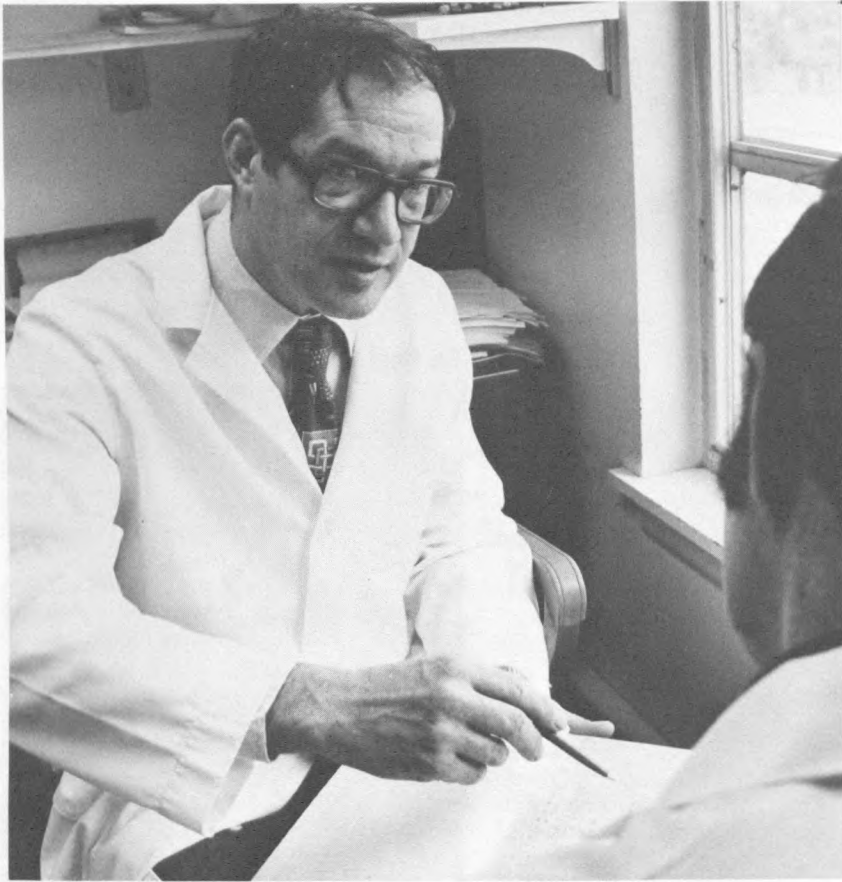
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January 15-17 Annual Conference for Veterinarians

Veterinary Viewpoints

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Dr. Bruce Calnek

International Focus on Marek's Disease

A disease that remains the most important cause of economic loss to the poultry industry brought researchers from 25 countries to the Cornell campus July 23-26 for an International Symposium on Marek's Disease. Hosted by the New York State College of Veterinary Medicine, the symposium examined Marek's disease, from the virus's molecular structure and function to host resistance factors, diagnosis, vaccination and field problems in the control of the disease. The four day event presented speakers from some of the leading universities in the U.S.A. and Canada; and from the U.S.D.A.'s Agricultural Research Service; Regional Poultry Research Laboratory in E. Lansing, MI; the Universities of Osaka, Hokkaido and Tokai in Japan; the Free University of Berlin and the Federal Research Centre of Agriculture in Dornbergstr., W. Germany; the Houghton Poultry Research Station, England; the Institut National de la Recherche Agro omique, France; and the Hungarian Academy of Sciences.

Marek's disease is a lymphomatous disease of chickens, caused by infection with a herpesvirus, Marek's disease virus (MDV). It is the only tumor-causing disease for

which a successful vaccine has been developed. Unfortunately, the very nature of a virus sometimes seems to change as vaccines are developed and used on a widespread basis. This appears to be the case with MDV in some regions. In recent years, the Department of Avian and Aquatic Medicine at the college has been responsible for field trials of a bi-valent vaccine combining a new Marek's disease virus vaccine strain SB-1 and the widely used HVT vaccine. Together, the two vaccines seem to offer significantly greater protection than a single vaccine against newly emergent "hot" strains of Marek's disease virus. The recent appearance of challenge strains of Marek's disease against which standard vaccines were apparently ineffective and the immediate need for vaccines that offer certain protection illustrates why research into the pathogenesis of the disease and immune response of chickens continues. The Symposium was a successful attempt to collect and report the results of this work from around the world.

The cause of Marek's disease, a herpesvirus, has also stimulated a separate line of research, one concerned with the role of

herpesviruses in the development of human cancers and disease. According to Dr. Bruce Calnek, Chairman of the Department of Avian & Aquatic Medicine, Cornell, it is possible that Marek's disease may serve as a model for herpesvirus induced cancers in man. Dr. Julius and Catherine Fabricant from the Departments of Avian & Aquatic Medicine and Microbiology, are also studying the connection between Marek's disease virus and atherosclerosis in chickens. As they reported at the Symposium, research shows that infection with MDV results in atherosclerotic lesions in chickens regardless of their diet, whether low or high in cholesterol. Uninfected chickens did not develop the lesions of atherosclerosis. This suggests that a vaccination, much like the present vaccines against Marek's disease, could be developed against the herpesvirus causing atherosclerosis. Unfortunately, humans are widely infected with up to five different types of herpesvirus and it may take years of research before we can expect

(Below) Dr. Julius and Catherine Fabricant

to receive immunization against atherosclerosis along with our routine shots against whooping cough, tetanus, measles and other diseases.

The International Symposium was organized by Drs. Bruce Calnek and K. A. Schat from Cornell University, and by K. Nazerian and R. L. Witter, USDA Poultry Research Laboratory, E. Lansing, Michigan. J. L. Spencer from the Animal Diseases Research Laboratory, Ottawa Canada was also a member of the Organizing Committee. Drs. J. Fabricant from Cornell, R. Hein from Intervet International in Holland and G. Waters from DeKalb Ag. Research in DeKalb, IL also assisted. Financial support for the program was provided by the Department of Avian and Aquatic Medicine, New York State College of Veterinary Medicine; Intervet International BV & Inter-Continental Biologics, Inc.; ISA/Babcock Breeders, Inc. & ISA Poultry Services, Inc; Merieux Laboratories and many other sponsors and contributors.



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