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The Blue Cross Book

for the Veterinary Profession

Hoechst Marion Roussel Ltd.

Hoechst

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The Editor
'The Blue Cross Book'
Hoechst Marion Roussel Ltd.
Mumbai, India.

Dear Sirs,

At the outset, I take this opportunity to extend my sincere thanks to all Editorial Board Members and also all other personnel connected with 'The Blue Cross Book' publication in India.

A period of 25 years, i.e. from 1958 - 1983, Veterinary Department of HVG published a total of 66 editions of 'Blue Book' with a novel intention to highlight new research findings in veterinary medicine and also publish reports from experienced veterinary practitioners in the field. I am really glad to understand that 'The Blue Cross Book' is maintaining the same intention and the 6th issue will be published shortly.

I am confident that this effort will further strenghthen the relationship between Hoechst Veterinary Division and friends, involved in all areas of Animal Health care and welfare.

I wish you all the very best in your endeavour!

DIETER HAAS

Mr. Dieter Haas

After completing his school studies in 1954, Mr. Haas joined Pharmacy Graduation studies and obtained his degree in the year 1960. In 1961, he started BWL studies - which is the German equivalent to Business Administration in the USA and obtained his M.B.A. Degree in the year 1964.

Mr. Haas was with HAG (Bereich Pharma Vertrieb) in the Pharma Division from 1965 and during 1969, he joined Pharma Division of Hoechst Turkey. In 1972 and upto 1977 he was the Head of the International Product Management Group of the Pharmaceutical Division. In 1978, Mr. Haas again went back to Hoechst Turkey as General Manager and continued in that position till 1982. In the year 1983, he left Turkey and went back to Germany and is presently Managing Director of HVG, Wiesbaden, Germany.

– Editor

A Tribute

Dr. B. V. Rao
(1935-1996)

Dr. Banda Vasudev Rao, popularly known in India as Father of Modern Poultry Farming, was born in an agriculturist family in Andhra Pradesh in 1935. As a child, he evinced a keen interest in chicken, reared by his family members in the backyard. This interest made him a poultry farmer par excellence and he took it up as a mission in his life.

During 1960, Dr. Rao initiated modern poultry farming in association with a visiting professor Dr. Earl Moore of Kansas University. In 1969, he started Venkateshwara Poultry Farm at Hyderabad and thereafter, Dr. Rao never looked back and committed himself to providing "Total Poultry Support" and making India self-reliant almost in all aspects of poultry. As he was committed to develop India into one of the world's most integrated poultry operations, Dr. Rao's simultaneous effort was to develop also poultry farmers' welfare in India. The notable among them are, the establishment of National Egg Coordination Committee (NECC), The All-India Broiler Marketing Cooperative (BROMARK) and the Agro Corpes. He also contributed to establish the Institute of Poultry Management of India, the Poultry Diagnostics and Research Units.

Dr. Rao's contribution to international poultry is commendable. It is entirely due to Dr. Rao's major effort that the XX World Poultry Congress and International Poultry Exhibition will be held in India during September 1996.

Dr. Rao's untiring efforts for the development of Indian Poultry Industry and integrating with modern poultry industry has earned for him many laurels. To mention a few :

1) "Man of the Decade" in 1981 by the Maharashtra Poultry Farmers Association
2) National Citizen Award in 1988 by the then Prime Minister of India
3) Indira Gandhi National Unity Award in 1989
4) Padma Shri Award in 1990
5) The Kakatiya University Award of Honorary Doctorate (D Sc) in the year 1992
6) Recently, Europe Award for Quality in 1994 for his enormous contribution to Poultry Industry.

Today, India is the 5th largest egg producer in the world contributing more than Rs. 7500 crores to the GNP and providing employment to nearly 15 lakhs of people in India. This is largely due to the vision and dedication of a single individual, Dr. B.V. Rao – Father of Modern Poultry Farming in India.

We are shocked to learn of the untimely sad demise of Dr. B.V. Rao (61). We convey our heartfelt condolences to the members of his bereaved family.

Determination of Enrofloxacin in Rabbit Plasma by Reverse Phase Pressurized Liquid Chromatography

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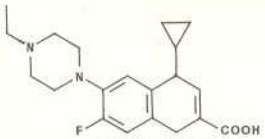
Introduction:

The fluoquinolone Enrofloxacin (1-cyclopropy1-6-fluoro-1, 4-dihidro-4-oxo-7-[4-ethy1-1- piperziny1]-3-quinoline-carboxylic acid) is an antibacterial agent which has been developed specifically for veterinary use. It has found applications in treating microbial infections in calves, poultry, rabbits, pigs and dogs.

The purpose of this study was to develop a high performance liquid chromatographic method for the analysis of enrofloxacin in rabbit plasma. This method was used to investigate pharmacokinetics, bioavailability and bioequivalence of injection (10%) and peroral (5%) solution formulations of Enrofloxacin developed at Hoechst India Limited (HIL).



ENROFLOXACIN

2. Method:

2.1 Apparatus: a) Waters model 510 liquid chromatograph with UV detector model 481, WISP 712 autoinjector of Waters and Shimadzu C-R4A chromatopac integrator or its equivalent, b) Sonicator, c) Centrifuge and d) Vortexing equipment.

2.2 Reagents:

Acetonitrile	AnalaR grade
Glacial acetic acid	AnalaR grade
Double distilled water	HIL
Enrofloxacin reference standard	Dr. Reddy's Lab
Ofloxacin reference standard	HIL
Dichloromethane	AnalaR grade
Potassium dihydrogen phosphate	AnalaR grade
Sodium hydroxide	AnalaR grade

2.3 Phosphate buffer pH 7.4 (USP 23)

Dissolve 27.22 g of monobasic potassium phosphate (0.2M) in water and dilute to 1000 mL. Similarly, dissolve 8 g of sodium hydroxide (0.2M) in water and dilute to 1000 mL. Place 50 mL of the monobasic potassium Phosphate solution in a 200 mL volumetric flask, add 39.1 mL of sodium hydroxide, then add water to volume.

2.4 Sample procedure:

In a 10 mL glass test tube spike 50 μL of methanolic solution of internal standard (5 ng). The methanol is evaporated under a purge of nitrogen.

The frozen plasma samples stored at - 30^{0}C are liquefied to room temperature before analysis. One half milliliter of plasma was accurately pipetted out and added to these test tubes. The drug is extracted from plasma samples under neutral conditions (pH 7.4 phosphate buffer USP) with 5 mL of dichloromethane. The extraction method consists of initial addition of 5 mL of dichloromethane to the plasma sample and vortexing for 1 minute. Then, 0.5 mL of phosphate buffer is added followed by vortexing for another minute. Next, the test tube was centrifuged at 4000 rpm for 15 minutes. The organic layer was separated by decantation in a 5 mL vial and dichloromethane was stripped under a stream of nitrogen. The residue was reconstituted with 500 μL of the mobile phase and injected in duplicate onto the HPLC column for assay.

2.5 Chromatographic conditions:

Column:	Octadecyl silane chemically bonded to porous silica (Nucleosil)® . Particle size 5 μm (125 x 3.9 mm stainless steel)
Mobile phase:	Water 764 volumetric parts Glacial acetic acid 16 volumetric parts Acetonitrile 220 volumetric parts
Flow rate:	1 μL/min
Injection volume:	15 μL
Column temperature:	Ambient
Detection:	UV absorbance at 278 nm
Detector range:	0.1 AUFS
Attenuation:	2. Adjust to maintain peak deflection of 50% to 100% of full scale for the largest peak of interest.
Chart speed:	2 cm/min
Run time:	10 minutes

The retention time of Internal standard is approximately 3.3 minutes and Enrofloxacin is 4.8 minutes.

2.6 Evaluation:

Quantification is based on the internal standard method. The concentration of Enrofloxacin in plasma of drug-treated rabbits was obtained by calculating the ratio of peak areas of the drug to the internal standard and relating this to a constructed calibration curve for the drug.

3. Results and discussion

Table 1 gives the recovery for four different concentrations. The mean recovery of Enrofloxacin from plasma was found to be 98.365%. Minimum quantifiable concentration was 20 ng/mL.

Table 1. Recovery data for Enrofloxacin from rabbit plasma

Concentration taken (mcg/ml)	Concentration found (mcg/ml)	% Recovery	S.D. (n = 3)
0.25	0.2372	94.87	2.87
0.50	0.5211	104.21	3.97
0.75	0.738	98.38	2.61
1	0.96	96	1.56
Mean		98.365	

A Report on the Efficacy of Floxidin in the Control of Early Chick Mortality due to Yolk Sac Infections

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Mortality during first two weeks of life due to various pathogenic bacteria is very common in chicks. An extensive field trial was conducted to test the efficacy of Floxidin in this regard in broilers.

Methods

The trials were conducted on three broiler poultry farms on five flocks (15,102 chicks treated with Floxidin and with 8302 chicks as controls).

In all these flocks, a moderate to high mortality was occurring in the first week. The necropsy conducted on the 3 day old dead chicks of each batch revealed mainly omphalitis, congested and infected yolksac with discoloured, watery or curdled yolk. In addition, chicks also revealed a combination of lesions viz air sacculitis, fibrinous pericarditis, liver bronzed with either necrotic spots or with perihepatitis.

