THIRTY SEVEN YEARS WORKING WITH CATTLE, HORSES
AND OTHER CREATURES.
WHAT DO THE NEXT THIRTY SEVEN HOLD?

R. M. Kenney, Professor of Reproduction
University of Pennsylvania School of Veterinary Medicine
New Bolton Center, Section of Reproductive Studies
382 West State Street, Kennett Square, Pennsylvania 19348

Introduction

It is a great honor to be awarded the opportunity to give the Bartlett Lecture. It is also a frightening undertaking for one who is really not a public lecturer but merely one who has been a presenter of clinical and research reports. As a consequence, it was with considerable trepidation that I have accepted this high honor and have been launched onto a very harrowing path leading to this lecture today. Since there are no guidelines for the lecture, one first has to decide on a subject. It is not easy to make such a decision when you must speak in front of long-time friends, mentors and, worst of all, total strangers. After much deliberation, I have decided to consider how veterinary medicine has changed, from my point of view in a few selected areas, in the time since I graduated from veterinary school in 1954 from Oklahoma A & M College. After considering the changes I would like to then think about how much was predictable. This approach has been prompted by my discussion with students - which is a common manner for ideas to be prompted - because in telling them how things used to be they are surprised to realize how much less we knew only 37 years ago. It is staggering to reflect on how much things have changed in my relatively short time in the profession. I won’t try to recall all the changes but will recall a few so as to remind us how far we have come and hopefully prod us to think about where we are going and whether we are going there for the right reasons. Like many others I have concern about veterinary education, where it is headed, why it is headed there and what we collectively should be doing to reach proper goals.

Title

In regard to my title, the past thirty-seven years is generalized from my personal exposure. I’ll watch as many as the next thirty-seven as possible. However, one hundred and three years is difficult to complete but nonetheless the developments should be interesting and I hope will be good for veterinary medicine. A subtitle for this talk could be “Change is Certain. Is it Predictable?”

Like many in this audience my early life was influenced by several veterinarians. As a boy, I was familiar with the routine chores on a dairy farm but in retrospect the most influencing "act" for me was the veterinarian who would put his arm up the backside of a cow and tell us if she were pregnant, how far along if so and if not what her problem was likely to be. The far-reaching implications of that "simple" act became increasingly fascinating the more I grew out of my naivete about reproduction. In preparing this talk I real-
ized that fascination and amazement of my early youth, in a sense, culminated in the report Dr. Garner Greenhoff and I prepared on the correlative examination of the mare's reproductive tract.(1)

Change

One of the early changes in my professional career was the name of my alma mater. From Oklahoma A & M College it was changed to Oklahoma State University (OSU). I guess it is progress to go from a college to a University - it certainly sounds more prestigious but I was just as proud of being from A & M as I am of being from OSU. There should also be a bit of concern over the existence of three OSU's in the United States.

Of far more significance has been the almost tripling of the number of veterinarians in the US and the percentage shift in category of employment. In 1955 there were about 17,500 veterinarians in the U.S. while in 1990 there were 46,300! That is 260% increase. Due to lack of data from the '50's it is not possible to make direct comparisons between categories of employment but it is interesting to look at a few. For instance in 1956 fifty-one percent (9000) of U.S. veterinarians were general practitioners(2) while in 1990(3), if we combine the large animal (6266) and mixed (3269) categories, there were 9535 practitioners involved. In 1956 there were 2173 in small animal practice exclusively while in 1990 there were 19,380 an 890% increase!! If we add to this the small animal predominant group, the total is 24,526: that is 53% of the veterinarians in the U.S.!! The number of large animal practitioners has remained stable while those in "small animal exclusively" has gone from 12.4 to 42% of a population which has tripled.

Society of Theriogenology

My introduction to this Society was a long time before Dave Bartlett devised the term Theriogenology.(4) In fact it was in the days of the Rocky Mountain Society for the Study of Breeding Soundness in Bulls, our parent organization which was organized in 1954.(5) The introduction occurred in 1959 while I was a graduate student at Cornell with Drs. McEntee and Hansel, having recently left dairy practice in Vermont. My wife and I had gone to Cornell to do a PhD in pathology under Dr. McEntee with the desire for me to become a better diagnostician of reproductive problems. One of Hansel's graduate students was Lloyd Faulkner, a veterinarian from Colorado State University. At that time Lloyd, among many other things, was transplanting rat pituitary glands beneath the renal capsule. Lloyd set up these rats with transplanted pituitary glands as an in vivo system, isolated from direct CNS influence, in a search for hypothalamic substances acting on the pituitary. He left it to others to fund GnRH! Also among his many other activities Lloyd was evangelizing for the Rocky Mountain Society. The origin of the Society is interestingly documented by Harold Hill in the Mobile, Alabama Proceedings (1979) of the Society.(5) Lloyd prevailed upon me to join the still fledgling Society. It frankly didn't take much pressure because the organizers' interests involved one of the areas I was woefully deficient in, that is, understanding male infertility. It still fascinates me that the impetus for forming the Society arose when the bulls in the Crow and Pawnee Valley Grazing As-
sociation range in North Central Colorado\(^5\) including those at the Wyoming Hereford Ranch\(^6\) suffered scrotal frostbite and "nearly nothing was known about semen quality in range bulls".\(^6\)

I regret having had to miss the 1988 Bartlett lecture in Orlando which Lloyd gave.

Back in the 50's and 60's members would receive the publication of the Society which was a set of mimeographed notes distributed when the "spirit moves and time permits". They were a great beginning from a bunch of busy guys operating in the right spirit. Life and the Society have changed mightily over the ensuing years but I shall always be grateful for the help and advice I have received from not only Lloyd but also Ed Carroll who came to Cornell for a master's program while I was there and to Les Ball who spent a sabbatic year with us and with whom we shared some research projects as well as watching a few hockey games when Cornell was National champion. Les gave the 1990 Bartlett Lecture last year in Toronto.\(^7\)

My involvement with the Society, other than being a faithful member, involved several years in the 70's when I served a couple of terms on the board of directors during which time I tried to be a force for moving the Society into multiple species and both sexes. I also played a role in the development of the stallion manual for the Society.\(^8\)

One aspect of the development of the Society which I would like to raise concerns the role played by Lloyd Faulkner. It is clear that Harold Hill was the founding father of our Society and that Dave Bartlett not only developed our name but also played a major role in our acceptance by the AVMA Council on Education. In between Harold and Dave what happened? The fate of the Society was primarily in the worthy hands of Lloyd Faulkner. He had not only a vision of what the Society should and could be but he manipulated and nurtured it to enable it to survive. He also had a dream of forming the College of Theriogenology. It was because of his persistence in following the necessary steps to take us from a narrow to a broad-based Society and to then develop the College (with suggestions from the AVMA and the help of Dave Bartlett) that we are where we are today. I believe we are here today primarily because of Lloyd's unsung efforts in the past. Because we all carry a debt of gratitude, I salute you Lloyd.

