

Theriogenologist of the Year in the SARS-CoV-2 pandemic

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To be nominated and chosen as the Theriogenologist of the Year (TOY) is a great honor and I am deeply humbled by this award. I am also deeply saddened that my colorful Big Apple New Yorker friend Peter Brunelli of Universal Ultrasound, who died of COVID19, and who has sponsored this award, is not here today for me to thank. Peter used to chide me about being “the theriogenologist who practices what she preaches,” reminding everyone within ear shot that I had 4 children and 2 stepchildren! Peter was an incredible supporter of the American College of Theriogenologists and the Society for Theriogenology, and I will miss him dearly.

This has been quite a year to reflect upon in the backdrop of the Coronavirus Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) pandemic. A word cloud of the Pandemic would be filled with: Zoonosis. Pangolins. Bats. Cats. Ferrets. Mink. SARS. MERS. Emerging disease. Public health emergency. Air born. Respiratory droplet spread. Pneumonia. Ventilator. Borders closed. Social distancing. Quarantine. N95. Facemasks. PPE. Community spread. Shelter in place. Vulnerable populations. Doubling rates. Flattening the curve. Fomites. Contact tracing. Self-quarantine. Supershedder. Reproduction number R0, Case Fatality Rate. Crisis.

Reviewing the past awardees of TOYs is impactful. My thoughts included: what an incredible list, how fortunate I am to have known these people, how our profession has been advanced by their scientific discoveries, how we need to encourage the nomination of more women, and how the heck did my name get on the list? This is my opportunity to thank those who illuminated my path. I want to acknowledge my formative years at Cornell University with mentors: Ron Gorewit, Bruce Currie, Peter Nathanielsz, Mary Smith, Joanne Fortune, my PhD supervisor Ron Butler, and my committee members Don Schlafer, and Bill Hansel; members of the Theriogenology section: Drs. Bob Hillman, Rob Gilbert, Barry Ball, Tom Little, Peter Daels, and Vicki Myers Wallen; and my fellow grad students Lisa Freeman, George Haluska, Rick Canfield, Charlie Elrod, and Susan Huyler. Your help and support were invaluable.

I owe a great deal to the dedication and iron work ethics of the students I supervised at the Western College of Veterinary Medicine’s combined residency and graduate program, including Drs: Shawn Haas, Stephen Manning, Theresa Burns, Natalie Bragg, Farshad Maloufi, Alejandro Rey, Alexandra Rauch, Farhad Ghasemi, Tal Raz, Sarah Eaton, Dawn Nairne, Mariana Diel de Amorim, and Maria Lopez Rodriguez, and the other graduate students I had the opportunity to mentor. You have all been an inspiration, and watching you become talented and sought-after clinicians and scientists has been a highlight for me. Similarly, thanks go out to my many collaborators over the years: Drs. Ed Squires, Jason Bruemmer, Irwin Liu, Don Thompson, Claudia Klein, Elemir Simko, Bernard Laarveld, Nadia Cymbaluk, Tasha Epp, Gregory Starrak, and Robert Foster along with the sea of undergraduate students, now veterinarians: Drs. Mark Corrigan, Jodyne Green, Sylvia Carly, Barb Hunter, Allister Gray, Ilse Dedden, Ellie Ripley, Jasmine Paulson, Patrick Roberts, Lyndsay Rogers, Megan Jurasek, Kayla Nielsen, Brad McKell, Mikayla Swirski, Brandi Bakken and Ashlyn Ketterer. Thanks to Tammy Kimmel and veterinary technicians: Mikhaela Thasher, and Rebecca Johnston, along with the Mason family’s Hilltopper Clydesdales, Ron Schreiner of D and R Ranch, and Jack and Linda Iveson of Jaclyn Quarter horses. A big thank you to all of our clients and referring veterinarians who have shown great trust in us over the years. Lastly all of the members of the ACT, SFT, and TF family who are my friends and whom I have had the pleasure of knowing and serving with over many years. You have made our veterinary speciality Theriogenology vibrant, relevant and progressive.

