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## EDITORIAL

# UNITY OF SERVICE

In South Africa, veterinary services, in the broadest sense of the term, started in a small way in the 19th century through the individual efforts of men like Duncan Hutcheon and Arnold Theiler. At the turn of the century, major epizootics, such as rinderpest and East Coast fever, created emergencies which stressed the urgent need for research, the training of veterinarians specifically equipped for South African conditions and an efficient State organisation to control and eradicate these diseases.

The emphasis fell on State Veterinary Services; a numerically small but inspired veterinary profession, ably assisted by auxillary personnel, rendered such good service to the country that they established a proud tradition both with regard to research and disease control. Only in 1936 did the total number of veterinarians reach one hundred, but diversification had already started. A few colleagues went into private practice, one or two entered medical research, some were appointed by local authorities to control the hygiene of food of animal origin.

After the economic depression of the 'thirties, and particularly after the second world war, private practice increasingly attracted veterinarians; today the majority of the profession renders services in this capacity. Simultaneously, veterinarians began to serve an ever widening biological field by entering the pharmaceutical and farm feed industry, AI services, poultry production, nature conservation, public health, medical research, training of agricultural and veterinary students, etc. In addition, the State also widened its range of activities to include animal health in general by the institution of specific health schemes, by assuming responsibility for the central control of meat hygiene and the development of regional diagnostic laboratory services. Because of this further diversification, it became necessary to adapt the training of veterinary students and to institute post-graduate "specialist" courses. At the same time, the need for more specifically trained paraveterinary personnel was felt, as the maximum potential of veterinarians could not be realized without their assistance. Their importance was no longer confined to the State Services.

## REDAKSIONEEL

# EENHEID VAN DIENS

Veeartsenydiens in Suid-Afrika, in die wydste betekenis van die woord, het in die 19de eeu klein begin deur die optrede van indiwidue soos Duncan Hutcheon en Arnold Theiler. Aan die begin van die 20ste eeu het ernstige episoötië noodtoestande geskep wat 'n meer omvattende diensorganisasie genoodsaak het. Daar was 'n dringende behoefte om ons eiesoortige probleme deur middel van navorsing op te los, georganiseerde bekamping van dieresiektes in te stel en veeartse op te lei wat spesifiek toegerus is om hierdie funksies te verrig. So het 'n betreklik klein maar besielde aantal veeartse (tot 1936 was daar slegs 100!) bygestaan deur hulpkragte, wonderlik presteer en 'n stewige tradisie vir die professie gebou.

Hoewel die klem vir die eerste veertig jaar hoofsaaklik op Staatsveeartsenydienste geval het, was diversifisering van dienslewering stadig maar seker besig om plaas te vind. Enkele veeartse het privaat gaan praktiseer, plaaslike owerhede het veeartse in beheer van die higiëne van voedsel van dierlike oorsprong geplaas, en enkeles is in mediese navorsing opgeneem. Na die depressie in die dertigerjare, en veral na die tweede wêreldoorlog, het private praktyk gaandeweg al meer kollegas getrek sodat die oorgrote meerderheid van die professie tans op hierdie wyse veeartsenydienste lewer. Terselfdertyd het veeartse 'n steeds verbredende biologiese werksveld bedien, bv. die farmaseutiese en veevoerbedryf, pluimvee, K.I.-dienste, wildbewaring, diereproduksie, mediese navorsing, voltydse landboukundige sowel as veeartsenykundige opleiding, ens. Ook die fasette wat die Staat behartig het, het toegeneem en opdragte soos sentrale beheer oor vleishigiëne, verskaffing van streekslaboratoriumdienste en die installering van spesifieke dieregesondheidskemas is aanvaar. As gevolg van hierdie diversifisering moes die opleiding van veeartse ook aangepas word en moes nagraadse kursusse en „spesialiste"-opleiding aangebied word. Terselfdertyd moes aandag aan die spesifieke opleiding en die aanwending van paraveterinêre personeel, waarsonder die veearts nie sy maksimum potensiaal kan bereik nie, verleen word. Hierdie hulpkragte het ook van groot belang geword weens die tekort aan veeartse en hulle gebruik is hoegenaamd nie tot die Staat beperk nie.

To a considerable extent this development and growth lacked co-ordination. As the spheres of activity overlapped, friction was inevitable. Because ours was a small profession, solutions could usually be found as between colleagues. The S.A.V.M.A. and its branches have played a significant role in smoothing the troubled waters. Now, however, the profession has grown to over 700; this makes planned co-ordination within the complexities of our modern society an urgent necessity. Efficient veterinary service to the country, with its still limited manpower, can only be rendered through planned dovetailing of our activities in the diversified spheres or fields of work. The services of individual veterinarians must be viewed as part of the whole, by the public, by the authorities, but first and foremost by members of the veterinary profession themselves.

Diagnostic laboratories are being developed to serve the public through more rapid and accurate diagnosis of diseases as well as by disclosing regional veterinary problems. They are there to serve all veterinary fields of activity. Control of meat hygiene is in the interest of the consumer as well as the stock farmer, but it can only be instituted on a national scale with the assistance of full- and part-time subsidized veterinary appointments. We are all concerned in the promotion of animal health, and the private practitioner has become particularly involved in the State's schemes, e.g., the bovine tuberculosis eradication scheme. Such collaboration is essential to the State for the execution of its functions. For the colleague in private practice it has economic advantages by bringing stability to the rural practice, which, in turn, makes veterinary services available to livestock owners in rural areas. All this is the most promising of more recent developments which must be nurtured by the profession as the starting point for more extensive and fruitful co-operation in the future.

If we are to render optimal service within our manpower limitations, we cannot allow for time and energy to be spent on duplications and the inevitable friction which it creates. We must take cognisance of the requirements of the country, the direction developments have taken and set our goal at a unified service.

In 'n groot mate het hierdie groei en ontwikkeling onbeheerd en gekoördineerd plaasgevind. Soos werksvelde mekaar begin oorvleuel het, was daár soms noodwendig 'n mate van wrywing, maar omdat die professie numeries klein was en die lede daarvan mekaar geken het, kon oplossings meesal op kollegiale vlak gevind word. In hierdie verband het die S.A.V.M.V. en sy takke 'n belangrike rol gespeel. Maar die Vereniging se lidmaatskap beloop tans meer as 700, en met die groei van die professie, die toenemende diversifisering en die kompleksiteit van die samelewing word dit egter nodig om hierdie belangrike taak met meer doelgerigte en beplande ywer voort te sit.

Afgesien van die werksveld wat die indiwiduele veearts betree, is dit noodsaaklik dat alle werkrigtings as aanvullend tot mekaar en as deel van 'n omvattende veeartsenykundige diens gesien moet word—deur lede van die professie, deur die owerheid, en deur die algemene publiek, maar veral, eerstens, deur lede van die professie self.

Streeksdiagnostiese laboratoria is nie slegs daar om die staatsveearts te bedien nie. Afgesien van ontbloting van veeartsenykundige probleme van algemene belang is hulle ook daar tot hulp van ander veeartsenykundige werkrigtings. Beheer van vleishigiëne is in belang van die verbruiker en die vleisbedryf, en kan alleen landswyd ingestel word deur Staatsubsidering van sowel deeltydse as voltydse veeartse. Almal is op een of ander wyse by dieregesondheid betrokke; by die Staat se bepaalde skemas, bv. die beestuberkuloseskema, is privaatpraktisyns die afgelope jare intiem betrek. Vir die Staat is hierdie samewerking onontbeerlik in die uitvoering van sy funksies. Vir kollegas in privaatpraktyk is daar finansiële voordeel en bring dit bestendigheid aan die praktyk. Vir die vee-eienaar, veral op die platteland, bring dit mee dat die dienste van 'n veearts beskikbaar is. Hopelik is dit alles die beginpunt van 'n grondslag waarop in die toekoms verder saamgetrek en uitgebou kan word.

Soos in ander fasette van die samelewing vandag, ondervind die veeartsenykundige dienslewering ook 'n tekort aan mannekrag. Daarom is dit nodig dat ons moet besin oor onderlinge skakeling en koördinering in ons verskillende werksvelde. Met die oog op optimale diens kan ons nie bekostig om energie en tyd te verkwis aan vermydelike oorvleueling en die gepaardgaande wrywing nie.

Matters have crystallized sufficiently for positive action, for which purpose improvement of communications within the profession is essential. Concomitantly, we must find a sound basis for the training, recognition and controlled use of paraveterinary personnel in all spheres of activity. An Association of Veterinary Technologists has already been formed and veterinary nurses will possibly be trained in the near future. Stock and meat inspectors are well established and essential for the work of the veterinarians concerned. Provision has been made in the Veterinary Act for the recognition and registration of such auxiliary personnel. As friction and other problems may result from unplanned and uncontrolled development, clear guidelines must be laid down where statutory provisions have not been made. The problems which may arise will not be as easily settled as between colleagues in the past.

Daar is nog gebrek aan voldoende en doeltreffende skakeling en koördinering binne die professie, en ons moet nou daaraan aandag verleen. Sake het ver genoeg uitgekristalliseer sodat ons dit kán doen. Die verdere ontwikkeling van 'n eenheidsdiens en -strewe wat tot voordeel van die land moet strek, vereis dat ons dit doen. Daaropvolgend moet die opleiding, erkenning en beheerde gebruik van paraveterinêre personeel in alle werksvelde op gesonde grondslag geplaas word. Die Vereniging van Veterinêre Tegnoloë bestaan reeds. Daar word beoog om eersdaags om veterinêre verpleegsters op te lei. Vleis- en veeinspekteurs bestaan reeds lank en hulle diens is vir die betrokke professionele amptenare onontbeerlik. Voorsiening word in die Veeartswet gemaak vir erkenning en registrasie van sulke hulpkragte. Vaste riglyne moet oordeelkundig neergelê word waar statutêre verpligtings en werksgebiede nie bestaan nie, want die wrywing en probleme wat as gevolg van onbeplande en onbekende ontwikkeling mag volg, kan nie meer so maklik as vroeër op kollegiale vlak geskik word **nie.**

## BOOK REVIEW — BOEKRESENSIE

# THE VETERINARY ANNUAL

C. S. G. GRUNSELL, EDITOR

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After ten most successful issues the eleventh issue of the Veterinary Annual hardly needs any introduction to the veterinary profession. It continues to provide a readable, concise review of current developments and literature in the veterinary field. Not only is it of value to practitioners who have little time to do extensive reading, but research workers will find the specific references useful. A complete subject index facilitates finding the information required.