**SELECTED CHANGES THAT HAVE OCCURRED OVER 37 YEARS**

In the next portion of this presentation I would like to discuss a few selected and memorable changes that I and many of you in the audience have witnessed over the years. For those too young to have witnessed the changes, you may be startled to learn how different our profession was only a relatively few years ago.
Surgery

The only reproductive tract surgery I would like to mention is the Caesarean Section of the mare. While it is commonplace today, in 1954 it generally was not attempted because of the susceptibility of the equine peritoneum to infection. The susceptibility of the cow was much lower so Caesarean Section in both beef and dairy cattle was routine. Antibiotics and sterile technique have removed a taboo.

Sexing Semen

We all learned in basic biology that the mammalian world starts off, at least at birth, as half male and half female. From time to time skewed ratios have been reported and such observations have added fuel to the dream that maybe we can tip the balance toward one sex or the other for some particular benefit. Examples of such desires are females for dairy herds or males for race horses. Many approaches have been tried but in August 1989 the first validated techniques for separating fertile X and Y sperm was reported by Dr. Larry Johnson and his collaborators. This is a landmark development and certainly we will see a dramatic unfolding of further improvements of man's ability to preselect sex. It was a dream in '54 and a fact in '91. Since the SRY gene was proven to be the male determinant this week (9 May 91), it will be interesting to watch the development of its role in sexing as well as in numerous other places. What will we be doing in 2028?

Control of the Cycle of Cattle

Manipulation of the cycle of the cow to achieve specific reproductive goals was in its infancy in 1954. In fact, the only effective technique to shorten diestrus that I can recall was "enucleation" of a "persistent" C. L. It was an effective technique in that the cow would come in heat in about 3 days. With the exception of pyometra and mucometra the problem was not persistence of the C. L., rather its presence indicated merely that the cow was cycling, the C. L. was normal and appropriate heat detection was the problem. In addition, enucleation resulted in serious fimbrial adhesions! Efforts to control the cycle began in 1948 when Christian & Casida delayed the onset of estrus by the daily administration of progesterone. Since that publication, increasing numbers of approaches and agents have been used with the objective of producing synchronous ovulation or ovulation within a limited time span. In addition to a series of oral, injectable and implantable progestins, some rather exotic, by 1954 standards, agents and approaches have been used. They include oxytocin, iodine, a number of variations of prostaglandin F2alpha and gonadotropin releasing factor.

After progesterone came the observation that systemic administration of oxytocin could shorten the life of the C.L. and thereby the cycle. About the same time we learned iodine in the uterus as well as uterine distention also shortened the life of the C.L. We subsequently learned these manipulations released prostaglandins. Then along came exogenous prostaglandins: the most effective, reliable endocrine product ever produced for
our practice bag. Imagine control of the cycle with a product originally found naturally in male accessory glands to control the C.L. yet commercially produced from sea weed! It's ready availability is largely due to the Upjohn Co.

These various compounds have been used to control the cycles of beef and dairy cows for a variety of management reasons. The present state of their use has been presented by Larry Rice and Brad Sequin for beef and dairy cows in the 1987 proceedings of the Society. The oldest reference in their bibliographies are 1961 and 1974 respectively.

Revolutionary to say the least and we can be sure there is more to come. Who knows from what direction and source? Some of you may, but I don't.

Control of the Cycle of Mares

The traditional way to control mare cycles in the 50's was uterine infusion of warm saline which was subsequently shown to cause the release of endogenous prostaglandins - if it is the correct pH. Prostaglandins have replaced the old infusion set-ups. For synchronization of ovulation, however, that short-term suppression of gonadotropin secretion with the progesterone and estrogen treatment of Loy has been much more precise. Loy has combined this technique with a lighting program on numerous breeding farms over the last ten years. When properly carried out, he has found that with the techniques combined he can have 50% of the open mares, including early foalers, in foal by the end of February! How's that for progress.

Johnson's discovery of the ability of GnRH to bring anestrus mares to successful ovulation has given us even more control over the mare's cycle. The inability of GnRH to induce multiple ovulations remains an enigma but at least we are a long way beyond the knowledge of the 50's.

An overview of control of the mare's reproductive cycle has recently been given by Frank Bristol.

Repeat Breeder Cows

The syndrome termed the "repeat breeder" cow was with us in 1954 and is still with us in 1991. In Europe, what we in the U. S. call the "repeat breeder" had similarities to what they called "enzootic infertility". This condition was first shown to be due to Vibrio fetus by Stegenga, Terpstra and the great Vandeplasche who, with his collaborators in the early stages of the development of our knowledge of the disease, put together the pathogenesis, effects and treatment of this disease. Vibrosis became widespread with the implementation of artificial breeding since semen extenders provided fine culture media for Vibrios. Probably it is a sign of my age but you will note I have trouble talking about Campylobacteriosis. Even freezing extended semen preserved the Vibrios along with the sperm. Many famous investigators are associated with our vastly improved methods of diagnosing, preventing and treating vibriosis. They include such
names as McEntee, who sustained a critical research program for many years at Cornell, Gilman, Frank, Plastridge, Hoerlin, Seger, Carrol, Clark and Winter. The contributions of Winter are particularly important in regard to elimination of the diseases from bull studs. Since diagnosis in individual bulls is dependent on culture, the demonstration of reliable techniques was critical. The best media were based on a formulation originated by Plastridge. One of Winter's graduate students developed a fluorescent antibody (FA) technic for use in the bull, which when accompanied by good culture techniques virtually assures that no carrier bulls will be missed. A fascinating finding was that of another of Winter's students who, while using the FA technique, demonstrated that the Vibrios colonized the penile epithelial crypts thereby making it more difficult to gain access to them with medication. This observation also formed the basis for the explanation of seasonal spontaneous cures in young bulls since they have many fewer crypts thereby facilitating ready clearance of the organisms. When these improved diagnostic technics were put together with the stopping of bull to bull transmission at collection time reliable removal of Vibrio from bull studs became possible.

