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Prof. B. B. Mallick
Vice-Chancellor

No. ..... Date 6-9-1995

MESSAGE

I am very glad to know that Vth edition of "The Blue Cross Book" is going to be published shortly. My association with this publication has been since its Ist edition and I have been watching the progress in the improvement of standard of this publication constantly.

The Blue Cross Book, dedicated to the Veterinary profession more so for the Veterinarians actually engaged in field work. The valuable information published in this book are enriched by the information obtained from the professionals engaged in field work and also the materials based on critical analysis of such data by experienced Senior Veterinary Scientists. Therefore, information coming out from this book is quite useful for the Veterinary profession in general and for those who are engaged in promotion of professional cause in particular.

Dr. A.K. Datta, the Editor of the Blue Cross Book, has a long association with me in various capacities in different forum at different institutions. He is capable of handling such work most ably. I have no doubt that this Book will gather a unique place in the history of professional publications in this country. I take this opportunity to congratulate all concerned and express my sincere wishes for Excellent future progress.

(B.B. Mallick) 6/9/95

सत्यमेव जयते

ARVIND NETAM

कृषि और सहकारिता राज्य मंत्री
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NEW DELHI-110 001

13 SEP 1995

MESSAGE

It gives me great pleasure to know that publication of the Blue Cross Book by Hoechst India Limited has been resumed after a long gap and the 5th Edition is going to be published. I take this opportunity to congratulate you and the Editorial Board Members for publication of this kind of journal. I am confident that regular publication of this book will help Hoechst India to go ahead not only in the pursuit of its commitment to Animal Health, but also beneficial to all veterinary clinicians and academicians at large.

Arvind Netam

(ARVIND NETAM)

Tribute To A Great Scientist

Prof. Sinha was born on January 1, 1921 in Dhaka, Bangladesh. He obtained B.Sc. degree from Dhaka University and then graduated from Bengal Veterinary College, Calcutta. He got M.Sc. degree from University of Bombay. He had his Ph.D. degree from Missouri University, U.S.A. He was Professor of Pathology and Preventive Veterinary Medicine, Bengal Veterinary College, Calcutta from 1966-68. From 1968-70 he was Research Officer, Research Division under the Directorate of Veterinary Services, West Bengal. Thereafter he joined as Vice - Principal, Bengal Veterinary College and continued upto 1976. Then he joined as Dean, Faculty of Veterinary and Animal Sciences, Bidhan Chandra Krishi Viswavidyalaya (University), West Bengal. Later he was chosen as the Dean, Faculty of Veterinary Medicine, University of Maiduguri, Nigeria in 1981 and in that capacity he functioned with distinction bringing lustre and dignity to the post. He returned to India in 1989. He was also member, West Bengal Veterinary Association, Zoological Society of India, Helminthiological Society of India and American Society of Parasitologists. Besides guiding a number of M.V.Sc and Ph. D. candidates he authored about 100 research papers. He earned a name for his outspoken, frank, constructive and progressive views.

We are shocked to learn of the sad demise of Prof. P.K. Sinha (74) former Dean, Faculty of Veterinary and Animal Sciences, Bidhan Chandra Krishi Viswavidyalaya, West Bengal and Faculty of Veterinary Medicine, University of Maiduguri, Nigeria on February 20, 1995. We convey our heartfelt condolence to the members of the bereaved family.

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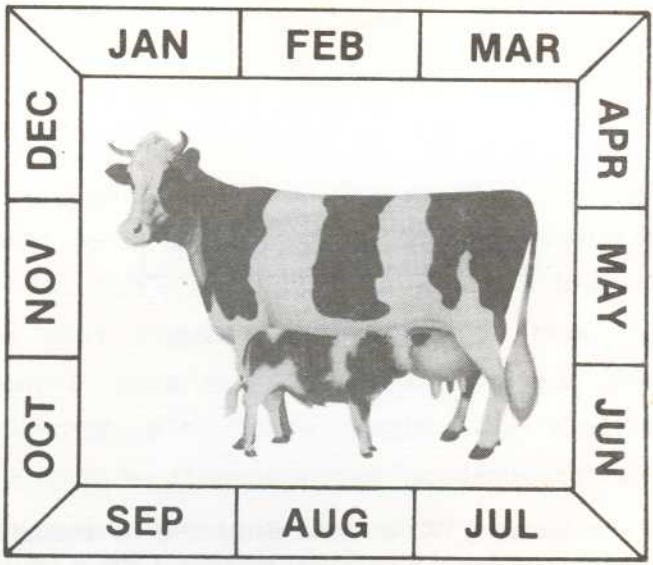

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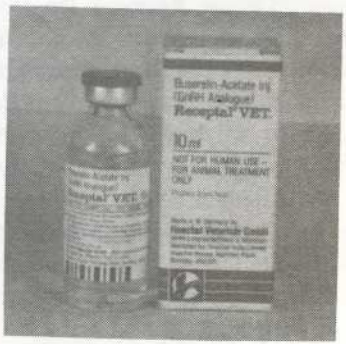

INDICATION

- DELAYED OVULATION, ANOVULATION
- ANOESTRUS
- FOLLICULAR CYST
- IMPROVEMENT OF CONCEPTION RATE AFTER ARTIFICIAL INSEMINATION AND OESTRUS SYNCHRONIZATION
- PROPHYLAXIS OF FERTIUTY DISORDERS BY EARLY INDUCTION OF CYCLE

PRESENTATION

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The Use of Receptal® Post Mating To Increase Pregnancy Rates In Dairy Cattle

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Abstract

The effect of Receptal on conception rate in cattle when injected after insemination is widely proven by several studies as well as by practical experiences. Recent findings, however, suggest that Receptal improves fertility as well when administered 11-13 days post mating. The effect may be explained by the prolonged lifespan of the Corpus luteum, which increases the probability of maternal recognition of pregnancy . Thus, the conceptus is protected from early embryonic death, and higher pregnancy rates can be expected in repeat breeders. The aim of this review is to give more details about the mechanism of action of Receptal in this indication as well as to present some trial results. Official registration of this new use of Receptal is ongoing in all countries where Receptal is on the market.

General

According to several studies, embryonic death is one of the most important causes of repeat breeding in dairy cattle. Especially high yielding diary cows suffer from embryo loss during early pregnancy. The majority of these losses occur between days 12 and 18 following mating, and coincide with the period of the maternal recognition of pregnancy. Healthy bovine embryos produce an anti-luteolytic alpha interferon from day 10 to day 25 after mating, which inhibits the development of the luteolytic mechanism in the cow and is partly responsible for the maternal recognition of pregnancy. A delay in the timing of this signal or a decrease in its intensity, may be responsible for the high rate of embryo loss. The sex hormone status of the cow contributes to the strength of her luteolytic drive during this critical period and so manipulation of this represents an appropriate technique for treating embryo mortality (Lamming, 1993).

There had been considerable experimental work on the possibility of using various hormonal compounds to decrease the rate of early embryo loss, and one of the most successful has proved to be a single injection of Receptal on day 11-13 following mating.

Previous experiments have shown that cows suffering from early embryo loss generally have lower plasma and milk progesterone levels during the period day 10 to day 16 following mating (Lamming, *et al* 1989). Subsequent experiments have shown that cows with low progesterone levels may suffer an enhanced luteolytic activity (Lamming and Mann 1993), which could contribute to the rate of loss.

There is an increased luteolytic drive in cows which have normal plasma levels of oestrogen but low levels of progesterone. All mated cows experience some ovarian follicle development post mating; these follicles produce a transitory rise in the plasma level of oestradiol. It is appropriate therefore in all cows and especially those which have low plasma levels of progesterone to investigate the effect of reducing the circulating level of oestradiol during the natural period of in-

creased luteolytic drive in the cow. The use of Receptal is designed to limit the level of oestradiol production during the period when it would increase the strength of the luteolytic drive in the mated animal. If Receptal is administered too early in relation to the maternal recognition of pregnancy or too late then it cannot be expected to be effective. The timing of the administration of Receptal is therefore critical in terms of the success of the treatment.

Mode of action

The observed effects are considered to be due to a luteoprotective effect occurring at about the time of maternal recognition of pregnancy. More detailed experiments have shown that injection of 10 µg buserelin in the luteal phase changes the pattern of ovarian follicle development. Furthermore, repeated treatment with burserelin at 3-day intervals extended the luteal phase of the cycle in non-pregnant cows (MacMillan *et al.*, 1989). The mechanism by which these effects operate are discussed in detail by Thatcher *et al*, 1989 as well as by Mann and Lamming, 1992 and in further studies by Mann *et al*, 1995.

1. Oestradiol secretion by follicles growing during the luteal phase, stimulates the synthesis of oxytocin receptors on the endometrium.

2. Oxytocin from the corpus luteum (or posterior pituitary) then stimulates the secretion of $PGF_{2\alpha}$.

3. In the non-pregnant animal, prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) released from the endometrium in response to oxytocin which binds to newly developed receptors, causes luteolysis.

4. The presence of a corpus luteum is essential for maintenance of pregnancy.

5. The embryo produces α_2 interferon (bTP-1) which inhibits endometrial oxytocin receptors and therefore prevents luteolysis.

6. It is probable that subtle changes in follicle development induced by early embryonic development, contribute to the failure of the luteolytic mechanism.

7. For some reason the link between the early embryo and follicle dynamics is abnormal in a high proportion of cows and therefore early embryo loss occurs as a consequence of luteolysis.

8. However, if oestradiol production is disrupted during the luteal phase, this may block the luteolytic cascade process, thereby preventing $PGF_{2\alpha}$ release.

9. Treatment with Receptal between days 11-13 of the luteal phase reduces oestradiol seretion and the luteolytic process is impaired.

10. Faced with weaker luteolytic drive by the cow, the embryo is more likely to be able to prevent luteolysis.

11. The use of Receptal can therefore be expected to prevent early embryonic death and therefore increase the pregnancy rate of mated cows to some extent.

12. Therefore, based on this principle of action, treatment of recipient cows five days after the normal date of embryo transfer could be expected to improve pregnancy rate in some circumstances (Ellington *et al.*, 1990).

Results from published papers

Several papers have been published regarding the use of Receptal post mating in dairy cattle. In the following summary the results obtained by different authors in terms of improvement of conception rates are presented.

Use of 10 mcg of buserelin (2.5 ml Receptal) 11-14 d post mating

Triallists	Animals (n)	Service	Treatment post service (d)	Conception rate improvement over control
MacMillan *et al.* 1986	225	1	11.13	11,5%
Bostedt and Okyere 1988	153	2 3	12	5,8%
Ryan *et al.* 1991	1.019	1	12	8.7%
Lajili *et al.* 1991	210	1	12-14	16%
Sheldon and Dobson 1993	1.040 272 134 80	1 2 3+ 3+	11 11 11 11	9,4% 13,2% 28,3% 30,0%
Drew and Peters 1994	643	1	12	12%

Discussion

These trials have demonstrated that the use of Receptal between day 11-14 after first, second, third and subsequent inseminations increases significantly pregnancy rates in dairy cows. In further trials Receptal was used before day 11 but no benefit was observed. This emphasizes the need to use Receptal either on day 11 or day 12 after service. When it is used earlier i.e. day 8 or 10, presumbly the embryo is insufficiently developed to produce its own protective protein bTP-1 and the luteoprotective effect of buserelin is too short lived to maintain the corpus luteum's lifespan for further 7-9 days that the embryo requires to establish itself. On the other hand, administration of Receptal after the day 14 may be too late for a positive effect on embryo survival. The presented papers indicate a distinct variability in the obtained results.

