Upon completion of this treatment regime, fluid balance may be maintained with oral solutions for the remainder of the convelescent period.

The mystic of fluid therapy is no longer veiled behind teaching hospital walls. Once we understand its application, fluid therapy becomes a palatable addition to bovine ambulatory practice that will foster therapeutic success as well as client satisfaction.

An Efficient and Safe Method of Castration for the Bovine By the Intra-Testicular Injection of Chem-Cast™

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The practice of castration, effecting elimination of the testes and reducing libido or virility, has for centuries been carried out in various ways. The method used has been largely dependent on the species, the opportunity to observe the animal following castration, and the nature of local disease problems. Such diseases as tetanus, black leg, malignant edema, and the presence of the screw worm fly may cause severe problems following castration by methods which result in an open wound or abrasion.

With these concerns in mind, there have been many attempts to find a method of castration as effective as surgical castration but free of the disadvantages of post-surgical inflammation and the risk of hemorrhage and infection. These latter two problems may result in 5 to 15% death loss depending on weather conditions, management practice and surgical technique. To avoid some of these problems, castration procedures have been performed using rubber bands above the testis to effect destruction of the testis, below the testes thereby pushing the testes against the body wall effecting hyperthermia of the testis and reduction of testical development and/or sperm maturation, knotting of the vascular supply and vas deferens by rotating (rotation) of the testis within the scrotum, and many other even lesser acceptable methods.

However the method that has previously met with the greatest acceptance, and until the advent of Chem-Cast, best meets the criteria of avoiding infection and hemorrhage, particularly in cattle, has been the method whereby the spermatic cord and its attendant vessels providing blood to the testis and drainage therefrom are mechanically crushed with a crushing instrument commonly known as a Burdizzo. This method of castration, generally called "clamping", usually renders the animal sterile by destroying the blood supply to the testis proper and effects varying degrees of testicular regression and resorption of the residual testis. This method also has its inherent drawbacks. The problems most commonly observed with the use of the Burdizzo are 1) complete scrotal and testis necrosis with and without secondary hemorrhage effected by completely transecting the crotal sack when "clamping" the testis/or testes; 2) edema that in some cases can be marked and persist for some time especially in older bulls; 3) "missed castration" whereby the spermatic cord slips out of the jaws of the Burdizzo or never was properly placed during "clamping"; 4) post-"clamping" distress which is exhibited by standing hunched up, lying down, reluctance to move and reduced appetites. Such stress may persist for several hours to several days depending on the age of the calf and the degree of post-"clamping" swelling that occurs; 5) difficulties with the use of the standard (18 inch or more) Burdizzo on small calves, 3 to 4 months of age or less; 6) secondary infections of the necrosed scrotum and testis or traumatized skin of the scrotum and/or hematomas of the genitalia following crushing and "breaking".

Therefore, it is evident that a method of castration that is easily accomplished, effective, and safe is needed. Chem-Cast, a chemical solution designed for intra-testicular injection, and restricted to use by the veterinarian, is such a product and offers distinct advantages over the other methods of castration. This Rx labeled Chem-Cast product is simple and fast to administer. It approaches the effectiveness of surgical castration and is superior, in this regard, to the Burdizzo method. The administration of Chem-Cast does not result in the pain, stress, edema, hemorrhage and unacceptable necrosis as inherent in the surgical and Burdizzo methods of castration; and further, it reduces the high risk if infection associated with the surgical procedure.

Chem-Cast field use data generated in twenty-one separate trials carried out in five different regions of the

United States using 1390 beef, dairy, dairy-beef and cross breed beef cattle substantiates Chem-Cast's superiority of effectiveness over Burdizzo clamping as a method of castrating cattle. Final evaluations of castrated, functionally castrated, or failures were made, these final clinical determinations as to the castration status of these calves were not made sooner than 110 days post treatment in nineteen of the twenty-one trials. In the two trials where evaluations were made sooner than 110 days, the first (20 calves) and fourth (76 veal calves) trials, final evaluations were made at 31-40 days and 48 days post castration respectively. In the first trial, surgical removal of the residual testicular tissue was carried out so as to obtain an early evaluation of the testis tissue response to Chem-Cast while in the fourth trial, the testicular response was evaluated at the time of slaughter. In the remaining trials final evaluations were made as follows:

7 trials	110-150 days
3 trials	151-200 days
8 trials	201-250 days, and

in one trial, 49 Chem-Cast treated cattle were followed to slaughter so as to evaluate residual spermatic cord tissues, serum testosterone levels and finished carcass weight and grade.