These findings helped the dairy industry but were inadequate for beef cattle which are handled more as herds than individual animals. For them Hoerlin and his workers Clark and his and Bouters and his have been the saviors with their vaccinacation technics. On a personal note, after running a few vibrio tampon tests (which are used to detect vaginal antibodies) with preputial mucus of infected bulls and not detecting antibodies in carrier bulls, I thought vaccination would not free a bull of the organism. What's the old story about fools venturing in where they don't belong?

When I first got out of veterinary school, it was felt by many that if we could "get on top" of vibriosis we could virtually eliminate repeat breeders. While the above men "put us on top" of Vibriosis to the point where the disease is no longer a serious factor in dairy cattle, repeat breeders are still with us.

The other infectious disease which contributed to repeat breeding was trichomoniasis. Our friend and leader Dave Bartlett, when I first heard of him, was in his first incarnation as an international authority of bovine trichomoniasis.

A couple of non-infectious areas of investigation seem worthy of further pursuit. Preliminary studies indicate that an in-depth evaluation of the embryos from repeat breeders as well as the survival of reciprocal embryo transfers between normal and repeat breeding cows would be fruitful areas. This was an area of much interest to me but from which I had to withdraw when my precious wife Ellie became terminally ill.

Of course there are many possible causes of the repeat breeder syndrome. Many of these have been outlined by Drost but even when all these have been eliminated as causes there remain too many repeat breeders without a diagnosis. That shall remain as a big challenge diagnostically and therapeutically.
Repeat Breeder Mares

Such mares have always been with us and no doubt always will. Although we have learned a tremendous amount about the biology of reproduction of horses since 1954, it is not clear how much the profession has progressed in improving equine fertility other than in individual instances. It is probably similar to the record in Germany where evaluation of records over 158 years revealed no change in overall foaling rate!\(^{(33)}\) These investigators postulated that veterinary contributions had a positive influence and therefore innate fertility had decreased! We won't know the real answer until a broad, multifactorial approach is completed. It has been repeatedly stated that the horse as a species is of low fertility. I doubt it but until we properly breed a significant portion of the population of this seasonal breeding species in "its" breeding season we really won't know if it is intrinsically subfertile. I suspect using the proper season and proper management would do more for maximizing foaling percentage than all the medical interventions we make. I say that because in 1969\(^{(34)}\) while designing a small program to minimize breedings and cycles per pregnancy, in collaboration with AH Rajamannon, twenty-nine mares were teased but not bred during April and May. All mares were then bred on their first heat in June which we had selected as the month for optimal fertility. Thirteen randomly selected mares received hCG on day 2 of their first June heat and were bred once on day 3 only. The sixteen controls received no hCG and were bred on day 3 and every other day thereafter until they went out of heat. Since the owner of the mare needed pregnant mares, he insisted mares not receiving hCG get bred more than once per heat.

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The three non-pregnant mares were bred repeatedly during June and July and failed to become detectably pregnant. They never received a fertility exam.

Therefore I suspect, the most salutary effect we can have on breeding efficiency would be to change the Universal birthday from 1 January to 15 March and begin breeding on 1 May. Because moving the birthday forward from January to March would cause the loss of one crop of two year olds for racing, the logical move is to go "backwards" and move the eligible breeding date backward from January back to March. By doing so the maturity of "two year olds" would be increased which is an additional benefit. The Standardbred industry attempted to do this in the 70's. They planned to move the birthday back 2 months at time in 5 increments until it reached 15 March. In their first move they allowed foals born after 1 November to be registered as of 1 January two months later. The problem is they stopped there and did not progress backwards. It was an enlightened,
landmark attempt and a pity it failed. It failed because of the dilemma in the minds of breeders who failed to appreciate the overall purpose. They stopped at the worst possible time - November - which is a nonphysiological time to breed therefore requiring artificial lighting. Furthermore they had to keep foals inside in the winter and they did not do well.\(^{35}\) Instead of stopping they should have kept moving back quickly. The studies of Cooper and Wert\(^{36}\) showed that it was a very feasible undertaking in that it was possible to obtain normal pregnancy and foaling rates during the winter on winter feed by the judicious use of lights.

Endometrial biopsies have helped greatly in the diagnosis of individual problem mares.\(^{37}\) It helps to detect endometria that possess serious problems detectable in no other way as well as those that are normal. The latter is a very useful finding too easily overlooked. On finding a normal endometrium one knows immediately to look "outside" the endometrium for the source of the problem. One interesting aspect of my involvement with the biopsy is that I worked for years on cow endometrial histology in the hope of eventually detecting causes of repeat breeding. With occasional exceptions the cow biopsies were essentially unrewarding. When the same approach was applied to the mare, things "fell right into place!" I wonder if they would have done so without the work on the cow?

Another diagnostic improvement that has helped avoid many false diagnoses is the doubly guarded, doubly occluded swabbing technic of Terry Blanchard\(^{37}\) that reduces contaminants to a minimum. He has shown why there are so many false positive swab cultures as a result of inadequate instrumentation and technique while simultaneously raising concern about non-infectious inflammation.\(^{39}\)

Swine Industry and Practice

The swine industry has gone through a greater revolution in the last 37 years than the other segments of animal agriculture. The changes in it were preceded by the same ones in the poultry industry and are now being followed by both cattle industries.

In the 50's much of hog practice centered on hog cholera. As students we learned how to balance virus and serum in simultaneous vaccination. After going through several phases of control, cholera was completely eradicated in the 60's, forcing the profession to take a broader view of maladies of the pig. This approach was also forced by the trend toward larger farms and confinement husbandry from which evolved a new set of problems largely centered on the digestive system. By a happy set of circumstances involving universities with good laboratory services to aid leading-edge practitioners the profession was able to understand and control enteric disease in the 70's. It was an era of traditional veterinary approaches using pathological diagnoses and therapeutics based on research findings. It was also a time of application of good biology to breeding herds. Swine practitioners became organized, with international relations becoming important after the International Pig Society meeting in 1969 in Cambridge.\(^{40}\)
The 80’s were different. There were many farm problems of an economic nature while there was an abundance of pigs which forced veterinarians to move out of the disease era into the broader view of hog farming as an economic enterprise. It was no longer reasonable to consider primarily disease problems in isolation - rather the veterinarians had to provide good biological and financial accounting as part of their service. Leading practitioners are now production advisors who provide traditional veterinary skills as well (40).