As there are too many factors which can influence the pregnancy rates, the treatment with Receptal can only affect part of these factors. This may explain, moreover, the cases of poor response or failure of the treatment. However, having in mind that embryo loss accounts as the single biggest factor for almost half of all pre-calving losses, the treatment with Receptal post mating should be considered when low fertility rates in dairy cattle are observed.

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Tests For Assessing The Viability Of Pre-implantation Embryos *In Vitro*

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In the recent years, concerted efforts of animal scientists are directed towards increasing the efficiency of farm animals, both in terms of production and reproduction. Following the tremendous achievements of artificial insemination programme in livestock improvement, the use of embryo transfer and related technologies are now being exploited to achieve quicker genetic gains from superior females. Newly developed technologies in this direction include embryo bisection, embryo sexing, embryo freezing, gene injection and in vitro fertilization (IVF)

All these techniques, however, involve some sort of insult to the embryo in terms of physical trauma. At present, there are no objective means of assessing the degree of damage caused to the embryos during manipulation, including collection, in order to predict the chances of their survival upon transfer to suitable recipients. This is particularly important in farm animals, where the number of suitable recipients is rather limited due to high costs. It is therefore, imperative that suitable objective tests are available for assessing the viability of embryos upon transfer.

To be useful, any test of viability must meet the following criteria:

i) Test must be efficient enough to be performed on individual embryos in order to allow evaluation on an embryo-by-embryo basis rather than group basis.

ii) Test should be rapid so that results can be obtained in hours rather than days.

iii) Test should be as non-invasive as possible so that embryos remain capable of further development and suitable for transfer following evaluation. However, even a test which kills a low percentage of embryos may be acceptable if higher pregnancy rates are obtained in comparison to those obtained without the viability studies.

(iv) Test should not make use of radiolabelled substances that are incorporated in embryos, as it may result in problems with handling and public perception.

(v) Test must make use of equipment and technologies that are readily available to research institutes and commercial embryo transfer companies.

For viability tests, limited systematic work has been done in farm animals due to the limited availability of embryos. Consequently, no suitable tests which meet all these requirements are available to the scientists and practitioners. Viability tests could be of great help in establishing the conditions required to support embryonic development *in vitro.*

The tests presently available to determine embryo viability can be divided into following categories :

A) Morphological
B) Development in culture
C) Metabolism of fluorescent substrate
D) Metabolic tests.

A. Morphological criteria

Principle and methods

Apart from development in culture, viability tests for pre-implantation embryos, till date, have been limited to morphological examination with light microscope as the most widely

used test. For visual evaluation, the general appearance of embryos such as presence of irregular or degenerated cells and stage of development of the embryo with regards to the time since fertilization, are considered.

Advantages and drawbacks

The advantage of morphological evaluation is that it is quick,easy, non invasive and requires simple equipments.

Morphological examination, however, is subjective and its accuracy and reliability as an indicator of embryonic viability is questionable in view of the observations that apparently abnormal embryos also result into viable pregnancies (Killeen and Moore, 1971). Moreover, quantification of visual appearance of cattle embryos has been on scoring systems that divide embryos into several arbitrary classes while the correlation between the score given and an embryo's ability to result in offspring has not been very high. The correlation improves substantially, only when the embryos with major morphological defects are separated from all other embryos. However, these tests require highly trained personnel and are subjective. Moreover, making comparisons between laboratories or even individuals, is difficult.

B. Development in culture

Principle and methods

Use of short-term *in vitro* culture, followed by morphological evaluation, has been used for assessing embryo viability. The embryos can also be incubated in the oviducts of the same or different species for 2-3 days. Embryos that fail to develop are eliminated. After incubation, the embryos are examined morphologically and only those embryos which are at proper stage of development are transferred to recipients. The rate of cleavage can also be used to assess viability. Greater pregnancy rate has been observed in human beings following the transfer of embryos dividing more rapidly in culture.

Advantages and drawbacks

This method provides sufficient selection to increase the pregnancy rates, but this procedure has also some limitations like :

i) Allowing sufficient time for the embryos to divide in culture greatly extends the time required between embryo recovery and transfer.

ii) Culturing of mammalian embryos require constant temperature incubators that are not often available for on-farm transfers.

iii) Keeping bovine embryos in culture for periods as short as 24 hours has been reported to cause an increased incidence of early embryonic death as compared to non-cultured embryos.

iv) Transfer and retrieval of embryos from oviducts of temporary foster mother results in loss of certain percentage of embryos. Using this technique, about 70% of the cattle eggs stored in rabbit oviducts can be recovered (Boland. 1984)

v) Variations in terms of time of ovulation in superovulated donors make it difficult to differentiate the stage of development following culture. Resultantly, a developmental stage less than that expected at the time of *in vivo* recovery from donors may be observed in some cultured embryos. Transfer of such embryos to recipients often result in low pregnancy rates (Trounson *et al.*, 1982).

C. Metabolism of fluorescent substrate

Principle and methods

(a) Diacetyl fluorescine (FDA) Test

This test is a measure of both esterase enzyme activity and membrane integrity. Diacetyl fluorescine (FDA), a non-polar substance which can readily pass into cell, is commonly used for this test. In the cell, FDA is hydrolysed into fluorescin by estrases. This fluorescin accumulates intracellularly as it is polar in nature and cannot readily cross the cell membrane. When the embryo is exposed to FDA, mitosis occurs. It has been reported that the

embryos that failed to exhibit fluorescence following exposure to FDA did not show mitotic activity. However, about 85% of the fluorescent embryos have been reported to be mitotically active (Schilling *et al.*, 1979). FDA exposed embryos are examined under phase-contrast microscope using ultraviolet rays and fluorescence is graded.

(b) Fluorescence of dead cells

Another alternative fluorescence test is using a DNA dye, diamidinophenyl indole (DAPI) which stains only the nuclei of dead blastomeres. It has been reported that 90% of the embryos that did not fluorescence continued to develop when placed in culture, while those exhibiting fluorescence did not show further development. If this test is combined with FDA which stains living cells then it makes the assessment of the embryos more certain.

Advantages and drawbacks

FDA has been reported to be non-toxic to embryos as it did not prevent the ability of the embryo to develop further and even the implantation is also not prevented.

The limitation of this test is that fluorescence measures only the basic cell function, not the developmental potential, since estrase activity may remain in embryos with morphological or biochemical defects, while these defects may prevent continued development.

D. Metabolic tests

Principle and methods

(a) Carbohydrate metabolism

Initial studies assessed the viability of the embryos by measuring the quantity of lactate and various enzymes in the medium following *in vitro* culture, but with a low accuracy. Subsequently, radiolabelled glycolytic substrates (C^{14} glucose and C^{14}lactate) were used with greater accuracy. Following the addition of these substrates into the culture medium, radiolabelled CO_2 released by the embryo is measured.

It has been observed that the embryos which have a high rate of glucose utilization develop better both in vitro and in vivo, than those using little or no glucose, regardless of their morphological appearance.But during early days, most of the workers were unable to detect glucose utilization by Day 7 or Day 8 bovine embryos. This was considered possibly either because of relative insensitivity of the assay methods or inability of the bovine embryos, like that of mouse embryos, to utilize glucose extensively during this period. The techniques have been further refined and currently glucose uptake even by a single blastocyst can be measured. Gardner and Leese (1987) measured glucose uptake by each blastocyst using ultramicrofluorometric technique and reported a higher glucose uptake by viable than nonviable blastocysts. But most of the workers have concluded that glucose uptake by the embryo may be a useful measure for optimising in vitro culture conditions rather than using it for assessing viability.

(b) Oxygen metabolism

Oxygen uptake is the most accurate, rapid, noninvasive method being employed as the viability test. Embryos remove oxygen from the culture medium and release CO_2 and this O_2uptake is measured. Initially, the methods were relatively insensitive and in order to obtain accurate readings, group of embryos were required. But now-a-days, the availability of the micro-oxygen electrodes, which can measure the O_2 uptake of single blastocysts, has made this technique more popular.

(c) Amino acid metabolism

Radiolabelled histidine, converted into histamine by an enzyme histidine decarboxylase of the embryo, is another substitute for assessing the embryonic viability. During this process also, labelled CO_2 is released which is then measured (Reiger, 1984). Viability can also be assessed by measuring the degradation of the amino acids to CO_2 by the embryo.

Advantages and drawbacks

The metabolic tests are very accurate measures of functional viability of the embryos. However the use of radiolabelled substrates has several pitfalls that may limit their usefulness as a routine measure for viability. The drawbacks of this technique are listed below:

i) It requires strict licensing practices with regard to handling and disposal of the radiolabelled products. While it may not be a problem for many research institutes, but may present considerable problems to commercial ET companies.

ii) The incorporation of labelled carbon or amino acids into embryos would result in a certain amount of radioactivity being transferred to recipient females which may be released into maternal system, if the embryo dies. Although the amount of the radioactivity would be very small, but the perception of radioactive cows and calves by the public would severely limit the use.

iii) Labelled substances especially amino acids may be harmful to the embryos (Fritiated leucine significantly reduces the viability of mouse embryo; Wiebold and Anderson, 1985).

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Efficacy Of Deltamethrin In Porcine Mange

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Sarcoptes scabiei var suis is the most important parasite of swine, distributed all over the world. The disease is posing a serious problem to the pig farmers, and maintaining pigs mange free is very difficult because of the prevalence of symptomatic carriers (Penny *et al.*,1980). The disease is of economical importance, since the diseased animal fails to attain proper growth , have poor feed conversion ability and low pork quality (Griffiths, 1970). Among acaricides for treating mange organophosphorus compounds are highly toxic for animals and human beings (Gupta *et al.*, 1981). Deltamethrin (Butox) is a synthetic pyrethroid, is highly effective against all external parasites, with no undesirable side effects and is safe for the handlers and for the environment (Sharma *et al.* 1992).

Materials and Methods

Thirty six (36) affected Landrace crossbred adult pigs of either sex were randomly selected for this study. These animals were divided into 4 equal groups, each consisting of 9 animals. Blood for eosinophil count and skin scraping from affected parts was collected from all the animals before treatment and on 7th day, 15th day and 30th day post-treatment. The first 3 groups of animals were sprayed with aqueous solution of Butox (Hoechst) i.e. 0.2%. 0.3% and 0.4% respectively, the 4th group was treated with cythion 1.5% (Northern Minerals). Depending upon the clinical/parasitological findings the medicine was repeated at 10 days interval. The efficacy of the drugs was noted on the basis of clinical and parasitological recovery (Table -1)

Results and Discussions :

Clinico-parasitological changes, eosinophil response to drug treatment in porcine mange are presented in Table 2 & 3.

On parasitological examination of skin scrapings, all the animals were found positive for mange mite i.e. *Sarcoptes scabiei*. All the animals were badly affected and showed heavy lesions all over the body, however, most noticeable parts were ear, head and tail. The animals showed abnormal behaviour because of intense itching, running, shaking of head were common observations. The infested areas became thick, hyperkeratinized and thrown into stiff folds, ulcers and abscess were also common in many animals, bare patches were scattered all over the body.

