

The 2009 Bartlett Address

Theriogenology Experiences and Reflections

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Dr. Bartlett's Influence

To start this story I go back to my first year in veterinary school at the University of Minnesota. I worked in the Anatomy Department, and one of my duties was to make bone preparations for teaching and display purposes. One day I was asked if I would like to take on some extra work in this area and if so I should contact a Dr. Bartlett at American Breeders Service (ABS) in DeForest, WI. I did not know Dr. Bartlett but I certainly knew of the ABS Company, and was therefore very excited to find out what this might be about.

Now I'd like to go back several years before to my teenage years in my hometown of Alma Center in west-central Wisconsin. I was a "city-kid" if that is possible in a town of some 400 people. My dad introduced me to all kinds of animals but he especially liked birds and we raised chickens, ducks, pheasants and homing pigeons. I was more interested in dairy cattle. All six of the major breeds were raised on farms in our area. But Guernseys were my favorite as they were raised by my good friend Fred Moseley and on the Seguin family farm near Eau Claire, WI. As artificial insemination (AI) increased in popularity, I

became intrigued with bull studs, semen technology and the work of AI technicians. So I was well aware of the ABS Company. The local veterinarian lived just a few houses away. I found his practice in general, but especially the reproductive part, compelling. So my intention for going to veterinary school was to work with cattle, and especially cattle reproduction in dairy practice or possibly the AI industry.

So I was very excited to find out what Dr. Bartlett had in mind. (Wouldn't a four-year scholarship be wonderful!)? As you can guess, what he was looking for was someone to provide pelvis preparations for use in their training programs for AI technicians. I was able to provide the specimens so my first paycheck for theriogenology work was thanks to Dr. Bartlett! But the real reward for me was the chance to get to know the veterinary staff at ABS: Drs. David Bartlett, Les Larson and Willis Parker. From that point on, the possibility of a career similar to theirs was my motivation whenever needed to get through veterinary school. A fact that is not well known is that Dr. Bartlett was the first head of the Ob/Gyn Department in the College of Veterinary Medicine at the University of Minnesota. In 1984 Dr. Bartlett gave the first of these addresses at this same meeting in Denver, Colorado. I encourage you to read that paper as it is a classic reflection of Dr. Bartlett's professionalism, intellect and dedication to our profession and specialty.¹ So I am deeply honored to speak to you today as this is the 25th anniversary of the first Bartlett address given of course by Dr. Bartlett himself.

Student at the University of Minnesota Veterinary College

As veterinary students at Minnesota in the 1960's most of us had heard the legend of Dr. Ray Zemjanis long before we were to have him as a teacher. He was on sabbatical for our 3rd year when we started our therioenology courses. However we were not shortchanged, as a very capable group remained to carry on: Dick Schultz, Mel Fahning, Louis Archibald, Charles Gibson, Dennis Copeland, John Ellery and Bob Wescott. They were all superb teachers, strong mentors and excellent therioenologists. During that year we took cow palpation lab, which included several early morning trips to the Bartusch slaughterhouse about 3 miles from campus. On these trips cows to be slaughtered that morning were palpated and findings recorded by each student. The reproductive tracts were recovered and returned to the Therio lab for review (and grading) that noon. This nearly instant feedback helped us master the art and science of cow palpation and reproductive physiology. This slaughterhouse resource was the backbone of the Minnesota program and where we really learned the techniques described in the Zemjanis textbook *Diagnostic and Therapeutic Techniques in Animal Reproduction*.² Ray Zemjanis returned as we started our 4th year. Those of you who knew him you can imagine the surprise we experienced that first day in lecture. Even though his reputation had proceeded him and we knew we could learn a great deal from this man, his hardcore, old school, no nonsense approach was a shock to say the least. If we answered when doing cow palpation with "I think I found -----", he would respond, "Your clients won't care about what you THINK you found, they expect you to KNOW what you found." Of course he

was right and we gained great respect for the teaching system he established and the principles he professed.

