

## HYPOTHESES, HURDLES AND HUNCHES

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I want to begin by expressing my appreciation for the honor which you have bestowed on me today. I want to thank my family which put up with my long hours of commitment to this chosen profession, sometimes at the expense of family activities. If you will permit, I want to extend this honor to include all of the colleagues with whom I worked, and the many graduate students and postdoctoral fellows.

I can not recall a time when I did not want to be a veterinarian. As a young boy I had imaginary herds of cattle that I tended faithfully. In a rather naive way I just assumed that I would be able to go to college and would be accepted into veterinary college. It never occurred to me that there were heavy odds against my succeeding, with over 300 applicants for 50 spaces at Cornell. I was not a brilliant student in the first years of veterinary school but I was given other opportunities and managed to redeem myself. I think of Dr. Myron Fincher, an Honorary Diplomat of the ACT, who would state in his gruff voice: "If you really want to do a good job for your client, take that sleeve and glove off so you will really be able to palpate the pelvic structures". Frankly, all that ever did for me was to produce "prune" fingers with which I could feel almost nothing. Perhaps the best training I got in the clinical reproduction arena was with Dr. Howard Fuller in Interlaken, NY. Dr. Fuller had operated the Seneca County Breeding Cooperative and, in the mid 1950's, was still doing artificial insemination for farmers in the Cooperative but buying the semen from American Breeders Service. His requirement that all cows must be palpated first to ensure normality prior to insemination was the impetus to begin to really learn how to do rectal palpation in the cow.

Subsequently, Dr. Francis Fox, who started me on chewing tobacco, was instrumental in my getting a job working with Dr. Kenneth McEntee. I want to express my appreciation to both Dr. McEntee, who tried his best to make me into a pathologist and to Dr. William Hansel, who also tried his best to make me into a physiologist. Others will have to judge the success of their efforts. Lennart Krook and Willard Visek were the other members of my doctoral committee and assisted in making me into some semblance of a scientist.

I was blessed over the years with a number of excellent collaborators including Bill

Adams and Dick Ross at Iowa State, Jim Hixon at Illinois, and two German scientists, Bernd Hoffmann and Franz Ellendorff. The major part of the science which was done in my program resulted from the work of my graduate students and postdoctoral trainees. At times I seemed to be operating an international center, especially with the "Brazilian Mafia". Over the years, we had a few successes in research such as the parturition induction work with Bill Adams in the early 70's, the demonstration of the impact of adrenal steroids on LH secretion by the bovine pituitary gland, the long series of studies on the synthesis of estrogens by the bovine placenta with Bernd Hoffmann and the experiments on the effect of endotoxin on prolactin secretion in the pig by Brad Smith, now at Oregon State University, which got us on the cover of Science.

I also wish to acknowledge the efforts of three research technical people who were more than just technicians and participated in all aspects of the work: Ron Strohbahn and Pat Harris Larson at Iowa State University and Pat Weston at the University of Illinois. The numerous veterinary students who worked with me in our research program and contributed their nights and weekends to the 24 hour blood collection schedules were a very important part of the total program. Although we worked hard at what we did, we also had some fun. I never considered it to be work. It was always too exciting, wondering how the next experiments would turn out, and where our studies would next lead us.

There have been some interesting events in the course of our research efforts. When I arrived at Iowa State University in January, 1968, Dr. Ed Wedman told me that I could work on any reproductive problems in animals as long as I also was doing research on the agalactia problem in sows. Thus, a collaboration with Dick Ross was started. This research involved three graduate students and culminated in our report that endotoxin administration would cause a marked depression of prolactin secretion in sows and that the loss of prolactin secretion would result in immediate termination of lactation. This was in clear distinction to reports that growth hormone, not prolactin, was the critical hormone for lactation in the cow.