After treatment with deltamethrin, lesions started disappearing and there was growth of fine hairs. Recovery was 100% in group III on 26th day Post treatment with single application. However, in group I and II 67% and 89% recovery was achieved on 30 days P.T. with no hair growth by 2 and 1 applications respectively. In group IV only 3 animals were partially recovered with 2 applications, in this group animals showed no signs of recovery.

The eosinophil/ul count (EC) was very high in all the group of animals before treatment (BT). No. significant change in eosinophil count could be observed at 7 and 15 days P.T. in all the groups. However, in group III on 30th day P.T. significant reduction in EC wasobserved, whereas no change could be observed in rest of the group on 30 days P.T.

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Similar observations have been observed by Kenneth (1986) in feline mange.

Deltamethrin is a synthetic pyrethroid with potent insecticidal action. It is highly effective at 0.4% dilution. Similar observations were observed by Sharma *et al.* (1986) in canine mange, Rossi *& Lanfranechi* (1992) in ovine mange and Soni *& Rao* (1993) in bovine mange. Cythion failed to treat porcine mange at 1.5% dilution this may be due to frequent use of this drug in the piggery, the mange mites may have developed resistance to Cythion, Butox found most effective at 0.4% dilution with no undesirable side effect.

TABLE 1. Treatment schedule with Deltamethrin in Porcine Mange

Sl. No.	Group	No. of animals	Medicine/ concentration	No. of applications	Interval of applications
1.	I	9	Butox (0.2%)	2	10 days
2.	II	9	Butox (0.3%)	1	-
3.	III	9	Butox (0.4%)	1	-
4.	IV	9	Cythion (1.5%)	2	10 days

TABLE 2. Clinico - parasitological observations in Porcine Mange

Sl. No.	Parameters	Observations				
1.	Groups	I	II	III	IV	
2.	No. of animals	9	9	9	9	
3.	Animals found positive for mange mite.	9	9	9	9	
4.	Skin scraping found positive upto (days Post Treatment)	28	6	6	30	
5.	Disappearance of clinical lesions (days Post Treatment)	30	10	8	-	
6.	Clinical recovery of animals.	6	8	9	3	animals partially recovered.
7.	Appearance of fine hair (days Post Treatment)	-	-	26 days	-	

TABLE 3. Eosinophil count in response to drug treatment

Sl No.	Parameters	Eosinophil/µl of blood			
1.	Group	I	II	III	IV
2.	Average value of eosinophil/ul before treatment (BT).	620 (7%)	580 (6%)	630 (7%)	570 (6%)
3.	- do- 7 days PT	620 (7%)	570 (6%)	650 (7%)	560 (6%)
4.	-do- 15 days PT	600 (7%)	550 (6%)	600 (7%)	560 (6%)
5.	- do - 30 days PT	600 (7%)	560 (6%)	500* (5%)	540 (6%)

* Significant reduction in eosinophil count.

Summary

Butox and Cythion were used for the treatment of porcine mange in 36 affected animals. 0.2, 0.3 and 0.4% Butox and 1.5% Cythion was used, once or twice at 10 day intervals. The efficacy of the drug was assesed on the basis of clinical and parasitological recovery upto 30 days P.T. It was observed that 100% animals were treated at 0.4% dilution. Cythion was found ineffective.

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Efficacy Of Fenbendazole Against Natural Infection Of *Ancylostoma caninum*

K. Purdhvi Reddy[1] and **Md. Hafeez**[2]

Reports on the efficacy of Fenbendazole against *A. caninum* are few (S.S Banerjee *et al,* 1978; Bhagherwal and Nanavati, 1989). Hence, a drug trial was conducted against infection of *A. caninum* in dogs at Veterinay Hospital, Anantapur.

The dogs belonged to mainly local, Pomeranian and Alsatian breeds aged between 3 months and 2 years. Out of 30 dogs chosen 6 were kept at infected control and other 24 were treated with Fenbendazole (Panacur Hoechst) 50 mg/kg. daily in milk for four days.

Faecal examination with egg counting was done employing Stoll's method before treatment and again on 3rd, 5th and 7th day of post treatment. In control group also, the faecal examination was similarly carried on identical days.

E.P.G. in the treated dogs varied between 200 and 500 before treatment. Out of 24 dogs treated 5 (20.84%) were negative for *A.caninum* ova on 3rd day, while 16 (66.67%) and 3 (12.49%) were totally free from ova on 5th day and 7th day post-treatment respectively. The drug did not produce any side effects. In untreated dogs the E.P.G. showed an ascending trend. Thus Fenbendazole was found to be effective against natural infection of *A. caninum* when given orally at the dose rate of 50 mg/kg body weight for 4 consecutive days. This observation gains support from the findings of Bhagerwal and Nanavati (1989). While Bhopale and Bhatnagar (1984) observed that Fenbendazole at 200, 400, 600, 800 and 1000 mg/ml concentration was ineffective against *A.caninum* under in vitro tests, Burke and Roberson (1984) reported 100% efficacy against larvae at the dose rate of 50 mg/kg body weight.

Groups	Mean, E.P.G.					Efficacy of the treatment
	No. of dogs examined	Pre-treatment	Post - Treatment			
			3rd day	5th day	7th day	
I	24	310	87	25	0	100%
II	6	270	350	440	500	-

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A Clinical Report On The Treatment Of Anaplasmosis In Cattle

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Anaplasmosis is an important rickettsial infectious disease of ruminants. It occurs singly or mixed with other blood protozoons.Many Chemotherapeutic agents have been found effective against anaplasmosis. This paper deals with the treatment of anaplasmosis with 4,4 - diamidino - diazoamino - benzene diaceturate tetrahydrate (Berenil - Hoechst) with supportive treatment in field condition.

Eighty five cases of anaplasmosis in cross bred cows were recorded and treated during March'94 to June'94. Symptoms exhibited by these cows were : dullness, cachexia, swelling of prescapular and / or prefemoral lymphnodes, temperature ranging from 39.5°C to 42°C, anorexia, icteric mucous membranes of eye and vulva, hypogalactia and yellow coloured urine. Some animals showed hydraemia and recumbancy.

Blood smears collected from the tip of the ear were sent to the Department of parasitology, Veterinary College and Research Institute, Namakkal and Animal Disease Intelligence Unit, Madurai for identification of the aetiological agents. Both laboratories have confirmed the presence of *Anaplasma marginale* . In some blood smears presence of both *Anaplasma marginale* and *Theileria annulata* were identified.

Ailing cows were divided into three groups. 54 cases which had above symptoms except icterus of mm were grouped as 'A'. 28 cases which had all the above symptoms with icteric mm were grouped as 'B' and three cases which had all the above symptoms with icteric mm and recumbancy were grouped as 'C'.

For all the groups; on first day single dose of 5 gms of Berenil dissoved in 30 ml of distilled water was given intramuscularly. For group 'B' third day onward daily 10 ml of Liver extract with B complex vitamins (Livobex - TTK Pharma Ltd.) and Ferric hydroxide 500 mg (Inferon - Rallis India Ltd.) were given intramuscularly till 10th day. 82 cases of group 'A' and 'B' recovered completely in 7 to 15 days. Recovery was assessed by the disappearance of all clinical symptoms and reappearance of normal conditions and yield. All the 3 cases of group 'C' died in spite of all required treatment.

This successful treatment of anaplasmosis with Berenil was in agreement with the findings of Bauer and Hochheimer (1974); Sarup *et al,* (1981) and Sharma *et al,* (1984).

Summary : Anaplasmosis in cross bred cows was treated with Berenil and supportive drugs and the percentage of clinical recovery was found to be 100% , 100% and 0% respectively.

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Application Of Butox (Deltamethrin) - In A Recent Plague Sporadics In Bombay To Control Rat Flea In Laboratory Animal Facility

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Deltamethrin is a recent synthetic pyrethrin which is extensively used for therapeutic as well as for prevention of the ectoparasitic infestations in large animals. It has marked cidal properties against ticks (Sharma *et. al,* 1991) in mites and (Upendra, 1991) in dogs. Besides the drug has an excellent ovicidal and larvae cidal activity (M.M. Gatne *et. al*) against dog tick *Rhipicephalus sanguineus.* This insecticide thus has been found to be quite sage in treating ectoparasitic infestations in dogs (Ranade V.V. *et. al, 1991*) as well as in other animals.

So far the drug has not been studied in this respect in laboratory animals. We have made use of this drug as a precautionary measure to control the rat flea besides other ectoparasites in our laboratory animal facility which was being frequently visited by some bandicoot and wild rodents through the airconditioning ducts.

It was used in the form of dips at the concentration of 3 ml. per liter of water. The rats were dipped in butox solution, taken in a bucket, at a time for minimum of 1-2 minutes, so that they get completely wet. They were then replaced in the cages containing absorption paper sheets for getting rid of extra solution and enabling them to drv earlier. The animals were then put back in their original cages with proper bedding (rice husk).

This treatment of butox was used only as a precautionary measure to avoid ectoparasitic infestation. Its efficacy for this could not be evaluated as our animals did not have any clinical or subclinical symptoms of ectoparasitic infections. However, the butox solution at this concentration was found to be quite safe as we did not find induction of any toxic reaction or skin rashes on the treated animals.

Our observations, however are of preliminary and precautionary nature. Its therapeutics effect needs to be assessed further in the laboratory animals.

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Sarcocystosis As Zoonosis With Special Reference To India*

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Lindemann was first to report the sarcocysts, supposedly of *Sarcocystis*, in the musculature of 3 human cases in 1863 which were christened in 1878 as *Sarcocystis lindemanni*, a new species named after its discoverer. In the ensuing years, sarcocysts were continued to be reported from time to time in human muscles and were assigned to this species irrespective of the fact that these were often different in shape, size and morphology. This was the sum total of our knowledge pertaining to human sarcocystosis until 1972 (Shah, 1984).

In this fateful year, the pattern of life-cycle of *Sarcocystis* was unravelled which paved the way for subsequent global upsurge in research on *Sarcocystis* and Sarcocytosis. In order to get a proper understanding of what follows, it is imperative that we should have a general idea of this life cycle pattern and be acquainted with the terminology used in this connection.

Sarcocystis has a typical coccidian life-cycle, but with one major difference it is divided between two obligatory hosts having prey-predator relationship. Harbivores (cattle, buffalo, sheep, goat etc.) and omnivores (pig and man) act as its intermediate hosts because asexual stages of the parasite, culminating in the formation of sarcocysts occur in their muscle and develop in them.