The swine industry continues to evolve and as it does, it is difficult to be certain what will happen. Veterinarians will be challenged to be prominent players in the industry. There is no question but that the systems analysis approach will be critical, while there will be increasing numbers of specialists in nutrition, ventilation, cash-flow needs and genetic programs (40).

With an increasing amount of research being conducted by private organizations as university dollars shrink, veterinarians will need much stronger training in experimental design and interpretation of research results. Veterinarians should be trained to become not only science advisors but information managers of both financial and biological information. Veterinarians have and should continue to have the best training of person available if our veterinary academic programs can meet the challenge to produce astute, solid, applied scientists (40).

For the next ten years the swine industry will be in dire need of information managers but over the next 37 years biotechnology will increase greatly in importance (40). Practice will not be biotechnology but the application of the products of biotechnology. With swine and other species if we go away from the whole animal, we are in danger of self destruction as a profession.

Dairy Herd Health

Major veterinary concern about fertility occurred when artificial breeding of cattle became widespread. The first bull stud to switch to completely frozen semen was in Canada in 1954 (41) - the year of my graduation. Naturally, veterinary education in 1954 included courses in normal and abnormal reproductive processes. By and large the focus in the 50’s was on individual animals and the biology of reproduction (42). Artificial breeding programs for cattle were run largely by cooperative bull studs which tried to bring to the farmers management ideas and techniques for breeding. They helped. It impresses me that in the 50’s heat detection of dairy cattle was a major problem and now 37 years later it impresses me even more that it remains a major problem! The cow exhibits homosexual behavior when in estrus so detection should be easy. The mare in contrast does not exhibit homosexual behavior yet heat detection is not such a large problem because detection has been made labor intensive out of necessity.
As discussed earlier artificial breeding of cattle early on was less successful than its first bright promise until it was discovered that many failures were due to Vibriosis. Nutritive extenders were as good for the Vibrio as for sperm! Artificial breeding began to reach its potential with the discovery that Vibrios were sensitive to streptomycin and the industry immediately became an inverted pyramid balancing on streptomycin until the industry was put on a much safer footing with the elimination of Vibriosis from the studs.

In the 40's and early 50's several prominent veterinarians who delivered herd health programs based primarily on reproduction. Men such as Elmer Woelffer in Wisconsin, who gave the 1986 Bartlett lecture, Wilson Haubrich in New Hampshire and Earnest Deubler in Pennsylvania showed the way in early attempts at herd health practicing in elite herds. I am sure there were others of whom I am not aware. Nonetheless, the concept of what they were doing by providing routine periodic, broad-based service rather than providing emergency or "on request" service was eventually picked-up by the veterinary schools and included in the curricula.

Since the '50's herd health management has increased in importance alongside the pre-existing concern for individual animals. This move has also been facilitated by the control of catastrophic disease and the necessity to be concerned about subclinical disease. Concern for the herd, as a unit, rather than individual animals has moved further, faster and more completely in swine practice but cows are catching up.

The shift of emphasis from the individual to the herd veterinary economists is demonstrating the economic benefits of herd management of subclinical problems. There are considerable economies of scale to be derived by spreading the fixed costs for "treatment" over many animals. The accounting process becomes more difficult because of the dynamism intrinsic in all matters concerning a herd.

In swine and cattle herds the objective now is to attain the economic optimum, not necessarily the biological optimum. Disease is of concern, of course, but rather than try to eliminate it (because to do so is too costly) disease is controlled and interventions are selected on their economic benefits. My colleagues Dave Galligan and Jim Ferguson at Penn are using their analytical systems and application of derived solutions to make routine savings of 12-15% in feed costs (which are 50% of total costs) when first working with a new dairy farm while simultaneously boosting milk production! It is the rare disease whose control yields such benefits.

This fascinating, worthwhile approach is here now and will be widely practiced by veterinarians in the immediate future. No other profession will be in a position to match what we can train our students and practitioners to handle. Veterinarians will know good biology but they will also know the value of and be capable of information processing in order to make informed, sound economic decisions - thereby becoming critical elements of the management team. They will be trained to use their heads along with their brawn. Our profession is looking at a golden opportunity to benefit society for the next 37 years but the opportunity won't last. Opportunities are grasped by someone. It may be our best
chance to be a major part of the miracle of American agriculture which has had so much to do with the strength of this country. Will our schools grasp this one now or will we end-up wishing we had? And which schools will it be? Veterinarians are the logical ones to provide this service because no one else with such a broad education visits farms on a routine basis. So while we properly discuss ways to expand into relatively new and promising areas let’s not forget some of our prime responsibilities - agricultural animals - for which information and its management are revolutionizing production and therefore practice.(44)

"Small (Companion) Animals"

The role of companion animals in our society and in our profession has taken on an increasing importance, for a variety of reasons, since the mid 50's. As of 1990 fifty three percent of all U. S. veterinarians were in exclusively or predominately small animal practice!(3) Our knowledge of reproduction has not kept apace but has recently improved considerably. The general outline of the seasonality of breeding in dogs and cats and the general features of their estrous cycle were known in the mid 50's, while in subsequent years this general knowledge has been filled in with detail. For example, timing of ovulation has been precisely pinpointed enabling increased efficiency of breeding practices.(45)

In the '50's the rule was to breed bitches 2 days after the bloody discharge became clear. The range in ovulation after this change is 2-24 days! By using the progesterone assay to detect the LH surge and therefore the time of ovulation, it is now possible to time breeding to maximize pregnancy rate, litter size and time of parturition.(46) We have also learned how to safely use prostaglandin for termination of early pregnancy.(47)

In the 50's we thought the relatively seasonal cycling of bitches was controlled by light but know now that it is not. In contrast, cycling of queens can be controlled by light.