Clinically, dullness, huddling and ventpasting were the marked symptoms.

Floxidin was administered in water at the dose of 1 ml per 2 litres of drinking water from 3rd to 6th day of age in trials 1,2, 4a and 5a and from 1st to 4th day of age in trial no 3. In trials 4b and 5b Floxidin was not given but instead Tetracycline and Strexia were given respectively from 3rd to 6th day of age.

The bacterial culture test was done in trials 2,3,4 and 5 to find out the organisms involved.

Daily mortality was recorded from all the batches to evaluate the effect of treatment.

Results and conclusions
(Refer Table I and Graph I)

1) In all the batches which received Floxidin treatment from 3rd to 6th day of age, (Trials 1,2,4a and 5a), daily mortality which had peak of 0.5% to 1.35%, declined to nil within 5 to 7 days after the commencement of treatment.

2) In the batch which received Floxidin treatment from 1st to 4th day of age, daily mortality reached a lower peak, declined rapidly to negligible level on fifth day after commencement of treatment.

3) Trials no. 4 and 5 were controlled trials with half of the batch being treated with Floxidin and the remaining with either Tetracycline (4b) or with antistress drug with no antibiotic (5b). The results showed that while mortality reduced to negligible levels on 9th day in Floxidin treated groups, in both others it continued at significant levels.

4) The culture test wherever done indicates that Floxidin is effective in checking mortality where organisms like E.*coli.*, *Salmonella* spp., and *Pseudomonas* spp are involved.

Early chick mortality caused by bacterial inflection showing lesions of yolk sac infection, air sacculitis, congested lungs, bronzing of liver etc. is common in most of the hatches. The chicks which are worst affected die in spite of treatment with antibiotics and mortality may decline after two or three weeks. The surviving birds from such flocks grow poorly and many remain stunted. Proper selection of antibiotic drug and early treatment would minimise losses on both counts.

Present trials indicate that Floxidin at 1ml/2 lits in drinking water administered either from 1-4 days or 3 to 6 days of age is effective in controlling early chick mortality caused by bacterial infections.

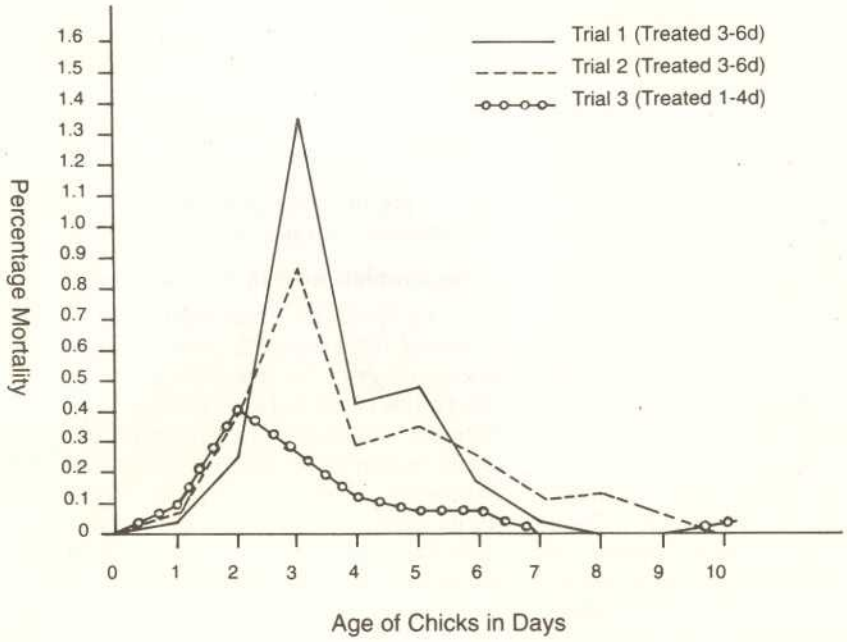
Table - I

Summary of five trials on the efficacy of Floxidin treatment in control of early chick mortality in broiler chickens.

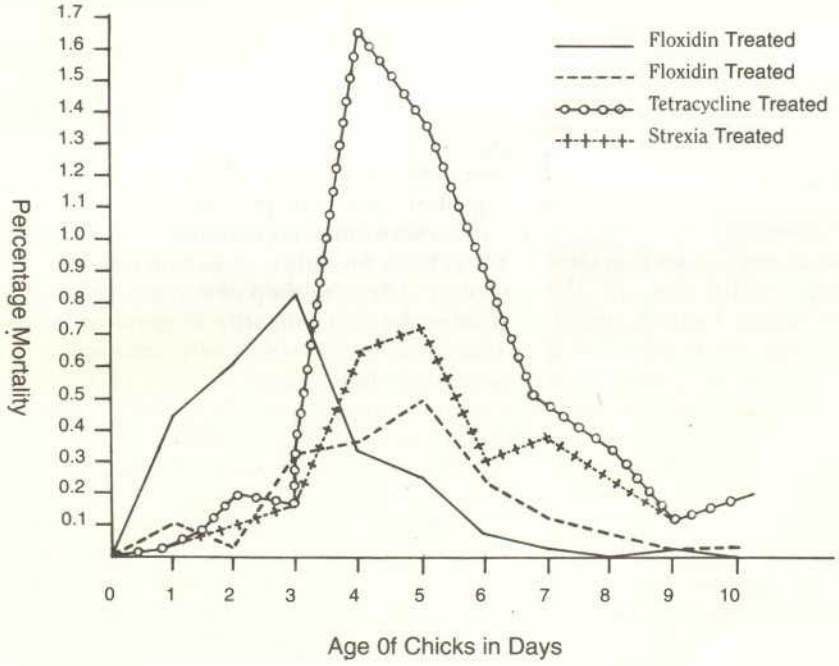
Trial No.	Farm (Location)	Batch size chicks	Treatment and age of treatment	Mortality chart (day)										Organisms in culture test	Reduction in daily mortality percentage
				1	2	3	4	5	6	7	8	9	10		
1	A (Sanjan)	2300	Floxidin 3rd to 6th day	1	6	31	10	11	4	1	0	0	1	Not done	1.35% to nil on 8th day.
2	A (Sanjan)	2300	Floxidin 3rd to 6th day	2	9	20	7	8	6	3	3	2	0	E.*coli* and *Salmonella* spp.	0.87% to nil on 10th day
3	B (Vasai)	2200	Floxidin 1st to 4th day	2	9	6	3	2	2	0	0	0	1	*Pseudomonas* sp. and *Staphylococus* sp.	0.41% to nil on 7th day
4.	C (Shed-a)	4235	Floxodin 3rd to 6th day	20	26	35	14	11	3	1	0	1	0	E. *coli* and *Salmonella* sp.	0.84% to nil on 8th day
	(Shed-b) Sanjan	4235	Tetracycline 3rd to 6th day	1	8	7	70	58	35	20	15	5	7	E.*coli*	1.67% to 0.12% on 9th day
5	C (Shed-a)	4067	Floxidin 3rd to 6th day	4	1	13	15	20	9	5	3	1	1	*Pseudomonas* sp. E.*coli* and *Salmonella* sp.	0.5% to 0.02% on 9th day
	(Shed-b) Sanjan	4067	Strexia 3rd to 6th day	1	3	7	26	29	12	15	9	6	7	–	0.72% to 0.15 on 9th day

Graph 1

Floxidin Treatment Trials 1, 2 & 3



Floxidin Treatment Trials 4 & 5



Overview of Antimicrobial Treatment of Uterine Infection in Bovines

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Introduction

Uterine infection is a common sequela to dystocia and retained fetal membranes in bovine. Uterine infection in post partum animal is characterised by purulent foul smelling uterine discharge and in a severe form by systemic signs of illness. In cycling animals uterine infection results in mucopurulent discharge and infertility. But on many occasions purulent discharge does not necessarily indicate infection and justify antimicrobial treatment. The discharge could be the normal defence mechanism wherein there is leucocytic infiltration. The ideal procedure in uterine infections is to eliminate bacteria from uterus without inhibiting the normal uterine defensive mechanism. Antimicrobials can be used to eliminate bacteria but the selection of the correct drug should be based on the bacterial sensitivity and the minimum inhibitory concentration. It is not feasible to test a selected number of cases in a herd to get a microbiological profile for the herd. Further, the microbiological pattern also changes from time to time so it is necessary to re-examine the animal at suitable interval (Vandeplassche 1984).