Colorado State University

Toward spring of my 4th year, a notice was posted that the veterinary college at Colorado State University (CSU) was looking to fill an internship position in bovine reproduction. Anyone interested should contact Dr. Ed Carroll at the "Bull Farm". That address sounded perfect! I went to the library to see what I could learn about Dr. Carroll and found his paper on BSE of 10,940 beef bulls,³ which was the basis for the formation of the group that would become the Society For Theriogenology. I applied and was fortunate to be offered the position. The Bull Farm was an exciting place where I worked with Drs. Carroll, Les Ball and Lloyd Faulkner. We did lots of bull work and more cow work (both beef and dairy) than I had imagined. Also present at CSU were Dr. Bill Pickett with his equine research program and Dr. Jim Wiltbank working on beef cow reproductive management systems. Their detailed approach to controlled experimental design in animal reproductive studies made a strong impression. I had many "interesting" mornings with Dr. Pickett and his graduate students collecting semen in their seasonality study in stallions and in a boar project. These experiences plus a growing concern at that time about seminal vesiculitis in bulls started me thinking that research in bovine reproduction and possibly even graduate school might be something to consider. Dr. Carroll and I did a small trial on seminal vesiculitis in yearling bulls in the hopes of creating the

basis for a possible graduate degree project. [Unfortunately Ed's life was far too short; he was a valuable resource to our profession.] The days at CSU flew by.

Michigan State University

Fortunately for me there was a bovine theriogenology residency/MS spot at Michigan State University with Drs. Dave Morrow, Wayne Oxender and Fayne Oberst. I got off to rocky start with Dr. Morrow when he wanted me to write an application for an NIH postdoctoral fellowship. My first reaction was to question if a veterinarian was even eligible, but indeed we are (or were). About the last thing I thought I wanted to be doing was to be confined to a desk when there were field trips, clinic cases and experiments to be done. But I did the application and have been grateful to Dr. Morrow ever since as it was funded about 2 years later. My Master's thesis was on the cycle-altering effects of endometrial irritation in cows,⁴ which started my career-long search for better control of the timing of estrus and ovulation in cattle. Two review papers by Dr. O.J. Ginther were available on the utero-ovarian relationship in cattle.^{5,6} I still feel these should be must read literature for graduate students and/or residents in theriogenology. At that time we were still talking about the uterine luteolysin and the luteolytic factor, but this would soon change.

The Dairy Science Department at MSU had a very active Reproductive Physiology group that included Drs. Harold Hafs, Alan Tucker, Ed Convey, Jack Britt and Wayne Oxender plus a large number of graduate students. It was the exciting place to be. I was accepted into a Ph.D. program with the Dairy Science group with Wayne Oxender as my advisor. Graduate students were officed six

per room so there were many stimulating discussions. There were always lots of trials being planned and conducted and many needed the assistance of a veterinarian so my days were always busy.

If you know Wayne Oxender, you know that something interesting was always going on when he was around. In those days, Select Sires and Michigan Animal Breeders had a bull stud on the edge of campus. They allowed us to use 25 two-year-old Holstein bulls housed in tie stalls for our experiment. The purpose was to study five anterior pituitary hormones possibly involved in the process by which false mounting bulls increases the number of sperm per ejaculate. Each bull was treated and then bled via the tail vein eight times in a 24-hour period. That barn was all muscular energy, testosterone and flying hooves. Somehow we all survived and I was able to present the project at the ASAS meeting in Lincoln, NE.

Prostaglandin! Today the activity of prostaglandin $F2\alpha$ ($PGF2\alpha$) in cattle is taken for granted but in 1972 prostaglandin was pretty much unheard of. One day at the weekly graduate seminar Tom Louis reviewed some recent work in lab animals that showed some negative effects on corpus luteum (CL) function by a compound, which was thought to be what we had been calling the uterine luteolysin. As I remember many of us present thought “This is a Dairy Science Department, what in the world does this work have to do with cows?” Little did we appreciate where this was going to take us. Shortly thereafter, Dr. Hafs went to visit Dr. Jim Lauderdale at the Upjohn Company about the possibility of some trials with a new compound that was $PGF2\alpha$. Soon Tom Louis, John Stellflug,