The award is often given to acknowledge significant recent research contributions. Our research contributions from Dr. Diel de Amorim's PhD work have centered on the role of oxytocin (Oxt) and oxytocinase,^a an enzyme that metabolizes oxytocin, in the maternal recognition of pregnancy (MRP) in mares, most of that is under review. If I had to describe the foundation for our research work, it was built on the work of those who came before. Ground breaking work was done in the early days by Dan Sharp on prostaglandin,^{1,2} Pat Sertich on embryonic and endometrial prostaglandin secretion,³ Elaine Watson^{4,5} on endometrial and luteal oxytocin, Gordon Woods and Jim Weber on embryonic PGE section,⁶ Dirk Vanderwall on PGE and the effects of oxytocin on the corpus luteum,⁷ Claudia Klein and Mats Troedsson⁸ on molecular aspects of MRP, Bob Douglas and Ollie Ginther on prostaglandin,⁹ Christine Aurich and Sven Budik on interferons and oxytocin receptors,¹⁰ Tom Stout and Twink Allen on embryo migration and the endometrial luteolytic pathway,^{11,12} along with many others. We have expended considerable effort to understand some of the complexities of MRP in the mare. We confirmed that oxytocinase was present in many equine tissues, including luteal, uterine and trophoblast tissue. Oxytocin is produced as a prohormone bound to neurophysin -1 and is then processed into the active hormone Oxt. We showed that whereas luteal tissue expresses Oxt, there is little hormone produced, making luteal origin oxytocin a possible intraluteal paracrine regulator, but an unlikely regulator of endometrial prostaglandin secretion. There is more work to be done to understand the role of Oxt gene expression and posttranslational processing of the oxytocin/neurophysin prohormone Oxt protein in MRP.

We have also another research focus from the thesis work of Dr. Maria Lopez Rodriguez, that is related to equine thyroid function and fetal development. In the early North American veterinary literature, the birth of contracted legged abnormal foals was identified.¹³ Gross and histologic thyroid abnormalities were reported and associated with low concentrations of iodine in the prairie soil.^{14,15} Outbreaks of disease¹⁶ and foals with severe musculoskeletal abnormalities including: dysmaturity, hypothermia, severe limb contracture, rupture of the common digital extensor tendons, mandibular prognathism, abnormal umbilicus, thyroid metaplasia and carpal/tarsal bony dysgenesis were identified¹⁷. This collection of abnormalities was termed congenital hypothyroidism dysmaturity syndrome (CHDS).¹⁸ Equine fetal studies including thyroidectomy¹⁹ proved that fetal thyroid hormone was actively secreted in the last third of gestation²⁰. Equine fetal thyroidectomy showed the critical importance of the thyroid in equine fetal development, and recreated many of the clinical signs of CHD.¹⁹ Research work by others highlighted the epigenetic effects of thyroid hormone on fetal development.^{21,22} Investigators identified that no trace mineral supplementation¹⁷ and exposure to mustard plants^{23,24} were a risk factor for CHDS. Mustard plants contain compounds called glucosinolates that are metabolized into goitrogens and alter thyroid function²⁵. Our studies showed that feeding glucosinolates combined with a low iodine diet resulted in reduced serum iodine concentrations similar to the effects on other species^{2,5-27}. We demonstrated that broodmares often have insufficient concentrations of iodine, in spite of access to salt blocks and mineral supplements.²⁸ Depending on the voluntary consumption of salt blocks or mineral products by broodmares to meet their iodine and other trace mineral needs may lead to insufficiency. We also reported that equine mammary tissue concentrates iodine and is a source of iodine for the foal.²⁸ Equine neonates have very high concentrations of serum iodine, total thyroxine and total triiodothyronine, all of that decrease rapidly over the first 10 days of life and play a key role in neonatal adaptation. However, questions still remain and further studies are needed with known and confirmed intakes of iodine to confirm the appropriate reference concentrations.

What have my years in research taught me? What would that word cloud look like? Team. Determination. Hard work. Repeat. Redo. Redesign. Focus. Literature. Hypothesis. Gene. Protein. ELISA. Western Blot. Mass Spec. Immunohistochemistry. Resilience. My family, my husband Peter Barnacle, daughters Kirstin, Ursula, Johnna and son Ryan, step-children Shawn, Tricia and grandchildren

^a Oxytocinase is also called leucyl-cystinyl-aminopeptidase (LNPEP), insulin responsive aminopeptidase (IRAP) and placenta leucine aminopeptidase (PLAP)

Owen, Jake, Nicholas, and Samantha, along with my good friends helped me survive. Much of my success is due to their support. It was not easy being a female large animal veterinarian and I hope that my efforts have made it easier for those who follow.

Key messages I wish to give to others is that the amount of funding for equine and small animal research remains woefully inadequate and needs to improve. This will rely on our profession's advocacy for changes in government policy and continued private and industry support for foundations such as TF and other granting agencies. My partnership with rural women farmers in Uganda has taught me that the true measure of one's life is not about the things money can buy, but in how much we give to others.

As investigators, I encourage everyone to continue to ask questions, and to keep checking your sources. Additionally, to members of the public, respect science, it is the pathway out of ignorance, out of the pandemic and out of the pernicious challenges that lie ahead, including rapid species extinction and climate breakdown.

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