

The 2021 Bartlett address

Find your niche



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Thank you for this honor.

Who am I?

I spent most of my career as a practicing veterinary anatomic pathologist on faculty at the Veterinary College at Cornell University. During this time, I developed a keen interest in diseases that involve reproductive organs of domestic animals. A substantial amount of my time was spent as the pathologist-in-charge of the surgical pathology or necropsy pathology services of the NY State Diagnostic Laboratory.

What a fantastic position to be in; what more could one possibly hope for? For over 30 years, colleagues from around the country and occasionally from around the world would send us tissues and carcasses from cases they had worked up. They were seeking help. They needed answers. That was our job as diagnosticians, to give them answers. But the selfish reality is that we had all this material, all these cases given to us for study and use in our teaching, research and training programs. Such a gift, such an opportunity. To paraphrase: if you build a... if you provide a service, the cases will come (my field of dreams). The more cases, the greater our experience became and the better we got at providing answers.

The formula was simple: offer a service (providing answers), express enthusiasm, do good work, be timely, and relish the opportunities you are presented with. A great place to find and to establish a niche. You are known by your work. You are known by the niche you occupy.

My background

I was trained at Cornell during the 1960's and 1970's. I worked for 2 years in a mixed animal practice on the western edge of Albany, NY. In 1977, I left practice and began an anatomic pathology residency and graduate training program at the University of Georgia.

I then moved into an academic appointment in anatomic pathology at Cornell in 1982 where I worked until my retirement in 2014. Additional study and board certifications (ACVP, ACT, and ACVM) followed during the first few years of as a faculty member. Once tenured, there arose opportunities for sabbatical leave.

My first sabbatical involved a fellowship at the University of Oxford, then a few years later I had 2 stints at the San Diego Zoo as a visiting scientist. These times included the chance to work with the comparative placentologist/pathologist Dr. Kurt Benirschke. Part of my last sabbatical leave was as a visiting professorship at the University of Padova in Italy teaching some classes in theriogenology and pathology courses.

I had many memorable experiences during those times. I will briefly mention 3 that I recall fondly.

I had learned early on that one needs to seek out opportunities. That turned out to be good advice. I won a scholarship during my undergraduate pre-veterinary years to study in Sweden for a year. Shortly after arriving there, I began to plan the year. I somewhat boldly wrote a letter to the Nobel Committee asking if I might attend the Ceremonies (1969) in Stockholm that December. A couple of weeks later, a ticket for the ceremony arrived. That December, I took a train down to Stockholm from Uppsala and I checked into a student hostel. Getting dressed in a rented tuxedo in the student hostel generated some attention and interesting comments as did the ride in the subway across the city. I made my way through the crowd watching outside Stockholm's Opera house (it seemed that nearly everyone else was arriving in large cars). After presenting my invitation, as I was waiting in the main foyer, I was approached by an older, very distinguished gentleman with a very large greying beard and with his chest covered with medals. As he came up to me, he handed me his invitation, and, in Swedish, asked me to show him where his seat was. After a moment's reflection, to give myself time to mentally compose my response in Swedish, rising slightly taller and with all the propriety I could muster, I told him that I was afraid I could not, as I was also a guest.

Indeed, a fond memory that I cherish still. As for the ceremony itself, King Carl Gustaf XVI of Sweden presided. My seat was in the very last row, way up in the top balcony next to the guy running the lights (he was the only one there not wearing a tux). I was relishing my good luck.

A few years later, I had the opportunity to meet royalty in the form of a sheep. During a trip to the Rosland Institute in Scotland, I gave a talk on comparative placentation to the group of scientists who were working on animal cloning. This was after the world learned that this group of researchers had succeeded

in producing the world's first cloned mammal. After my talk, I was graciously taken to meet Dolly (Figure 1). (My wife has suggested I might be aging myself, so, if you do not know who Dolly the sheep is, I suggest you look her up.)