Carnivores (dog, cat etc.) and other predators (man), on the other hand, play the role of definitive hosts in which the sexual stages of the parasite develop leading to the formation of sporulated isoporan type oocysts/sporocysts. The intermediate host acquires the infection by swallowing the oocysts / sporocysts shed in the faeces by the definitive host and the definitive host, in turn, gets infected by feeding on the tissues of the intermediate host containing the sarcocysts (Shah, 1984). Against this backdrop, man has a unique position *vis-a-vis Sarcocystis,* he plays a dual role either as a definitive host or as an intermediate host for a number of species of *Sarcocystis.* Thus human *sarcocystosis* has two aspects :

(1) intestinal sarcocystosis wherein man is a definitive host and (2) muscular sarcocystosis wherein man is an intermediate host (*Dubey et al., 1989*)

Intestinal Sarcocystosis

Man serves as a definitive host for two species of *Sarcocystis*, viz. *S. hominis* of the cattle and *S. suihominis* of the pig, both of which have been reported from their respective intermediate hosts i.e. cattle and pig in India (Shah and Chaudhry, 1994). As for intestinal sarcocystosis, it has been encountered only 3 human-clinical cases from India (at Lucknow). Since these were natural cases, it was rather difficult to determine, on the basis of the morphology of sporocysts present in their stools whether these belonged to *S. hominis* of the cattle or to *S. suihominis* of the pig. Very recently, Banerjee *et al.* (1994) found at Pantnagar (U.P) 14 out of 20 children, that had been feeding on pork, positive for ocysts/ sporocysts of *S. suihominis* in their faeces, but exhibited no deleterious effects.

Shah (1990) drew attention to two parallel studies, one on *S. hominis* of the cattle and another on *S. suihominis* of the pig, from the same location i.e. Jabalpur (M.P.). According

* (Abstract of V Dr. S.R.Rao Memorial lecture 1995, delivered by the author at Bombay Veterinary College)

to the former, the prevalence of *S. hominis* was 12.18% of the 238 cattle carcasses examined. This low percentage was explained in terms of human behaviour by Shah (1990) who argued that people in India, by and large do not consume beef on religious grounds, thus effectively preventing them from acquiring the infection. According to the latter the prevalence of *S. suihominis* of the pig was 49.5% of the 200 pig carcasses examined. Surprisingly it was higher than that of *S. miescheriana*, a dog transmitted-species of the pig, which was 34.5%. This implied that human exposure to *S. suihominis* was more frequent. This proved to be the case on epidemiological grounds as detailed by Shah (1990).

There is sufficient evidence to show that intestinal sarcocystosis, as revealed by experimental infection of human volunteers as well as on observations based on natural cases, causes mainly abdominal pain and severe diarrhoea (Pethkar, 1990).

Muscular Sarcocytosis

While assessing the available reports of muscular sarcocystosis in man from all over the world Beaver *et al* (1979) reached a startling conclusion that the cysts, on the basis of which *S. lindemanni* was created, bore no resemblance to *Sarcocystis* or to any other related organisms. Hence they pronounced the species invalid. It is ironic to realise that this species which stood the test of time for well over a century as the only human species of *Sarcocystis*, has disappeared from the scene.

However it must be added in parenthesis that some authors (Pethkar, 1990) still adhere to it. Of the 40 genuine cases of muscular sarcocystosis accepted by Beaver *et al.* (1979), 8 were from India. This number has since increased by the addition of 3 more cases (Dubey *et al.*, 1989). However the species of *Sarcocystis* to which these sarcocysts belong have not yet been established. The circumstantial evidence rules out the possibility of the existence of a *Sarcocystis* species exclusively of man. Since all species of *Sarcocystis*, hitherto known, requires a prey predator relationship for their maintenance and since no where humans are eaten on regular basis by predators, the life-cycle of these parasites cannot be sustained in man acting as a sole intermediate host. Tardros and Laarman (1982) for this reason, opined that man is unlikely to act as a natural intermediate host of a predator but most likely to acquire infection by ingesting the sporocysts infective to other primates (i.e.monkey and ape). Beaver *et al.* (1979) reinforced this view by insisting that *Sarcocystis* infection of human muscles is always zoonotic. In support of this contention, it is significant to point out that the sarcocysts reported from human muscles in India resemble those of one or two species of *Sarcocystis* found in rhesus monkeys (*Maceca mulatta*). Unfortunately it has not been possible to verify whether such is the case by experimentation for the reason that the definitive host/s of monkey *Sarcocystis* is/are yet to be discovered. This is a big gap that still exists in our knowledge of *Sarcocystis*.

Only harmful effect associated with muscular sarcocystosis in humans is attributed to sarcocysts. These were associated in clinical cases with muscle soreness or weakness, subcutaneous swellings and periarteritis or polyarteritis nodosa (Beaver *et al* 1979). This, however is a part of the story.

Numerous studies (in cattle, sheep, goats, pig etc.) have conclusively proved that the pathogenicity of *Sarcocystis* is mainly due to schizogonous stages that precede the formation of the sarcocysts (Dubey *et al.*, 1979, and Shah and Chaudhry, 1994). We have therefore, every reason to suspect a similar pathogenic role being played by *Sarcocystis* in man also. But this is unlikely to be tested in humans. Our best bet, in the circumstances, is to infer for man from the pathogenicity of monkey sarcocystosis, as and when it is determined on discovery of its intermediate host/s, by experimentation. Till then, we have to agree with Dubey et al. (1989) that " the clinical significance of sarcocysts in humans is unknown".

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Immunological Infertility In Females

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Reproductive immunology is a powerful tool for unlocking normal fertility problems and various forms of infertility are due to antigens on hypothalamic cells, pituitary cells, gonads, gametes placenta and fetus, and the induction of a specific antibody could alter their function. In addition antibodies can be induced against gonadotropin-releasing factors, gonadotropins, steroidal hormones and pregnancy associated hormones. Antibodies against antigens of reproductive tissue and hormones can be used to quantitate, qualitate, destroy, neutralize or enhance specific reproductive events associated with normal fertility and infertility in the bovines.

The female reproductive tract is capable of generating an immune-response to ejaculated sperms that can result in infertility.

How Antisperm Antibodies Interfere in fertilization

Sperm transport

1. Binding of immunoglobulins to the surface of spermatozoa within semen impairs their ability to penetrate cervical mucus, immunoglobulins binding also leads to alter the motility of spermatozoa within the cervical mucous-shaking, vibration or complete immobilization.

2. The presence of sperm-reactive antibodies within the cervical mucous subjects spermatozoa to complement mediated cell membrane damage. Tail directed antibodies that fix complement (IgM and IgG but not IgA) promote loss of motility. Head directed antibodies may not impair sperm motility.

3. Opsonization of antibody-coated spermatozoa through the binding of complement components (C3) could lead to an increased rate of phagocytosis of sperm by macrophages within the female reproductive tract.

Gamete Interaction

1. Antibodies directed against the sperm head may include binding sites for the zona pellucida preventing sperm attachment.

2. Complement-fixing antibodies (IgM and IgG) directed against the sperm head may impair the ability of spermatozoa to penetrate eggs without a loss of motility by promoting damage of the acrosomal and plasma membranes.

Effect of Antibodies of egg yolk containing semen extender

In artificial insemination of cattle the genital tract is exposed not only to isoantigenic semen but also to potentially antigenic proteins used in dilution such as hens egg yolk, antibiotics and enzyme additives that are routinely present in the semen extender. It has also been claimed that an immune response to egg yolk antigen within the cows genital tract inhibits fertility in cows bred by artificial insemination.

Infertility with freeze dried semen

Protein stability in an aqueous medium is dependent in part upon its bound water content. Removal of this water can lead to alteration in the protein structure and function. The absence of fertility with semen freeze dried to 2% residual moisture was hypothesized to be from alteration of the tertiary structure of certain essential seminal proteins.

Immuno suppression

The bovine female reproductive tract is exposed to many known antigens during coitus. The potential antigenic challenge comes from sperm seminal plasma, components of the egg yolk, semen extender, micro-organism and cellular debris of marked origin. Although bovine seminal antigen evoke strong immuno-

logical response in foreign heterologus species, they are rarely isoantigenic. The uterine endometrium of most higher mammals is abundantly endowed with lymphatics which can deliver either antigenic sensitized or peripherally sensitized immunologically competent cells to a draining lymphnode. The reason for the antibody-synthesizing lymphatic system not being activated may be because bovine seminal plasma has immuno-suppressive activity towards lymphocytes involved in immune reactions. Another potential site where iso-immunization to sperm might occur is the cervix. However bovine cervical secretions also contain immunosuppressive substances.

In the bovine, cases of immunological infertility are rare because the cow is exposed to an antigenic dose of semen only once every 21 days at estrus. In addition the high concentration of estrogen which is known to possess anti bacterial action suppresses immune response and promote phagocytosis of non-fertilizing sperm. The neutrophilis that normally phagocytose sperm are elicited by a non-antigenic stimulus that destroys excess sperm without providing further antigenic stimuli. This phagocytosis in uterine secretion flushes sperms from the cow's tract without stimulating the lymphnodes in the genital tract.

Investigation Of The Inability Of Bovines To Get Up On Their Legs *

W. Hofmann** and **S. El Amrousi*****

As already reported, we found in earlier experiments that in atypical parturient paresis there is hypophosphotaemia, only occasionally hypocalcaemia, an increased sodium and phosphorus content in the milk, in addition to inability of the animals to get up on their legs, the general condition mostly being undisturbed, while in contrast to parturient paresis normal blood glucose and blood cholesterin levels are found. The changes in the phosphorus metabolism which stand to the fore, of necessity lead to the question whether the disease condition can be influenced by the administration of phosphorus. A further question which is of interest is whether the phosphorus concentration in the blood rises following the administration of phosphorus.

The literature provides no comprehensive information on whether calcium or phosphorus infusions in healthy bovines and especially cows incapable of getting up on their legs, lead to a raising of the blood phosphorus level and to a direct influence on the disease.

Our investigations

We administered phosphorus and calcium solutions in various dosages to healthy bovines and cows incapable of getting up on their legs. Eighteen clinically healthy cows were divided into 4 groups : group I comprised 3 spotted cows and 2 black-pied cows, each receiving 10 ml Tonoshosphan " Hoechst". Group II also comprised 3 spotted and 2 black-pied cows; they were injected with 35 ml Tonophosphan. Group III comprised 3 spotted cows and 1 black-pied cow, each of these receiving 50 ml Tonophosphan. Group IV was made up of 3 spotted cows and 1 black-pied cow, each being given 100 ml.

Before the intravenous injection, as well as 30 minutes, 1,2,3,4,8 and 24 hours after injection, the calcium and inorganic phosphorus levels of the blood were determined. The keeping and feeding conditions of all animals were the same, all animals produced 10 -13 litres milk per day and the injection was given at 8 a.m.

In addition there were 26 cows which were incapable of getting up on their legs; these animals were split up into 3 groups as follows: group A comprised 8 cows, i.e. 6 spotted cows, 1 red-pied cow and one red cow. All of them suffered from atypical parturient paresis and were given 500 ml "CMC" of OWG-Chemie and 20 ml " Tonophosphan" of Farbwerke Hoechst. Group B comprised 12 animals, i.e. 9 spotted cows, 2 black-pied cows and 1 red-pied cow. These also suffered from atypical parturient paresis and were given 500 ml "CMC" only. Group C comprised 6 animals, i.e. 5 spotted cows and 1 red-pied cow; these all exhibited the typical symptoms of parturient paresis. They also received 500 ml "CMC".

Before treatment all diseased cows were thoroughly examined. The findings have already been reported (Hofmann and Amrousi, 1970). The blood samples were taken and examined in the same order and at the same times as for the healthy cows of groups I to IV. During infusion the temperature, pulse, heart, respiration and general condition were checked.