Our increase in knowledge is not restricted to females. We now know about prostatic hyperplasia and infection associated with advancing age and know much more about frozen and slow cooled semen although their problematic state raises hope for the future improvement. Now if someone will only improve the anatomy of the cervix of the bitch so we will be able to put the semen in the cervix or uterus readily.(48) Why improve the product if you cannot put it where it belongs?

Recently we have learned much more about the abnormalities of sexual differentiation in dogs and that Mullerian Inhibiting Factor has a role in this species as well.

Thus small animal reproduction has clearly taken on a life of its own after playing second fiddle for so long to the efforts expended in behalf of the larger domestic animals. Since 53% of the veterinarians in the U.S.(3) are small animal practitioners it is appropriate that they be armed with broad, deep, accurate reproduction information. This renaissance is best expressed by the publication of the Proceeding of the 1st International
Symposium on the subject. It also considers all the above topics and much more in detail. We can expect much future improvement of the efficiency of reproduction for man's favorite companion animal - the dog.

Three persons who have been particularly prominent in the renaissance of small animal reproduction are Drs. Shirley Johnson, Patty Olson and Pat Concannon whose clinical and endocrinological efforts are so complimentary.

In the future there will be a continuous struggle to exert control over the estrous cycle which will probably include the use of GnRH. We can also anticipate considerable effort toward the improvement of techniques for freezing and "slow-cool" of dog semen for transport or short term storage. To maximize the benefits of these methods of semen handling I wonder who is going to improve the anatomy of the bitches cervix? Why improve the product if you cannot place it where it belongs?

On the downside is the lack of control of dogs and cats neglected by the citizenry of the United States. From 1985 to 1988 10.3 to 28 million dogs entered shelters and 5.8 to 16.6 million were euthanatized. The numbers for cats are a bit lower. If we put average weight of each dog at approximately 35 lbs it amounts to 581,000,000 pounds or 290,500 tons to be disposed off! As a society we must face and solve this disgrace and we as a Society must do even more. We should all take time to examine the serious loose pet problem as presented in the April 1991 JAVMA put together by Pat Olson. Hopefully it won't take 37 years to solve this serious problem.

Endocrinology

Progesterone assays in the 50's required a liter of plasma which was extracted with large amounts of organic solvents then purification on thin layer chromatography and finally analyzed by UV spectrophotometry. It was pretty easy to run one sample a week!! Imagine the time and effort to develop baseline data on the bovine CL or follicular function to say nothing of dynamics. No wonder incorrect data was published concerning reproductive endocrinology in domestic animals in the 60's.

This was all changed as a result of the observation of Berson & Yallow that certain plasma proteins (transcortin) could be used to bind hormones. Subsequently Beverly Murphy used transcortin to devise the competitive protein binding (CPB) assay for progesterone (P4) using only 2 ml amounts of plasma.

Then along came radioimmunoassay (RIA) using antibodies derived against the desired hormone rather than natural proteins used in CPB. The protein hormones can be measured without extraction! With only 25-50 ul samples required, sampling can be frequent. RIA has remained one of the main assay techniques for reproductive endocrinology since the late 60's. Along with radioimmunoassay, the radioreceptor assays were developed, enabling the gaining of critical knowledge about the interaction of hormones and target tissues since the response to trophic hormones depends on the number of avail-
able receptors and amount of hormone. Hormone profiles alone can only suggest meanings.\textsuperscript{[51]} In the 80's the advance has been in enzyme-linked steroid endocrine assay techniques. These assays are already finding application in new and practical ways and will probably be available in the near future for solving practical clinical reproductive endocrinological problems.\textsuperscript{[51]}

There are numerous avenues opening in the future. One specific avenue judging by the studies of Don Holtan \textsuperscript{[53]} on the pregnant mare and fetus, is that we have more to learn about the control of well being of the equine fetus - particularly in regard to the pregnancies - but we may be on the threshold of having accurate assays for monitoring fetal viability.

An entire new exploratory frontier seems to be coming into view in regard to the endocrine, paracrine and autocrine role played by the transforming growth factors (TGF) family of genes. We learned some time ago that gonadal inhibin inhibited FSH secretion. Now an entire family of these peptides is known in numerous locations and only in time will we learn their roles. It is a bit reminiscent of prostaglandins. We first heard of prostaglandin F\(_2\)alpha and its role of involuting the C.L. We now know it is only one of a big family with both reproductive and non reproduction roles.

Embryo Transfer

In 1954 no one considered transferring embryos between cows or between mares on a commercial basis. Now it is widely practice with international shipment of frozen bovine embryos. How far away is transfer of genes and cloning on a commercial basis? Will veterinary medicine play a role?

Genetics

In a sense, after infectious disease have come under greater control and close to elimination, genetic disease and nutrition take on major concern. In 1954 numerous genetic conditions of domestic animals had been identified although the precise mode of inheritance too often was not known. Control of some of these conditions could be achieved by selective breeding but all too often such breeding was not implemented when there was some financial gain to avoid it - at least in cattle, horses and probably other species as well. Who remembers when short-coupled, compact Angus were the rage and bulldog calves were the result? How many breeders would rather you did know they produced bulldogs? However, the cooperative bull studs have been a major factor in removing from service bulls which are carriers of proven genetic traits. Such control in other species must rest on the breed associations which often seem reluctant to take action. The veterinary profession could play a much larger role, in the next 37 years, in the identification of genetic problems, the definition of mode of inheritance as well as knowing how to diagnose known disease while helping to develop effective programs for selection.
against deleterious genes in livestock, companion and recreation animals.\(^{(54)}\) The bellwether program in this area is directed by Don Patterson\(^{(54,55)}\) in which they have shown that the dog and cat genetic research helps both the animals and man.