Uterine defence mechanism

Natural uterine defence mechanism is evident by the leucocytic infiltration in the endometrium and the uterine luminal content. The uterine defence response to infection is influenced by the estrogen and progesterone hormones. Estrogen promotes and strengthens the uterine defence mechanism while progesterone decreases the defence mechanism. This could be the reason for the increased chances of uterine infection in progesterone sensitized uterus. Change in the uterine PH favourable for bacterial growth and uterine epithelium becoming less permeable so that stimulation for the appearance of leucocytes is delayed are the other unfavourable effects of progesterone (Olson, *et al* 1987)

Antimicrobials used in uterine infection :

Many antibiotics have been used to treat uterine infections, often with little or no regard, for the pharmacology of the antibiotics used or for the effect on the uterus and upon subsequent fertility. Optimum pharmacologic properties of intra-uterine antibiotics are rapid dissolution and even distribution of an active drug throughout the uterine cavity, limited systemic absorption, lack of irritation and not to inhibit the natural antibacterial function of the uterus (ziv, 1980).

a. **Penicillin:** Penicillin acts by interfering with bacterial cell wall synthesis. Resistance to penicillin is conferred by production of an enzyme penicillinase, which is released into the immediate environment of bacteria to destroy penicillin before it can bind to the enzymes of cell wall synthesis. Consequently penicillin resistant organism in the uterine environment can provide protection for penicillin sensitive pathogens as well. Since, in addition to common pathogens, penicillin resistant organism are usually present in the uterus for 2 to 3 weeks following parturition, penicillin is not a choice for early post-partum intra uterine therapy. After 3 weeks post-partum, the uterine flora is reduced primarily to gram negative anaerobes, which are usually susceptible to penicillin. Intra uterine infusion of 1 to 1.5 million units of penicillin after 3 weeks post-partum will provide therapeutic levels of antibiotic in both the lumen and wall of the uterus for more than 24 hours. Penicillin is a sound choice for systemic treatment in the puerperal period because it is effective against the bacteria invading endometrium from uterine lumen. The dose must be at the minimum of 9000 Iu/kg as I.M. injection.

Present address : 1 Associate Professor, Dept. of Animal Biotechnology, 2 Professor and Head, Dept. of Clinics.

b. **OTC :** Oxytetracycline inhibits protein synthesis in the bacterial ribosome. The mechanism for bacterial resistance to Oxytetracycline is a reduced uptake of the antibiotic in the bacterial cell. This is an individual cell phenomenon which is not rapidly transferred to adjacent OTC susceptible cells. Therefore OTC is likely to be an effective form of intra uterine treatment even when a mixed bacterial population is present in the uterus. In addition OTC is only slightly inhibited by the purulent exudate and its activity is only mildly reduced in an anaerobic environment. However, intra uterine infusion of OTC does not penetrate the endometrium, hence local therapy alone is not likely to be effective if systemic involvement is also present. The vehicle in which OTC is dissolved should be non-irritating. Povidone or polyvenyl pyrolidine are relatively less irritating and are the vehicles of choice. When OTC is used for I/U treatment, preparation with propylene glycol causes irritation to the uterus.

c. **Aminoglycosides :** Antimicrobials like gentamycin, kanamycin, streptomycin and neomycin are of questionable value for the treatment of uterine infections. They do not affect bacteria that are anaerobes and are also considered to have a less bactericidal activity in an acidic or anaerobic environment which normally exist inside the uterus.

d. **Nitrofurazone :** Nitrofurazone has been commonly used for the treatment of uterine infections. However, it is a poor choice for I/U treatment because its action is inhibited by blood, pus and high concentration of bacteria all conditions commonly prevalent in post-partum uterus. It is also irritating to endometrium and causes infertility.

e. **Sulfonamides** : Sulfonamides inhibit bacterial growth by inhibiting the Para Amino Benzoic Acid (PABA). As the necrotic tissue debris in the post-partum uterus supplies adequate environmental PABA, sulfonamide loose their effective bactericidal properties in the uterus. They are not recommended for the treatment of uterine infection. (Frank *et al* 1983).

Route of administration of the Antimicrobials

In uterine infections antimicrobials are administered by systemic route (IV, IM,SC) or by intra-uterine route.

In general effective distribution of the drug depends on blood flow of the genital tract, concentration gradient between blood and genital tissue, lipid solubility of the drug, difference between blood and tissue fluid PH. In addition in the post-partum uterus, involution process of the uterus denudation of the epithelium necrotic tissue debris, production of lochia and presence of retained fetal membranes will also interfere with the effective antimicrobial action of the drug. In general it has been observed absorption and distribution of the drug in the genital tract with pathology was significantly slow when compared to healthy genital tract.

For antimicrobial to be effective an effective concentration of the drug must be achieved and maintained at the site of infection ie. in the uterine lumen or deeper in the uterine wall for an adequate period. Intra uterine medication may help to achieve the desired concentration of the drug inside the lumen but it remains localised without having any effect on the other parts of the genital tract. But systemic administration helps in achieving adequate concentration in sub-endometrial tissues, vagina, cervix, ovaries and oviduct. Perhaps the most important reason for the apparent failure of intra-uterine treatment is the alteration of leucocyte function of the uterus. All antimicrobials destroy phagocytes for several days after administration. The removal of this most effective defence mechanism of the uterus nullifies the beneficial effect of the antimicrobials and failure to get complete cure occurs (Dawson, 1977).

Systemic administration of antimicrobials has several potential advantages over I/U. application. Systemic administration results in antibiotic concentration in the uterine tissue and lumen that are similar to blood and plasma concentration (Gustafsson and Ott, 1981). The concentration achieved would not interfere with uterine leucocyte function (Ziv *et al* 1983). The drug also reaches all the parts of the genitalia,

however, its concentration in the lumen will be minimum compared to other parts. Absorption and clearance of the systemically administered drugs are more rapid than from I/U. administration (Seguin *et al* 1974). Therefore, repeated doses may be required to maintain therapeutic levels of antibiotic (Gustafsson and Ott 1981). This, however, can be carried out easier than with I/U treatment and the risk of introduction of new infections or injuring the endometrium and depressing phagocyte activity can be avoided.

Criteria for drug selection for systemic treatment of uterine infections include rapid and complete absorption from the injection site, a large volume of distribution, minimum binding or inactivation by endometrial tissue or secretions and slow elimination rate from the body (Ziv, 1980) . In the case of oxytetracycline. I/V dose of 11 mg/kg body wt. given twice daily, maintain a serum concentration of only 5 mg / ml which is far below the MIC of 20.4 mg/ml for C. *pyogenes*. Pharmacologial studies suggest that chloramphenicol should be the most effective antibiotic for treatment of uterine infection (Ziv, 1984) but it is banned for use in food production animals.

Characteristics of the antimicrobials

Many factors relevant to the antimicrobials have influence on their *In vivo* activity (Bretziaff, 1986).

1. The binding of antimicrobials to blood plasma proteins could affect the therapeutic efficiency of the drug. Binding of the drug to uterine secretions or to endometrium surface will also prevent absorption of the drug from the uterus into the system.

2. The nature of the drug (week acid or weak base) and PH of the local environment plays a role in absorption of the drug. When a differential PH occurs across biological membranes eg. endometrium and blood vessels, a corresponding differential in the degree of ionization of certain drugs occurs at equilibrium. Ionized drug is then trapped on the side of the membrane.

3. Appropriate volume of the drug should be used particularly for I/U administration. Presence of tissue such as placenta and fluid already present inside the uterus should be noted before determining the volume.

4. Formulation of the antimicrobial is another factor to be considered for I/U administration. It is also shown that the tonicity of the infused solution can influence absorption of the dissolved drug from the uterus.

Antimicrobial treatment in the uterine infection of cycling animals

Intra uterine antimicrobial treatment are often given to cycling animals that have mild endometritis and to 'repeat breeder' cows. Intra uterine antimicrobials has been used as post insemination intra uterine treatment in an attempt to rid the uterus of organisms that might be detrimental to the survival of the conceptus. However, there is no covincing result to support this practice. This practice not only produces drug resistant bacteria, it also inhibits the phagocytosis of the uterine endometrium the natural defence mechanism. Further irritating drugs may alter the length of the estrous cycle in cows.

Post partum infection in cow often result in chronic endometritis in the cycling animals. These animals will have mucopurulent discharge, enlarged uterus and irregular cycle. Spontaneous recovery occurs if the animal is allowed to pass through several estrous cycle. This is because of the positive effect of estrogen on the natural defence mechanism of the uterus. The number of estrus periods can be induced to occur at a short interval of time. Two methods can be adopted 1) Treatment with prostoglandin F2 alpha 2) Shortening the estrous cycle by intra uterine infusion of iodine.

Prostaglandin treatment can be repeated one or two times at 10 to 14 days interval. Since luteolysis occurs progesterone inhibition on the uterine defence mechanism is reduced. Estrogen produced during the repeated estrus at frequent intervals helps in stimulating the phagocytosis and uterine defence mechanism and contraction and tonicity of the uterus brought about by the estrum helps in expulsion of the purulent material.

Regarding intra-uterine administration of iodine, 4 percent lugol's solution (4ml of commercial lugol's solution per 100 ml of saline) on day 4 or 5 of the cycle. The volume can be 5 to 25 ml but should be infused into each horm. Oestrus occurs within 5 to 7 days of treatment. Repeat breeder cow can be bred on the induced estrum. In case of mild to moderate endometritis it is recommended to breed the animal on the next spontaneous estrus (Hemelda *et al* 1986)

Conclusion

In uterine infection systemic antimicrobial treatment is considered superior to intra uterine treatment. However, care should be taken to select the most appropriate drug. Indiscriminate use of the antimicrobials particularly as a prophylactic measure and to promote fertility should be avoided as they have questionable value. Whenever possible natural defence mechanism of uterus should be strengthened by using alternative non antimicrobial agents.