The work from my doctoral thesis had been concerned with the postpartum cow and the resumption of ovarian function. This topic has been recycled on a periodic basis and continues to draw interest. At the same time, it must be said that we have not truly solved the problem of how to control the return of ovarian function in the postpartum cow. Our interest in this area led, however, to studies on the interaction of increased adrenal activity and the impact of the increased blood concentrations of cortisol on pituitary and ovarian function. The culmination of these experiments was the demonstration that the addition of low levels of cortisol to cultures of bovine pituitary cells could suppress the secretion of luteinizing hormone. The other component was to investigate the impact of hormonal changes at parturition on neutrophil function. This series of studies culminated in our publication in 1994 of data which demonstrated that the number and function of neutrophils is reduced significantly in cows during the

parturient period, especially in those cows which develop metritis or mastitis.

When I graduated from veterinary college, a major cause of anestrus and/or infertility was considered to be the retained corpus luteum. It is hard to even estimate the number of normal corpora lutea that were removed by manual expression per rectum as we struggled to "treat" this problem. Of course more recent research and information clarified this issue and demonstrated that any pathologic alteration of the uterus can delay the regression of the corpus luteum but otherwise the "retained" corpus luteum probably does not exist. The death of a cow due to fatal hemorrhage after manual removal of the corpus luteum was a truly memorable event.

The other main interest in our research program was the physiology of pregnancy and the fetus itself. This particular line of research benefitted from my interactions with Bernd Hoffmann and Franz Ellendorff in Germany and the many interactions with other scientists in Europe, Australia and New Zealand. This work began with the interest of Bill Adams in inducing parturition with corticosteroids and ended many years later with studies on control of estrogen synthesis by the bovine placenta. Along the way we learned that: 1) the maternal ovaries and adrenals were not involved in regulation of parturition in sheep; 2) the lungs of the fetal lamb do not provide signals to the adrenal or pituitary for initiation of parturition; 3) the bovine placenta does make significant amounts of progesterone; and 4) the bovine placenta can use steroid precursors like pregnenolone or androstenedione to make estrogens, especially in the very late stages of pregnancy. However, we still do not have the definitive answers about the exact mechanism by which the fetus initiates the process which leads to its birth.

Those of you who know me well are probably expecting me to leave you some philosophical statements before I finish and I do not wish to disappoint you. We have a very strong record in theriogenology for the past 25+ years. The movement from consideration of only individual animals to the development of the reproductive herd health concept was an early move toward what is now considered production medicine. While the demand for theriogenologists to work with individual animals remains high for some species, this is not true for some of our large animal species. Given the structural changes within the swine industry, there is a lesser need for veterinarians with a special focus on reproduction. The emphasis is on disease control and prevention with much less attention to the individual animal.

In the dairy industry, what is the economic impact of a total herd reproductive health program vs the same time spent on nutrition consulting or other management issues such as mastitis control? If a reliable and inexpensive pregnancy test was available would we now be "out of business"? The situation is much different for the canine and feline area at the present time where individual animal diagnosis and treatment is very much in vogue and the demand for services continues to increase.

The continuing focus on the clinical aspects of theriogenology with less effort in some of the contributing disciplines such as pathology, bacteriology or immunology may need to be reviewed. There has been a tendency to place emphasis on the physiology of reproduction to solve our problems with less attention to infectious problems, including a full understanding of host immune function. The need for information about infectious infertility has been somewhat neglected. This is reflected in the fact that most studies on such disease problems as the PRRS virus in swine and the problems with Neospora abortion in cattle have not been given strong leadership by individuals identified as theriogenologists. In this regard, I commend people such as Dr. Bondurant for establishing linkages with researchers which have facilitated his work on trichomoniasis.