Coincidentally, in the recent past, the field of molecular biology has developed the tools and knowledge to enable biomedical scientists to make major inroads on genetic disease. Much of the impetus for such studies will come from the need to study mammals with genetic disease which are homologous to those in humans.\(^{(54)}\) Such diseases exist in the livestock, companion and recreation animal populations. However the emphasis of research is on diseases of laboratory animals, dogs and cats which are homologous to the same disease in man. Dogs are already known to have over 200 different genetic disorders. With so much live and inbreeding in horses we should be prepared to recognize genetic diseases in horses in addition to the classic combined immunodeficiency.\(^{(56)}\)

The truly remarkable change in genetics that was not predictable in 1954 is the potential opened by the development of transgenic animals. What veterinary school graduates of the '50's could have dreamed that in their life time they could be isolating genes to say nothing about inserting them in oocytes or other cells and thereby modifying gene pools?! Such a vintage veterinarian - Ralph Brinster - is one of the major pioneers in the production of transgenic animals.\(^{(57,58)}\)

While there are great hopes for what transgenic animals can do for animal agriculture, it appears that there is a long road from the promise of a new technique in mice to its application in agricultural animals.\(^{(59)}\) None are yet commercially feasible.\(^{(60)}\) In fact it appears that, in this DNA age, some of the less flashy techniques will be quietly making contributions before the high visibility ones do. The "quiet" techniques include such significant items as vaccines produced with recombinant DNA techniques (such as the \textit{E. coli} vaccine), new diagnostic tools and marker assisted selection of animals.\(^{(60,61)}\)

For the transgenic procedures knowing and using the proper gene controls and proper constructs is critical. For instance in mice transgenic animals are produced 2.5-6\% of the time \(^{(62)}\) while gene transfer of growth hormone in pigs results in an integration frequency of a mere 0.6\%! An unexpected finding in the transgenic pigs with the growth hormone gene\(^{(59)}\) was an increased incidence of pathological changes of the skeletal, digestive and other systems as well as anestrus in gilts and lack of libido in boars. These findings require basic research to unravel the many aspects of genetic control. While acknowledging that the application of gene transfer to domestic animals has come a long way it is clear there is much still to be learned regarding transgenic regulation. Given the current rapid rate of discovery, a few years might turn promise into reality.

Where does the veterinary profession fit into this picture? We need more Ralph Brinsters; where do we get them? As far as I can see it is fortuitous that Ralph is a veterinarian at a veterinary school. No one planned to produce him. What we need and what part of the thrust of the Pew National Veterinary Education Program aims to encourage is the formation of programs which can produce the type of veterinary scientists
that can successfully compete at the forefront of biological science. Do we have the resources to redirect our mission toward competitive basic research and still maintain our obligation toward maintenance of animal health?

Producing transgenic animals is only the beginning since the next step in our progress for control of genetic material seems to be the use of embryonic stem cells (ESC). Some of the potentials of which have recently been presented. Essential the use of ESC "has both extended and refined the types of genetic modifications that can be transferred into the germ line". The hopes for manipulation of mammalian genomes will probably come to fruition with ESC.

Whales and Falcons

While my life as a veterinarian has been largely devoted to horses and cattle, there have been a number of sidetracks - two of which I will mention briefly. One such interest involved the peregrine falcon which at that time was close to the extinction because of DDT. There was a remarkable young insurance man, by the name of Bob Berry, who lived near New Bolton Center and was learning how to capture, breed, raise and release peregrines. This was a major activity for Bob to which he devoted much time, effort and money. He conditioned birds to accept him as a mate and was able to get the males to mount and ejaculate on his hand. He would aspirate the semen and deposit it in the females who were also conditioned to "mate" with him. I tried to help Bob by finding some semen extenders to pick up the semen and store before depositing in the females in his effort to save these magnificent birds. The implication of what he was doing and why - saving a sensitive and wonderful part of our environment that we were destroying - made me even more concerned about man's impact on this his only world.

The other wild animal I worked with briefly also concerned environmental issues. Since there was interest in drilling oil wells off the north slope of Alaska the Bureau of Land Management was asked to develop an impact statement of the effect of such activity on the fate of bowhead whales. These whales migrate eastward past Point Barrow in the spring with the break-up of the off-shore ice and pass back through again before the fall freeze. In the spring the eskimos are permitted subsistence hunting of the whales. It is the carcasses of these whales that are used by a variety of scientists to study numerous aspects of the biology of the whale. I was fortunate to be invited to join Tom Albert's group which was the principle biology group. While I was concerned with the reproductive systems, two others from University of Pennsylvania were also involved - Bill Medway studied blood and urine, while Jeff Everett studied the respiratory and lymphatic systems.

It was interesting to deal with ovaries as big as a loaf of bread but whose oocytes are in the size range of a cow or a cat and probably the same amount of DNA!

The uterus is much like that of a sow yet the penis is like that of a bull! This means ejaculation is "instantaneous" and all that supposed "foreplay" in the mating season may include the real thing. We never got to the point of developing an AV!
It was a fascinating project with the promise of many interesting insights to come although embryo transfer, as a means of saving this endangered species, seems remote. I withdrew from the project to allow others to continue when my Ellie became ill with ovarian carcinoma.

Knowledge and Communication

A major difference between our profession in 1954 and 1991 has been the increase of knowledge coupled with its rapid, widespread distribution. We have moved from an era when much of clinical practice was based on experience (empiricism) to one in which much more of clinical practice is based on scientifically derived evidence.

Look at the books available in 1954. Just for the fun of it go to the library and look over Runnels (Pathology), Udall (Medicine), Frank (Surgery), Milks (Materia Medica and Therapeutics), and Williams (Reproduction)! Look at what the students have today. I am jealous. I remember borrowing a precious mimeographed copy of Nieberele and Cohr’s book on pathology painstakingly translated by the Drs. Georgie from the German. They had undertaken this large task personally because there was nothing even approaching its breadth and depth in the English literature until Jubb & Kennedy published their first volumes. It is a whole new world now. Look at the texts available today in surgery and medicine. Imagine, if you can, what it was like without the availability of the encyclopedic Roberts’ text.\(^{(64)}\)

A good simile of what has happened is to compare, if you will, the slide rule of 1954 with the personal computer of today! Could you have predicted in the mid 50’s the availability of the personal computer we enjoy today and what it is enabling us to do?

That comparison serves as a good example of the difference in our knowledge base of 1954 compared to 1991. There is no comparison. It also is a good comparison of our ability to communicate our knowledge as well as all sorts of information. The tools of today were all unimaginable, or only in dreams, in 1954. From slide rules, mechanical calculators (the abacus never caught on) and telephones who would have dreamed of electronic calculators, personal computers, FAX machines, Xerox copiers and Internet.