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B.C.J.

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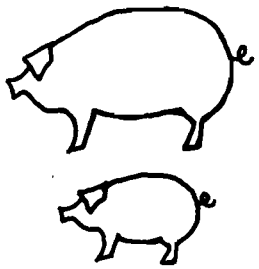

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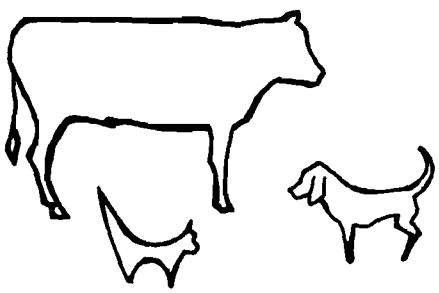

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# *SCIENTIAM COLIMUS*

## SOUTH AFRICAN ASSOCIATION OF VETERINARY TECHNOLOGISTS*

The South African Association of Veterinary Technologists was founded about two years ago. Although the various stages of technical laboratory practice date back to the days of Sir Arnold Theiler, it remained a vague concept without recognition as a definite profession. That Veterinary Technology has earned a rightful place in Veterinary Science cannot be disputed.

The designation of Veterinary Technologist was adopted, as the word Technician had become the current descriptive term applied to persons doing anything technical, mechanical or otherwise, and as such would impose limitations on the veterinary technological profession. The term has already become an accepted one in the medical field.

The Association was founded with the following aims:

(a) To promote Veterinary Technology with its own identity as a profession and to stimulate fixity of purpose, status and pride in its practice among members.

(b) To endeavour to obtain a more suitable training course.

(c) The holding of regular seminars, lectures and talks of a technical nature or interest.

(d) To establish an ethical, moral code of conduct.

The veterinary technological profession must not be seen as one of quasi-veterinarians. Tasks in a laboratory, together with the various facets of their application, e.g. serological tests, parasite identification, preparation of histological material, microbiological work, clinical pathological tests, are mainly the work of a technologist. Included is also the handling and care of laboratory animals. These duties are executed under or with the co-operation of a veterinarian.. This is where the limitations of the profession not only are outlined but already exist in practice. In the past the veterinary technologist has contributed profoundly to veterinary service in general and there is no reason why this cannot be extended in the future.

The foundation of the Association with the motto "Scientiam Colimus" is aimed at the stimulation of proficiency and pride, and a healthy liaison between the veterinary technologist and his senior, the veterinarian, with the acknowledgement of his bounds within the veterinary field.

The intentions are not to restrict these aims to veterinary technologists in the service of the state, but to extend them so as to include those working in the private sector as well.

Trained technologists are in the employ of firms manufacturing pharmaceutical products, but this service is unknown to practising veterinarians and remains a field for future development.

Whether the South African Veterinary Medical Association can accept this Association constitutionally as an affiliated body on the ground of common interest on a different level is not clear, but it is an ideal to strive for. As with all scientific bodies, the Association believes it has a contribution to make on an international level as well. It therefore welcomes the co-ordination and co-operation of all existing veterinary technological bodies, orientated under one common purpose, namely the maintenance and growth of Veterinary Technology.

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# REFRESHER COURSES IN PHARMACOLOGY

## 4. THE BIOTRANSFORMATION OF DRUGS

W. L. JENKINS*

### INTRODUCTION

During the course of any animal's life it is presented with thousands of different substances which are not nutrients and which must be removed from the body in order to maintain a normal *milieu intérieur*. Drugs which have been administered for therapeutic or prophylactic purposes are included amongst such compounds and their possible metabolic fates following absorption and intracorporeal distribution will be reviewed here.

### GENERAL CONSIDERATIONS

There are, in broad terms, two fundamental categories of foreign chemicals with which the body has to contend and which must ultimately be eliminated, namely:

(a) water soluble polar compounds which are generally not metabolized and are readily excreted unchanged;

(b) lipid soluble non-polar compounds which are metabolized to more polar compounds which are then excreted.

Thus the general principle which governs biotransformation processes is for drugs to be converted by enzymes to compounds with an ever-increasing polarity until they are polar enough to be eliminated from the body. This feature has an important consequence in renal and biliary excretion and will be discussed in the next article in this series.

From a pharmacological point of view, the biotransformation of drugs may be classified into five distinct types which may be briefly described as follows:

1. The conversion of an inactive drug into an active drug. This is a nonsynthetic biochemical reaction which leads to the activation of a drug. Examples include chloral hydrate, prontosil and parathion.
2. The conversion of an active drug into another active drug. This is also a nonsynthetic biochemical reaction which leads to an alteration in drug activity. Examples include codeine, heroin and phenylbutazone.
3. The conversion of an active drug into an inactive drug. This is once again a nonsynthetic biochemical reaction, but in this case it leads to the inactivation of a drug. Examples include barbiturates, phenothiazine derivatives, succinylcholine and many other commonly used drugs.
4. The conversion of an active drug into an inactive drug by the formation of a new, larger compound. This is a synthetic biochemical reaction and the process is usually described as detoxication. Examples include the conjugation reactions, methylation and thiocyanate formation.
5. The incorporation of an active drug into a normal body biochemical process which then becomes disrupted. This is often a synthetic reaction which is usually described as lethal synthesis and which leads to intoxication. Examples include fluoroacetate, 5-bromouracil and 8-azaguanine.

These metabolic processes are all based on enzyme-catalysed reactions which take place in various organs of the body. The nonsynthetic reactions involve oxidation, reduction or hydrolysis, whereas the synthetic reactions are based on the conjugation of an endogenous substrate with the drug or its metabolite.

It is important to realize that a drug may undergo biotransformation by more than just one of the five processes noted above. In fact, this is generally the case and the metabolites of most drugs following nonsynthetic reactions often undergo conjugation prior to being excreted from the body.

*Department of Medicine, Faculty of Veterinary Science, University of Pretoria, P.O. Onderstepoort.

### SITES OF BIOTRANSFORMATION

The enzymes involved in drug metabolism are located in many tissues, especially the liver, and may even be present in body fluids such as plasma. These enzymes or groups of enzymes characteristically are not as absolutely substrate specific as many of those in normal intermediary metabolism; they are often responsible for the metabolism of many foreign compounds within a particular chemical group. There are, however, some enzymes encountered in intermediary metabolism which do play a role in the biotransformation of drugs. The sites of the more important enzyme systems involved in drug metabolism will be discussed briefly because of their clinical significance when pathological processes interfere with their normal function.

*The Microsomal Drug Metabolizing Systems*

"Microsomes" refer to fragments of smooth-surfaced endoplasmic reticulum which are harvested by various techniques primarily from hepatic cells. These microsomal fractions consist of aggregates of enzymes with very low orders of specificity but which are generally specific for a functional group rather than for a particular substrate. Furthermore, at least a degree of lipid solubility appears to be a necessary property for a drug to react with microsomal enzymes; the product of the reaction is usually a more polar water-soluble compound. The microsomal enzymes catalyse many of the nonsynthetic and synthetic biotransformation reactions noted above. These enzymes have a requirement for TPNH, molecular oxygen, magnesium ions and nicotinamide. Furthermore, an unusual cytochrome termed P-450 also plays a key role.

*Mitochondrial and Soluble Fraction Enzyme Systems*

There are enzymes present in the mitochondria and in the soluble fraction of various cells, which may also play a role in the biotransformation of drugs. These enzymes are usually those involved in normal metabolic processes and thus have natural substrates. It is, in fact, simply fortuitous that they metabolize some foreign compounds. Examples of this type of enzyme include alcohol dehydrogenase, aldehyde dehydrogenase, monoamine oxidase, purine nucleotide phosphorylase and xanthine oxidase.

*Plasma Enzymes*

Esters and amides frequently undergo hydrolysis within the body. The enzymes responsible are often present in the plasma as well as in the tissues. A good example of such a plasma enzyme which plays a significant role in drug metabolism is pseudo- or nonspecific cholinesterase which is responsible for the hydrolysis of drugs such as procaine and succinylcholine.

Although the liver is the major organ involved in drug biotransformation, other tissues may, in certain cases, make considerable contributions. The most noteworthy amongst these are kidney, intestine, skin, lung, muscle and nervous tissue.

From the above discussion it should be apparent that, following the absorption and intracorporeal distribution of a drug, biotransformation will take place as the compound is presented to appropriate enzyme systems. This process will continue until all the remaining drug has been metabolically altered to the forms which are excreted.

### CHEMICAL PATHWAYS OF DRUG METABOLISM

The clinical significance of drug biotransformation really revolves around the factors which may influence the process and for this reason the possible chemical pathways of drug metabolism will simply be listed here. Readers may refer to the suggested texts for any detailed information required.

*Oxidative Transformations Mediated by the Liver Microsomal Enzymes*

(a) Side-chain (aliphatic) oxidation, e.g. barbitone —> hydroxybarbitone.

(b) Aromatic hydroxylation,
e.g. acetanilid —> p-hydroxyacetanilid.

(c) N-dealkylation, e.g. morphine —> normorphine.

(d) O-dealkylation, e.g. codeine —> morphine.

(e) S-demethylation,
e.g. 6-methylthiopurine —> 6-mercaptopurine.

(f) Oxidative deamination, e.g. amphetamine —> phenylacetone.