We need to consider where future research must be focused in theriogenology. If you do not have a clear goal or destination, then any road will get you there. Who is setting the agenda for reproduction research? At the USDA, the National Research Initiative program in reproductive biology is largely controlled by physiologists from animal science and physiology departments. A few years ago, I issued a challenge to the members at this meeting. I challenged you to step forward and take some leadership in animal reproduction research. Has it happened? Are we not the best group to set that agenda? Are we not the group that sees the clinical problems and knows what the needs are? Are we doing anything about securing more resources for our area of interest? I must acknowledge that, on the companion animal side, the theriogenology community has been more active in giving leadership. I especially note the efforts of Dr. Pat Olson with respect to the pet overpopulation problem and the efforts of Dr. Shirley Johnston in promoting programs at the international level.

My concern is about who makes decisions on the research and education agenda. Are we masters of our own fate or are we leaving it to others? The advent of rapid and sensitive assay systems had a profound effect on what biological events could be studied. More recently the advent of molecular biology techniques have led to even more detailed experiments at the subcellular level. At the same time our clientele is expecting that we should provide a more integrated set of answers to their problems and that it is better if diseases or problems are prevented rather than treated after they occur. Commodity groups regularly state their need for more effort on adaptive or applied research to solve their immediate problems. What I hear from producers is a frustration that the research community does not work on the things that they think are important. I believe that our interests should be similar to those of the producer community.

In cattle, especially dairy cattle, the issues of retained placenta, metritis, mastitis and postpartum infertility continue to surface. Do we know a lot more about the animal's pathophysiologic state during these problems? Of course we do. Have we significantly reduced the costs to the industry of these problems? Probably not. There are serious questions about these diseases that relate to host animal defenses, cellular responses such

as neutrophils, and general cellular function. The topic of apoptosis in the parturient cow and its role in placental separation in cattle, needs to be investigated. The reasons for the decline in neutrophil numbers and functional status at parturition, especially in cows which develop metritis and mastitis, need to be discovered.

My association with the American College of Theriogenologists (ACT) has been an important part of my career. I believe that the past 25 years have been sort of a "golden era" in the field of reproductive biology and theriogenology. I can recall the early days of the ACT when some of us would meet in an airport motel from Friday afternoon to Sunday afternoon writing examination questions. Bob Hudson, Bush Bierschwal and the late Ed Carroll come to mind as some of the participants in these marathon events; Bierschwal telling bad jokes, while Hudson and Carroll provided the nervous energy for the rest of us. Perhaps the most exciting annual meeting was the one that did not occur - in Mobile, Alabama in 1979 - when the hurricane arrived before the meeting started but after the examining committee and the examinees were already there. A close second might be Oklahoma City when Borje Gustafsson and I shared a "weekend" suite because all of the double rooms were filled. This was the only time I have experienced the following: a round bed, orange and peach colored walls and a shower surrounded with mirrors, plus having Borje as a roommate.

The problems faced by the College were different in 1971 when the ACT held its first meeting, and there was concern about whether we would survive the probationary stage. An appropriate quote comes from Elbert Hubbard: "Progress comes from the intelligent use of experience". If true, we should have made a lot of progress because we had a lot of experiences. There was also thought given to the future of the organization and how to develop a plan for including private practitioners through an alternate route. I can assure you that the other clinical specialty groups watched our efforts with much interest. At the meeting in 1971, Dr. Dave Bartlett commented that "he was disappointed that during visits to large herds of dairy cattle, tracks of dinosaurs were more evident than those of veterinarians". At that same meeting Dr. Raimunds Zemjanis commented that "in serving the livestock industry we are dealing with an economy issue. If what we do is not economically justified, we will not be called back".

I wonder if our current secretary would be able to insert the parenthetical and often quite personal comments which our first secretary, Dr. Lloyd Faulkner, did with such regularity. They certainly added some spice to the discussion at the next meeting when the minutes were up for approval by the membership. The minutes also listed all members who were present and who were absent, plus indicating if the absentees had been excused for sufficient reason. I also remember the first class of diplomates by examination. Four of those individuals, Bart Gledhill, Bob Hudson, Ed Mather and Dick McFeely were a major force over the past years in both the College and the Society. We were not blessed with large diplomate classes in those first years, but we had some outstanding quality.