and I were sent to the University's dairy to select heifers and cows for the initial trials with this product. Late one night we were in the research barn getting everything ready for the start of the project when the manager of the dairy farm walked through. It must have been obvious to him that we could hardly contain our excitement. He asked what company was sponsoring the project. We were only thinking about how the project would get us started on our graduate work but he was looking for an investment opportunity! In the first trials cows were treated by intrauterine infusion in the ipsilateral vs. contralateral horn to the CL and the heifers by intravaginal deposit vs. IM injection in diestrus vs. metestrus. There were no adverse reactions and to our amazement, the CLs that were present at the time of treatment were soon disappearing. When the heifers went out for heat detection on the third day after treatment they lined up in standing heat like elephants in the circus. These two projects resulted in two of the first publications on the action of PGF₂ α in cattle.^{7,8} Many other experiments with PGF₂ α followed to further define dose effects, routes of administration, intervals to estrus and ovulation, etc. Then it was time for fertility trials where we had very good results.⁹ A review of potential uses of PGF₂ α in cattle was presented at the first SFT conference by Wayne Oxender.¹⁰

There were some other PGF₂ α experiments and experiences with unexpected events. Several surprises occurred at the Chatham Experiment Station in the Upper Peninsula of Michigan where we used beef cattle for one of the first PGF₂ α fertility trials. The first was that we would take a commercial plane to Chatham, which sounded great, but it was a very bumpy ride in a small

commuter plane and it made 3 or 4 stops! A second surprise was the weather. We left Lansing on a beautiful spring day but in the UP it was still winter with more than a foot of snow still on the ground. Another surprise was the cattle. Some of you will remember the Chianina beef breed that was imported from Italy for crossbreeding to add some size to our native beef cows. It turned out their other highly heritable traits were how high they could jump and how slow they were to reach puberty. The heifers used were $\frac{1}{2}$ and $\frac{3}{4}$ Chianina yearlings. Although well grown and in good condition, many were not yet cycling and they all could jump. It was a long day. You have probably seen the warning on the Lutalyse® bottle that says exposure to this product may cause breathing problems or an asthmatic attack in some people. I have never seen such a problem with the commercial product but for these first trials PGF2 α came to us in powder form that we had to dissolve in PSS. I had usually done this in a large well-ventilated room but that day I did it in a closed up car. As I mixed the two, some of the PGF2 α powder became airborne and I experienced a weird respiratory episode. This did not last long but I was convinced of two things: PGF2 α is a potent substance and it is true that it's half is very short. On our last trip to Chatham an experiment station cowboy named Blacky took us Coho fishing in a local river. When we could not get a bite by hook and line, he just illegally used a dip net to catch a few under a state highway bridge.

There was also some mare reproductive research done in our group. Pat Noden was another of the graduate students. Her Ph.D. thesis was on using PGF2 α for estrus control in mares.¹¹ The day the first mare was treated I was at

the campus dairy barn. I received a phone call that there was an emergency at the Bennett farm where the research horses were kept. By the time I was contacted and got over there, all was quiet and no one was around. The only thing that seemed unusual was a large wet spot in the treatment area! While we had never seen any side effects from PGF₂α in cattle, Pat had just seen the first sweating reaction in a mare caused by PGF₂α treatment. This reaction in mares to PGF₂α is well known now but was a shock that day.

Another surprise occurred when Dr. Hafs wanted to try PGF₂α in bulls. He had a research interest in sperm output and collection efficiency of AI bulls. He wanted to see if an injection of PGF₂α might mimic the affect seen with false mounting. The initial trials were done in rabbits where the most obvious affect was a marked increase in fecal expulsion.

One disappointing aspect of the early PGF₂α work for me personally was that we did not have approval to do research trials in lactating dairy cows. This was my major interest area and where most of us thought the greatest use would occur.