Figure 1. A visit to the Roslin Institute in Scotland provided the opportunity to meet Dolly

A third story I will tell occurred on a day in 1990 while I was working in the placental lab at the John Radcliff Hospital at Oxford University. I was the 'token' veterinarian in the unit. I was being exposed to the inner working of a University Obstetric Unit.

I was standing in the corner of a delivery room trying to be as inconspicuous as possible, holding a medium sized stainless bowl under one arm as I awaited the delivery.

I had come for a placenta. After the baby was born (my gracious) the placenta was delivered. I carried 'my' placenta up one floor of steps that led from the delivery suite to the back of the placental trophoblastic research lab for examination, sampling and further processing. I had been in the lab about 6 months into my fellowship, working in a research group investigating the pathogenesis of preeclampsia in young women.

There were usually between 5 and 10 deliveries each day in the delivery unit. I had gone down those back steps that join the lab and delivery suite to retrieve placentas many times before. Nearly all patients delivering in the hospital would sign consent forms donating their placentas, (technically

more part of the fetus than the mother) for research. This particular hospital clinic was limited to care for, and delivery of women considered to have high-risk pregnancies. A considerably mutually beneficial relationship existed between patients and the pregnancy/placental researcher working a floor above.

The wait was never very long. A system had been worked out over the years in which by one of the researchers, or a technician who needed access to fresh placental tissues at a particular time on any day (literally), would carry a beeper. When a patient was entering the later stages of delivery, one of the delivery nurses would send a message to the beeper to let us know we should quickly come down to collect the placenta that would come shortly after. That particular day was a special one for me as arrangements had been made for me to be in the delivery room for a delivery. The delivered baby was a girl. She and her placenta were normal in every way. Beautiful baby, beautiful placenta. That delivery was nearly 21 years ago now. I wonder what her life has been like?

As a veterinarian, I have been admonished for using the word 'comparative,' as in comparative veterinary pathology, or comparative veterinary medicine. The point being, that by nature and definition, most of our work as veterinarians involves multiple species. Perhaps one might get away with using the term comparative placental pathology if it includes aspects of human reproduction?

Finding a niche

My work in surgical and necropsy pathology gave me exposure to a large amount of case material. Over time there was a steady increase in reproductive cases. There were more referrals and invitations to speak at meetings. A niche in reproductive pathology was developing.

Training became an important and very rewarding part of my job. With faculty from Cornell's theriogenology section, we started holding joint rounds on a regular basis. These became the nidus that brought us together and became an important training activity for both pathology and theriogenology residents.

Dr. Rick Miller at the University of Guelph and I had shared cases and had been on programs together. We enjoyed working with each other. With his enthusiastic cooperation, we started to hold regular traveling 'Repro Rounds' across the border. These became a twice a year exchange. Guelph residents and graduate students would come to Ithaca once every 6 months, stay with our residents and join us for a couple of days of case presentations and talks. About 6 months later we would go with our trainees to Guelph, staying with their students and trainees and again spend a lively time, sharing cases and presentations. This went on for many years with considerable success. Reproductive pathology was alive and well.

The work was fulfilling, and the opportunities seemed endless. I was finding a niche.

That is an interesting term; as it comes from the old french 'nichier' which means 'to nest' (The Free Dictionary). A niche is a place 'well suited' to the person who occupies it. It is being unique for a given person, not unlike a pair of well-worn slippers.

It is also an architectural feature. A niche is a recess in wall in which an object, or stature is placed (Figure 2).



Figure 2. A structural niche in a wall. «Niche» is derived from a word that means 'a nest'. (image is from <https://www.shellwoodcraft.com/images/Products/Custom-Niche-805-x-452.jpg>)

Given sufficient time, personal interests, abilities and circumstances, we develop areas of interest followed by expertise. Our niche can be identified by the work we are confident in, and happy to be doing. This is also a good way to look at one's professional development. It is a helpful concept in assessing and guiding others in their careers. It allows for one to define their life's work.

With time, my niche continued to evolve with a greater focus on placentation, placental pathology, and placental pathophysiology. Do you have a niche? Can you describe it in 2 sentences? If colleagues were to read them, would they recognize the niche as yours?

