

## SESSION OVERVIEW

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### Dr. Julie Levy

*Panel members were Sean Hawkins, Dr. Carlos Esquivel LaCroix, Dr. Don Polley and Don Landers (see separate documents for individual presenters' materials).*

The Holy Grail of nonsurgical contraception is permanent sterilization with a single treatment that is inexpensive, safe, and uncomplicated. Of all the approaches presented during the symposium, only Neutersol<sup>®</sup> meets these objectives in its current form. Neutersol<sup>®</sup> is a zinc compound (zinc gluconate neutralized by arginine) delivered by an intratesticular injection that results in sclerosis of the testes and permanent sterility. The product first became available for use in the U.S. in 2003, but by 2005 it was no longer in production, and the patent holder and the distributor severed their ties. Neutersol<sup>®</sup> is currently approved only for use in puppies 3-10 months of age with testicles measuring 10-27 mm in width, but it has undergone widespread off-label use in large adult dogs as well.

**Sean Hawkins** of Saving Animals Across Borders shared standard operating procedures used in the large-scale Neutersol<sup>®</sup> clinics he has organized, located primarily in the U.S. These clinics are offered to the community free of charge and take on a light-hearted, enthusiastic tone. The events have been held in both indoor and outdoor public spaces such as fire stations and parks. The availability of a nonsurgical procedure delivered directly in the neighborhoods captures a target audience that is often missed in traditional neutering campaigns. Although extremely well-organized, the clinics are relatively low-tech and highly portable. They do not require medical facilities and can even be managed without electricity, making the U.S. clinics a promising model for developing countries, where fully outfitted veterinary clinics for companion animals are not always available.

These outpatient clinics are capable of treating up to 200 male dogs in a few hours, making them highly efficient. The group has observed that while testicles in puppies may atrophy after treatment, that does not appear to be the case in dogs treated as adults. Preservation of the classical male silhouette following neutering may increase acceptance of chemical neutering, since fear of “emasculating” male dogs is one reason that dog owners fail to have their male dogs castrated. However, this also requires that dogs sterilized with Neutersol<sup>®</sup> be identified so they do not needlessly undergo surgical castration in the future. In the Neutersol<sup>®</sup> clinics, the ear is tattooed to identify treated dogs.

**Dr. Esquivel LaCroix**, professor of reproduction at the Faculty of Veterinary Medicine at the Universidad Autonoma Nacional de Mexico and president of the Mexican Veterinary Medical Association, presented interim results from a very large field trial of Neutersol<sup>®</sup> in Mexico. The study, just completed, was a collaboration between public health officials and veterinarians to deliver Neutersol<sup>®</sup> to 10,000 adult pet dogs in three Mexican states. Following treatment, dogs were evaluated daily for the first week, then at

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weeks 2, 4, and 26. Adverse events were uncommon. The most significant concern was the appearance of ulcers at the injection sites in 2.6% of cases. A majority of these were severe enough to require orchiectomy for treatment. Over the course of the study, veterinarians learned specific injection techniques to reduce the ulcers dramatically. One technique was to use one needle to draw the solution and a different one to inject it.

A subset of approximately 50 dogs underwent detailed measurement of testosterone concentrations and semen analysis. Of these, all but one dog was sterilized by one month post-treatment. In the U.S. licensing trials conducted in puppies, testosterone was reduced by approximately 50% in treated dogs. Thus, it was somewhat surprising to learn from this Mexican study that testosterone appears to remain normal in adult dogs. However, this is consistent with Mr. Hawkins' observation that testicular atrophy is not observed in dogs treated as adults. This can be considered both an advantage and a disadvantage. One traditional reason for surgical castration is to control undesirable behaviors and medical conditions associated with testosterone production, and Neutersol<sup>®</sup> may not achieve this. However, a reason many male dogs are not castrated is a fear that desirable male behaviors such as protection will be decreased, and maintaining testosterone production following sterilization may be viewed as desirable.

A much smaller project was carried out by the group Animal Balance in the Galapagos Islands. The benefits of Neutersol<sup>®</sup>, including low cost, ease of use, and cultural acceptance of a sterilization technique that does not require removal of the testicles, were significant in this remote location. A slightly higher complication rate of 4% was observed in the 97 dogs treated with Neutersol<sup>®</sup>. All of the adverse reactions occurred in adults and were treated with surgical castration. Zinc gluconate is highly irritating to the subcutaneous tissues, requiring precise intratesticular injection. It is possible that flawed injection technique or leakage of the solution via the needle track contributed to the injuries.

**Mr. Don Landers** announced that the Neutersol<sup>®</sup> patent-holder and Abbott Animal Health were making plans to re-launch Neutersol<sup>®</sup> in the U.S. market. He noted that he could not give a date because even though the product is already approved by the FDA for use in dogs, the FDA would need to inspect and approve the new manufacturing facility before the drug could become available for use.

**Dr. Don Polley** was the director of veterinary services for Addison Biological Laboratory when the company launched Neutersol<sup>®</sup> as the first FDA-approved drug for sterilization of companion animals. He reported firsthand from his experiences with the challenges of launching a product that required a radical change in the way veterinarians, animal welfare workers, and dog owners viewed canine contraception. From the lessons learned during the launch and then withdrawal of Neutersol<sup>®</sup>, Dr. Polley presented the audience with a series of questions that will likely prove relevant not only to the return of Neutersol<sup>®</sup>, but also to any of the nonsurgical contraceptives presented at this meeting which seek acceptance from society at large. The questions are:

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- Will the pricing be consistent with providing a distinct advantage over surgical sterilization, both in the U.S. and internationally?
- What does a reduction of testosterone by approximately 50% mean related to both health and behavior?
- Will there be a focus on educating veterinarians regarding the sterilization technique?
- Will there be a focus on educating veterinarians concerning the pros and cons of surgical sterilization vs. nonsurgical sterilization?
- Will there be sufficient capital to insure a long-term commitment to success?