In these twenty-one trials the 1390 calves were randomly treated by one of six veterinarian investigator-consultants or the veterinarian study director or assistant study director. The method of Burdizzo castration, as well as the instrument used, was as routinely practiced by the individual doing the castration.

Chem-Cast and Burdizzo success rates achieved for castration (complete elimination of both testes), functional castration (remaining residual testicular tissue in one or both sides <2.5 cm round) and clinical failures (remaining residual testicular tissue >2.5 cm round one or both sides) are as presented in Table I, page 5.

Chem-Cast treatment results with regard to calves successfully castrated, functionally castrated and clinical failure clearly favors Chem-Cast over Burdizzo at all weight groups evaluated (Page 5, Table I). A direct linear relationship of Chem-Cast dose to efficacy is also readily evident in all weight categories for these 998 Chem-Cast and 160 Burdizzo treated calves weighing up to 250 pounds at the time of treatment. While the table presented here is limited to calves weighing <250 lbs. at the time of treatment, there were 207 and 25 additional calves weighing 251 to 500 lbs. treated with similar or higher doses of Chem-Cast or the Burdizzo instrument, respectively. While an acceptable intra-testicular dose of Chem-Cast to effect acceptable castration rates in calves weighing more than 251 pounds at the time of treatment has yet to be established a similar linear dose to weight to effect relationship is present.

Based on this and other supporting data the Bio-Ceutic Division of Philips Roxane, Inc. has petitioned FDA-BVM for approval of a prescription product labeled for sale to licensed veterinarians only. It will carry the following intra-testicular injection label dose to weight recommendations for use in normal bull calves:

<100 lbs. - 1.0 ml per testis
101-150 lbs. - 1.5 ml per testis
151-200 lbs. - 3.0 ml per testis
201-250 lbs. - 4.0 ml per testis

With regard to those Chem-Cast calves having residual testicular tissues remaining subsequent to 110 or more day post treatment, it has been demonstrated histologically and by procedures of attempted electroejaculation that those calves evaluated as functionally castrated are unable to ejaculate seminal fluid and those tissues remaining are infantile in size and inactive. This inactivity appears permanent for the siminiferous tubules contain only primary and secondary spermatocytes and few if any degenerative or dying cellular debris even in tissues removed five to seven months following Chem-Cast treatment.

In contrast to this and as is evidenced in Table 1, higher percentages of the Burdizzo treated calves have residual testicular tissue remaining. The residual tissues in these Burdizzo cattle are more active as evidenced histologically by more active seminiferous tubule basement membrane, presence of tubular secretions, large numbers of vaculated and dying cells and in some cases, mature spermatocytes.

It has also been demonstrated that serum testosterone levels for steers castrated with Chem-Cast are no different than the serum testosterone levels for Burdizzo castrated steers. The following data was submitted to FDA-BVM to support such a statement.

AVERAGE BLOOD SERUM TESTOSTERONE LEVELS OF BULLS CASTRATED BY CLAMPING WITH A BURDIZZO AND INJECTION WITH CHEM-CAST™ AS COMPARED TO NON-CASTRATED BULLS

		Blood Serum Testosterone Levels (ng/ml)**		
Castration Procedure	No. of Bulls	Prior To Castration (No. of Bulls)	Inter-mediate (No. of Bulls)	Final (No. of Bulls)
Injected Intra-Testicularly with Chem-Cast	20	0.643 (20)	0.006 (8)	0.159 (20)
Clamped with a Burdizzo	24	0.355 (24)	0.005 (9)	0.132 (24)
Bulls Not Castrated	9	x	x	4.660

**Testosterone quantitated by radioimmunoassay (sensitivity = 15 pg/ml)
* 400 lb. or more
x = No Serum Sample

TABLE 1: Clinical Efficacy Results For Calves Treated With Chem-Cast™ and Burdizzo Treated Controls.