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Bacterial Profile of Clinical Samples from Animals and Poultry

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The department of Bacteriology, Bombay Veterinary College receives a variety of clinical samples from the SPCA hospital, large animal and poultry farms around the Bombay city for cultural and antibiotic sensitivity. These assays are of importance in the proper treatment of the infected animals and birds. It also reduces the risk of unwanted misuse of antimicrobial agents.

A total of 217 clinical samples which included milk, cervical and vaginal swabs, urine, faecal swabs, pus, liver, lung and spleen were subjected to bacteriological isolation, using various nutrient and selective media. The isolates were identified upto genus level by the method of Covan and Steel (1993). The *In vitro* drug sensitivity of the isolates were carried out by employing disc diffusion technique using commercially available antibiotic disc (Hi-Media).

Table I shows the isolates obtained from various samples. Many of the samples revealed mixed infections of two or more organisms. E. *coli* was most commonly isolated from cervical and vaginal swabs of cattle and buffaloes, faecal swabs of dogs and liver of poultry. Milk samples and urine of dogs had a predominance of *Streptococcus* spp. and *Staphylococcus* spp. *Salmonella* spp. was notably isolated from liver, lung and spleen of poultry.

All the E.*coli* isolates from milk were sensitive to Pefloxacin whereas 50% of E.*coli* isolates from vaginal and cervical swabs of cattle and buffalo were sensitive to gentamycin and 5% were sensitive to Kanamycin, Doxycycline, Metranidazole and Oxytetracycline. All *Streptococcus* spp. isolated from milk were sensitive to Pefloxacin and 70% were sensitive to Norfloxacin. In general all the isolates from cervico-vaginal swabs from cattle and buffalo were sensitive to gentamycin, which was found to be the most widely used antibiotic in treatment of uterine infections. In an earlier Study Ramaswamy *et.al.* (1992) also found gentamycin to be effective in treatment of repeat breeding cases, involving cattle and buffalo.

Gastrointestinal and urinary tract infections were commonly encountered in dogs and on culturing of faeces and urine, E.*coli* and *Staphylococcus* spp. were the predominant isolates respectively. The antibiogram study reveals that all the isolates from faeces (Table I) were sensitive to gentamycin except *Klebsiella, Acinetobacter* and *Serratia* spp. 40% E.*coli* isolates from faecal samples were sensitive to gentamycin, 4.5% to Kanamycin and 4% to Neomycin. From urine, 50% of the *Staphylococcus* spp. were sensitive to gentamycin, kanamycin and neomycin and 70% to Ampicillin. S. *aureus* appeared to be the principal isolate from urine as also observed by Dwivedi *et. al.* (1990) who found them resistant to Ampicillin as compared to the present study. Pus samples from dogs showed variable sensitivity to antibiotics.

In poultry, colibacillosis has the highest prevalence. Combined infections of E.*coli* with *Proteus* spp. or E. *coli* with *Salmonella* spp. have been recorded in this laboratory by Paranjape and Das, (1985). All isolates from poultry samples were mainly sensitive to Pefloxacin followed by Neomycin, Neodox and Lincospectin and were resistant to most of the routinely used antibiotics like Nitrofuran and tetracyclines.

All the faecal samples from monkey yielded mixed infection of E.*coli* and *Klebsiella* spp. which were sensitive to Ampicillin. Whereas E.*coli* from faecal samples of dogs were

Table - I

Isolates obtained from the sample

Species	Types of sample (No. of sample collected)	E.*coli*	*Strepto-coccus*	*Staphylo-coccus*	*Pseudo-monas*	*Bacillus*	*Proteus*	*Klebsiella*	*Acineto-bacter*	*Serratia*	*Salmo-nella*
Cattle	Milk (22)	5	10	5	1	1	--	--	--	--	--
	Cervical/Vaginal swabs (54)	35	1	8	1	5	5	8	--	--	--
Dog	Cervical/Vaginal swabs (13)	4	2	3	4	1	2	--	1	1	--
	Urine (21)	3	6	10	--	1	--	1	--	--	--
	Faeces (40)	33	--	1	2	--	9	2	--	--	--
	Pus (10)	2	5	3	--	--	1	--	--	--	--
Monkey	Faeces (4)	4	--	--	--	--	4	--	--	--	--
Poultry	Liver (35)	26	4	5	3	3	6	2	--	--	4
	Lung (8)	3	--	--	2	--	2	1	--	--	1
	Spleen (10)	8	--	--	--	--	2	--	--	--	3

sensitive to gentamycin and resistant to Ampicillin, which may be due to the development of Ampicillin resistant strains in dogs due to the wide spread use of broad spectrum antibiotics in canine practice.

In this study, most of the clinical samples showed highest prevalence of E.*coli* sensitive to gentamycin. Newer antibiotics like Pefloxacin are now being used in Intra mammary preparations for treatment of acute cases of mastitis and in feed and water for treatment of colibacillosis and other mixed infections in poultry.

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A Field Trial of Floxidin in Poultry at Gurgaon

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Mortality in poultry may be caused due to bacteria, viruses, parasites, fungi, nutritional deficiency diseases and managemental problems. Data collected on the epidemiology of diseases in this laboratory revealed that most of the casualities in poultry farms were due to managemental deficits resulting into bacterial infections. Among bacterial diseases E. *coli, Salmonella* or combination of Enterobacteria were encountered.

Early chick mortality in the first week of rearing is quite common in many poultry farms. Therefore, a field trial of Floxidin 5% oral solution was conducted in poultry with the following objectives:-

1. To stop/minimise early chick mortality;
2. To check and record the bacterial sensitivity; and
3. To study weight gains and FCR.

Materials and methods

400 day old broiler chicks of a reputed brand (Cobb) were selected for the trial in the month of October, 1995, after necessary culling at hatchery level (approx. 1% chicks were culled). Two hundred chicks were kept as control. Trial was conducted at one of the organised broiler farms near Gurgaon. Before conducting the trial water of the farm was tested for potability and was found to be fit for consumption. Different bands were used on the treated and control (Untreated) groups to avoid mixing. Necessary vaccinations were carried out in both the groups.

Pipped and culled chicks of the same lot were subjected to culture and sensitivity test. Weekly mortality was recorded both from the treated and control groups. Postmortem of the birds was routinely done in the laboratory so as to detect the cause of mortality. Weight gain/FCR data was recorded weekly for final calculation of gain over control.

5% Floxidin oral solution was administered in the chicks from 0 to 3 days @ 0.5 ml/liter water. Medication was further repeated in the 4th week for 3 consecutive days (day 24 to day 26) only in the treated group. Total duration of experiment was 6 weeks.

Observations

E. coli isolated from the pipped and culled chicks of the same lot was subjected to drug sensitivity test. Bacteria were found to be sensitive to Enrofloxacin (5+), Chloramphenicol (3+), Neomycin (2+), Ampicillin (2+), Doxycycline (3+), Furaltadone (1+), and was resistant to Oxytetracycline, Gentamycin and Co-trimoxazole.

Therefore, the need of field trial of Floxidin in poultry arose to confirm the findings of In-vitro drug sensitivity test. Following observations were recorded.

It was evident from the table that FCR in the treated group was 2.21 and mortality was 4.0% as against control (FCR 2.4 and mortality 12.0%). In the treated group chicks died mostly due to non specific reasons such as weakness and emaciation, piling, traumatic injury etc. Whereas chicks in the control group invariably showed bacterial infection as the cause of mortality. In this case pattern of drug sensitivity was the same as observed earlier. Thus, the use of Floxidin in the early age to combat early chick mortality is very much justified. In the

treated group there was no evidence of CRD whereas in the control group CRD was the consistent feature. Present observations srongly suggest the use of Floxidin in the poultry, first course early in the chick life and then in the fourth week to take care of bacterial infections including CRD, for better FCR and uniform growth of the birds.

Table

Treated Group (400)						Control Group (200)					
Age (Wks)	Number	Mort. %	Body Wt. Kg.	Cumm. Feed Kg.	FCR	Age (Wks)	Number	Mort. %	Body Wt. Kg.	Cumm. Feed Kg.	FCR
1	400	–	38.0	36.4	0.95	1	200	1.5	18.4	19.6	1.06
2	400	0.75	112.0	140.0	1.25	2	197	1.0	54.2	67.9	1.25
3	397	0.75	190.6	280.0	1.46	3	195	1.5	89.3	135.8	1.52
4	394	0.75	309.7	488.5	1.57	4	192	3.0	131.2	241.5	1.84
5	391	1.25	427.1	801.9	1.87	5	186	2.0	193.2	408.5	2.11
6	386	0.75	521.1	1155.9	2.21	6	182	2.0	230.4	584.9	2.53
Total Mortality %	–	**4.00**	–	–	–	**Total Mortality %**	–	**12.0**	–	–	–

Conception Rate in Repeat Breeding Cows Following Uterine Flushing and Antibiotic Therapy

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Abstract

Forty eight repeat breeding cows were subjected to therapeutic uterine flushing with normal saline at estrus. In the experimental animals forty cows were allotted to the treatment group I and eight repeat breeding cows acted as group II with eight untreated control animals as group III. Cervical mucus samples from the treated group were collected aseptically prior to uterine flushing and subjected to antibiotic sensitivity test. Systemic administration of the antibiotics was carried out to the treatment group for five days from the second day of uterine flushing. All the cows were bred by artificial insemination in the subsequent estrous cycle. The overall conception rate in treated group I was 80 per cent compared to 75 per cent in the group II whereas 37.75 per cent conception was observed in untreated control group III. The average number of services required per conception was 2.50, 2.56 and 6.30 for the group I, II and III, respectively. Therapeutic uterine flushing alone or in combination with systemic antibiotic therapy increased the fertility of repeat breeding cows by stimulating the uterine endometrim for increased leucocyte activity.

