Intratesticular Approaches, Going Forward

ACC&D Symposium

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Calcium Chloride: Brief History, Recent Research and Transition to Field Use

Background and going forward

- Linda Brent, PhD, MBA
  - Parsemus Foundation, San Francisco, CA, USA

Refinement through research on CaCl

- Raffaella Leoci, DVM, PhD
  - University of Bari Aldo Moro, Bari, Italy

Field use of CaCl

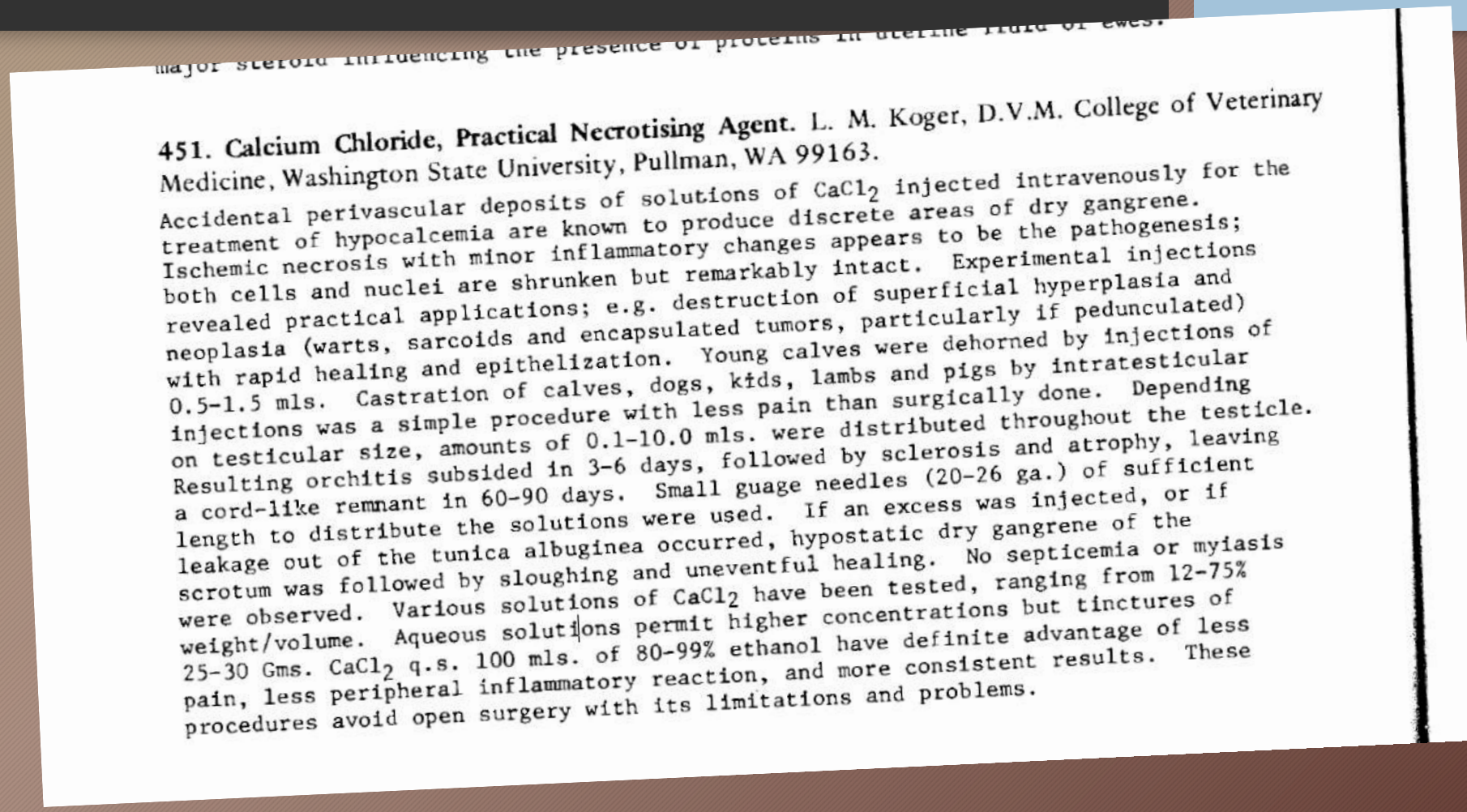
- Marcela Pineda, DMV
  - Amici Cannis, Cotacachi, Ecuador

What is it?

- Calcium chloride dihydrate is a salt, usually derived from limestone or brine
- It is a common substance used for diverse purposes (e.g., food additive, de-icing agent, medical applications)
- Mixed with a solvent to form a tissue-necrosing agent, it has been used for chemical castration, dehorning and tumor removal in a number of animal species
- Non-surgical neuter at low-cost, making it appealing for resource-restricted locations
- Unlikely to be taken through regulatory approval process as a pet sterilant

Calcium chloride sterilant: Historical perspective

- Early work by Koger
- Publications dating back to 1977
- Study including dogs published in 1978
- Various concentrations and diluents used, but alcohol as the solvent reported to have less inflammation and pain.



451. Calcium Chloride, Practical Necrotising Agent. L. M. Koger, D.V.M. College of Veterinary Medicine, Washington State University, Pullman, WA 99163.