*) The trials were conducted with the financial support of the Hessian Minister for Labour, Welfare and Health

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Table 1. Administration of different doses of "Tonophosphan" to clinically healthy cows with simultaneous control of the calcium and phosphorus blood levels

Dose "Tonophosphan" ml	Blood level mg%	before injection	Time of blood withdrawal hours after injection 1/2	1	2	4	8	24
10	Ca	10.48 ± 0.207	11.52 ± 0.421	11.16 ± 0.436	11.104 ± 0.416	10.8 ± 0.507	10.46 ± 0.201	0.2 ± 2.06
	P	5.16 ± 0.390	5.86 ± 0.389	5.88 ± 0.479	5.36 ± 0.381	5.26 ± 0.204	4.94 ± 0.303	4.89 ± 0.32
35	Ca	9.65 ± 0.31	9.55 ± 0.430	9.62 ± 0.320	9.95 ± 0.401	10.22 ± 0.531	9.97 ± 0.521	9.72 ± 0.23
	P	5.22 ± 0.21	6.075 ± 0.392	7.65 ± 0.231	5.47 ± 0.401	5.05 ± 0.230	4.90 ± 0.22	5.05 ± 0.35
50	Ca	9.975 ± 0.230	9.70 ± 0.341	10.1 ± 0.272	10.02 ± 0.513	10.5 ± 0.421	10.2 ± 0.380	9.8 ± 0.4
	P	4.77 ± 0.213	5.375 ± 0.394	4.975 ± 0.412	4.95 ± 0.273	5.125 ± 0.198	4.725 ± 0.207	4.55 ± 0.27
100	Ca	9.825 ± 0.525	11.05 ± 0.721	10.15 ± 0.341	10.25 ± 0.482	10.425 ± 0.521	10.075 ± 0.231	9.9 ± 0.24
	P	4.650 ± 0.472	5.225 ± 0.414	4.825 ± 0.358	4.80 ± 0.132	4.95 ± 0.253	5.150 ± 0.372	4.97 ± 0.20

Table 1 shows the calcium and phosphorus blood levels of the healthy animals. Thirty minutes after administration of Tonophosphan the calcium level had risen, but dropped again, and 8 hours at the latest after infusion had again reached the initial value. After 35 and 50 ml only slight fluctuations occurred; at 100 ml there was a distinct increase in the calcium level after 30 minutes which did not drop to the initial value until 8 hours after infusion. The phosphorus blood level rose only slightly after administration of 10 ml Tonophosphan up to 1 hour after infusion, then dropped and 8 and 24 hours respectively after infusion dropped to below the initial value. Similar findings were made after the injection of 35 ml. The value 1 hour after infusion was higher compared with the initial level. However, 50 and 100 ml Tonophosphan brought about slightly raised phosphorus levels only in the first half-hour. Thus there was no prolonged increase in the calcium and phosphorus levels.

The animals of group A with atypical parturient paresis exhibited normocalcaemic and hypophosphotaemic blood serum levels (Table 2). 24 hours after the administration of CMC and Tonophosphan the calcium level had on average risen slightly and the phosphorus level markedly; after a further period of 24 hours Ca had risen a little more, whereas P had not increased any further. On an average the phosphorus levels at 3.36 mg% remained below the norm. The healthy animals also tolerated the administration of Tonophosphan well.

Merely after administration of 100 ml there was a slight increase in the heart rate and a decrease in the internal body temperature by an average of 0.2 degree C.

Finally, 11 cows with atypical parturient paresis were initially given 20 ml Tonophosphan and after 2 hours 500 ml CMC. The group comprised 8 spotted cows, 1 red-pied cow and 2 black-pied cows. Two of the animals got up on their legs immediately after the Tonophosphan injection and 9 after the administration of CMC. The blood levels can be seen Table 3. These data show that the initially much reduced calcium levels rose distinctly to the limit of the normal range after the Tonophosphan injection alone, whilst the subsequent calcium injection only led to a transient, slightly further increase. The phosphorus content of the serum rose initially but was further increased after the calcium infusion, without reaching the physiological range within 24 hours. Nevertheless the animals had already got up on their legs. The administration of Tonophosphan thus had a favourable effect on the blood levels and symptoms of disease in these cases of atypical parturient paresis.

Any possible effect the therapy might have on the Ca and P content of the milk was also examined. A total of 43 milk samples was taken from 17 cows, immediately following the therapy and 24-28 hours later, and tested. The investigations which have not been completed show that the calcium content of the milk from cows unable to get up on their legs does not rise much, but in some cases even drops.

In contrast, the phosphorus levels of the milk dropped both after Tonophosphan alone and after calcium infusions, and in several cases were still elevated compared with the norm after 24 and 48 hours. In several animals from whom milk samples had been taken 2 hours after the Tonophosphan injections the phosphorus concentrations were considerably higher than before the treatment: after 24 and 48 hours respectively a marked drop in the P content of the milk had come about.

The outcome of the examinations suggests the following:

1. In healthy cows intravenous injections of Tonophosphan lead only to transient, slight increases in the phosphorus level.

2. By means of simultaneous administration of calcium and Tonophosphan solution to cows with atypical parturient paresis, normocalcaemia and hypophosphoraemia, both the calcium and phosphorus levels are increased. However, the latter remains below the physiological norm even 48 hours

Table 2. The influence of calcium and Tonophosphan infusions on the calcium and phosphorus blood levels in cows with atypical and typical parturient paresis (for the separation into groups see text)

Group	Time after blood withdrawal: before treatment		24 hours after treatment		48 hours after treatment	
	Ca	P	Ca	P	Ca	P
A	9.263 ± 0.725	2.025 ± 0.266	9.60 ± 0.599	3.36 ± 0.491	9.70 ± 0.374	3.30 ± 0.548
B	8.984 ± 0.540	1.97 ± 0.330	8.89 ± 0.377	4.40 ± 0.48	9.27 ± 0.552	3.60 ± 0.215
C	8.733 ± 0.605	2.45 ± 0.82	10.06 ± 0.469	2.90 ± 0.298	9.93 -	4.93 -

Table 3 . Calcium and phosphorus content of the blood serum before treatment, 2 hours after the administration of Tonophosphan and 24 and 48 hours after subsequent calcium injection.

Before treatment		2hrs. after Tonophosphan		24 hrs. after CMC		48 hrs. after CMC	
Ca	P	Ca	P	Ca	P	Ca	P
7.563 ± 0.759	1.90 ± 0.228	8.93 ± 0.726	2.42 ± 0.256	9.345 ± 1.01	3.309 ± 0.256	8.96 ± 0.229	3.33 ± 0.225

after the injection. Further experiments will be required in order to find out whether it is possible by means of an increased phosphorus dose to achieve a rise to the normal range.

3. The exclusive administration of calcium to animals with atypical parturient paresis only leads to a transient increase in the phosphorus level and later to a further drop.
4. Calcium infusions lead to increases in the calcium and phosphorus blood levels in cows suffering from true parturient paresis, thus suggesting a direct or indirect dependence of the phosphorous level on the calcium content of the blood.
5. It is surprising to note that on the other hand the administration of Tonophosphan alone also leads to an increase in calcium and phosphorus in the blood.
6. By means of combined therapy with calcium and phosphorus, which on the basis of these investigations is to be considered the method of treatment to be most highly recommended, a reduction in the phosphorus excretion in the milk is achieved. This stopping of phosphorus losses with the milk thus has a similar influence as air insufflation into the udder and consequently brings about the increase in blood levels.

Summary

Whilst parturient paresis when it takes a typical course can be cured swiftly and safely by intravenous application of calcium solutions, the atypical form of the disease poses considerable difficulties. There are no satisfactory reports in the literature. The hypophosphotaemia accompanying the disease and the increased phosphorus excretion in the milk are reduced after intravenous calcium and phosphorous ad-

ministration. Similar observations are reported in the literature, a reduced release of parathormone being held responsible. Thus calcium and phosphorus infusions have the same effect as air insufflation into the udder previously practised, and must be employed in the treatment of atypical parturient paresis for the time being.

Reference:

Hofman, W. and S. El Amrousi (1970): Dtsch. tierarztl. Wschr. 4, 73.

Editor's Note

Administration of phosphorus injection will recoup or compensate for the deficiency of phosphorus in the animal suffering from hypophosphotaemia. It may not be possible to demonstrate sustained higher levels of phosphorus in blood as the efficacy of phosphorus injection. The phosphorus and calcium, being the physiological ingredients of the blood, milk and tissues, the body always shows homeostatic tendency to keep the concentration of phosphorus and calcium in the blood within physiological normal limits.

Effect Of Combined Adjunct Therapy With Special Reference To Herbal Drug And Different Levels Of Grain In Feed In Induced Hepatopathy In Caprine

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Eighteen healthy goats conditioned for six weeks on standard feeding after treatment for endo and ecto parasites were divided into 3 groups of 6 each randomly. The 3 diets contained 25, 50 and 70 percent crushed maize; 52, 31 and 14 percent wheat straw; and 10, 6 and 3 percent deoiled groundnut cake in group 1, 2 and 3 respectively with optimum protein. All diets contained 10, 2 and 1 percent molasses, mineral mixture and common salt respectively. The goats were group fed experimental diets for 8 weeks and at the end acetaminophan was administered i/v @ 400 mg per kg. body weight as a single dose for the induction of hepatopathy. After 24 hours of drug administration, goats of each group were sub-divided into 2 sub-groups of 3 each. No therapeutic drug was used in subgroup 1A, 2A and 3A, while herbal drug @10 ml/day was given orally for 10 days to goats in sub-group 1B, 2B and 3B. Clinical changes were recorded periodically upto 18 days from the day of induced hepatopathy. Dry matter intake was recorded before and after 10 days of induced hepatopathy.

Symptoms of induced hepatopathy appeared in all goats within 24 h of paracetamol administration which were most severe in group 1 and least in group 3. Treatment with herbal drug reduced severity and it was most effective in group 2B and 3B. The levels of aspartate aminotransferase, alanine aminotransferase, cholesterol, globulin, bilirubin and BSP percent retention increased significantly on the induction of hepatopathy. However, the levels started decreasing at a faster rate in the treated animals from day 7-11 in groups 2B and 3B and from day 18 in group 1B. More or less similar trend was observed in the decrease of serum protein, albumin and glucose. Cholecystography revealed non-visible gall bladder after hepatopathy which showed reversal in treated goats being first in group 3B followed by group 2B and 1B. High energy diet of grain with treatment provided considerable protection and helped in quicker recovery in comparison to low energy and high fibre diet.

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On The Use Of Oxyclozanide In Natural Outbreaks Of Amphistomiasis In Bovines

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Three outbreaks of amphistomiasis affecting bovines were recorded during the last three years 1991 - 93 in the villages namely Khandur Distt. Ferozepur and Jhangerhi, Distt. Ropar and village Diva (Distt. Ludhiana) of Punjab.

Three adult buffaloes and one heifer died at Khandur, 25 cows and buffaloes died at Jhangerhi and ten cows and two buffaloes at Diva due to amphistomiasis.

Animals in all three villages were severely affected. The animals showed bottle-jaw condition and foeted diarrhoea.

Faecal samples from affected were collected and eggs per gm. of faeces was done by McMaster Chamber. The average EPG was 110 and ranged between 30 - 330. One crossbred heifer which died due to amphistomiasis was subjected to post-mortem. It was observed that the mucosa of duodenum was studded with immature amphistomes.