If we have come this far in 37 years and innovations and knowledge are increasing at an accelerating rate, where will we be in 2028?

Another form of communication which has increased drastically since 1954 is travel. It is now common to have frequent colleagues and even students visiting us from outside North America and for us to reciprocate. What a rewarding and enriching way to communicate professional as well as societal matters. I have learned much by visiting and being visited by people from England, France, Germany, Poland, Czechoslovakia, Finland, Sweden, Italy, Spain, Africa, Brazil, Venezuela. Through such contact, the world gets smaller. While we discuss and try to solve professional and biological problems we come
closer as human beings. Hopefully these contacts will enlarge so that our Society and our general society will become more international by 2028. What form will our professional societies take? Even what forms will the general society be in?

Environment

We are daily made aware of what we are doing to our environment and a realistic view of what we are doing is a gloomy one. The process of deterioration of our environment is advanced and accelerating. It seems that the world economies are growing to keep up with a soaring population that will double to 10 billion in the next 40 years! Our air, our water, our soil, our wetlands, our forests and therefore our future are being sacrificed by pollution, waste and consumption of the planet's resources. It seems to me that all citizens of the U.S., as a society, must become an active force for making the earthshaking transitions that must be made in the immediate decade(s) ahead to make a sustainable future possible. The environmental foe, modern technology, must be made a friend. We of the developed world who are at the root of the problem, must become part of the solution. We of the profession, and specifically the reproductive segment, as pointed out by Dr. Theirs, that is the members of the Society and College, must contribute through increase in fundamental knowledge and importantly in its application for increased fertility and efficiency of reproduction in some species or segments of species while decreasing it drastically in other species - maybe including our own. Environmental problems are to be one of veterinary medicine's targeted, non-traditional areas.

Since the most effective population growth control of humans comes through an increase in economic status and increase in the latter results in increased deterioration of the environment - how are we to separate the two and save the environment and ourselves?

It took all of human history to build an economy that produced about $600,000 billion in output in 1990. Today the world economy grows by this amount every two years! With it has come unprecedented pollution, waste and consumption of resources.

We as a medical profession have an obligation to participate in the corrective measures involving animals and other areas where appropriate. If we want to be a part of solutions - not just discoveries - we must become activists for the necessary social changes.

THE FUTURE

After looking at the large changes that have occurred in the last 37 years involving all aspects of the profession one has to think about what this is prologue to in 2028. Because the rate of change is accelerating in society and in biological sciences it will be difficult to know which of the various predicted scenarios will come true. Much has been talked about at all levels of the profession and quite a bit has been written including some contributions from deep thinkers and philosophers. The most important prognostications have occurred under the provocation of the Pew National Veterinary Education Program and the very able leadership of Dr. William R. Pritchard. I can heartily recommend that all
of us read with care the publication entitled "Future Directions of Veterinary Medical Education" and then the Proceedings of the Tenth and Eleventh Symposia on Veterinary Medical Education. Thanks to the foresight and money provided by The Pew Charitable Trusts, whose president is Dr. Tom Langfitt, formerly a distinguished professor and neurosurgeon in the School of Medicine of the University of Pennsylvania, we are looking at ourselves introspectively while keeping an eye on our role in the nation and the world. It is clear that as a profession we are headed for social and biological challenges.

Dr. Samuel Thiers gave the keynote address to the Eleventh Symposium. He is a physician and president of the Institute of Medicine of the National Academy of Sciences. In his address Dr. Thiers made numerous important comments, from which all veterinarians can benefit. One in particular seemed directed to members of the Society and College of Theriogenology (as well as the components of the veterinary schools involved with teaching, providing service for and conducting research on animal reproduction). He addressed our profession as a whole when he said "... the one area where we (society) are absolutely dependent on you, reproductive biology." Have "we" (the reproductive segment of the profession) yet begun to address or even begun to think about such a responsibility? It must be very subtle if we have! This is a very serious challenge to our Society and College of Theriogenology as well as academia.

By and large the leadership in veterinary medicine has been primarily concerned with assuring that graduating seniors are prepared for handling the day to day aspects of reproduction. Only here and there has existed the vision to develop leaders in the development of fundamental knowledge of the reproductive processes and then apply them. For "us" to accomplish a proper response to Dr. Thiers will take great changes in the way reproduction, in both its research and applied forms, is viewed by veterinary schools. Such changes will, in turn, require substantial new funding sources. To accept the change and the challenge will mean new directions which will require appropriate leadership with substantial increases in funding. It will also mean increased competition with scientists with comparable research interests in medical schools and animal science departments. Is the profession up to it? We shall see. We are completing the discussion phase and entering the critical planning phase where we must turn to our strengths.

Veterinary schools should not become primarily research institutes. They must have a strong research component which in large measure should relate closely to whole animal problems, domestic, zoo, feral, wild, exotic and aquatic. The lot. Our most significant client has always been and probably always will be the animal industry. With the push toward basic science, we have to be careful that the clinical side of veterinary medicine is not slighted - for which there seems to be a disturbing tendency. Rather a strong concerted effort should be made to integrate the clinical and basic sciences in veterinary schools more than they ever have been.
TWO AREAS OF CONCERN

While I am a strong admirer and supporter of the profound influence the Pew Foundation's efforts is having on our profession I am concerned that more thought and effort is not directed toward two particular areas; firstly, there are too many unfilled openings for food animal veterinarians and secondly the insufficient concern about the development of academic clinicians. For me these are two essential areas of our profession. As we turn toward new areas to enter while emphasizing basic research, I would like to see and hear more discussion and see action on these two critical areas.

Insufficient Numbers of Food Animal Veterinarians

One of the problems which has been nagging the profession for a relatively long term is the insufficient number of properly trained veterinarians coming out of school to fill the openings in food animal practice. Even the federal capitation grants to veterinary schools in the 50's, which required 50% of the student body have a primary interest in food animals, failed to fulfill the need. There are numerous reasons these positions are open including the fact that while total pay is comparable to other segments the hourly income is less, work load is greater, working conditions more difficult, as well as relative social and professional isolation. There seems to be this problem with most professional people - certainly all the health professionals. In fact health care delivery in all its forms, not just veterinary medicine, to rural areas and inner cities is a matter of great concern. The possible solutions need wider discussion and implementation to solve the crisis. Several schemes have been tried in New Zealand, Canada, and Scandinavia with the intention of helping veterinarians maintain rural practices. An approach being tried in this country consists of consortia of veterinarians and other professionals formed to provide production advice on a contract basis to groups of farms. Another approach may be forced on us by producers - that is the big, consolidated producers which are vertically integrated. They will be the Frank Perdus of the swine and cattle industries. They will hire veterinarians to work for them in production management as well as to direct and interpret their research.