(g) Sulphoxidation, e.g. chlorpromazine —> chlorpromazine sulphoxide.

(h) Desulphuration, e.g. parathion —> paraoxon.

(i) N-oxidation, e.g. trimethylamine —> trimethylamine N-oxide.

*Oxidative Transformations not Mediated by the Liver Microsomal Enzymes*

(a) Alcohol and aldehyde oxidation, e.g. ethanol —> acetaldehyde —> acetic acid. Alcohol dehydrogenase and aldehyde dehydrogenase are rather nonspecific enzymes found in the soluble fraction of the liver.

(b) Monoamine oxidase (MAO) recations. Monoamine oxidase is a relatively nonspecific mitochondrial enzyme whose potential substrates include both endogenous and foreign compounds. Examples include the catecholamines, tyramine and serotonin.

(c) Diamine oxidase (DAO) and histaminase reactions. These enzymes catalyse the oxidation of the terminal amine in a number of di-amines and may be found in the soluble fraction and in plasma.

(d) Purine oxidation,
e.g. theophylline —> methyl- and dimethyluric acid. Xanthine oxidase is the enzyme which appears to participate in this type of reaction.

(e) Dehalogenation,
e.g. DDT —> DDE.
Dehalogenation reactions include displacement by a hydroxyl group, splitting out of hydrogen halide and displacement by an acetylcysteine residue (mercapturic acid formation).

*Reductive Transformations Mediated by Microsomal Enzymes*

(a) Azo-reduction,
e.g. prontosil —> sulphanilamide.

(b) Nitro-reduction,
e.g. chloramphenicol —> reduction product.

The enzyme systems that reduce azo- and nitro- compounds are present mainly in the liver but are also found in other tissues.

*Hydrolytic Reactions*

Drug metabolism by hydrolysis is primarily restricted to esters and amides, i.e. esterases and amidases.

In general, esters are subject to hydrolysis by enzymes in the blood, liver, kidney and other tissues. Examples of drugs which undergo cleavage by esterases, with loss of pharmacological activity, include the following: atropine, cocaine, procaine, pethidine, succinylcholine and methacholine.

Amides are frequently hydrolysed more slowly than alcohol esters and advantage is taken of this in therapeutics, e.g. the use of procainamide rather than procaine as an antiarrythmic drug.

Esterase and amidase action does not always inactivate drugs. Many drugs are administered as esters, and enzymatic hydrolysis, either within the body or the gastro-intestinal tract, liberates the active principle. Examples of such drugs include cortisol succinate, chloramphenicol palmitate and phthalyl- and succinylsulphathiazole.

Glucosidases are also hydrolytic enzymes which play a role in the biotransformation of cardiac glycosides and the anthraquinone purgatives.

*Synthetic (Conjugation) Reactions*

Conjugating enzymes occur mainly in the liver but also in other tissues, particularly the kidney.

(a) Glucuronic acid conjugation.
In the synthesis of glucuronides, uridine diphosphate—glucuronic acid serves as a donor of glucuronic acid to various acceptors, the enzymes mediating the process are called transferases. Normal constituents of the body that are conjugated with glucuronic acid include bilirubin, thyroxine and steroid hormones. Examples of compounds which undergo glucuronidation include phenols, primary, secondary and tertiary alcohols, carboxylic acids, aromatic amines and drugs containing a sulphydryl group.

(b) Amino acid conjugation.
(i) Acetylation reactions, e.g. acetylation of sulphonamides. Acetylation usually involves the conjugation of acetyl coenzyme A with an acceptor amine.

(ii) Glycine conjugation,
e.g. salicylic acid —> salicyluric acid.

(iii) Mercapturic acid formation,
e.g. nitrobenzene —> p-nitrophenylmercapturic acid.

(iv) Glutamine conjugation.
Glutamine conjugation is confined to man and the arthropoid apes and the compounds involved are usually arylacetic acid.

(v) Other amino acid conjugations.
A few compounds are conjugated with serine and lysine; ornithine conjugation occurs in birds and reptiles.

(c) Sulphate conjugation.
Aromatic and aliphatic hydroxyl groups and certain amino groups may react with an activated form of sulphate to form compounds known as "ethereal sulphates". Examples of drugs which undergo sulphate conjugation include simple phenols, phenolic steroids, alcoholic steroids and chloramphenicol.

(d) N-, O- and S-methylation.
Methylations proceed by a pathway in which S-adenosyl-methionine serves as a methyl donor. A good example of this type of conjugation reaction is the inactivation of noradrenaline and adrenaline by the enzyme catechol O-methyltransferase.

(e) Transsulphuration.
An important example of a transsulphuration reaction is encountered in the metabolism of cyanide in which the cyanide ion is converted to thiocyanate by a mitochondrial sulphurtransferase which was formerly called "rhodanese".

## FACTORS INFLUENCING THE BIOTRANSFORMATION OF DRUGS

Since the metabolism of drugs is carried out by means of enzymes, then, if the enzymes are influenced in any way, drug metabolism can be altered. Many of the factors which may play a role are of very great practical significance.

### *Species differences*

In many cases there seems to be little difference between species in the pharmacodynamic response to drugs. Nevertheless, great interspecies differences exist regarding the biotransformation of drugs. A few examples will serve to illustrate this most important concept. Dogs are unable to acetylate aromatic amines, cats do not readily form glucuronides and guinea pigs can not acetylate arylcysteines. Furthermore, there are widely different rates of drug metabolism between species and thus the duration of pharmacological effects will vary. Finally it should be noted that different species may metabolize the same drug by different pathways simply because of variations in the enzymes which are available.

These considerations should serve as a constant reminder to the danger of extrapolation of drug data between our domesticated animal species.

### *Genetic variation in drug metabolism*

Pharmacogenetics is a very new research field. Nevertheless, a number of genetic or strain differences have already been recognized and it is likely that many more may exist. Once again examples will serve to illustrate the significance of genetic differences. There are strain differences in the hexobarbitone sleeping times in mice. Atropine esterase only occurs in certain rabbits. Defects in glucuronide synthesis have been noted in certain rat strains and in man. A hereditary defect involving an atypical pseudocholinesterase and other variants of plasma cholinesterase occurs in man: in affected individuals the duration of action of succinylcholine is markedly increased. Similarly the phenomenon of slow acetylation of isoniazid in humans results from a genetically determined amount of liver acetyl transferase.

### *Age*

The drug-metabolizing microsomal enzymes are either absent or present in neglible amounts in the immature liver of a newborn animal. Thus the neonate is more sensitive to drugs than is the adult of any species: in general it requires a period of about four to six weeks before microsomal enzyme activity attains approximate adult levels.

This situation has important clinical implications. Neonates are likely to be more sensitive to some drugs than are adults and therefore liable to show more prolonged effects when given a drug at an equivalent dosage rate. Furthermore, a drug that is relatively harmless to a dam may cross the placenta and have an adverse effect on the foetus. In obstetrical practice it should always be remembered that after parturitition the newborn no longer has the use of the maternal liver system to metabolize drugs, so that very prolonged effects may be encountered.

The effects of old age on drug metabolism have not been studied extensively but it is a sound general principle to utilize the lowest effective drug dosage possible in very old animals.

*Sex*

Sex differences in the rate of drug metabolism have been demonstrated in a few instances. The hexobarbitone sleeping time in certain strains of rats and mice is very much longer in the females than in the males. Similarly, where toxic metabolites are formed from parent compounds, e.g. aldrin, the females appear to be somewhat less sensitive. These differences can be reversed by pretreatment with the appropriate hormones.

It is also well known that stallions have a higher susceptibility to poisoning by *Senecio* spp.

*Other physiological conditions*

It has been observed that during pregnancy the activity especially of the conjugating reactions may decrease. There is also recent evidence that the endocrine status of an animal may influence drug metabolism to some degree. The adrenal steroids, thyroid hormone, oestrogens, progestagens and androgens may all play a role.

*Nutritional status*

A very important dependence of drug-metabolizing enzyme activity on nutrition has been frequently demonstrated. The availability of adequate liver glycogen, protein for enzyme synthesis and vitamins and minerals as biochemical co-factors, is essential for optimum biotransformation. These factors should always be considered when dealing with an undernourished or starved patient.

*Pathological conditions*

Depression of the microsomal drug-metabolizing systems and other biotransformation enzymes can be expected in pathological states where there is a deleterious effect on liver function. Examples of such conditions would include hepatitis, liver cirrhosis, hepatocellular damage due to poisons and toxins, obstructive icterus, hepatic neoplasmata and diabetes mellitus. In addition, pathological changes in other organs which may play a role in drug metabolism will have a similar effect. It is noteworthy, however, that these effects are not invariably present and that recovery may also completely reverse the impaired enzyme function.

*Inhibition of drug metabolism*

If the drug-metabolizing systems, particularly the liver microsomal enzymes, are depressed, excessive or prolonged responses may occur to ordinary doses of drugs. The exception will be for those drugs whose effectiveness or toxicity is enhanced by metabolic biotransformation, in which case the drug effect will be reduced.

Several compounds inhibit drug metabolism in animals. These include "SKF 525A" (a drug often used experimentally) and many drugs commonly used in clinical practice. Examples of the latter include the following documented instances. Tolbutamide metabolism is depressed if bishydroxycoumarin is administered simultaneously. The p-hydroxylation of phenytoin in man is inhibited by the concurrent administration of phenylbutazone, p-aminosalicylic acid or disulfiram. Both stimulation and inhibition of drug biotransformation have been observed in animals treated with steroid hormones.

There are also more obvious mechanisms of inhibition of drug metabolism which are therapeutically useful. Examples here include the monoamine oxidase inhibitors which delay the metabolism of noradrenaline, adrenaline and serotonin, and the use of disulfiram in alcoholism to inhibit the conversion of acetaldehyde to acetic acid.