Gonadotropin Releasing Hormone: At the same time that the PGF₂α research was starting at MSU, Drs. Jack Britt and Ed Convey and several graduate students were studying uses of gonadotropin-releasing hormone (GnRH) in cattle reproduction. An early project by Britt et al. described the basic effect of GnRH on LH release and showed great promise for the use of GnRH to induce early postpartum ovulation and CL formation in cows.¹² Another project that became my Ph.D. thesis compared the luteotropic effects of hCG and GnRH

in normal cattle and in dairy cows treated for ovarian follicular cysts.^{13,14} An interesting part of this work happened when several bovine practitioners were asked to find cows with follicular cysts for this trial. Even though it was specified that the cysts had to be follicular in type, 40% had enough progesterone to be luteal cysts if not normal CLs. When in 10 to 14 days I went to examine and treat the cows, most of that 40% no longer had the ovarian structure originally thought to be a follicular cyst. A review of potential uses of GnRH in cattle was presented at the first SFT conference.¹⁵

University of Minnesota Faculty

With completion of my graduate program at MSU, it was time to find a real job. Back at the University of Minnesota there was a temporary position to be filled while Ray Zemjanis went to Africa to teach for two years. The Theriogenology group had changed greatly since my graduation. Now Ed Mather, Howard Whitmore, Borje Gustafsson (newly hired from Sweden) and Bob Wescott were the faculty, and residents included Shirley Johnston, John Hurtgen and Rolf Larsen. Also working closely with the Theriogenology group were the Reproductive Physiology group from the Department of Animal Science: Ed Graham, Bo Crabo, Alan Hunter and Jon Wheaton. Members of both departments participated in the Theriogenology Graduate Program, in which 12 to 15 veterinarians were enrolled. Later Ed Mather moved to Michigan State University and Borje Gustafsson and Howard Whitmore went to the University of Illinois. They were replaced by Ray Zemjanis returning from Africa, Norm Williamson from the University of Melbourne and myself. After completing her

Ph.D., Shirley Johnston joined the faculty as Small Animal Theriogenologist. Dr. Mel Fahning returned to the program after several years in private practice and bovine ET business. These were rewarding times with an excellent teaching and clinic program for veterinary students, and productive teaching and research with veterinary residents and graduate students in Theriogenology.

With a series of graduate students we continued studying applications for PGF2 α and GnRH in cattle. Now we had two PGF2 α products (Estrumate® and Lutalyse®) to work with. Despite ads to the contrary we could find no significant difference in the luteolytic potency between these two products in dairy cows.¹⁶ We did however make some interesting observations on factors affecting results with either product when treating unobserved estrus in dairy cows. We did several fertility trials in cooperating private beef herds. Cooperating farmers would assure us that the entire herd was ready for the breeding season when we planned for the first PGF2 α injection. But a pretrial palpation would almost always find at least a few pregnant cows! A good lesson for everyone involved was that, at least in the first year of a PGF2 α controlled breeding program for beef herds, never treat cows prior to checking that some might still be pregnant. We also looked at the efficacy of the PGF2 α products to induce abortion in feedlot heifers¹⁷ and causes of the variation in the timing of estrus after PGF2 α treatment. Then the fun began when it became possible to do PGF2 α application trials in lactating dairy cows; first in individual cows with unobserved estrus¹⁸ and later in herd breeding programs.^{19,20} Today many dairy herds use

multi-product, multi-treatment programs for breeding that eliminate estrus detection altogether.

One of the real highlights of my faculty career came in 1984-85 when I was able to go on sabbatical leave at the Swedish Veterinary College. At that time the Ob/Gyn Department included Drs. Stig Einarsson, Kjell Larsson, Hans Kindahl as well as many excellent staff and graduate students. Their courses, facilities, clinical service and research were first class. I could not speak Swedish so I did very limited lecturing; rather I mostly helped the graduate students with their research projects. My own research efforts that year were to focus on measuring a PGF₂ α metabolite. This was thwarted by a small technical detail that became a painful lesson. We changed to a new source of tubes for blood collection without testing to see if the new tubes affected assay results. After all samples had been collected, we learned that the new tubes somehow interfered with the assay negating nearly a years' work. My family and I will never forget the hospitality and friendships we enjoyed that year.

We returned to Minnesota to some changes. Ray Zemjanis retired and was replaced by Harry Momont. Norm Williamson moved to the veterinary school in New Zealand and Jerry Olson joined us. Shirley Johnston moved into administration. Harry Momont moved on to the veterinary school in Wisconsin. Margaret Root Kustritz came on board to work in small animal theriogenology and Mats Troedsson joined our group specializing in equine theriogenology.