Introduction

Repeat breeding is a perennial problem recognised as one of the most serious threats affecting the economy of the dairy industry. The specific reason for this condition cannot be pinpointed as the factors contributing to this syndrome are multifarious. Cycling cows that are devoid of any palpable abnormalities in the genitalia possess apparently normal estrous cycle and exhibit genital discharge without visible changes in abnormality. But the presence of micro organisms may be one of the predominant factors playing a significant role in the failure of conception. Microbial examination and antibiotic sensitivity testing of the cervical mucus would help to overcome the genital tract infection which contributes a major factor in this syndrome. Information regarding the intra uterine infusion and parentral therapy of antibiotics either alone or in combination were reported to increase the fertility. Literature concerning the therapeutic uterine flushing and its impact on conception rate is very limited. In view of the above perspectives and considering all the facts this work was carried out.

Materials and method

Fifty six cross-bred cows available at Livestock Research Station, Kattupakkam which had failed to conceive after three inseminations were utilised for the study. All the experimental animals were subjected to therapeutic uterine flushing with sterile normal saline at the rate of 500 ml in each cornua of the uterus as per the method described by Napolean *et al.* (1995). Care was taken to monitor the uterine engorgment during the process of flushing on both sides of the cornua separately.

Cervical mucus samples were collected from forty cows prior to the uterine flushing which served as the treated group I. Aseptical measures were taken to aspirate the cervical mucus with the help of the AI gun and sheath as the method described by Dabas and Maurya (1988) with slight modification. All the samples were subjected to antibiotic test by the standard single disc method as per Bauer *et al.* (1966). Eight cows in which their uteri were flushed at estrus served as group II and eight cows acted as untreated control group III.

Treatment with antibiotics commenced on the second day following uterine flushing with the

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amenable drug which showed the maximum zone of inhibition in the sensitivity tests. The standard dose of drug recommended as per the body weight was followed for five consecutive days with specified intervals.

Parenteral injections were preferred to intra uterine therapy in order to avoid the endometrial irritation and to have a maximum concentration in the systemic circulation. All the animals were inseminated in the subsequent estrous period. The conception rate was worked out following three inseminations by confirming pregnancy after 60 days of last AI.

Results and discussion

In the present investigation out of the forty cervical mucus samples tested for antibiotic sensitivity using different discs viz. Gentamycin, Chloramphenicol, Ampicillin, Oxytetracycline, Penicillin and Streptomycin to identify the appropriate drug, the tune of sensitivity were found to be 30, 25, 22.5, 7.5, 7.5 and 7.5 per cent, respectively (Fig - 1). It was observed that the sensitivity was limited to a higher range of antibiotics only. This might be due to the indiscriminate usage of lower antibiotics for various infections towards a considerable period by which the organisms develop resistance. The present findings are in agreement with those of Sharma *et al.* (1978), Kavani *et al.* (1985), Maurya *et al.* (1992) and Dabas *et al.* (1995).

Increase in the conception rate following the antibiotic therapy in repeaters have been reported by many workers with varied results. Antibiotic therapy was followed for the treated animals with their respective amenable drug available in the market by parental injections. In the present work an overall conception rate of 80 per cent was recorded in the treated group I and the percentage for different antibiotics are shown in the Table - 1. The results observed in this study are in accordance with the earlier reports recorded by Sharma *et al.* (1978), Kavani *et al.* (1985) and Sharma *et al.* (1988) with an improved performance. However in the present study, uterine flushing was carried out followed by parenteral antibiotics which might be the cause for non interference of the normal uterine defence mechanism. The conception rate of 70 per cent was observed in group II and it was 37.75 per cent in the untreated control group III. The average number of services required per conception was 2.56 in the treated group I, 2.50 in the group II and 6.30 in the untreated control group, respectively. Better response in the group II with uterine flushing alone could be due to the stimulation of endometrium with increased leucocytic activity and supports the findings of Seguin *et al.* (1974), Coe (1984) and Paisley *et al.* (1986).

Hence it is suggested that uterine flushing with systemic administration of appropiate antibiotics at repeated doses will maintain the therapeutic level in cases of uterine infection causing repeat breeding problem. This method is also easier than intra uterine therapy by avoiding the risk of introducing new infection, injury to the endometrium and depressing the uterine phagocytic activity.

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Fig. 1

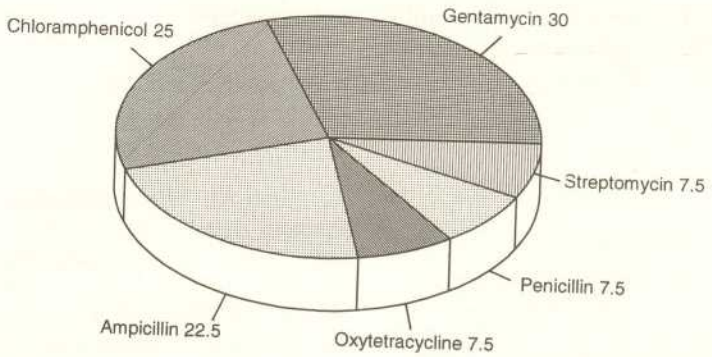

Table - I

Pregnancy rate in antibiotic treated and/or uterine flushing and control groups.

Group	No. of animals	Pregnancy % during the estrous cycle			Overall conception	Avg. no. of services
		I	II	III		
Gentamycin (Gentavet)	12	33.33 (4)	25.00 (3)	25.00 (3)	83.33 (10)	2.50
Chloramphenicol (Phenivet)	10	40.00 (4)	20.00 (2)	30.00 (3)	90.00 (9)	2.22
Ampicillin (Roscillin)	9	33.33 (3)	11.11 (1)	33.33 (3)	77.77 (7)	2.86
Streptopenicillin (Dicrysticin)	6	50.00 (3)	16.66 (1)	– –	66.66 (4)	2.75
Oxytetracycline (Terramycin)	3	33.33 (1)	33.33 (1)	– –	66.66 (2)	3.00
Treated group I (Uterine flushing + Antibiotics)	40	69.50	20.00 (15)	22.50 (8)	80.00 (9)	2.56 (32)
Group II (Uterine flushing)	8	50.00 (4)	12.50 (1)	12.50 (1)	75.00 (6)	2.50
Group III (Untreated control)	8	25.00 (2)	12.50 (1)	– –	37.75 (3)	6.30

Bacterial Isolates of Cyclic Non-Breeder Cows and their Treatment

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Introduction

Repeat breeding is one of the most common reproductive disorder in dairy animals (Agarwal and Buch, 1968) It accounts for greater economic losses as a result of loss in milk production and inability of animals to reproduce and increasing the intercalving period. Bacterial Infection of the uterus is a frequent cause of repeat breeding (Singla *et al.* 1991 and Verma *et al.* 1994). Hence, the present study was planned to assess the type of bacterial infection and for suggesting rational drug for treating them.

Materials and methods

Uterine discharges from 26 cyclic non breeder cows of different breeds were collected aseptically and studied for bacteria and its load. The samples were collected from ambulatary clinic service in the adopted villages of Ludhiana district of Punjab. The samples were streaked on to 10% sterile blood agar plates and on MacConkey's lactose agar plates and incubated at 37°c for 24 hrs. The samples were processed within 4 hours of collection. The colonies were studied for their morphological, cultural and biochemical characters (Buxton and Fraser, 1977; Carter 1984). The bacterial load in the liquid suspension was counted adopting plate count technique (Malik, 1967). *In vitro* drug sensitivity test was carried out against 9 different chemotherapeutic agents by standard disc diffusion technique (Bauer *et al*, 1966).

On the basis of bacteriological examination, all the animals were given Intra uterine infusion with gentamycin 400 mg. dissolved in 30ml of distilled water for three consecutive days and all the animals were inseminated on next oestrus and examined for pregnancy between 60-90 days after AI. The animals were dewormed by Panacur 6gm, orally, on the day of sample collection and 2 weeks after that.

Results and discussion

Bacteriological examination of uterine swabs of all animals yielded 28 different bacteria belonging to 8 genera (Table 2) Among these 24 (92.3 %) samples yielded a pure growth of bacteria belonging to a single genus whereas the remaining 2 (7.7%) yielded a growth belonging to different genera.