Drugs such as chloramphenicol, morphine, pethidine, isoniazid and chloral hydrate have also been incriminated as depressants of liver microsomal enzyme activity.

These findings obviously suggest great caution in multiple drug therapy of any kind.

*Stimulation of drug metabolism*

If the activity of microsomal enzymes is stimulated, the result would be that drugs will be metabolized much more rapidly and their plasma halflives will be reduced. This would lead to a shorter drug effect time in most cases, except in those instances where a drug metabolite is more active than the parent compound.

The activity of these enzymes can, in fact, be markedly increased by treatment with a large number of commonly used drugs, insecticides, herbicides, polycyclic hydrocarbons, carcinogens and even endogenous compounds. This stimulating effect is known as "microsomal enzyme induction" and the process is

associated with increased liver weight, increased synthesis of microsomal protein and cytochrome P-450. Electron photomicrographs show that there is an increase in the amount of smooth endoplasmic reticulum in the liver cells. It should, however, be noted that enzyme induction may also occur in other tissues.

A fundamental and important concept to be appreciated is that a drug may stimulate its own metabolism or that of many other drugs.

A wide variety of drugs in common use may increase the activity of drug-metabolizing enzymes in animals. A few of the more important compounds will be listed here: barbiturates, phenylbutazone, chlorinated hydrocarbons, androgens, adrenocorticoids, diphenhydramine, primidone and phenytoin. In many cases it may take three to four months for the microsomal enzymes to return to pretreatment levels.

The pharmacological significance of this phenomenon revolves around the development of tolerance and the reduction of therapeutic effect unless larger and more frequent doses are given. In addition, clinical trials may be very difficult to interpret if the drugs studied are inducing agents.

Induction can be clinically useful and phenobarbitone and DDT have been utilized to promote the conjugation of bilirubin in neonatal hyperbilirubinaemia and familial unconjugated jaundice in man.

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## ANNOUNCEMENT OF PUBLICATIONS

## AANKONDIGING VAN PUBLIKASIES

# SPECIAL PUBLICATIONS OF THE INDEX-CATALOGUE OF MEDICAL AND VETERINARY ZOOLOGY

The National Animal Parasite Laboratory of the U.S. Department of Agriculture has begun a series of Special Publications as part of the Index-Catalogue of Medical and Veterinary Zoology. These will be sent as a matter of course to the Index-Catalogue's regular mailing list, and to other interested scientists upon request.

*Special Publication No. 1,* a Checklist of the Internal and External Parasites of Deer, *Odocoileus hemionus* and *O. virginianus,* in the United States and Canada by Martha L. Walker and the late Willard W. Becklund, appeared in 1970, and is now available.

*Special Publication No. 2,* a comprehensive, subject-indexed bibliography on Chagas Disease is being prepared under the direction of Dr. Louis Olivier, in collaboration with the Pan American Health Organization, and should be ready for distribution in 1971.

*Special Publication No. 3,* Ticks and Tick-Borne Diseases, is being compiled under the direction of Dr. George Anastos and Miss Mildred A. Doss of the University of Maryland and will probably be published in 1972.

*Special Publication No. 4,* a bibliography on Piroplasmosis, is in the early stages of preparation. Any suggestions on format or content will be welcomed, as would any personal bibliographies or available reprints. Please contact: Martha L. Walker, Index-Catalogue of Medical and Veterinary Zoology, National Animal Parasite Laboratory, Veterinary Sciences Research Division, Agricultural Research Center, Beltsville, Maryland 20705.

Jl S. Afr. vet. med. Ass. 42 (3): 217-221 1971

# THE PASSAGE OF *COWDRIA RUMINANTIUM* IN MICE

J. L. DU PLESSIS* AND N. A. L. KUMM*

SUMMARY

The white mouse was found to be susceptible to a strain of *Cowdria ruminantium* (Cowdry, 1925) isolated from a goat. The organism was passaged for more than 20 generations in mice by subinoculation of spleen and liver suspensions via the intraperitoneal route. The mice consistently died from 10 to 14 days after injection. Sixteen susceptible sheep inoculated intravenously with similar material developed pronounced febrile reactions 8 to 10 days later and 6 died or were destroyed. After 23 passages there was no indication of attenuation of the organism for mice or sheep.

The organism passaged in mice was identified as *C. ruminantium* by demonstration of Rickettsia-like colonies in mouse spleen and liver impression smears and in sections of the liver, spleen and lung, as well as in brain smears of the six sheep which succumbed after inoculation with mouse tissues. The fact that the surviving sheep were partially immune to challenge with infective sheep blood harbouring a different strain of *C. ruminantium*, provided supporting evidence.

## INTRODUCTION

Attempts to propagate *C. ruminantium* in guinea pigs, rabbits, rats and mice have hitherto been unsuccessful[1]. Mason and Alexander[1] reported the susceptibility of the ferret to this organism. Buffy coat prepared from infective blood and administered intraperitoneally was used as inoculum. They observed no modification in virulence for sheep after five ferret passages. Adelaar in a personal communication to Haig[2], stated that the virulence of this organism for ferrets increased with continued passage and that there was no attenuation for sheep.

## MATERIALS AND METHODS

*Mice.* Twelve white mice, 3 weeks old, were infected with *C. ruminantium* by the intraperitoneal inoculation of a saline suspension of mesenteric lymph nodes from a sheep reacting to an intravenous injection of lymph node suspension obtained from a goat that had acquired the disease naturally (goat strain). Two further groups of mice were similarly inoculated intraperitoneally with lymph node suspensions from two other sheep harbouring respectively the Ball 3 strain and a Hammanskraal strain of *C. ruminantium.*

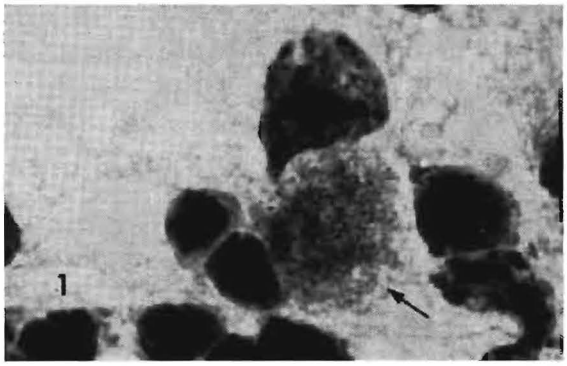
When the mice started dying 10 days later, separate suspensions of spleen and liver were prepared from moribund mice in buffered lactose peptone (181 g $Na_2HPO_4$, 26,4 g $KH_2PO_4$, 30 l distilled water, 2% Difco peptone, 10% lactose) and 0,2 ml inoculated intraperitoneally into two groups of 12 three weeks old mice. Serial liver and spleen passages were subsequently made and are still being continued.

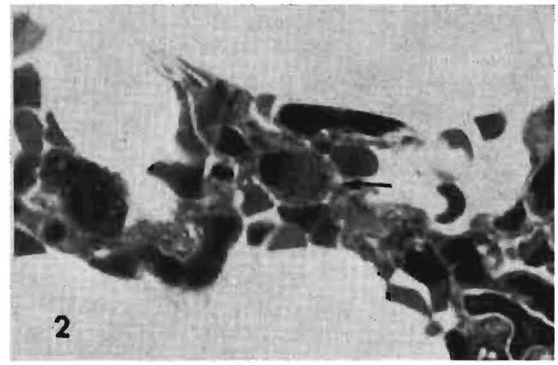
Smears and sections from the mice were examined for evidence of infection. Impression smears were prepared from liver and spleen and crush-smears from brain and were stained with Giemsa. Portions of liver, spleen, lung, kidney and brain were fixed in 10% buffered formalin, sectioned and stained with haematoxylin-eosin and Giemsa. Sections were also prepared from liver, spleen and lung fixed in 4% glutaraldehyde, post-fixed in buffered 2% osmium tetroxide and embedded in araldite. Sections, 0,5 to 1 $\mu$m thick, were stained with Giemsa.

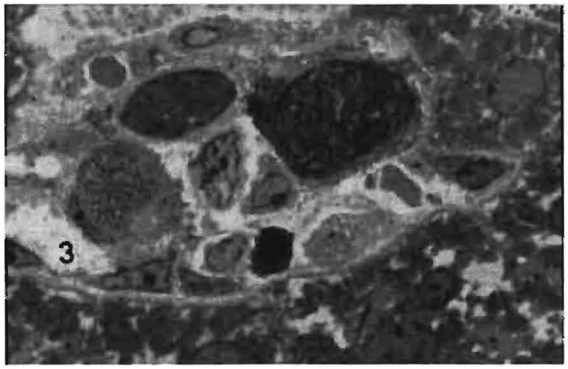
The infectivity of the agent in spleen and liver was titrated in two groups of mice after 22 passages by inoculating them with 0,2 ml of $10^{-1}$ to $10^{-4}$ dilutions of the organ concerned.

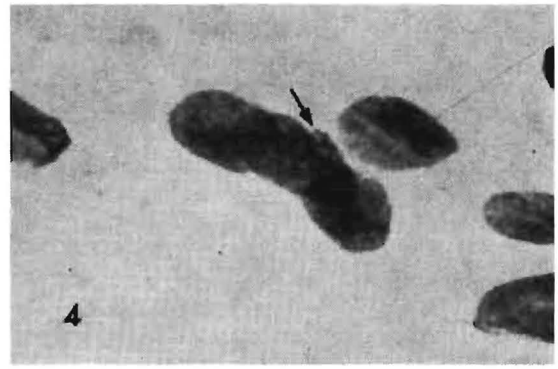
*Sheep.* From time to time spleen and liver suspensions from moribund mice were inoculated intravenously into susceptible sheep (Table). At the height of the temperature

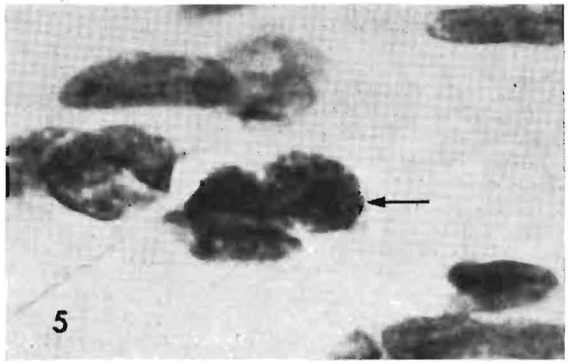
*Section of Pathology, Veterinary Research Institute, Onderstepoort.