Accidental perivascular deposits of solutions of $CaCl_2$ injected intravenously for the treatment of hypocalcemia are known to produce discrete areas of dry gangrene. Ischemic necrosis with minor inflammatory changes appears to be the pathogenesis; both cells and nuclei are shrunken but remarkably intact. Experimental injections revealed practical applications; e.g. destruction of superficial hyperplasia and neoplasia (warts, sarcoids and encapsulated tumors, particularly if pedunculated) with rapid healing and epithelization. Young calves were dehorned by injections of 0.5-1.5 mls. Castration of calves, dogs, kids, lambs and pigs by intratesticular injections was a simple procedure with less pain than surgically done. Depending on testicular size, amounts of 0.1-10.0 mls. were distributed throughout the testicle. Resulting orchitis subsided in 3-6 days, followed by sclerosis and atrophy, leaving a cord-like remnant in 60-90 days. Small guage needles (20-26 ga.) of sufficient length to distribute the solutions were used. If an excess was injected, or if leakage out of the tunica albuginea occurred, hypostatic dry gangrene of the scrotum was followed by sloughing and uneventful healing. No septicemia or myiasis were observed. Various solutions of $CaCl_2$ have been tested, ranging from 12-75% weight/volume. Aqueous solutions permit higher concentrations but tinctures of 25-30 Gms. $CaCl_2$ q.s. 100 mls. of 80-99% ethanol have definite advantage of less pain, less peripheral inflammatory reaction, and more consistent results. These procedures avoid open surgery with its limitations and problems.

Research on CaCl as a sterilant

Samanta and Jana, India

Published a number of dose-finding studies with extensive physiological measurements, including: testosterone, cortisol, LH/FSH, testicular function measurements, blood values and histology.

- 1998 – 48 dogs plus controls — Indian J Anim Health
  - ❖ First controlled study of CaCl
- 2002 – 48 rats plus controls — Veterinary Res Comm
- 2005 – 18 goats plus controls — Animal Repr Sci
- 2006 – 48 rats plus controls — Contraception
- 2007 – 24 dogs plus controls — Contraception
- 2011 – 18 cats plus controls — BMC Vet Res

Research on optimization of formula and technique

Leoci and colleagues, Italy

- 2014 – 40 dogs plus controls: Dose-finding, 12 month study. 20% CaCl concentration determined to be most effective with fewest complications.
- 2014 – 42 dogs plus controls: Evaluation of diluents, 12 month study. Alcohol determined to be most effective solvent.

Paranzini and colleagues, Brazil

- 2017 – 6 cats: 20% $CaCl_2$ with 0.5% DMSO, 80 day study using infrared thermography to evaluate inflammation. Method was effective with minimal adverse reactions.

Field use and continued research on refinement

-SpayFirst!

- Field use in U.S. for several years
- Website with videos and detailed training information
- Currently working on confirmatory study for modified technique

-Amici Cannis, Ecuador

Interest in CaCl sterilant

- CaClCa.com provides vials of sterile-filled calcium chloride to veterinarians. Pharmaceutical grade ethanol is added onsite.
- Table indicates the number of contacts to CaClCa.com regarding use of CaCl sterilant over past 3 years
- At least 25 groups have obtained the product, with >12 groups having used it

Country	Considering use	Have product - use unknown	Used product
Argentina			1
Bangladesh	4		
Canada	1		
Cuba		1	
Dominican Republic			5
Ecuador			1
Grenada			1
India			>1
Iran		4	
Kenya		1	
Mongolia		1	
New Zealand		1	
Peru		1	1
Singapore	1	1	
South Africa		2	
Suriname		1	
Tanzania			1
Thailand	1		
USA			>1

Thanks to Peter Denooij, CaClCa.com for sharing data

Calcium chloride: Going forward

A foundation's perspective and role

PARSEMUS FOUNDATION

- Parsemus Foundation's mission is to create significant improvements in human and animal health and welfare by advancing innovative and neglected medical research
- Established in 2005 by Elaine Lissner to support proof-of-concept studies and disseminate the results, to encourage uptake and/or larger trials

Role in non-human contraception and welfare

- Parsemus Foundation supports research, advocacy and education:
  - Calcium chloride male sterilant
  - Other nonsurgical options for sterilization
  - Hormone-sparing surgical alternatives to traditional spay/neuter
  - Tumor bulk reduction with injectable calcium chloride
  - Online listing of veterinarians offering alternative spay/neuter procedures
  - Marking dogs after nonsurgical treatments
  - Supporting open-access publication of results

Learnings

Action taken	Expected outcome	Actual outcome
Supported long-term research studies to determine optimal formula and methodology	Field use could commence once best practices identified.	Active research on alternative formulations and injection methods continues.
	Practitioners would use optimal methods.	Small changes made by individual users; difficult to distinguish improvements from hindrances.
Provided copious information via website, including research findings, videos and training info	Online written and video training information would support uptake	Some locations experienced complications. Success is very technique-dependent. May require more than online education.

Where to go from here

- Additional controlled studies to directly compare new techniques and formulations for dogs and cats
- Complication rate needs to be consistently acceptable before advocating for more field use
- Determination of optimal training methods
- Testing in smaller pets, such as rabbits, rodents, guinea pigs

Thank you!

Thanks to ACC&D for inviting us to participate in the Symposium