Staphylococcus aureus was the main causative organism followed by E. *coli* and *Klebsiella* spp. Most of the isolates were sensitive to Gentamycin (71%) and chloramphenicol (46%) while the sensitivity was minimum with Furazolidone and Erythromycin. No organism was found sensitive to Ampicillin and Penicillin. *Bacillus* sps, *Coryne bacterium pyogenes* and *staphylococcus epidermidis* were the most resistant organisms. They were 100 percent resistant to 7,6 and 6 of the 9 antibiotics tested respectively (Table 2). These findings corroborate with the findings of Singla *et. al* (1991) and Verma *et al* (1994). Most of such organisms isolated in the present study have been termed as "opportunists" since they are the normal inhabitants of various organs including urogenital organs. When immune system of these animals goes down due to stress factors (poor sanitation, overcrowding, summer stress, poor nutrition etc.) these organisms may become pathogenic. This all depends upon the physiological status of animals and organs (Terpstra and Eisma, 1951). Pateria *et al* (1988) concluded that these organisms cause uterine infections and inflammation of endometrium of uterus resulting in endometritis which is a common cause of infertility in cattle.

Table 1. *In Vitro* drug sensitivity pattern and average number of live organisms isolated from cyclic Non breeder cows

	Name of bacteria	Total No.	Average Isolates count	Number of Isolates sensitive to								
			Load	G	C	Co	F	T	S	E	A	P
1	*Staphylococcus aureus*	8	$28x10^7$	5	3	2	-	3	2	-	-	-
2	*Escherchia coli*	5	$25x10^7$	4	2	1	-	-	3	-	-	-
3	*Klebsiella* sp.	5	$40x10^6$	4	2	3	1	-	1	-	-	-
4	*Streptococci*	2	$47.31x10^7$	1	2	1	-	1	-	-	-	-
5	*Corynebacterium pyogenes*	2	95.7×10^6	1	1	1	-	-	-	-	-	-
6	*Bacillus* sp.	2	34.7×10^7	1	-	-	-	-	1	-	-	-
7	*Proteus vulgaris*	1	$4.9x10^6$	1	1	1	1	2	-	-	-	-
8	*Pseudomonas aeruginosa*	2	$12.5x10^7$	2	1	1	-	-	-	1	-	-
9	*Staphylococcus epidermidis*	1	10.8×10^6	1	1	1	-	-	-	-	-	-
	Total	28		20	13	11	2	6	8	1	0	0

G=Gentamycin; C = Chloramphenicol; Co = Co-trimoxazole; F = Furazolidone; T = Tetracycline; S = Streptomycin; E = Erythromycin; A = Ampicillin; P =Penicillin.

Table 2. Percentage efficacy of various antibiotics against the pathogens isolated from cyclic Non breeder cows

S. No.	Name of antibiotic	Concentration/ disc	Total No. of Isolates tested	Found sensitive	Percentage
1	Gentamycin	10 mcg	28	20	71
2	Chloramphenicol	30 mcg	28	13	46
3	Co-trimoxazole	25 mcg	28	11	39
4	Furazolidone	50 mcg	28	2	7
5	Tetracycline	30 mcg	28	6	21
6	Streptomycin	10 mcg	28	7	25
7	Erythromycin	15 mcg	28	1	4
8	Ampicillin	10 mcg	28	0	Nil
9	Penicillin	10 units	28	0	Nil

Out of the 26 cows treated with gentamycin, 16 conceived following treatment and became pregnant with conception rate of 61.54 percent. Ten animals did not conceive, which suggests that either dose of gentamycin was not sufficient to clear off the uterus from infection or there may be some factors other than infectious causes responsible for repeat breeding.

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Case Report : Successful Post-operative Treatment with Floxidin 10% Injection alongwith other Supportive Treatment

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A buffalo was brought to the hospital with a huge swelling at the chest region near the elbow joint. Swelling was not painful but it was hard. (Fig. 1)

A mass of about 15 Kg. was hanging from the same spot. The buffalo was not in a position to move much; moreover, her production had came down from 12 litres to 3 litres. It was very painful to animal.

It was decided that the mass had to be detached from the body because of the painful condition to the animal. The animal was given 4 ml. Sequil i/v and Xylexin 3 ml i/m for restraining the animal. A longitudinal incision was given to avoid thick veins because the heavy mass was having rich blood supply. It was full of pus which came out along with blood. The mass was a tumourous growth. It was ascertained that nothing was embeded in the chest cavity or this growth had no roots in thoracic cavity. An eliptical incision was given on healthy skin and after ligating the major blood vessles, the growth was detached.

After detachment, continuous sutures were applied after putting antibiotics. Tinc. Iodine was applied on the sutured area.

Injections of antibiotic Floxidin 15 ml daily alongwith Novalgin 15 ml morning and evening were given. Rintose 540 ml along with Tonophosphan 30 ml and Avil 10 ml was given intravenously on the same day of operation.

The antibiotic Floxidin 10% Inj. and Novalgin were given for 5 days and dressing was done regularly on alternate days, with Charmil. To reduce the stress, Gerifort 50 ml daily was given for 5 to 6 days. The operated site healed nicely. So, sutures were opened and the animal was monitored for two to three weeks.

The animal came back to normal in production and was relieved from pain and stress. (Fig. 2)

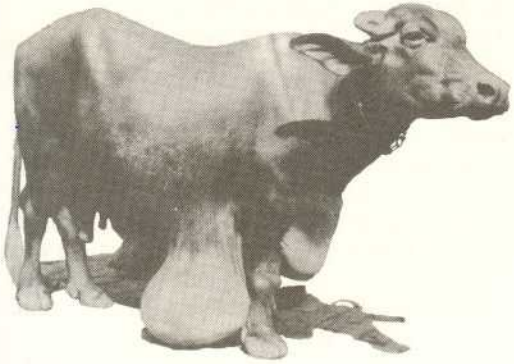

Fig. 1

Fig. 2

Case Report : Treatment of Ventricular Bigeminy with Mexiletine in a Dog

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Jain Samaj Europe Cardiac Centre, Bai Sakarbai Dinshaw Petit Hospital, Parel, Mumbai.

A ten year old female pomeranian was referred for evaluation of a severe cough and orthopnoea. Physical examination revealed an abnormal (slapping) apex impulse, a mitral systolic grade IV murmur and a marked pulse deficit. Bronchovesicular breath sounds and rales were prominent.

Radiography revealed a symmetrically enlarged cardiac silhouette.

The ECG showed ventricular bigeminy, in which ventricular premature contractions (VPCs) are seen alternating with normal beats. The diagnosis of VPCs is based on the presence of premature, wide and bizarre QRS complexes with the T wave usually oriented in the direction opposite to the QRS complex. (see Fig. 1).

The dog was given Lidocaine as an i/v bolus @ 2 mg/kg, and an ECG was repeated. Lidocaine was successful in converting the bigeminy to a sinus rhythm. Lidocaine is a type 1B antiarrhythmic and is usually the drug of choice for treatment of VPC in the canine patient, since it has minimum effect on blood pressure, cardiac contractility and cardiac output.

The dog was then prescribed Quinidine, a Type 1A antiarrhythmic, @6 mg/kg Po tid. Treatment with diuretics (furosemide) was also started simultaneously to treat the congestive cardiac failure due to mitral regurgitation. An ECG was repeated after 2 days of treatment with Quinidine. The bigeminy persisted, although the dog had improved clinically and the rales were absent. The dog was then put on Mexiletine, a type 1B antiarrhythmic @ 5 mg/kg po bid. Conversion to sinus rhythm was achieved after three days of treatment with Mexiletine. Mexiletine was then weaned off gradually over a period of three weeks. The dog showed a remarkable improvement after treatment with furosemide and Mexiletine. The arrhythmia did not recur after Mexiletine was finally stopped. (see Fig. 2) Maintenance dose of furosemide was continued to treat the congestive cardiac failure.

Discussion

An arrhythmia is defined as an abnormality of impulse formation, conduction, rate and regularity. Any arrhythmia should be classified into benign or clinically insignificant, requiring no treatment or clinically significant, which requires treatment with antiarrhythmics and/or antifailure drugs.

The recognition of arrhythmias and identification of animals requiring treatment for the same is important for proper case management. Since the malignant arrhythmias may lead to hypotension myocardial ischemia, syncope, seizures, shock or death.

Antiarrhythmic treatment is warranted for dogs with hemodynamically significant arrhythmias.

The current criteria for treatment of ventricular arrhythmias is

1) Presence of multiform VPCs.
2) More than 20-30 VPCs / min.
3) Rapid, sustained rates.
4) Presence of heart disease.
5) Whether the patient is symptomatic.

At the same time, since the arrhythmogenic potential of antiarrhythmic drugs is now widely recognised, one has to be careful with drug selection and dosage. In this case, the valvular disease may have caused a pressure - volume overload, leading to altered myocardial function and ventricular ectopics. Since the patient was symptomatic, had an organic heart disease (mitral regurgitation) and had 80 VPCs / min. therapy had to be initiated immediately.

Although Mexiletine is not very commonly used in Veterinary medicine it proved to be useful in this case which was refractory to Quinidine.