The close collaboration and interaction between the ACT and the Society of Theriogenology (SOT) has been most beneficial. As one who wrote the material for a 1961 issue of the Journal of the Society for the Study of Breeding Soundness of Bulls (published when the spirit moves and the time permits), I have been very pleased to see this occur. Lloyd Faulkner was instrumental in convincing me to do that, expressing his opinion that the Westerners needed to know how we did bull examinations and semen evaluations in the East. I also remember indoctrinating Lloyd into the harsh realities of winter weather in the East when I took him on an overnight trip to visit two dairy herds in Malone, NY where the temperature was -35 the next morning. And his biggest complaint was that I did not let him have coffee every 25 miles on the way from Ithaca to Malone.

I complement the organizers on having a session at this meeting on educational programs in theriogenology. This reminds me of the earlier efforts to bring some standards and uniformity to programs at our veterinary colleges. One of these sessions was in Oklahoma and I can still recall Dr. John Simon getting up after listening to considerable wrangling over how much time to devote to specific topics and issuing his commandment on the subject: "You ought to spend 70% of the teaching time on things that you will spend 70% of your time doing in practice". Maybe a slight overstatement but not a bad guiding principle to keep in mind. In his comments on the occasion of receiving the Bartlett Award, Dr. Bierschwal lamented the lack of respect being given to people in clinical service, particularly in clinical theriogenology. My observation is that some of that has changed, especially with the increased interest in good teaching and the education of the undergraduate student at many universities. Gaining credit for teaching is possible if you can convince your faculty colleagues to look at it that way.

We have many capable people in this organization but do not be content to rest on your past accomplishments. You, individually, need to step forward and provide leadership. Remember that "if you straddle the fence, you'll never have your feet on the ground".

We need to have both good leaders and good followers. It is hard to be a good leader unless your followers display some trust and willingness to accept some (a few) decisions on trust. Having served in both faculty and administrative positions I am aware of the frequently adversarial tone which affects this relationship. I believe that is unfortunate especially in our present times when budgets are continually being squeezed and no one is getting the resources needed to continue to operate our programs as we would like to do. This is just as true at the Federal level as in the land-grant universities. Our budgets for support of research on animal topics continue to shrink as the down-sizing of government becomes a reality. If there are to be funds available to support the research topics of interest to us, then each of you as individuals need to be actively involved.

I have appreciated very much my involvement in these organizations and the friendships

which I have made. And I regret that some of those friends are not able to be with us here today. I note especially three people - John Kendrick - with whom I visited the herd from which John got his first isolates of what we then called Infectious Pustular Vulvovaginitis until we got smart enough to realize that it was the same as IBR virus; Ed Carroll - who let us pitch our family tent in his backyard in Ft. Collins; and Elmer Woelffer - a true pioneer in clinical reproduction. I also note that two of these men were Cornell graduates and the third, Ed Carroll, spent a sabbatical leave at Cornell.

I look forward to attending many more of these meetings in the future. As many of you know, I retired from the University of Illinois in November, 1993, taking up my current position as Principal Veterinary Scientist in the Cooperative State Research, Education and Extension Service. Whether I will hold up as well in my second career as my former mentor and colleague Steve Roberts has done in his second career remains to be seen. If you are coming to Washington, DC, give me a call and we can do a spicy Thai meal somewhere in town.

I wish to close with one or two personal comments. The first is that each of us is responsible for our own state of happiness. No one else can make you happy. If you are unhappy, it is in your power to change that. Worrying is like standing in a mud hole; it gives you something to do, but it doesn't get you anywhere. Many years ago, John Kendrick alerted me to a quote from George Eliot: "Friendship is the inexpressible comfort of feeling safe with a person, having neither to weigh thoughts nor measure words". Perhaps all of us could reconsider how we interact with our colleagues and help make the places where we live and work kinder and gentler for everyone.

Thank you again for this signal honor. I hope I bring credit to the award and to both of these organizations.