Graduate dissertation research

I spent 3 years on Plum Island doing my dissertation research

in virology and reproductive pathology of African Swine Fever (ASF).

Outbreaks of ASF had spread to 3 countries in the western hemisphere during the 1970's and the US government was concerned. Abortions had been reported as the most consistent clinical manifestations during some outbreaks in Haiti and the Dominican Republic. The Western Hemisphere viral isolates circulating in those countries caused less lethal infections than African isolates, so recognition of less dramatic forms of the disease was important. My research confirmed that in controlled laboratory settings, ASF infection caused pregnant swine to abort and we studied the pathogenesis of those abortions.

In another series of studies, we looked for evidence of immune protection against ASF. No vaccine that is effective in preventing ASF had or has been developed to date. There were scattered field reports that some pigs that had recovered from infection were somewhat protected when rechallenged with the same isolates.

We designed studies to determine if passive protection through ingestion of colostrum collected from recovered sows (yes, I was milking sows) and given to normal piglets could be demonstrated by challenging those piglets with viral inoculations. The results showed that the clinical course was indeed lessened, confirming that some degree of immunity could be transferred between animals.

After a time, ASF infections were stopped in South America and in the Caribbean Islands, lessening the immediate threat, but massive outbreaks have spread throughout domestic swine populations in Eastern Europe, Russia, China (2018; OIE reports) and Far East over the last few years. Mortality rates of 65% percent occurred. Reports in the popular press suggest that over one-quarter of the pigs in world have died from ASF! While I was doing ASF research, neither I nor anyone else could have predicted that ASF outbreaks would become such a crisis to the swine industries of the world. Africa Swine Fever has become a great swine pandemic!

Knowledge gained through diagnostic cases

The large number of cases that came through our diagnostic services provided a rich source of material for study. A few examples of insights gained through our regular service work:

- Enhanced interpretation of endometrial lesions in endometrial biopsies from mares and bitches.
- Gross and histologic diagnostic findings in abortion cases; many species.
- Conduction of thorough placenta examinations.
- Recognition and characterization of both macroscopic and microscopic lesions of diagnostic significance in

placental tissues.

- Histopathology assessment of canine uterine biopsy material collected by trans-cervical procedures.
- Tissue changes of diagnostic importance in canine testicular biopsy.
- Recognition and characterization of immune-mediated orchitis in dogs.
- Recognition of lesions of diagnostic importance during gonadal histopathology.
- Characterization of abnormalities of sexual differentiation

Placental Research

I was very fortunate to have started at the Veterinary College about the same time that Dr. Peter Nathanielsz joined the faculty. Peter is an MD fetal physiologist with extensive experience using various research approaches to study fetal life in utero. He quickly established a large research program at the Veterinary College.

He was very generous in helping me gain experience in the use of surgical instrumentation in various fetal sheep models. Our research included studying the fetal effects of endotoxin exposure on sheep pregnancy, placentomal eversion, and development of placental embolization techniques to model placental infarction leading to placental insufficiency leading to fetal growth retardation.

After some years, my research interests turned to using chronic fetal instrumentation to investigation of placental function (Figure 3) in other species. I established research projects studying placental function in the fetal calf and foal based on implanted probes. These studies later involved use of surgically implanted flow probes to quantitatively study umbilical and uterine blood flow dynamics under varying conditions (Figure 4).

Some aspects of our placental research will be described in more detail during my address.

Acknowledgements

As I was preparing this paper, I made a list of my mentors and colleagues who each deserve sincere thanks and acknowledgment. But the list grew to considerable lengths, so much so it became obvious I could not include them. I also became very fearful that I might leave someone out. Let me give a heartfelt 'thank you' to each and all and ask you to know that you share this honor with me.