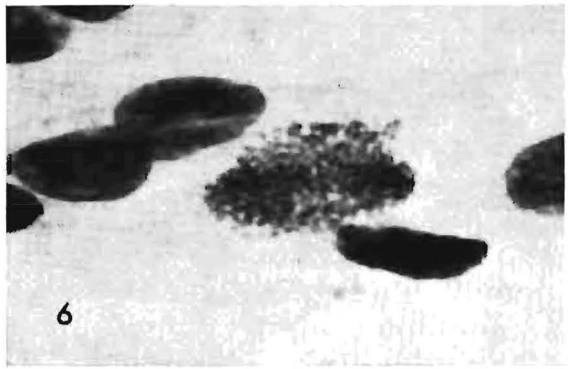


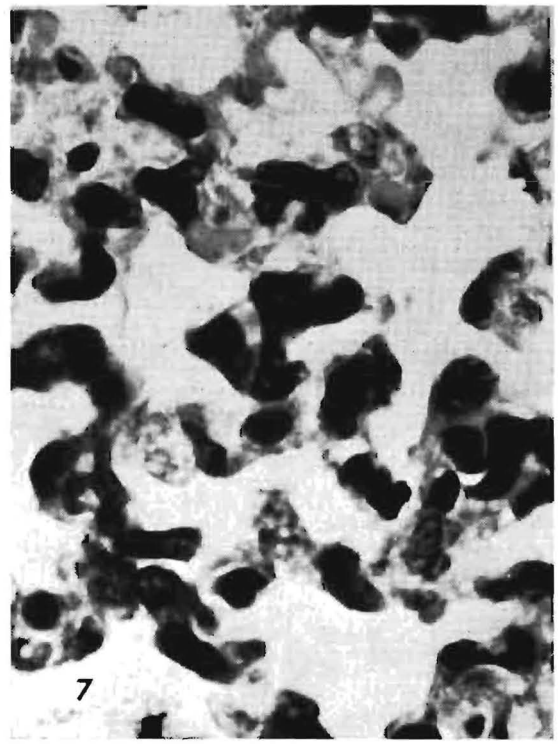



Table: RESULTS OF SHEEP INOCULATED WITH MOUSE LIVER AND SPLEEN AND SUBSEQUENTLY CHALLENGED WITH HEARTWATER BLOOD

*E.g. 8/4/105,4 = Febrile reaction commenced on 8th day after inoculation of infective material, lasted for 4 days and reached a maximum of 105,4°F.

| Sheep No. | Passage level in mice | Infective inoculum | Reaction | Challenge | Reaction |
|---|---|---|---|---|---|
| 1 | 3 | 10 ml mouse liver | 8/4/105,4* | 10 ml infective sheep blood | 10/7/106,6 |
| 2 | 6 | 10 ml „ „ | 9/11/107 | 10 ml „ „ „ | 11/5/106,8 |
| 3 | 8 | 10 ml „ „ | 10/12/107,2 | 10 ml „ „ „ | 13/4/106 |
| 4 | 9 | 10 ml „ „ | 9/7/107,6. Killed | | |
| 5 | 9 | 10 ml mouse spleen | 6/9/107,8. Killed | 10 ml „ „ „ | |
| 6 | 11 | 5 ml „ „ | 15/3/105,6 | 10 ml „ „ „ | 8/6/107. Died |
| 7 | 11 | 10 ml mouse liver | 9/11/106,4 | | 10/4/107 |
| 8 | 13 | 5 ml mouse spleen | 9/3/106,4. Died | 10 ml „ „ „ | |
| 9 | 13 | 10 ml mouse liver | 8/5/107,2 | | 10/6/107,6 |
| 10 | 14 | 5 ml mouse spleen | 6/5/106,6. Died | | |
| 11 | 15 | 5 ml „ „ | 7/8/107,4. Died | 10 ml „ „ „ | |
| 12 | 15 | 5 ml „ „ | 6/7/106,8 | 10 ml „ „ „ | 10/10/108 |
| 13 | 16 | 10 ml mouse liver | 13/6/108 | | No reaction |
| 14 | 17 | 5 ml mouse spleen | 10/3/106,6. Died | | |
| 15 | 17 | 5 ml „ „ | 12/3/108 | 10 ml „ „ „ | 10/4/107 |
| 16 | 19 | 5 ml „ „ | 10/7/108 | 10 ml „ „ „ | 11/2/104,2 |
| 17 | — | 10 ml infective sheep blood | 10/4/107,8 | 5 ml mouse spleen | 11/5/108 |
| 18 | — | 10 ml „ „ „ | 6/7/107,4 | 5 ml „ „ | 11/4/107,6 Died |
| 19 | — | 10 ml „ „ „ | 6/7/107 | 5 ml „ „ | 12/5/107 Died |

*E.g. 8/4/105,4 = Febrile reaction commenced on day 8 after inoculation of infective material, lasted 4 days and reached a maximum of 105,4°F.

reaction, blood from one of the sheep was subinoculated into three sheep. One was susceptible to heartwater, the second immune to the Ball 3 strain of heartwater and the third had survived a previous infection with mouse spleen.

The sheep that survived inoculation with mouse organs were challenged from three weeks after the reaction with infective citrated blood, employing the Ball 3 strain (Table). At the same time two fully susceptible sheep were inoculated with the infective blood used for the challenge.

Three sheep, which had survived infection with the Ball 3 strain of heartwater after treatment with oxytetracycline, were challenged with a suspension of infective mouse spleen (Table).

## RESULTS

*Mice.* The first group of mice inoculated with the goat strain and the mice of the subsequent passages died from 10 to 14 days after inoculatioon. In the case of the Ball 3 and Hammanskraal strains no deaths occurred and no symptoms were observed.

Lesions consistently observed at autopsy after inoculation with the goat strain were splenomegaly and hydrothorax. Rickettsial colonies were observed in Kupffer cells of the liver and reticulum cells of the spleen in impression smears (Fig. 1). They could not be demonstrated in brain smears. In histological sections intracellular organisms were seen in alveolar capillary endothelial cells of the lung (Fig. 2), in reticulum cells of the spleen and in Kupffer cells of the liver (Fig. 3). A moderate degree of pneumonitis was in evidence in the lungs of the mice (Fig. 7).

The $LD_{50}$ of both spleen and liver of moribund mice was $10^{-2,4}/0,2$ ml as determined by the method of Reed and Muench[3].

*Sheep.* Of the 16 sheep inoculated with either mouse liver or spleen, four died, two were destroyed *in extremis* and 10 survived,

LEGENDS

FIG. 1. Rickettsial colony in mouse spleen smear. Giemsa.
FIG. 2. **C. ruminantium** in mouse alveolar endothelial cell. Araldite section, Giemsa, X1200.
FIG. 3 Two rickettsial colonies in Kupffer cells of mouse liver. Araldite section, Giemsa. 1200.
FIG. 4, 5 and 6. **C. ruminantium** in endothelial cells in brain smears of sheep. Giemsa.
FIG. 7. Pneumonitis in section of mouse lung in response to infection by **C. ruminantium**. H. & E. X1200.

six after treatment with oxytetracycline (Table). *Post-mortem* examination of the six sheep revealed lesions which closely resembled those usually seen in heatrwater but which were usually less pronounced. These lesions were: moderate to marked tumour splenis, slight to moderate hydrothorax and hydropericardium and moderate pulmonary oedema. Brain smears contained a small number of rickettsial colonies, which were small and, in many cases, poorly defined (Figs. 4 and 5).

The results of the cross-immunity tests between the goat strain passaged in mice and the Ball 3 strain are also shown in the table. One of 10 sheep inoculated with mouse material succumbed to a subsequent challenge with the Ball 3 strain, whereas nine withstood the challenge. Most of them developed pronounced febrile reactions, but no other signs of illness were seen. Two susceptible sheep inoculated with infective blood used for the challenge, died of heartwater.

Sheep 18 and 19, which were immune to the Ball 3 strain, died after being challenged with a suspension of infective mouse spleen, whereas sheep 17 survived. Autopsy revealed lesions similar to those seen in sheep inoculated with infective mouse organs only.

Blood from a sheep reacting to mouse passage material produced fatal heartwater in a susceptible sheep. At autopsy lesions were typical of heartwater and a small number of typical rickettsial colonies were demonstrated in the brain smear (Fig. 6). The injection of blood from the same donor into a sheep immune to the Ball 3 strain resulted only in a moderate febrile reaction. A sheep which had survived a previous inoculation with infective mouse spleen proved to be solidly immune to a similar challenge.

## DISCUSSION AND CONCLUSIONS

Evidence in favour of the fact that *C. ruminantium* was the infective agent passaged in mice, was the consistent demonstration of Rickettsia-like organisms in their spleen and liver impression smears as well as in sections of the lung, liver and spleen. Furthermore, the inoculation of mouse spleen and liver passage material into 16 susceptible sheep constantly resulted in a temperature rise in all the sheep and death of four sheep (40%) that were not treated. Lesions indistinguishable from, but milder than those of classical heartwater, were observed. In these cases the brain smears differed from those of typical heartwater in that the rickettsial colonies were rare and of relatively small size.

Confirmation that the infective agent passaged in mice was *C. ruminantium* was provided by the fact that its inoculation into susceptible sheep conferred partial immunity to a challenge with the virulent Ball 3 strain. None of the challenged sheep was treated during the febrile reaction. Although the animals developed a febrile reaction as result of the challenge, it was considered that they were partially immune, as susceptible sheep challenged with the same blood consistently died of heartwater.