Weight Range-Pounds	Treatment Chem-Cast™ or Burdizzo	Successfully[a] Castrated/ Total Treated	Functionally[b] Castrated/ Total Treated	Clinical[c] Failures/ Total Treated	Castrated Plus Functionally[a+b] Castrated/ Total Treated
100	0.50 ml	6/16 (38%)	0/16 (0%)	10/16 (62%)	6/16 (38%)
*	1.00 ml	54/55 (98%)	1/55 (2%)	0/55 (0%)	55/55 (100%)
	2.00 ml	2/2 (100%)	0/2 (0%)	0/2 (0%)	2/2 (100%)
	Burdizzo	11/15 (73%)	1/15 (7%)	3/15 (20%)	12/15 (80%)
101-150	0.25 ml	0/2 (0%)	0/2 (0%)	2/2 (100%)	0/2 (0%)
	0.50 ml	7/32 (22%)	6/32 (19%)	19/32 (59%)	13/32 (41%)
	1.00 ml	69/88 (78%)	5/88 (6%)	14/88 (16%)	74/88 (84%)
*	1.50 ml	121/128 (95%)	4/128 (3%)	3/128 (2%)	125/128 (98%)
	2.00 ml	5/5 (100%)	0/5 (0%)	0/5 (0%)	5/5 (100%)
	2.50 ml	18/18 (100%)	0/18 (0%)	0/18 (0%)	18/18 (100%)
	3.00 ml	1/1 (100%)	0/1 (0%)	0/1 (0%)	1/1 (100%)
	Burdizzo	50/66 (76%)	7/66 (11%)	9/66 (14%)	57/66 (86%)
151-200	1.00 ml	9/23 (39%)	1/23 (4%)	13/23 (57%)	10/23 (43%)
	1.50 ml	44/70 (63%)	2/70 (3%)	24/70 (34%)	46/70 (66%)
	2.00 ml	34/43 (79%)	2/43 (5%)	7/43 (16%)	36/43 (84%)
	2.50 ml	80/93 (86%)	5/93 (5%)	8/93 (9%)	85/93 (91%)
*	3.00 ml	98/104 (94%)	4/104 (4%)	2/104 (2%)	102/104 (98%)
	3.50 ml	8/8 (100%)	0/8 (0%)	0/8 (0%)	8/8 (100%)
	4.00 ml	1/1 (100%)	0/1 (0%)	0/1 (0%)	1/1 (100%)
	Burdizzo	39/43 (91%)	0/43 (0%)	4/43 (9%)	39/43 (91%)
201-250	0.25 ml	0/6 (0%)	0/6 (0%)	6/6 (100%)	0/6 (0%)
	0.50 ml	0/18 (0%)	0/18 (0%)	18/18 (100%)	0/18 (0%)
	1.00 ml	0/20 (0%)	2/20 (10%)	18/20 (90%)	2/20 (10%)
	1.50 ml	3/26 (12%)	6/26 (23%)	17/26 (65%)	9/26 (35%)
	2.00 ml	21/38 (55%)	0/38 (0%)	17/38 (45%)	21/38 (55%)
	2.50 ml	23/32 (72%)	0/32 (0%)	9/32 (28%)	23/32 (72%)
	3.00 ml	23/38 (61%)	2/38 (5%)	13/38 (34%)	25/38 (66%)
	3.50 ml	63/80 (79%)	10/80 (13%)	7/80 (9%)	73/80 (91%)
*	4.00 ml	46/50 (92%)	3/50 (6%)	1/50 (2%)	49/50 (98%)
	5.00 ml	1/1 (100%)	0/1 (0%)	0/1 (0%)	1/1 (100%)
	Burdizzo	20/36 (56%)	10/36 (28%)	6/36 (17%)	30/36 (83%)

a = Clinically Castrated - Calves with no remaining testicular tissue.
b = Calves with minimal (2.5 cm round) residual testicular tissue remaining.
c = Tests from animals considered failure by virtue of residual testicular tissue exceeding 2.5 cm round.
* Proposed Label Dose

In addition to this, one trial lot of cattle were followed to finished weight slaughter so as to obtain finished weight data with regard to serum testosterone values and spermatic cord observations so as to satisfy an additional FDA request. The results achieved were as follows:

1) Appearance, Weights and Grade:

Grade and carcass weights of these 45 head of Holstein, Holstein-Beef cross steers (11 months post castration)
29 graded choice
15 good All 45 yield graded - 2
1 standard