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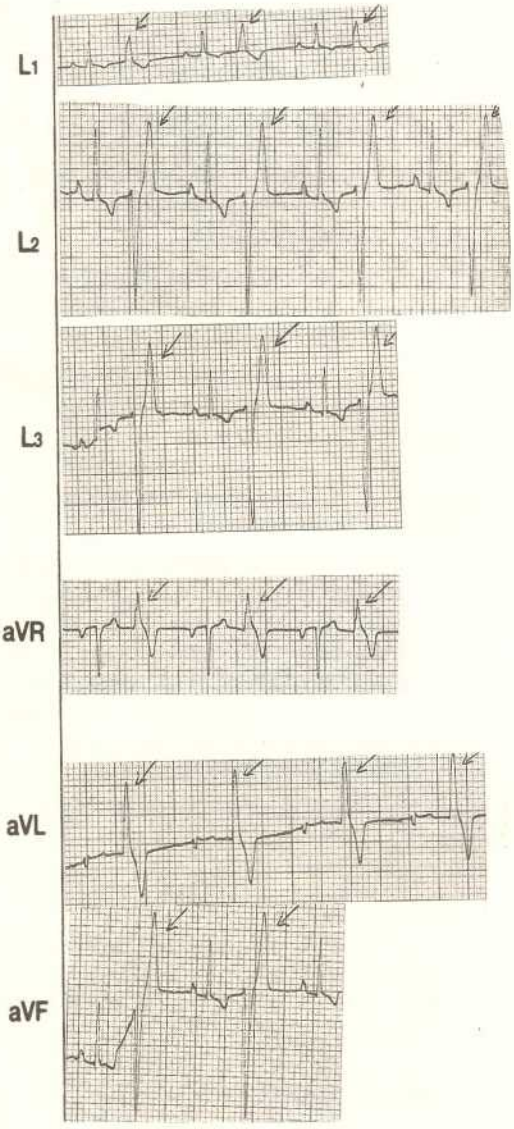

Fig. 1 – Ventricular bigeminy. Note the normal complexes alternating with the bizzare ectopic beats. (arrows)

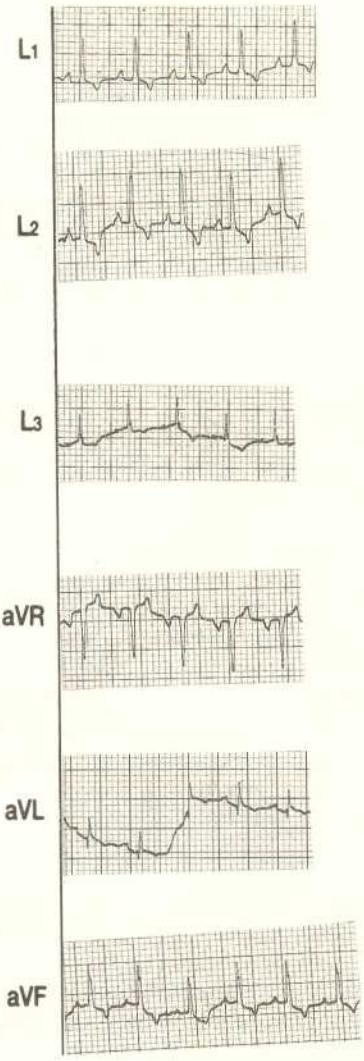

Fig. 2 – Normal sinus rhythm established after treatment with Mexiletine and Lasix.

Review : Enrofloxacin – A New Drug

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Enrofloxacin is the latest antimicrobial of fluoquinolone group available to the veterinary clinicians. The broad spectrum of activity, greater bioavailability, penetrability in various tissues, long serum half life and general safety have made fluoquinolones very attractive agents for treating acute infectious and several diseases (ziv. 1994). Besides, enrofloxacin also possesses some attractive pharmaceutical features viz., it can be made available in different dosage forms for administration by enteral as well as parenteral routes. It is a very stable compound. It is readily mixed in water for poultry.

Enrofloxacin – A Veterinary Speciality

Enrofloxacin was developed synthetically in 1983. It is the fluoquinolone group of anti-bacterial agent.

Spectrum of activity of Enrofloxacin

The spectrum of activity of enrofloxacin encompasses both Gram-negative and Gram-positive bacteria including some anaerobic bacteria. Significant activity has been demonstrated against some species of Mycoplasma and persistent intracellular animal pathogens such as *Brucella, Listeria, Chalmydia species.*

E.*Coli, Actinobacillus and Moraxèlla* are highly sensitive to enrofloxacin with MIC Values ranging from 0.008 to 0.06 mcg/ml. *Serratia Proteus, Citobacter, Campylobacter, Brucella, Bordetella, Vibrio, Staphylococcus, Erysipelotherix, Bacillus and Mycoplasma* are moderately sensitive (MIC 0.125-0.5 mcg/ml).

Unique mode of action of Enrofloxacin

- Enrofloxacin is a very rapidly acting bactericidal/mycoplasmacidal agent.
- Inhibition of the cell division is the first action of enrofloxacin which ends with total lysis.
- Enrofloxacin impairs the bacterial gyrase – the enzyme which plays one of the major roles in the replication of DNA.
- The susceptible organism cannot survive beyond 30 minutes of exposure to optimum antibacterial concentration.
- The action against bacterial cell wall and cytoplasmic membrane is also suggested (Dahloff, 1986).

Absorption, Distribution, Metabolism and Excretion of Enrofloxacin

Enrofloxacin is readily absorbed after oral or parenteral administration. In monogastric species and in preruminant calves upto 80% of oral dose is absorbed. It is distributed to a very great extent in almost all body tissues. High concentrations are particularly achieved in liver and urinary tract (Vancutsem *et al;* 1990) Enrofloxacin has very low protein binding (10-40%) property.

In poultry enrofloxacin also appears in hatching eggs and is effective in reducing vertically transmitted infections such as *Mycoplasma, Salmonella.*

Enrofloxacin is rapidly metabolized to ciprofloxacin which is also a potent antimicrobial. Enrofloxacin is eliminated slowly mainly via urine.

Pharmacokinetics of Enrofloxacin

The peak serum enrofloxacin concentration is achieved at 1-2 hous after oral administration. The most attractive pharmacokinetic parameter of enrofloxacin is its large volume of distribution in almost all kinds of tissues. The elimination half life is 7.3, 1.4, 1.2, 2.1 and 3.3 in the chicken, turkey, calf, dog and horse respectively (Vancutsem *et al:* 1990).

Safety & Toxicity of Enrofloxacin

The adverse effects of enrofloxacin are not of severe consequence when compared to the beneficial features it exhibits (Vancutsem *et al;* 1990).

Enrofloxacin is well tolerated by oral route in poultry, dogs and cats and by parenteral routes in calves, dogs and cats.

There is no interaction of enrofloxacin with other oral constituents like milk, milk substitutes, electrolyte solution in calves and other coccidiostats in poultry.

The LD 50 values of enrofloxacin are very high (< 5000 mg/kg in rats and mice and 500-800 mg/kg in rabbits) after oral administration.

Enrofloxacin does not affect feed consumption, body weight, haematology and biochemical parameters after repeated adminstration.

It is neither embryotoxic nor teratogenic.

Clinical Indications of Enrofloxacin

Enrofloxacin can be used in all domesticated animals and poultry for following clinical ailments.

Cattle and buffalo calves :

- Coli diarrhoea and coli sepsis and diarrhoea of non bacterial origin for prevention of intercurrent bacterial infections.
- Broncho pneumonia due to primary bacterial infections and secondary bacterial infections of respiratory organs in complex diseases.
- Salmonellosis.

Poultry :

- Mycoplasmal infections
- Colisepticaemia
- Coryza contagiesa avium *(Haemophilus paragallinarum)*
- Pasteurellosis
- Salmonellosis
- Staphylococcal infection
- Erysipelothrix infection
- Mixed bacterial infections and secondary infections in viral disease.

Dogs and Cats :

- Infections of digestive organs
- Infections of respiratory organs
- Infection of urinary tract and sex organs
- Infections of the skin
- Infections of auditory canal
- Wound infections

Contraindications

Juvenile cartilage is reported to be the site of adverse effect in young growing animals. This is the reason of its contraindication in young growing pups below eight months of age.

Enrofloxacin is not recommended for treatment of horses (Pyorala *et al;* 1994).

Dose

Cattle:

In calves 2.5 mg - 5 mg/kg. once daily by oral or parenteral route. In complicated infections or salmonellosis treatment can be increased to 5 mg/kg for 3 to 5 days.

Dogs and Cats:

In dogs and cats the recommended oral and parenteral (s.c.) dose is 5 mg/kg/day in two divided (morning and evening) doses or a single dose for 5 days. In protracted cases such as pyoderma, chronic/recurrent urinary tract infection treatment can be given for 10 days.

Poultry:

Enrofloxacin is administered as 10% & 5% oral solution in drinking water for therapeutic and protective purpose respectively.

In chickens and turkeys, daily dose of 8-10 mg/kg body weight is recommended. It is therefore added at the rate of 50 ppm in drinking water (50 mg/L i.e. 1 ml 5% oral solution or 0.5 ml of 10% oral solution/litre of water) for 3 days or 5 days in salmonellosis.