One Last Trial

Over the years we had done many projects looking at various means to maximize control of the timing of estrus and ovulation in cattle. These included endometrial irritation, estradiol cypionate (ECP), PGF2 α , GnRH, hCG, removal of the ovary containing the preovulatory follicle,²¹ etc.

The last experiments I undertook involved two protocols that were tested for potential to improve AI submission and pregnancy rates achieved by using PGF2 α (Lutalyse®, Pfizer Animal Health, New York, NY, USA) in dairy cows with unobserved estrus judged to have a PGF-responsive CL by ovarian palpation. In Expt 1, 151 cows were selected and treated with PGF2 α . Cows in the experimental group were treated with 1.5 cc (3 mg) of ECP IM at 30-34 hrs after PGF2 α while controls had no further treatment. Significantly more cows treated with PGF2 α plus ECP were seen in estrus and AI'd within 6 days of PGF2 α than were cows treated only with PGF2 α (91% vs. 53%). Estrus behavior was more tightly synchronized for cows treated with PGF2 α plus ECP than for cows treated only with PGF2 α . Resulting conception rates were similar (55% vs. 58%). Therefore pregnancy rate 6 days after PGF2 α was higher for cows treated with PGF2 α plus ECP than for cows treated only with PGF2 α (50% vs. 31%). In Expt 2, 197 cows were similarly selected and treated but all cows were AI'd at 72-76 hrs after PGF2 α without regard for estrus behavior. There was no significant difference in pregnancy rates between groups, 40% for 98 PGF2 α plus ECP cows versus 35% for 99 cows treated only with PGF2 α . Results showed that a 3 mg dose of ECP 30-34 hrs after PGF2 α treatment 1) can increase AI submission and pregnancy rates in unobserved estrus dairy cows judged by palpation to

have a functional CL when AI'd based on detection of estrus, 2) can tighten the estrus response pattern of responding cows, and 3) but did not improve pregnancy rate results when cows were AI'd by appointment at 72-76 hrs after PGF2 α .

I did not publish this research although I believe it demonstrates significant results for controlling estrus and ovulation with the combined use of PGF2 α and ECP. Unfortunately, the work is now nearly irrelevant because of public health concerns regarding estradiol in the human food supply and the fact that ECP is no longer marketed for use in dairy cattle. Nonetheless, these findings were a rewarding culmination to 35 years of theriogenology research. I am pleased to have had the opportunity to share them with you today.

Graduate Students

Working with graduate students has probably been the most rewarding part of my career. I totally enjoyed the chance to help them search for goals, answers and their future. In fact most of these ladies and gentlemen gave more to me than I gave to them. Every one of them educated me in some way. I have been able to visit many places and do many things. With Ahmed Tibary, I saw great horsemanship and some of the world's most beautiful Arabian horses in Morocco. I saw beef production and the AI industry in Argentina with Miquel Fortin. I reviewed theriogenology curricula and graduate programs at 3 veterinary colleges in Thailand with Preeyphan Udompresert. By the recommendation of Juan Ramono, I visited dairy farms and gave CE lectures for veterinary practitioners in Uruguay. With translation help from Stephano

Romagnoli, I lectured at the veterinary school in Pavia, Italy and to practitioners in Sardinia. From Ting Q. Zhang, I learned about China. When I started, my world was quite small but by these relationships it is now much more complete. I cannot list you all here but please know that I am grateful for the experiences we shared. Thank you!

Retirement and Beyond

Bovine theriogenology and academia have been very good to me and my family (wife Trish, daughter Ann, son Tony, daughter-in-law Sarah Beth, and granddaughter Avery). I cherish the memories. After 35 years it was time to walk away – while I could still hit a golf ball. Since golf season is short in Minnesota, I soon needed another activity. It has been surprising what a veterinary education and a theriogenology career prepared me for. For 6 years now I have done corneal excisions on organ donors as an eye procurement technician for the Minnesota Lions Eye Bank. This too has been an interesting and rewarding experience.

If you have not already done so, I encourage you to register as an organ donor, discuss your wishes with your next of kin and give the gift of life or sight to someone in need.

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