A possible explanation for the febrile reaction of the challenged sheep is that the two strains were not antigenically identical. This may also explain the death of two of the three sheep immune to the Ball 3 strain that were challenged with infective mouse spleen. In an homologous challenge, however, a solid immunity was present. It is also possible that a modification in the antigenic structure of *C. ruminantium* could have occurred during the passage in mice. Although the goat strain was perhaps antigenically identical to the Ball 3 strain before its passage in mice, it could have been altered subsequently and hence did not confer a solid immunity to a challenge with the Ball 3 strain. This possibility is supported by the fact that in an earlier attempt to passage the Ball 3 strain in mice, it was found that after three passages, sheep inoculated with mouse material were only partially immune to a challenge with the mother strain [4].

There was also a difference in the three strains dealt with in these experiments as far as their infectivity to mice was concerned. Whereas the goat strain readily infected and killed mice, inoculation of lymph node suspensions from sheep reacting to the Ball 3 and the Hammanskraal strains failed to establish infection in mice . Although the possibility that an agent lethal to mice was passaged simultaneously with *C. ruminantium* was not investigated specifically, it is highly probable that the latter was responsible for the regular mortalities in mice.

It is noteworthy that there was no definite evidence of attenuation of the organism for mice or sheep after 23 passages in mice.

ACKNOWLEDGEMENT

We thank Mr. A. M. du Bruyn for photography.

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## BOOK REVIEW BOEKRESENSIE

# INFECTIOUS DISEASES OF WILD MAMMALS

JOHN W. DAVIS, LARS H. KARSTAD AND DANIEL O. TRAINER, EDITORS

First edition. The Iowa State University Press, Ames, Iowa, Pp. XI and 421. and: Baillière, Tindall & Cassell, Ltd., London.

Price $18.00/£10.50.

This excellent book on the infectious diseases of wild mammals fills a dire need by condensing the rapidly expanding information on the subject into an easily accessible, up-to-date form. It will be a most useful addition to the library of anyone who is interested in the diseases of wild animals, no matter from what point of view.

Forty-two authors, all well-known specialists in their fields, have contributed. The subject matter has been divided into four major portions: Part 1 deals with 22 viral diseases, Part 2 with 27 bacterial, rickettsial and mycotic diseases, Part 3 with skin tumors of deer and Part 4 with the effects of toxic substances on wild mammals. Although no excuse is offered for inclusion of the latter topic in this book on infectious diseases, it is a useful contribution.

The 43 chapters each give a brief definition of the disease (or diseases) considered, followed by particulars on the history, distribution, epizootiology, clinical signs, pathology, immunity, diagnosis, treatment and control. A list of selected references concludes each chapter. Where appropriate, a vast amount of information on the host range is condensed into most useful tables.

Since only one of the authors is not resident on the North American continent, it is perhaps not surprising that most chapters have a distinct geographical bias. In mitigation it must be conceded that most of the work in this field is being done in the U.S.A. A notable omission from the viral diseases is African swine fever, a much more important disease than hog cholera. Heartwater is another important African disease that might well have been included.

Typographical and factual errors, such as the statement that sheep are refractory to *A. marginale* infection, are rare and do not detract from the overall excellence of the book.

R.D.B.

Jl S. Afr. vet. med. Ass. 42 (3): 223-226 1971

# VIBRIONIC ABORTION IN EWES IN SOUTH AFRICA: PRELIMINARY REPORT

A. P. SCHUTTE*, E. E. MCCONNELL** AND P. P. BOSMAN***

SUMMARY

An outbreak of ovine vibriosis, thought to be the first recorded in South Africa, ran a course similar to that reported from elsewhere, namely a sudden outbreak of abortions near or at term, still-births and post-natal deaths, initially affecting about 40% of the lambs and tailing off subsequently. The total mortality for the lambing season was 17%, dropping to zero for the next one.

The organisms isolated from one submitted abortus and from cases produced experimentally by this isolate were identified as *Vibrio fetus*, resembling *V. fetus intestinalis* biochemically, except for producing small amounts of $H_2S$ on cystine-free media, but with no serological relationship to bovine *V. fetus* strains.

Macroscopic focal necrotic hepatitis was present in the submitted abortus. In the experimental cases only microscopic evidence of a similar focal coagulative necrosis could be found. Large areas of necrosis accompanied by a purulent exudate were observed in many of the cotyledons.

## INTRODUCTION

Ovine vibriosis, a disease characterized by late abortions, full-term dead lambs, or the birth of weak lambs, has been recorded in various parts of the world[1]. It occurs as an enzootic of sudden outbreaks with abortion rates of 5 to 70% (average 25%), which then stops abruptly and occurs only rarely in successive seasons. Unlike bovine vibriosis, where transmission occurs mainly through coitus, this disease in sheep spreads by oral ingestion of infected material[2-6]. It has also been postulated that other vectors, such as birds, as well as immune carrier ewes, may perpetuate the infection[6-12]. This report describes a recent outbreak of the disease thought to be the first recorded in the Republic of South Africa.

## HISTORY OF OUTBREAK

The first abortions occurred in August, 1970, on a farm in the Memel district of the Orange Free State, in a flock of 550 merino ewes. Seven ewes aborted about one week prior to expected lambing. The lambs were at full term or slightly premature. Some were born dead, while others were alive but died soon after birth. Of the first 50 lambs born, about 20 were dead or died soon after birth. This initially high mortality rate of about 40% tailed off subsequently: a total lamb mortality rate of 17% (88/515) was registered for that season. No abortions were recorded during the following lambing season.

Two of the first seven aborted lambs were referred to Onderstepoort by a practitioner (Dr. S. D. Cilliers) of Ingogo, Natal.

## MATERIAL AND METHODS

The first foetus, about two weeks premature, was in an advanced state of decomposition, negating significant *post mortem* findings. The other foetus appeared to be at full term and was still covered by the foetal membranes. These were dessicated, making pathological examination impossible. The foetus itself, however, was in an excellent state of preservation, evidently having been aborted soon after death. A complete necropsy was conducted and the liver was collected for bacteriological and histopathological examination.

*Department of Genesiology, Faculty of Veterinary Science, University of Pretoria, P.O. Onderstepoort.

**Major, USAF, VC, Staff member of the Geographic Pathology Division, Armed Forces Institute of Pathology, Washington, D.C., Temporarily assigned to the Section of Pathology, Veterinary Research Institute, Onderstepoort.

***Section of Artificial Insemination, Veterinary Field Services, Onderstepoort.

*Isolation of organism*

A small quantity of material from the foetal liver was plated onto brilliant green cystine heart agar [13] and thioglycolate blood agar plates [14]. These were incubated at 37°C in McIntosh jars from which $\frac{2}{3}$ of the atmosphere had been evacuated and replaced by a gaseous mixture of 95% nitrogen and 5% $CO_2$. Plates were examined for growth after three and five days.

*Identification of organism*

Vibrio-like colonies were checked for catalase activity (rapid slide method, Florent [13]) and wet preparations examined with a phase contrast microscope for motility and morphology.

Vibrio isolates were also checked biochemically against known strains of *Vibrio fetus venerealis* and *Vibrio fetus intestinalis*. Albimi broth plus 0,2% agar was used as basal medium for all biochemical tests. The serologic relationship to known *Vibrio fetus* strains was examined by a fluorescent antibody technique previously described for the identification of *Vibrio fetus* carrier bulls [14].

The isolates, which were classified as *Vibrio fetus*, were lyophylized and stored at 5°C for further studies.

*Experimental transmission*

Four clinically healthy merino ewes, selected at random from available experimental stock, were mated to rams. Three to four months later, all four were infected intravenously with 4 ml saline suspension (opacity: Wellcome tube No. 5) prepared from the Vibrio isolates cultivated as previously described.

The aborted foetuses were autopsied, and specimens from the following tissues and organs were collected: For histological examination: mesenteric lymph nodes, spleen, heart, lung, liver, kidney, stomach, small intestine, large intestine, skeletal muscle, brain and placenta. For bacteriological examination. mesenteric lymph nodes, spleen, heart, lung, liver, kidney, gallbladder contents, brain, stomach contents and placenta.

## RESULTS

The Vibrio-like organisms isolated from the liver of the submitted aborted lamb, as well as those isolated from lambs aborted following experimental infection, proved to be *Vibrio fetus*. They resembled *Vibrio fetus intestinalis* biochemically, except for producing small amounts of $H_2S$ on media without cystine (Table). No serological relationship to bovine *Vibrio fetus* strains could be demonstrated.

Two of the four infected ewes aborted. The first after 9 days and the second after an 11-day interval. The third ewe lambed normally 46 days after exposure, while the remaining ewe was not pregnant. All ewes remained clinically healthy until slaughtered three months later.