References

Brander G.C., Pugh D.M., Bywater R.J. and Jenkins W.L. (1991) Veterinary pharmacology and therapeutics, Edn. 5th Bailliere Tindall, London, pp 484-485

Dahloff A. (1986), Wirkung der Chinolone, Vortrag, Ludwing Heimeyer – Symposium in Koln Gorg Thieme Verlag Stuttgart i.m. Druck.

Pyorala S. Panu S. and Kaartinen L. (1994) Proc VI International Cong., European Assn. for Vet. Pharmacology and Therapeutics, pp.45

Richer P, Dellac B. and Froyman R. (1994) Ibid pp. 207.

Vancutsem P.M., Babish J.G. and Schwark W.S. (1990) Cornell Vet. 80(2) 173-183

Ziv G. (1994), Proc VI International Cong., European Assn. for Vet. Pharmacology and Therapeutics, pp. 194.

Abstracts

(1) Ivermectin toxicosis in kitten

Three month old kitten which received a subcutaneous injection of Ivermectin Co. 3 mg/kg body weight) for persistent ear mite infection, exhibited mild tremors ataxia, weakness, myosis and depression within 12 hours of treatment. Intravenous fluid therapy, enteric nutrition therapy failed to recover the kitten which died on day 7th. Caution must be taken in the treatment of kittens with Ivermectin.

Lewis DT., Merchant S.R. and Neer T.M. (1994)
J. Am.-Vet Med. Assn. **205** : 284 - 285.

(2) Dose titration study of enrofloxacin (Baytril) against respiratory coli bacillosis in muscovy ducks.

Four week old SPF muscovy ducks were inoculated with reo-virus and one week later with 078 : K80 strain of E. coli intra tracheally. Next day enrofloxacin treatment was given in drinking water. Comparing rate of mortality, weight gain, macroscopic lesions and E. coli reisolation among treated and untreated birds showed that a five day treatment with 12.5 or 25 ppm enrofloxacin in water for four hours in the morning provided good therapy against respiratory coli bacillosis.

Kempf I; Gesbert F; Guittet M., Froyman R; Delaporte J and Bennejean G. (1995).
Avian Diseases **39** : 480 - 488

(3) Persistence of Foot and Mouth Disease virus on wool.

Based on the experimental studies on persistence of FMD virus on contaminated wool the authors recommend that either i) Simple storage of contaminated wool for four weeks at temperature of 18^{0}c or higher or ii) Scouring of contaminated wool at 60-70^{0}c would be sufficient to remove the threat of FMDV contaminated wool being infectious to other animals.

Mc Coll K.A; Westbury H.A; Kitching R.P. and Lewis V.M. (1995)
Austr. Vet J. **72** (8) : 286 - 292.

(4) Evaluation of three water suspensible formulations of Fenbendazole against Ascaridia galli infection in broilers.

Three formulations of water suspensible Fenbendazole at target doses of 30.3 or 60.6 PPM in drinking water were administered to broilers infected with Ascaridiagalli. Medication was given in water through automatic medicators for 6 hours on 3 consecutive days. Three days after treatment, chicks were killed, and worms were counted. Efficacy of the drug was 99.2 to 100 % and 69.0 to 89.6 in 60.6 PPM. and 30.3 PPM. respectively.

Sander J.E. an Schwartz. R.D. (1994)
Avian Diseases **38** : 350 - 353.

(5) Dose titration of moxidectin oral gel against migrating Strongylus vulgaris and Parascaris equorum larvae in pony foals.

Moxidectin is a broad spectrum anthelmintic with structural and functional similarities to other macrocyclic lactones viz. Ivermectin and Milbemycine oxime. It is shown to be effective on gastro intestinal adult and larval parasites of horses.

At all doses (300 mg, 400 mg and 500 mg per kg) the Moxidectin was 99.6 to 100% effective on migrating larvae (L4 & L5) of S. vulgaris and P. equorum in trials.

Monalian C.M; Chapman M.R.; Taylor A.W. French D.D. and Klei T.R. (1995)
Vet Parasitrology **60** : 130 - 110

(6) The effect of route of inoculation on protection by killed vaccines in chicken.

Trials to immunize chicken by administration of killed vaccine intra tracheally, intranasally, per os, by crop gavage and intramuscularly were conducted using killed Haemaphilus gallinarum, Mycoplasma gallisepticum and IBD virus. The protection against challenge with respective agent showed that immunizations with intratracheal administration was equivalent to those produced by parental administration in all the killed vaccines tried.

Yogi Nagasawa and Susumu Ueda (1995)
Avian Diseases **39** : 507 - 573.

(7) Egg dipping in Hydrogen peroxide Solution to eliminate salmonella typhimurium from egg shell membrane.

Double dipping using positive pressure differential method (PPD) in 6% H_2O_2 (VV) reduced average number of organisms in shell membrane by 75% and number of Salmonella typhimurium on positive eggs by 55%. This does not affect hatchability.

PPD method consists of dipping eggs in a pressure cooker type container to which positive pressure 1.1 kg/cm^2 was applied for 5 minutes and later pressure released to allow eggs to be dipped in atmospheric pressure for 20 minutes.

Mario Padron (1995) Avian Diseases **39** : 627 - 630.

(8) Abortion due to Neospora sp. in dairy herd

Neospora caninum is identified as a cause of neurological disease and reproductive abnormalities in dogs; but has been since shown to affect cattle in various parts of the world.

Authors have reported an abortion storm due to Neospora sp. in a cattle herd in U.K. and confirmed by immuno histochemical staining of the brain of an aborted foetus and presence of antibodies (by IFA test) in 9 out of 10 affected cows. The authors advise examination for the parasite should be carried out as a part of abortion investigations particularly in multiple abortion incidents.

Dannatt L; Guy F an Trees A.J. (1995)
Vet Record **137** : 566 - 567

(9) Characterisation of cell mediated responses to Eimeria acervulina antigen.

Merozoite and sporozoite fractions of E acervuline were separated by electrophoresis and injected into mice to study coccidia specific antibody titres, lymphocyte proliferation and interferon production.

Antibody response was high with Merozoite fractions 4 (MW 12700 - 18400) and 3 (MW 18400 - 29000).

Lymphocyte proliferation was marked with merozoite fraction 2 (MW 29000 - 43000) and sprozoite fractions 1 and 2 (MW 200000 + and 68000 - 200000 respectively). High interferon production was noticed in case of Merozoite fraction 4(MW 12700 - 18,000) and Sprozoite fraction 2 (MW 68000 - 200000).

Thus different antigens preferentially elicited different T. cell responses.

Martin A; Awadalla S. and Lillehoj H.S. (1995)
Avian Diseases **39** : 538 - 547.

(10) Ascitis in broilers

(a) Bronchodilators, oxygen level and temperature effects on ascitis incidence in broiler chicken.

Ascitis is a primary cause of death in rapidly growing broilers resulting in 15-20% mortality .

Low oxygen pressure in air (high altitude, poor ventilation) elevated oxygen needs (rapid growth), Low environmental temperature are responsible factors leading to pulmonary hypertension and ascitis. Metaproterenol. (bronchodilators) 2mg/kg in water reduced the incidence of Ascitis.

Van hooser SL, Beker A and Teefer RG,
Poultry Science **74** (10) : 1586 - 1590 (1995)

(b) **Pulmonary arteriole hypertrophy in broilers with pulmonary hypertension syndrome (Ascitis).**

Two experiments were conducted to determine the effect of low ventilation or cool temperature on pulmonary hypertension syndrome (PHS).

Pulmonary arteriole hypertrophy was observed in birds having PHS in both experiments and it was without co-incident inflammatory response in lung tissue.

Enkvetchakul B; Beasley J. and Bottje W. (1995) Poultry Science **74** (10) : 1677 - 1682.

(11) Xenotransplantation of animal organs to man.

''Jeff Getty who had HIV for about 15 years received bone marrow transplant from baboon in December' 95 in USA left hospital for home in first week of January 1996. In his case only immature cells from baboon's bone marrow were transplanted to avoid immune rejection".

" In 1995 Spring Duke University Medical Centre in North Carolina produced transgenic strain of pigs whose heart was successfully transplanted in three baboons, though for a short while".

" British biotechnology company Imutran has produced a herd of 300 transgenic pigs and expects to carry out first organ transplant from transgenic pigs to human subject later this year".

"The knowledge in this field has moved so rapidly that according to John Logan of Princeton New Jersey, every thing that we know today was hypothesis two years ago".

"Possibility of animal viruses & other microbes entering human body receiving transplants is a distinct danger".

"Pigs are ideal organ donors to man than primates or other animals since they can be bred rapidly, can be reared in SPF conditions, and its organs in shape, size and weight etc are suitable".

"After all we have been pumping pig insulin into diabetic people for generations and any virus that can jump from pigs to man viz. Swine Flu. probably already has".

Based on articles by Christine Gorman in Time (Vol 147 No3. 15.1.96) and by L.M. Fisher Times of India (Dt. 9.1.96)

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References	:	**For periodicals:** name and initials of author/s, year of publication in parenthesis, title of article, abbreviated title of journal, volume number, first and last page number.
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