80 affected animals at Jhanger and 25 at Khandur and one heifer at Diva were treated orally with oxyclozanide (TOLZAN - F - a trademark of Hoechst) @ 20 mg./kg. body weight. Faecal samples from treated animals were again collected 15 days after the treatment.

During this period none of the treated animals died. The faecal samples from all the animals were negative for any egg of amphistomes.

In fact the clinical cases of amphistomiasis occur due to immature worms which infest the duodenum. The recovery of treated animals proved that the drug effectively controlled the immature as well as the mature forms, because no egg could be detected in faeces. The drug did not produce any untoward effect in treated animals. Therefore oxyclozanide could be safely and effectively used in case of an outbreak of amphistomiasis in bovines.

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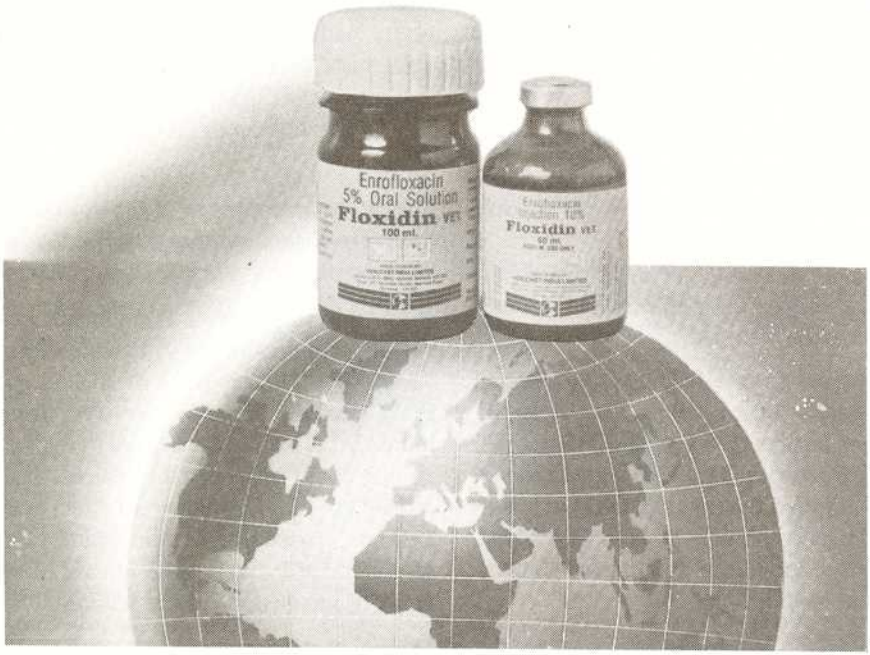

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Studies On Blood And Cerebrospinal Fluid Alterations In Induced Hepatopathy In Ovine

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Liver, the largest glandular organ of the animal's body is located centrally in the metabolic pathway and has the responsibility to maintain the normal functioning of several other organs/systems of the body. Obviously, injuries to hepatic parenchyma or interference with hepatic vascular system may have serious and far reaching effects not only on the liver itself but also on the other organs/systems. But because of lack of specific symptoms of serious disorders of liver, the diagnosis of its dysfunction in farm animals often becomes difficult. Clinical symptoms suggestive of hepatic damage may be evident when a substantial damage to the organ has already taken place. Hence, tests which can indicate the preclinical stage of the disease will undoubtedly help in limiting the disease process. However, there is paucity of literature regarding various biochemical changes in the body fluids due to hepatic dysfunction in sheep. The present experiment was, therefore, undertaken to study the changes in blood, cerebrospinal fluid (CSF), and hepatic structural and functional status of sheep with induced hepatopathy.

Materials and Methods

Twelve adult healthy sheep (Dorset X Muzaffarnagari and Suffolk X Muzaffarnagari) of either sex were kept on standard feeding and managemental conditions for six weeks before including them in the experiment. During this period the animals were given anthelmintic and antibacterial coverage to exclude the possibility of infections. These animals were, then divided into 2 equal groups (group I and II) of 6 animals each. To induce hepatopathy paracetamol was administered @ 400 mg/kg body weight by single intravenous (I/V) injection (Gupta, 1989) to the animals of group II. The animals of group I served as healthy control.

Haematological studies were carried out as per the methods of Jain (1986). Various biochemical parameters were studied as per the methods of Folin and WU(1920) for blood and CSF glucose, Greenburg (1929) for total protein, Pandy's test for CSF qualitative protection, Wootton (1964) for serum cholesterol, and Reitman and Frankel (1957) for serum and CSF aspartate aminotransferase (AST) and alanine aminostansferase (ALT). The changes in these parameters of blood/serum were recorded before induction of hepatopathy (zero day) and thereafter on day 1,5,10,15, and 20, whereas the CSF studies were carried out on day 0,1,5,10 and 20. Bromsulfophthalein (BSP) percent retention test was performed as per the methods of Oser, 1965) on day 0,1,10 and 20.

Cholecystographs were taken by using Biligrafin Forte dye (O'5 g) N-methyl glucamine salt of adipic acid-di-(3-carboxy-2,4,6 triiodoanilic in 1 ml. of injection, schering, A.G. Berlin, Germany) as a contrast excretory agent. Twenty millilitre of the dye was injected slowly by intravenous route to the 24 hours (hrs.) fasted animals. Plain radiograph of liver region were taken at 60 - 65 KVP and 13 - 17 m as before injecting the dye and thereafter at 30, 60, 90 120 and 150 minutes. Exposed films were then processed for interpretation.

Histopathological changes in the liver of animals sacrificed on the last day of the experi-

Table 1. Showing changes in various parameters of sheep with induced hepatopathy (Mean+ S.E)

Group I is control

Parameters	Groups	Days					
		O	1	5	10	15	20
Hb (g/dl)	I	10'89 ± ^{A}O'72	12'10^{aA} ±O'87	11'82^{aA} ± O'98	10'72^{aA} ± O'98	10'53^{aA} ± O'51	10'47^{aA} ± O'62
	II	11'73^{aA} ± O'68	9'36^{bB} ± O'71	8'4O^{bB} ± O'49	8'7O^{bB} ± O'56	8'O6^{dB} ± O'63	8'26^{bB} ± O'59
TEC (x10^{6}/ l)	I	8'96^{aA} ± O'57	8'87^{aA} ± O'72	8'75^{aA} ± O'72	9'02^{aA} ± O'62	9'O7^{aA} ± O'47	8'89^{aA} ± O'38
	II	9'12^{aA} ± O'41	8'96^{aA} ± O'4O	7'91^{bB} ± O'43	7'51^{bB} ± O'38	7'69^{bB} ± O'39	6'83^{bB} ± O'39
TLC (X10^{3}/ul)	I	6'52^{aA} ± O'87	6'79^{aA} ± O'92	6'85^{aA} ± 1'O1	6'21^{aA} ± O'12	6'09^{aA} ± O'29	6'39^{aA} ± O'36
	II	6'89^{aA} ± O'28	7'03^{aA} ± O'34	11'34^{bB} ± O'3O	10'27^{bB} ± O'24	9'80^{cB} ± O'39	9'69^{cB} ± O'36
Clotting time (minute)	I	5'87^{aA} ± O'62	5'65^{aA} ± O'5O	6'01^{aA} ± O'39	5'89^{aA} ± O'31	5'89^{aA} ± O'12	5'79^{aA} ± O'82
	II	5'58^{aA} ± O'40	6'95^{bB} ± O'41	8'79^{cB} ± O'3O	8'16^{cB} ± O'22	7'25^{dB} ± O'18	7'16^{dB} ± O'12
Blood Glucose	I	46'12^{aA} ± O.69	47'47^{aA} ± O'75	46'53^{aA} ± O'83	44'33^{aA} ± O'83	45'87^{aA} ± O'97	46'72^{aA} ± O'82
	II	48'16^{aA} ± 1'3O	36'OO^{bB} ± O'93	30'66^{cB} ± O'61	28'5O^{cC} ± O'56	28'5O^{cB} ± O'67	29'5O^{cB} ± O'71
Serum Cholesterol (mg/cl).	I	63'98^{aA} ± 1'21	64'23^{aA} ± 1'87	64'88^{aA} ± 2'O1	62'19^{aA} ± O'98	63'13^{aA} ± 1'12	62'89^{aA} ± 1'01
	II	65'79^{aA} ± O'72	78'76^{bB} ± O'38	126'25^{cB} ± O'89	148'OO^{cB} ± 1'38	144'45^{cB} ± 1.22	123'O8^{cB} ± 1'O5
Total Serum Bilirubin (mg/dl)	I	O'15^{aA} ± O'O2	O'16^{aA} ±O'O3	O'15^{aA} ± O'O2	O'18^{aA} ± O'O2	O'18^{aA} ± O'O2	O'16^{aA} ± O'O2
	II	O'17^{aA} ± O'O1	O'34^{bB} ± O'O2	O'5O^{cB} ± O'O3	O'48^{cB} ± O'O2	O'48^{cB} ± O'O2	O'46^{cB} ± O'O3
AST (RSU/ml)	I	9O'23^{aA} ± 2'34	89'56^{aA} ± 1'44	95'33^{aA} ± 1'73	95'33^{aA} ± 1'73	96'25^{aA} ± 2'16	92'11^{aA} ± 1'56
	II	95'91^{aA} ± 2'43	144'33 ^{bB} ± 2'OO	203'13^{cB} ± 1'3O	2O7'85^{cB} ± O'35	2O3'82^{cB} ± 1'59	198'47^{cB} ± 2'43
ALT (RFU/ml)	I	3O'46^{aA} ± 1'92	32'45^{aA} ± 1'22	31'56^{aA} ± 1'54	29'32^{aA} ± O'98	34'53^{aA} ± 1'20	33'22^{aA} ± 1'89
	II	31'99^{aA} ± 1'24	73'19^{bB} ± 1'2O	130'56^{cB} ± 2'57	142' 4O^{cB} ± 1'54	131.59^{cB} ± 2'47	114'45^{cB} ± 2'88
BSP % retention	I	7'98^{aA} ± O'19	6'29^{aA} ± O'2O	-	6'87^{aA} ± O'27	-	7'23^{aA} ± 1'2O
	II	6'08^{aA} ± O'20	16'2O^{bB} ± O'6O	-	19'4O^{cB} ± O'20	-	16'O3^{bB} ± O'6O

N.B. Values with different small letters (within group) and capital letters (between the groups differ significantly (P<O'O5).

ment were studied according to the procedures described by Lillie and Fulmer (1976). Statistical analysis of data were made by the methods of Snedecor and Cochran (1967).

Results and Discussion

The animals which were healthy and active initially, started showing various abnormal symptoms viz. anorexia, incoordination in movement, stretching of head and neck, trembling of muscles and open mouth breathing just after administration of paracetamol.

Haemoglobin (Hb), packed cell volume (PCV) and total crythrocyte count (TEC) values showed a significant (P<O'O5) decrease whereas total leukocyte count (TLC) and blood clotting time recorded a significant (P<O'O5) increase following induction of hepatopathy in the sheep of group II. Reduction in the values of Hb. PCV and TEC might be attributed to the inability of the damaged hepatic parenchyma to produce erythropoietinogen and partly to the reduced feed intake, decreased absorption and metabolism of nutrients (Piperno *et al.*, 1978). In addition disintegration of erythrocytes in the circulation might also have resulted in reduction of Hb content of blood (Dixon *et al.* 1975) which inturn was associated with decrease in PCV and TEC values.