Macroscopic lesions were confined to the liver of the submitted foetus. It contained numerous focal, circular, tannish orange, necrotic areas 0,5 to 1,5 cm in diameter, randomly scattered over the diaphragmatic surface (Figure). The periphery of each area was slightly raised, which gave the darker centre an umbilicated appearance. On cutting through the lesions, they were found to extend into the parenchyma to a depth

Table: A COMPARISON BETWEEN THE BIOCHEMICAL CHARACTERISTICS OF VIBRIOS ISOLATED FROM SHEEP AND CATTLE

| | Catalase activity | $H_2S$ production | | Growth in 3,5% NaCl | Glycine tolerance | | Deep stab culture (Thiol+ Agar) | Aerobic growth |
|---|---|---|---|---|---|---|---|---|
| | | −Cystine | +Cystine | | 1,0% | 1,5% | | |
| **Vibrio fetus** isolated from aborted ovine fetus | + | + | + | − | + | − | − | − |
| **Vibrio fetus** isolated from lambs and vaginal secretions of ewes following experimental infection | + | + | + | − | + | − | − | − |
| **Vibrio fetus intestinalis** isolated from bovines | + | − | + | − | + | − | − | − |
| **Vibrio fetus venerealis** isolated from bovines | + | − | − | − | − | − | − | − |

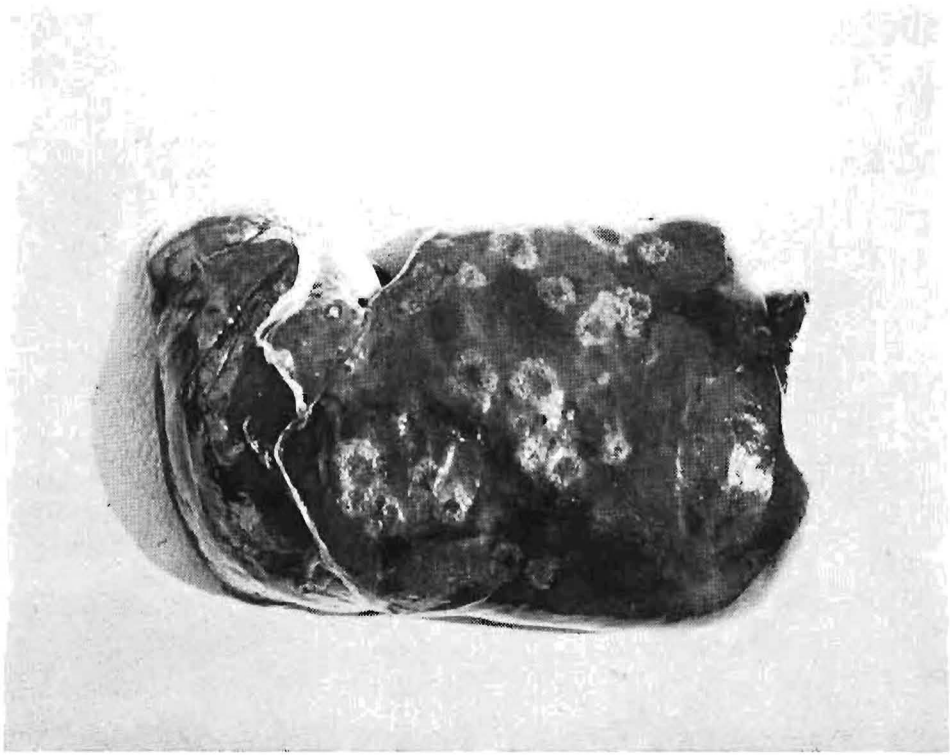

FIGURE — Foetal liver from original outbreak. Pale discrete circular lesions are characteristic of the disease.

which roughly corresponded to the surface diameter. Similar areas of necrosis were observed deep in the parenchyma. Microscopic examination of these areas revealed that they consisted of a focal but poorly circumscribed area of necrotizing hepatitis, without predilection for any particular area of the lobule. Approximately one third of the hepatocytes in these areas, however, still appeared viable. The reactive process appeared to be acute to subacute with many neutrophils scattered radomly throughout. The remaining liver tissue appeared normal in all respects.

Microscopy of the lung revealed mild to moderate suppurative bronchopneumonia with focal areas of serofibrinous exudate in the alveolar spaces. A Gràm's stain (MacCallum and Goodpasture) of the liver and lung failed to demonstrate any bacteria. All tissues were in a good state of fixation with very little *post mortem* autolysis.

The 9-day post-inoculation (PI) foetus had evidently died a few days prior to being aborted, since autolysis was well advanced, making examination of the foetal tissues difficult. Besides mild ascites (2 ml), hydrothorax (50 ml) and hydropericardium (7 ml), the only significant changes involved the placenta. Several cotyledons had a yellow-brown, necrotic centre surrounded by a hyperaemic zone. Microscopic examination proved futile because of advanced autolysis.

Macroscopic examination of the 11-day PI foetus was unrewarding. The microscopic appearance of the liver, however, was markedly similar to the spontaneous case, with focal areas of coagulative necrosis. The lungs also contained small areas of necrosis with associated haemorrhage. The aerated appearance of the lung suggested that post natal respiration had taken place.

Large areas of necrosis accompanied by a purulent inflammatory exudate were observed in many of the cotyledons. MacCallum-Goodpasture stained sections of the placenta and liver were equivocal, but there was a suggestion of short Gram-negative rods in a few macrophages from both organs.

## DISCUSSION

The small trial undertaken to study the abortifacient properties of the Vibrio isolates confirms the experimental findings of other workers that abortion can be induced readily in ewes three to four months pregnant [5, 15]. The history recorded for this outbreak, namely abortions one to two weeks prior to the normal lambing time, the ewes remaining clinically healthy, corresponds closely to observations previously documented [1, 6].

The focal areas of hepatic necrosis (Fig.) are highly suggestive of ovine vibriosis [16]. Unfortunately, they occur only in a limited percentage of the abortions and were not found in our experimental cases. Microscopic evidence of hepatic pathology, however, is more consistent, but not particularly characteristic, with necrosis involving any area of the hepatic lobule. Differential diagnoses include *post mortem* autolysis and hepatic necrosis resulting from umbilical infection [16]. The former can be ruled out, because there is no inflammatory reaction, while the latter is restricted to lambs which have lived a few days and macroscopic changes of the umbilicus are evident.

The placental lesions are nonspecific and variable. The cotyledons are often enlarged, yellowish brown (necrotic) or haemorrhagic and may be covered with cloudy exudate [17].

The *Vibrio fetus* strain isolated during the abortion outbreak could be classified biochemically as an *intestinalis* variety. Serologically, however, it seems to differ from similar strains which were isolated from bovines. This is acceptable, since it has been shown by Marsh and Firehammer [18] and recently by Berg, Jutica and Firehammer [19], that several serotypes can be distinguished. Further studies to establish the relationship between ovine serotypes present in this country are warranted.

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# TICKS AND CASEOUS LYMPHADENITIS IN SHEEP: PRELIMINARY OBSERVATIONS

G. NAGY*

SUMMARY

A survey was undertaken to determine the general and breed incidence of caseous lymphadenitis in Karoo sheep and a study made of the aetiology and the possible role played by tick infestation.

Merinos were found to be more susceptible to caseous lymphadenitis than other breeds or crossbreeds. Of the Merino sheep examined, 3,93% were found to be infected during the first and 7,41% during the second phase of the experiment, while only 0,54% Blackhead Persians, 0—1,55% Dorpers and 0—2% Afrikaner sheep were positive during the corresponding phases of the experiment. Older Merinos had a much higher incidence of abscess formation and 7,41% of Merinos over 1 year were positive while only 2,4% of Merinos under 1 year were infected.

The two major tick species found on Karoo sheep were found to be *Hyalomma truncatum* and *Rhipicephalus capensis*.

No relationship could be established between tick infestations and the incidence of caseous lymphadenitis in Karoo sheep.

The typical manifestation of this disease is a caseous lymphadenitis of the superficial cervical (prescapular) lymph nodes.

Only *Corynebacterium pseudotuberculosis* could be isolated from infected lymph nodes.

## INTRODUCTION

Caseous lymphadenitis is typified by Blood & Henderson [1] as a chronic disease of sheep characterized by the formation of abscesses in lymph nodes which exert little effect on the general health of the sheep unless the abscesses become generalized. These authors consider *Corynebacterium pseudotuberculosis* (Buchanan, 1911) as the specific cause of the disease and that the infection gains entrance to the body through shearing wounds, less commonly through the navel and through docking wounds. No mention is made of the tick as a possible vector.

Ticks have been incriminated in a number of pyogenic diseases. According to Foggie [2], tick pyaemia, characterized by staphylococcal abscess formation in various parts of the body, is caused by the tick acting as a true vector. It carries the infection acquired from feeding on an infected lamb to the next host. Alternatively, the infective agent is present on the skin of the lamb and gains entrance through a tick bite. Manninger & Mócsy [3] described abscesses of the regional lymph nodes of horses caused by infected tick bites. Van Tonder [4] found that ticks seem to be the major cause of scrotal abscesses in rams.

From 1968—1970 a total of 5 833 Merino rams was clinically examined for abscesses in the scrotal region by the personnel at the Veterinary Investigation Centre, Beaufort West. A total of 71 (1,2%) rams was found positive for abscesses in this region [5].

In an endeavour to evaluate the possible role of ticks in caseous lymphadenitis, studies were undertaken on sheep of different breeds on various farms in the Karoo.

## MATERIALS AND METHODS

Examinations for the presence of abscesses and ticks were made on eight different farms in the Karoo area. On five farms only Merino sheep were examined while Dorper, Blackhead Persian and Afrikaner crossbred sheep were used for these observations on the three remaining farms.

The whole investigation was undertaken in three phases. During the first phase of six months every farm was visited once monthly and a total of not more than 100 randomly selected sheep was examined by inspection and palpation. Examinations were

*Veterinary Investigation Centre, Beaufort West.

terminated after finding three abscesses immaterial of the number of animals examined. All abscesses were then incised and material collected on sterile swabs for bacteriological examination at the Veterinary Investigation Centre, Beaufort West. Trans plantation on blood agar plates of all material from abscesses was done within four hours after collection on the farm. Bacterial isolations and identifications were done according to the existing techniques [6-9].

During examination all ticks observed were removed and cultures were made from the mouth parts on blood agar plates. All ticks removed were identified according to the descriptions by Lapage [10].

Pilocarpine hydrochloride (0,1 ml of 0,2% solution) was injected into female *Hyalomma truncatum* according to Howell's [11] technique to stimulate secretion of saliva. Saliva so obtained was cultured on blood agar plates and the resulting bacterial growth typed and identified.

On the strength of the results obtained during the first phase, the lay-out for the second phase, also of six months' duration, was changed, using different breeds of sheep on each of another four farms in the Karoo area. The frequency of visits and the techniques were unchanged.