Average slaughter weight 1021 lbs.
Average % dressed weight - 59.1%

2) Serum Testosterone Values - Blood collected on day of slaughter

AVERAGE SERUM TESTOSTERONE - 31 of 45 head - 126.9 pg/m; High - 466.01, Low - 50.04 pg/ml
(All cattle carrying original ID tags + 5 head)

AVERAGE SERUM TESTOSTERONE -

Chem-Cast treated cattle - 109.00 pg/ml -
High 292.32 pg/ml
Low 50.04 pg/ml
(with original ID tags - 24 head)

Serum Testosterone for #44, #9 - 131.4 pg/ml)
(only two Burdizzos carrying original ID tag)

Estrogen and progesterone data generated to support the human safety portion of Philips Roxane NADA and submitted to FDA demonstrated there are no differences between levels as demonstrated in Chem-Cast and Burdizzo castrated steers with regard to the hormones. Chem-Cast has also been declared as a GRAS item by FDA and has zero days tissue withdrawal with regard to slaughtering cattle having been treated with Chem-Cast.

When considering the safety of the animal being treated with Chem-Cast, Philips Roxane has demonstrated that 3.5 to 4.0 times the recommended label dose for calves weighing up to 150 pounds can be safely administered. However, at this time, only 2.5 times label recommended dose has been demonstrated to be safe for calves weighing 151 to 250 pounds. This lower safety margin for those higher weights occurred as a result of anticipating a lower dose requirement for actual castration than was demonstrated. Thus, a very wide margin of safety exists when using Chem-Cast as labeled.

It also has been demonstrated that Chem-Cast castration effects a more humane castration with reduced animal stress contributing to improved weight gains, lower grain to gain ratio and markedly reduced medical treatment days as compared to surgically and Burdizzo castrated calves for the four week period following castration. This stress data was generated by dividing 45 five-week-old calves into two groups that were then randomly subdivided into Surgical, Burdizzo and Chem-Cast treatment groups. All groups were treated on the same day, similarly housed and all nutrient consumption and medical treatments were regularly evaluated and recorded.

The Relationship of Environment to Respiratory Disease in the Dairy Calf

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Veterinarians have diagnosed enteric and pneumonic diseases in cattle for many decades. Causative organisms have been isolated on numerous occasions. Histopathological studies reveal typical lesions associated with specific organisms. Antibiotic sensitivities are conducted and treatment is now routinely instituted on the basis of sensitivity tests. Vaccines are produced against specific viruses and/or bacteria. Regimes for treatment have been offered. However, in spite of our best efforts as professionals many diseases continue practically unabated. Evidence for this conclusion is drawn from the yearly mortality rate in dairy calves of 8-25% in the United States (Agriculture Statistics 1980).

It is well accepted that infectious organisms and sometimes mildly or even non-infectious organisms cause disease. It is often very difficult for a veterinarian to draw a microbiological work picture that a client will understand. This is because it is human nature to believe what can be seen rather than believe what is unseen. It is often helpful in explaining the bacteriological process to clients to emphasize that 1 cm^3 of manure may contain up to 1 billion coliform organisms.

One of the major factors contributing to bacterial disease is sheer numbers of organisms or to put it another way, size of bacterial inoculum. A second bacteriological principle consists of virulence. An increase in virulence is achieved by serial passage of an organism through susceptible individuals. These two principles therefore play a great role in determining whether or not an animal does in fact sustain disease.

An animal's total defense mechanism consists of a number of parts. If sufficient numbers of organisms enter an animal's body, one or several of these defense mechanisms may be overwhelmed and disease can result. Further, environment is a stressor (Anderson, 1980). As a result of stress there is an elevation of endogenous steroids and the animal's defense mechanisms are thereby suppressed. This, in brief, explains the perpetuation process whereby clinical and sub-clinical disease becomes accentuated in undesirable confinement units regardless of species. A further observation is that it is important that as practitioners we become aware of when, how and under what circumstances vaccine studies are performed. If these studies are performed in undesirable environments, preventive medicine measures of the highest order are totally ineffective because of the overriding environmental effect (Anderson, 1980).

Calves which recover from severe enteric or respiratory diseases, depending on the causative organism, seldom achieve optimum growth rates (Anderson, 1976; Bates, 1976; Anderson & Bates, 1979). Many of these animals are stunted and are often inapparent carriers of disease. They exhibit no outward clinical signs and continue to serve as