Leukocytosis which was observed in group II animals following induction of hepatopathy might be due to stress coupled with inflammatory changes in body tissues which were responsible for phagocytosis of toxic substances. Similiar changes in haematological parameters of experimental animals with hepatopathy have also been reported by Peer (1987), and Singh (1988), Gupta (1989).

A marked increase in the blood clotting time was observed following administration of paracetamol. Almost all the clotting factors are produced in the liver and damage of hepatic cells might have led to reduced production of these factors which inturn resulted in delayed clotting of blood. In addition, inadequate absorption of vitamin K because of less quantity of bile in the intestines might have led to decreased production of vitamin K-dependent clotting factors (factors II, VII, IX, X and prothrombin). Coagulation abnormalities related to hepatic disorders have earlier been reported by Sen *et al* (1976); Verma (1982) and Prescott (1986).

Blood glucose level decreased significantly in all the animals of group II following induction of hepatopathy.Hepatic injury caused by paracetamol might have hindered the normal metabolism of carbohydrate and ultimate maintenance of normal blood glucose level. A similar reduction was observed in total serum proteins, albumin and albumin: globulin (A: G) ratio in group II animals. Serum proteins are synthesized mostly in the liver which became damaged by administration of paracetamol and resulted in such reduction. Decrease in blood glucose, total serum proteins, albumin and A:G ratio in experimental animals following induction of hepatopathy has been reported by Gupta (1989). Hypoglycaemia and hypoproteinaemia in liver diseases were also observed by Mezey (1978).

Hypercholesterolaemia following paracetamol administration was recorded in the present study which might be either due to utilisation of volatile fatty acids by damaged hepatic parenchyma for glycogenesis which entered the general circulation, or decreased excretion of cholesterol by the damaged liver cells. Serum total bilirubin level in group II animals also increased significantly which might be attributed to abnormal uptake, conjugation and excretion by damaged hepatic cells. Similar elevations in cholesterol and bilirubin levels in experimental animals with induced hepatopathy have also been reported by Gupta (1989).

Serum activities of AST and ALT showed a significant (P<O'O5) increase in the animals of group II following induction of hepatopathy. Gupta (1989) have recorded a similar increase in these enzyme activities which might be due to release of the enzymes from disrupted hepatic parenchymal cells either due to necrosis or altered membrane

permeability. A significant (P<O'O5) increase in the percent retention of BSP dye was observed in the group II animals and this might be attributed to the inability of the damaged hepatic parenchymal cells to excrete the dye at normal rates. Increased BSP percent retention following paracetamol intoxication has also been reported by Finco, *et al.* (1975).

There was no change in the colour and turbidity of CSF of sheep after induction of hepatopathy. However, a significant (P<O'O5) decrease in the CSF glucose level was observed similar to the observed in blood. This decrease might be due to hypoglycaemia as a result of hepatic damage and being the ultrafiltrate of blood, CSF glucose level also recorded a fall. According to Coles (1980) some of the chemical constituents of CSF changed in accordance with their changes in blood. He opined that diseases primary to other organs/systems might also alter its composition. Absence of protein (qualitatively) as indicated by negativity of Pancy's test and no significant change in leukocyte count, AST and ALT values in CSF of sheep with hepatopathy induced with paracetamol were observed during the present study. Some degree of variation from the normal values of sheep CSF have been reported by Thathoo (1986) in induced chronic malathion toxicity and by Patra (1991) in induced acidosis. However, because of paucity of literature regarding CSF changes in hepatopathy, the findings of the present experiment could not be substantiated.

In the present study the gall bladder could be visualised in the lateral cholecystographs taken after 60 minutes of dye administration . The dye concentration in the gall bladder further increased by 90 minutes and started decreasing after 120 minutes. But, after 24 hrs. of paracetamol administration cholecystographs could not visualise the gall bladder even after 150 minutes of dye administration. A similar result was also recorded on day 10 of the experiment suggesting either a very slow rate of excretion of the dye into the gall bladder or a total inability of the liver to excrete the dye. I/V administration of different dye compounds has been done in various species of animals to visualise the gall bladder and to assess the severity of liver dysfunction by various workers (Gupta, 1989 : Singh *et al.*, 1990).

The contrast material is conjugated with glucuronic acid in the liver to form a freely water soluble glucuronic acid conjugate before its excretion into the bile and this inturn makes the gall bladder visible on radiographs (Dowdy, 1969). Thus, in the animals with normal hepatic function the time required for the liver to excrete the dye is minimum which increases when the hepatic parenchymal cells are damaged. Construction to the intrahepatic biliary ducts in hepatic damage may also be a contributing factor to this delayed visualisation. Jones opined that severe hepatic dysfunction prevented ductal opacification because of inadequate excretion. Similar observations in experimental hepatopathy with paracetamol have also beenmade by Gupta (1989).

Histopathological studies of liver tissues regroup 1. The changes which were observed in group II animals included necrosis in the pericentral hepatocytes, foamy appearance of cytoplasm of hepatocytes, partial or complete loss of normal structure at places around the central vein and infiltration of cells of leukocytic series.

The abnormalities which were recorded in the different parameters of group II animals following induction of hepatopathy in the present study were absent in the group I animals.

Summary

Hepatopathy was induced in six adult healthy sheep with single intravenous injection of paracetamol @ 400 mg/kg body weight. Various haematological, blood/serum biochemical, changes in CSF, radiological and histopathological studies were carried out in these animals over a period of 20 days and the findings were compared with an equal number of healthy control animals. Following induction of hepatopathy significant decrease in haemoglobin, packed cell volume, total eryth-

rocyte count, blood and CSF glucose, total serum proteins, albumin and albumin: globulin ratio, and significant increase in total leukocyte count, blood clotting time, serum cholesterol, bilirubin, serum AST and ALT, and BSP % retention. Studies on CSF revealed decreased glucose level. Radiological changes included delayed visualisation of gall bladder. Various degenerative changes in the hepatic tissue such as necrosis of pericentral hepatocytes, foamy appearance of cytoplasm, loss of normal structure and infiltration of leukocytic cells were recorded histopathologically.

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New Challenges In Development Of Veterinary Clinical Pharmacology

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The development of Clinical Pharmacology in Veterinary is still in the infancy stage. J. Desmond Baggot had written the first book "Principles of Drug Disposition in Domestic Animals, the Basis of Veterinary Clinical Pharmacology" in 1977. The diversity of animal species makes Veterinary Clinical Pharmacology more challenging.

Most drugs in ruminants are injectables due to their unpredictable bio-availability after oral administration in compound stomach. Injectable anthelmintics, injectable pesticides, injectable neomycin, injectable Sulfa-Trimethoprim are new introductions in veterinary practice and recent one long acting oxytetracyclines. Species variations in half-life, protein binding capacity, metabolism, distribution and excretion patterns are diverse. Monitoring of drug residues in milk, meat and eggs should be also considered on priority as it may be a serious problem in Public Health. Pharmacokinetic studies of major drugs in animals and their residues in tissues and body fluids are interesting areas in Verterinary Clinical Pharmacology. Important clues can be derived from Veterinary Clinical Pharmacology to human Clinical Pharmacology.

Passage of Antimicrobial Agents into milk

Milk is a suspension of fat droplets in an aqueous phase in which lactose, inorganic salts and proteins mainly casein are dissolved. Studies of the penetration of antimicrobial agents from the systemic circulation into milk indicate that the mammary gland epithelium behaves as a lipoidal membrane which separates blood of pH 7.4 from milk which has a somewhat lower pH value (Normal pH 6.5 - 6.8). The passage of each drug into milk is determined by the extent of binding to plasma albumin, the pKa value and the degree of lipid solubility.

It has been shown that only the lipid-soluble, non-ionized moiety of an organic electrolyte in the water phase of blood plasma diffuses into milk. In normal lactating cows, weak acids give milk ultrafiltrate-to-plasma ultrafiltrate concentration ratio less than or equal to one. Weak bases excluding aminoglycoside antibiotics attain concentration ratios greater than one (Table 1). The limited extent of penetration of the aminoglycoside antibiotics into milk can be related to their extremely poor solubility in non-polar solvents and to their low lipid -to-water partition coefficient. The choice of antimicrobial agent for systemic therapy of mastitis should be based upon the susceptibility of infecting micro-organisms to the drug and upon the milk drug level which may be attained with usual dosage. The former can be determined *in vitro* and the latter may be predicted.

Penetration of drugs through the skin

The barrier properties of the skin vary with the site of application and with the species of animal. Species differences in skin penetration following topical application of a radio labelled organo-phosphorus compound to isolated skin sections are observed (Table 2). The efficacy of topical applications also depends on composition of vehicle and physical properties of drug. When skin infection is located in the deeper layers of the epidermis or in the dermis, systemic therapy is often more effective than topical application.

Table 1. Passage of Chemethorapeutic agents from the systemic circulation into milk

Drug	pKa	Milk pH	Concentration Ratio (milk ultrafiltrate : Plasma Ultrafiltrate)	
			Theoretical	Experimental
Organic Acids				
Benzyl Penicillin G	2.7	6.8	0.20	0.13 - 0.26
Cloxacillin	-	6.8	0.20	0.25 - 0.30
Ampicillin	-	6.8	0.26	0.24 - 0.30
Cephaloridine	3.4	6.8	0.25	0.24 - 0.28
Sulfadimethoxine	6.0	6.6	0.19	0.23
Sulfamethazine	7.4	6.6	0.55	0.59
Organic Bases				
Tylosin	7.1	6.8	3.0	3.5
Lincomycin	7.6	6.8	2.83	2.5 - 3.6
Trimethoprim	7.6	6.5 - 6.8	2.8 - 5.3	2.9 - 4.90
Erythromycin	8.8	6.8	6.1	8.7
Kanamycin	7.8	6.5 - 6.9	-	0.6 - 0.8

Table 2. Maximal penetration of radiolabled organo-phosphorous compound through excised skin from dorsal thorax of various species

Species	Rate (mcg/cm^2/min)
Pig	0.3
Dog	2.7
Monkey	4.2
Goat	4.4
Cat	4.4
Guineapig	6.0
Rabbit	9.3
Rat	9.3

Comparative Aspects of Drug Absorption

The domestic animals are divided into three groups

1) Herbivores (Horse, Ox, Sheep and Goat)

2) Omnivores (Pig)

3) Carnivores (Dog and Cat)

The pH gradients between plasma and the gastrointestinal fluids of various species play an important role in determining the extent of absorption of orally given drugs. Passage of weak organic bases by non-ionic diffusion from blood plasma into ruminal fluid, with subsequent ionisation therein (Ion-trapping) is an important aspect of the disposition of such drugs in ruminant species (Table 3).