Which approaches to satisfying rural needs should we take and which veterinary schools are going to provide the programs to develop the highly qualified veterinarians needed? For our survival as leaders in providing health care and now production management, we should remember that political support comes from the food animal industry - not small animals or horse industry. We are not now adequately serving that industry while we simultaneously consider entering new areas while emphasizing basic research. Is the profession not strong and resourceful enough to do both providing we get proper leadership?
Academic Clinical Research

Research is one component of the traditional triumvirate of clinical departments and clinical individuals of veterinary schools. At many times and locations satisfactory performance in research has been lacking for a variety of reasons including inadequate leadership, lack of money, inadequate training and lack of desire in the clinician but all too often it results from overload of cases. The cause of the latter is multifactoral. Teaching hospitals are expensive so administrators like to see them full, busy and a source of as much income as possible. As a consequence, clinicians are encouraged to keep up their case load. Big case loads may satisfy one's desires, administrators desires, clients desires, or one's view of self worth. Big case loads mean big obligations of time in the clinic or on the road, telephone time, letter writing and report writing. They are often barely compatible with meeting teaching obligations to say nothing of organizing and then maintaining a meaningful, focused research program. Yet, to my way of thinking, "clinical research" in the hospital and on the farm is one of the major reasons for the existence of veterinary medicine. High quality research should be done on the animals for their own sake, or on them when the findings have important biological relevance or when findings from basic laboratories should be tested in domestic animals to determine if potential benefits can be obtained.

While I greatly admire and strongly support the profound influence the Pew Foundation's efforts is having on our profession I am concerned that more thought and effort is not directed toward the development of academic clinicians. For me they are the essence of our profession. As we turn toward new areas and basic research, I would like to see and hear more discussion on this critical subject.

I believe that the bulk of academic clinicians, by the time they are ready for a permanent appointment, should have demonstrated an intense desire to do clinical work, have broad clinical experience topped by some systemic specialization, rounded off by training as an investigator in an academic program best exemplified by a sound PhD or DSc program. Such people are capable of doing fundamental research to solve or prevent real problems. They are also a link between problems and basic scientists. To become a productive experimentalist does not necessitate obtaining a PhD but doing so does shorten the time necessary to reach a proper level of competence for most people. An alternative to a PhD program is to become a functional component of a productive research team. I say functional because it is important for such a person in training to have increasingly heavy responsibility as (s)he benefits from chosen collaborators and colleagues who can demonstrate how research is done by providing advice, good examples and training. If this is done carefully and properly with appropriate timely publications such an approach could lead to a DSc and a very useful mechanism for producing academic clinicians.

These are not new ideas but as far as I can see they are seldom adequately fulfilled in our veterinary schools today. With the coming changes in our profession with increased emphasis on research, particularly in biotechnology, our clinicians and practitioners are in danger of being replaced by a host of technical services unrelated to formal veterinary medicine unless we meet the challenge. I think the three reports mentioned above (66,67,68)
are just what we as a profession need to generate the necessary dialogue and action. Hopefully concrete plans of action based on defined centers of strength will come out of these deliberations. We cannot do everything in all areas so we must turn to defined centers of strength. However, I can foresee an unfortunate fate for academic clinicians unless they become more significantly included in discussions and eventual actions than currently seems to be the case.

The 2 year residency plus the 2 year MS programs or the combined 3 year residency/MS programs I am aware of have not turned out the type of individuals I think are necessary for the growth of academic clinical programs which should become increasingly sophisticated. In the combined 3 year programs culminating in a residency certificate and an M.S., there is a strong tendency for the clinical portion to detract from the graduate training and vice versa. These programs serve very well for training people for passing the board exams and give a touch of training in the scientific method but are generally less than adequate to develop strong academic leaders. Unless a person has a unique background of training or experience I think a resident should receive intensive experience, responsibility and training in a specialty area for two years and then undertake graduate studies leading to a PhD or actively participate with a basic research group as discussed above. The PhD is becoming increasingly important for two reasons. First it is increasingly difficult to get "up to speed" in specialty areas without a PhD, or equivalent training, because of the increasingly rapid growth of (information) knowledge and secondly because more and more research money comes in open competition with graduates of other biomedical and agricultural science programs.

Another program which has some questionable aspects to it is that of the clinician-educator (CE) track. These non-tenured positions are filled by persons with service (clinical) and teaching but little or no research responsibilities. Selecting this track is a personal career decision since the position was not created to enhance the opportunity for a clinician to develop an academic career. Their presence in a clinic certainly helps cover the service responsibilities of a section thereby increasing the amount of teaching and income. There are also reciprocal benefits for both parties when clinician educators associate with individuals who are experimentalists. While clinical educators become increasingly skilled in technical details (journeyman), the individual is in a poor position for personal development or financial improvement under prevailing administrative leadership and academic strictures.

Many people have talked about the things that will change in the future. It is certain that there will be change. It will be rapid. Some overall directions are rather clear. We can influence some of the forces affecting us but as a profession we have to be more active than ever in determining the directions of these forces.

Summary

1. This is a rather personal view of some of the changes that have occurred in my 37 years in the profession.
2. Changes have been profound.

3. Many of the changes were not predictable.

4. The changes in the next 37 years will probably be more profound than the last 37.

5. We think we can foresee (to some extent) many of the changes which will occur.

6. Judging by the past experience we will be surprised by what actually occurs.

Writing this lecture started out as a frightening experience but now at the end it has turned out to be fun. Now I wish there had been more time between telephone calls, subfertile stallions and boring meetings to tie things up tighter. Time simply ran out. I have had the pleasure of discussions with numerous friends and colleagues some of whom are referenced. More are not. Due to limitations of time and space some subject areas have been dropped - even some which are of particular interest to me. Let's plan on getting together again in 2028 and look back another 37 years to evaluate where we are today.

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