Any career successes I have had are due in most part to generous good friends and colleagues and mentors, wonderful parents,

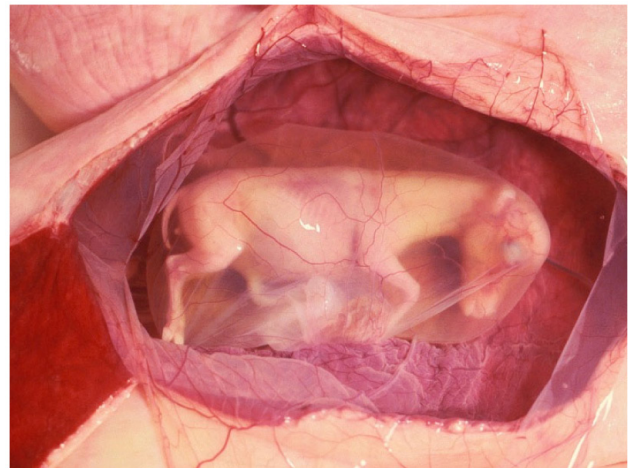


Figure 3. A normal equine fetus in utero encased in an amnion and surrounded by its chorioallantoic placenta. A major challenge to study of fetal life in utero is to gain access to various fetal and placental tissues in as unperturbed a state as possible.

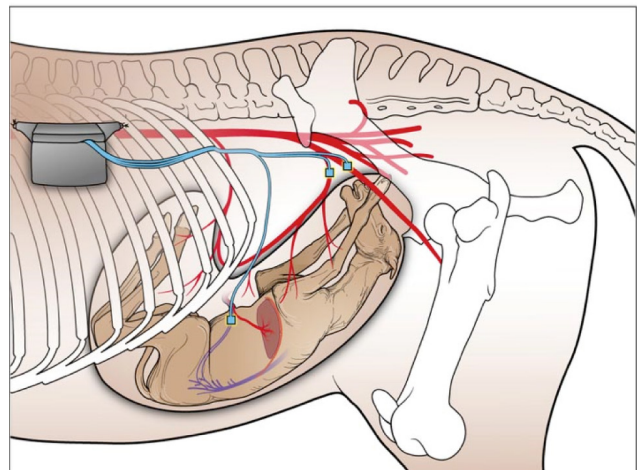


Figure 4. Investigating life in-utero - placental function research using chronically instrumented animals. This drawing shows placement of doppler flow probes (small square boxes) around fetal and maternal vessels, enabling detailed study of blood flow to the fetus's placenta and simultaneously maternal blood flow to the uterus.

and to many unique and fortunate circumstances. Good fortune has brought many opportunities and wonderful experiences. A broadened niche in the world of theriogenology and pathology.

We acknowledge the efforts extended by my fellow veterinary pathologists, Drs. Chris Premanandan and Robert Foster for presenting this year's Reproductive Pathology Symposium. Thank you.

I would especially like to mention Dr. Kurt Benirschke. We shared strong interests related to placentation and placental pathology. He was very good to me.

Kurt passed on in September 2018. He represented the strongest of links between the disciplines of human and animal reproductive

biology. I fondly remember Kurt's Friday afternoon's placental 'trim' sessions. Placentas contained in storage 'pots' that had been collected from all deliveries that week would be removed from the pathology refrigerator and with great care weighed, measured, photographed and studied before being sampled for histopathology, genetic testing, culture, etc. Dr Benirschke

was a fountain of knowledge, knew everyone it seemed, and had a great following in the human reproduction and animal conservation fields. He was equally at home examining placenta from women, or from any of an amazing number of different animals (Figure 5).



Figure 5. Dr. Kurt Benirschke examining a normal giraffe placenta with me at the San Diego Zoo. He was an authority on placentation and placental pathology.

Among his many achievement was the establishment of 'The Frozen Zoo' in 1972 at the San Diego Zoo. This unique repository of cells, gametes, and genetic material is and will have unimaginable benefits in the future.

Dr. Benirschke also created a web-based resource on placentation, filled with information about the reproductive cycle and

tens of species with detailed description of placentation and placental disease of each. If you have not visited his website (placentation.ucsd.edu) on comparative placentation developed based on his work at the San Diego Zoo, please do. It is superb. The niche Kurt occupied was very broad and very deep.

Again, thank you for this honor.