Table 3. Bioavailability of some drugs in domestic animals

Drug	Dose mg/kg	Species	Route	Availability	Time (min)	Ave. Conc (mcg/ml)
Ampicillin trihydrate	10	Cat	s/c	36	60	15
Kanamycin So4	10	Dog	i.m.	90	15 - 30	28
Kanamycin So4	10	Horse	i.m.	90	60 - 90	30
Salicylate (Aspirin)	50	Cow	oral	50 - 70	150	22
Tablets	100	Cow	oral	-	-	45

Pharmacokinetic Parameters

Pharmacokinetic parameters of drug with the same dose varies from species to species. There is lot of variation in biological half-lives, volume of distribution and clearance rate. Therefore, it is very necessary to investigate the drug disposition in all the species. Extrapolation of data from one species to other species is neither justified nor scientific (Table 4-5).

Table 4. Apparent specific volume of Distribution (litre/kg) of some drugs in goat (or cow), dog and horse

Drug	Goat (Cow)	Dog	Horse
Amphetamine	3.08	2.67	2.61
Tylosin	(1.10)	1.71	-
Chloramphenicol	1.33	1.77	1.02
Oxytetracycline	(1.04)	2.09	1.35
Kanamycin	(0.22)	0.25	0.20
Phenylbutazone	0.26	0.18	-

Table 5. Extent of binding of drugs to plasma (or serum) proteins at therapeutic concentrations

Drug	Conc. mcg/ml	Percent bound Human	Ruminant	Dog
Sulfadiazine	100	33	24	17
Cloxacillin	20	95	71	64
Phenytoin	10	81	82	81
Lincomycin	5	72	342	-
Kanamycin	5	28	40	-
Morphine	1	34	23	12.1
Digitoxin	0.05	92	86	88

Biotransformation

The species variations are found in the biotransformation of drugs, oxidation, reduction, hydrolysis and conjugation are important major processes of biotransformation of drugs and chemicals. Conjugation reactions convert drugs and natural metabolites of the body into products that are pharmacologically and biologically inactive. The metabolic pathways not only inactivate drugs but also facilitate their removal from body. Certain species are defective in certain conjugation reactions (Table 6). These factors are important in clinics while monitoring the treatments with drugs.

Microsomal enzymes in liver have important role in the metabolism of drugs. Certain drugs and chemicals have ability to stimulate microsomal enzyme activity (Table 7). This property of enhancing enzyme activity will facilitate metabolism of other drugs concurrently administered. Thus the duration of action of drugs can be influenced.

Elimination or excretion of drugs also shows species variation to a great extent. The half lives of drugs (Table 8) will decide the frequency of drug administration. The over dosage and toxicity can be avoided by knowing this variation in different species for specific drugs.

The pharmacokinetic parameters will show variations due to several variations in biotransformation, elimination, protein binding capacity etc. The example of kanamycin pharmacokinetics in different animals (Table - 9) is self explanatory.

Table 6. Animal species defective in certain conjugation reactions

Species	Conjugation	Extent
Cat	Glucuronide synthesis	low level
Dog	Acetylation	Absent
Pig	Sulfate conjugation	low level
Domestic Animals	Ornithine conjugation	Absent

Table 7. Drugs that stimulate microsomal enzyme activity

Phenobarbital
Phenylbutazone
Phenytoin
Griseofulvin
Chlorinated hydrocarbons
Chloral hydrate

Table 8. Half-life values (in hours) of drugs which are eliminated mainly by metabolism

Drug	Pony	Cow	Pig	Dog	Cat
Salicylates	1.0	0.54	5.9	8.6	37.6
Chloramphenicol	0.9	2.0	1.3	4.2	5.1
Trimethoprim	3.8	0.5	2.0	3.0	-
Amphetamine	1.4	0.6	1.1	4.5	6.5
Quinidine	4.4	0.85	5.4	5.6	1.9

Table 9. Pharmacokinetic parameters which describe disposition of kanamycin after intravenous injection of a single dose (10 mg/kg)

Kinetic parameter	Units	Dog	Sheep	Horse
A	mcg/ml	65.4	66.4	55.0
B	mcg/ml	38.4	42.4	54.0
$t_{1/2}$	min	44.4	99.0	84.5
Cl. B	ml/kg/min	3.51	1.52	1.43
Body weight	kg	11.4	36.4	77.3

Drug Delivery System

Various formulations are being designed to reach the drug to the target site. Various dosage forms for oral administration, capsules, slow releasing crystals, slow releasing granules etc. are being prepared. The long acting antibiotics are being prepared with slow releasing technique. Intramammary preparations will need some novel techniques of slow releasing in mammary gland. The estimation of various drugs in the tissues and various biological fluids is the vast area of scope for further understanding of drug disposition in animals. These areas of Veterinary Clinical Pharmacology are challenges to be met by the Veterinary scientists. The information thus generated will be of immense use to the Veterinary and medical profession. The advanced sophisticated technique of drug assay will also be required to be developed.

Reference

Baggot J. Desmond (1977)

" Principles of Drug Disposition in Domestic Animals, the Basis of Veterinary Clinical Pharmacology".

W.W. Saunders Company, Philadelphia, London, Toronto.

Abstracts

1) Protection studies with integral membrane fractions of Haemonchus contortus.

Immunization of sheep with various candidate protective antigen fractions of whole parasite revealed a Haemonchus galactose containing glycoprotein (H-gal-GP) complex to be highly protective, reducing mean challenge worm burden by upto 72% and mean faecal EPG by upto 93%. The antibodies produced were found to coat luminal surface of the intestine of *Haemonchus sp* recovered from sheep immunized with this fraction suggesting that protective effect was due to antibodies interfering with functions of the gut of the parasite.

Smith.W.D., Smith.S.K., Murray. J.M. (1994)
Parasite Immunology **16** (5): 231 - 241

2) Studies on seminal degeneration due to pesticide BHC intoxication in Mehasana buffalo bulls.

A group of 19 (6 adult + 13 young) buffalo bulls were found inadvertently exposed to BHC dust bags, received for agriculture purpose - stored in adjacent open yard for 28 days. In eleven days of initial exposure rejection rate of semen samples increased (to 70% ejaculates) due to high occurrence of flat (immotile) semen ejaculates: High percentage of dead sperms noticed (30 to 70% as against 17.8% in pretoxicity period): post thaw recovery rate dropped to 20% (from normal 60 to 65%). These effects were more in older bulls. Clinically all bulls were normal with no changes in libido and sexual behaviour.

Average CHC isomere residues in seminal plasma was 26.349 ± 2.907 in exposed bulls (against 8.175 ± 6.997 in unexposed bulls) and the values in blood serum were 19.421 ± 16.184 (as against 3.315 ± 0.512 in unexposed bulls). There was gradual recovery by stopping exposure, cleaning and hygiene with sexual rest to bulls.

Kodagali, S.B., Doshi.M.B. & Dhani.A.J. (1995)
Buffalo. J. **1**: 91-96.

3) *Neospora caninum* infection in three dogs ....case reports

Neospora caninum is a newly recognised, fatal apicomplexan protozoal parasite of dogs, structurally similar to but immunologically distinct from *Toxoplasma gondii.*

The clinical signs in the three cases confirmed by immunofluorescence antibody test, were of lower motor neuron deficit of the pelvic limbs, bladder and rectum. Dogs showed paraplagia and hyper extension of pelvic limbs. Parasite is sensitive to Clindamycine, Sulphatrimethoprim preparations but prognosis for complete recovery was poor.

Knowler.C. , and Wheeler. S.J. (1995)
Journal of Small Animal Practice **36** (172 -177)

4) Utilization of dried caged-hen manure and cassava peels for intensive sheep production.

A trial on 20 grower eves with dietary treatments to replace conventional protein by dried cage-hen manure, revealed that the cage-hen manure can be fed as sole protein supplement in cassava peel based diets to sheep.

Okeudo. N.J., Adegbol a (1993)
Tropical Animal Health Production 25 (234-238)

5) Food intake and growth in chickens given food in the wet form with and without access to drinking water.

In individually caged broiler growing chicken given commercial grower food mixed with 1.5 to 2.25 times the weight water (porridge like consistency), significant increased weight gain and improved conversion efficiency were noticed. It was not necessary to withhold drinking water to obtain this effect.

Yalda AY: Forbes J.M. (1995)
British Poultry Science 36:357-369.

6) On *Pneumocystis carinii,* which is a parasite of considerable medical importance as it is commonest opportunistic pathogen with human patients of AIDS, following papers point out to the possibilities of animals being reservoirs.

a) *Pneumocystis* carinii infection in foals in U.K.

Five cases of fatal pneumonia in 5 thorough bred foals of 6 week to 3 months age are reported one each in 1992, 1991 and three in earlier years. Diagnosis was initially based on presence of interstetial pneumonia and detection of intra-alveolar pneumocysts microscopically; later corroborated (in recent cases) by Steptavidin-biotin immunostaining and electron microscopy.

Whitewell .K. (1992) Vet Record 131 (1) : 19

b) *Spontaneous Pneumocystis carinii* infection in the dog with naturally acquired, generalised Demodicosis.

In a dog died of generalised demodicosis. *P.carinii* cysts were found in lung homogenate smears, confirmed by immunofluorescence and Polymerase chain reaction, which raises question, whether dogs are natural reservoirs of this zoonotic parasite.

Furuta. T., Nogami.S., Kojima.S., Fujita.M., Kamara.H., Kuwabara.M., Ohba.S and Yoshida. H (1994) Vet. Record 34 : 423-424.

7) Formulation and use of anthelmintic blocks for sheep and goats in Fiji.

Urea-Molasses feed block containing Fenbendazole at the rate of 0.5 g/kg was suitable anthelmintic in sheep and goats. Significant differences were noted between sheep and goats when plasma FBZ and FBZ sulphoxides were plotted against FBZ intake indicating that goats require higher dose rate 0.75 gm/kg in urea molasses feed block. Field studies in Fiji indicate that FBZ medicated urea-molasses can successfully control, benzimidazole resistant strains of nematodes in sheep and goats.

M.R. Knox, R. Single, R. Manudi, J.W. Steel and L.F. Le Jambre (1994) Proc. of 6th EA VPTA Congress pp 248 (Edinburgh)

8) Comparative pharmacokinetic of fenbendazole in buffaloes and cattle.

Three swamp buffaloes (Bubalus bubalis) and four drought master cattle *(Bosindicus x B taurus)* fitted with gastrointestinal cannulae, were dosed intraruminally with Fenbendazole (FBZ) at 7.5 mg/kg body weight together chromium oxide capsule and a pulse dose of NaCo EDTA to estimate flow dynamics of digesta in rumen and duodenum.Concentration of FBZ metabolites were measured in plasma and duodenal fluids over 120 h. In plasma significantly lower peaks and early disappearance of FBZ and its sulphoxide (OFZ) was observed in buffaloes than in cattle. The availabilities of OFZ in duodenal fluid of buffaloes was significantly lower whereas FBZ disposition was similar to that in cattle. The turnover rate of fluid in rumen was higher in buffaloes that in cattle, while the flow parameters for other digesta were similar in the two species. It is concluded that decreased absorption of drug in buffaloes was attributable to shorter residence time in rumen and probably entire G1 tract. This is also the cause for reduced systemic availability of the drug in buffaloes as compared to cattle as indicated in this study. This indicates need for higher dose rates for benzimidazole anthelmintics in buffaloes than in cattle.

Knox M.R., Kennedy, P.M. Hennessy, D.R., Steel, J.W. and Le Jambre, L.F. (1994) Veterinary Research Communication **18** (3) 209-216.

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