The effect of degree of tick infestation on the frequency of abscess formation was also studied in Merino sheep on four different farms. While the sheep on farms A and B were relatively tick-free, those on farms C and D were infested to a considerable degree.

During the last phase all sheep carcasses were examined daily at the Beaufort West abattoir over a period of three months for abscesses and the anatomical regions of the affected lymph nodes noted. These sheep come from different Karoo regions but not from the farms originally visited.

## RESULTS

*First phase*

A summary of results obtained during the first phase is presented in Tables 1, 2 and 3.

Table 2: SPECIES OF TICKS FOUND ON DIFFERENT BREEDS OF SHEEP ON EIGHT DIFFERENT FARMS

| Breed | Tick spp. found |
|---|---|
| Merino | **Hyalomma truncatum**<br>**Rhipicephalus capensis** |
| Dorper | **Hyalomma truncatum**<br>**Rhipicephalus capensis** |
| Blackhead Persian | **Hyalomma truncatum** |
| Afrikaner crossbred | **Hyalomma truncatum**<br>**Rhipicephalus capensis**<br>**Ixodes rubicundus** |

From Table 1 it is evident that the Merino is more prone to abscess formation than any other breed. While 3,93% of Merino sheep had one or more abscesses, only 0,54% of the Blackhead Persians were positive and Dorpers and crossbred Afrikaners were negative for abscesses. Tick infestation varied from 12,5% in the Blackhead Persian to 30,08% in the Dorper. Only 12,28% of the Merino sheep were infested.

As illustrated by Table 2, the only tick species found on all breeds of sheep was *Hyalomma truncatum*. *Rhipicephalus capensis* occurred on all breeds except the Black-

Table 1: INCIDENCE OF ABCESSES AND TICK INFESTATION IN DIFFERENT BREEDS OF SHEEP ON EIGHT DIFFERENT FARMS

| Breed | No. of animals examined | No. of animals with abscesses | No. of animals tick-infested |
|---|---|---|---|
| Merino | 1 701 (5 farms) | 67 (3,93%) | 226 (13,28%) |
| Dorper | 369 (3 farms) | 0 (0%) | 114 (30,08%) |
| Blackhead Persian | 552 (3 farms) | 3 (0,54%) | 69 (12,50%) |
| Afrikaner Crossbred | 272 (3 farms) | 0 (0%) | 50 (18,38%) |
| Total: | 2 894 | 70 (2,42%) | 459 (15,86%) |

Table 3: MICRO-ORGANISMS ISOLATED FROM ABSCESSES AND TICKS

| Specimen | Number | | | | Micro-organisms isolated |
|---|---|---|---|---|---|
| | Merino | Dorper | Blackhead Persian | Afrikaner crossbred | |
| Abscesses | 67 | 0 | 3 | 0 | **Corynebacterium pseudotuberculosis** |
| Tick mouth parts | 60 | 15 | 11 | 17 | **Staphylococcus** spp.<br>**Bacillus** spp.<br>**Salmonella** spp. |
| | 0 | 0 | 1 | 1 | **Corynebacterium pseudotuberculosis** |
| Tick saliva | 7 | 0 | 0 | 2 | **Staphylococcus** spp.<br>**Pseudomonas** spp. |

head Persian. Afrikaner crossbred sheep were also infested with *Ixodes rubicundus*.

Without exception *Corynebacterium pseudotuberculosis* was identified from all abscesses cultured for bacterial examination. Usually *S. aureus* and *Staphylococcus. epidermidis* were present on the mouth parts and in the saliva of ticks, while *Bacillus* spp., *Salmonella* spp. and *Pseudomonas* spp. were found infrequently. C. *pseudotuberculosis* could only be illustrated twice on the mouth parts of ticks that were removed from breeds other than the Merino (Table 3).

*Second phase*

In order to examine the higher incidence of abscesses in Merino sheep, all observations for the second phase were conducted on farms on which Merino as well as one or more of the other breeds of sheep were kept. The age of Merino sheep was also taken into consideration. A summary of results obtained is presented in Tables 4, 5 and 6.

Table 4: INCIDENCE OF ABSCESSES AND TICK INFESTATION IN DIFFERENT BREEDS OF SHEEP ON THE SAME FARM

| Breed | No. of animals examined | No. of animals with abscesses | No. of animals tick-infested |
|---|---|---|---|
| Merinos over 1 year | 135 | 10 (7,41%) | 28 (20,74%) |
| Merinos under 1 year | 334 | 8 (2,40%) | 220 (65,87%) |
| Merino crossbred over 1 year | 76 | 1 (1,32%) | 0 |
| Merino crossbred under 1 year | 124 | 0 | 0 |
| Dorper (Whitehead) | 76 | 0 | 76 (100%) |
| Dorper (Blackhead) | 254 | 4 (1,55%) | 97 (38,19%) |
| Namakwa Afrikaner | 50 | 1 (2%) | 2 (4%) |
| TOTAL | 1 049 | 24 (2,28%) | 423 (40,32%) |

Table 5: MICRO-ORGANISMS ISOLATED FROM ABSCESSES AND TICKS

| Specimen | Breeds | | | | | | | Micro-organisms *isolated* |
|---|---|---|---|---|---|---|---|---|
| | Merino >1 year | Merino <1 year | Merino crossbred >1 year | Merino crossbred <1 year | Dorper Whitehead | Dorper Blackhead | Namakwa Afrikaner | |
| Abscesses | 10 | 8 | 1 | 0 | 0 | 4 | 1 | **Corynebacterium pseudotuberculosis** |
| Tick mouth parts | 21 | 15 | 0 | 0 | 3 | 9 | 3 | **Staphylococcus** spp.<br>**Pseudomonas** spp.<br>Mixed infection |
| Tick saliva | 4 | 4 | 0 | 0 | 1 | 3 | 0 | **Staphylococcus** spp.<br>**Escherichia coli** |

Table 6: EFFECT OF TICK INFESTATION ON THE FREQUENCY OF ABSCESS FORMATION IN MERINO SHEEP

| Farms | Sheep examined | Abscesses | Tick-infested sheep |
|---|---|---|---|
| A, B | 198 | 11 (5,55%) | 38 (19,19%) |
| C, D | 271 | 5 (1,85%) | 210 (77,49%) |
| Total | 469 | 16 (3,41%) | 248 (52,88%) |

In Table 4 the susceptibility of the Merino to abscess formation is again emphasized. In old Merinos, however, a much higher incidence of abscess formation was found: 7,41% of Merinos over 1 year were positive, while only 2,4% of Merinos under 1 year were infected. In Merino crossbreds, Dorpers and Namakwa Afrikaners abscesses were of low occurrence. Ticks were especially found on Dorpers of the Whitehead variety (100%), young Merinos (65,87%) and Dorpers of the Blackhead variety (38,19%). All breeds were parasitized by *Hyalomma truncatum;* no other species of ticks were found.

As in the first phase of the experiment, only *Corynebacterium pseudotuberculosis* was isolated from cultures of abscesses. *S. aureus* and *S. epidermidis* were again frequently isolated from the mouth parts and saliva of ticks, while *Pseudomonas* spp. and *Escherichia coli* were of minor importance (Table 5).

The results given in Table 6 illustrate the absence of any direct correlation between the degree of tick infestation and the frequency of abscess formation in Merino sheep. While the relatively tick-free sheep on Farms A and B (19,19% infested) had a high frequency of abscesses (5,55%) only 1,85% of the more heavily tick-infested sheep (77,49% infested) on farms C and D were infected. The highest incidence of clinical caseous lymphadenitis was found in the superficial cervical (prescapular) lymph nodes.

*Third phase*

The results of weekly carcass examinations done at the municipal abattoir of Beaufort West are presented in Table 7.

From Table 7 it is evident that the superficial cervical lymph nodes were most often infected with caseous lymphadenitis, the incidence being 84,38%. Other lymph nodes affected totalled 15,7%.

## DISCUSSION

It is clear from the preceding evidence that the Merino is more prone to abscess formation than the other breeds or crossbreds examined. While 3,93% of Merino sheep examined during the first phase of the experiment were infected, only 0,54% of the Blackhead Persians were positive and no abscesses could be found in Dorpers or crossbred Afrikaners. In the second phase of the experiment this tendency was again found and 7,41% of Merino sheep over one year and 2,4% under one year suffered from clinical lymphadenitis, while only 1,55% Blackhead Dorpers and 2% Namakwa Afrikaners were affected. Even the crossbred Merinos had fewer abscesses than the purebred Merinos (Table 4).

Further research work, however, would be necessary to explain the reason for the

Table 7: THE REGIONAL INCIDENCE OF CASEOUS LYMPHADENITIS DURING CARCASS EXAMINATIONS AT THE BEAUFORT WEST ABATTOIR

| Year 1970 | Animals slaughtered | Animals infected | Lymph nodes infected | | | | |
|---|---|---|---|---|---|---|---|
| | | | *Lnn cervicales* superficiales (prae-scapulares) | Lnn subiliaci (prae-femorales | Lnn *mediastinales* | Lnn *poplitei* | Lnn *hepatici* |
| June | 2 030 | 141 (6,95%) | 100 (70,92%) | 33 (23,40%) | 3 (2,13%) | 1 (0,71%) | 4 (2,84%) |
| July | 1 903 | 139 (7,30%) | 121 (87,05%) | 10 (7,19%) | 4 (2,88%) | 0 | 4 (2,88%) |
| August | 1 573 | 149 (9,47%) | 141 (94,63%) | 0 | 4 (2,68%) | 0 | 4 (2,68%) |
| Total | 5 506 | 429 (7,80%) | 362 (84,38%) | 43 (10,02%) | 11 (2,56%) | 1 (0,23%) | 12 (2,80%) |

higher incidence of abscesses in the older Merino sheep.

Blood *et al*[1] mentioned *C. pseudotuberculosis* as the specific cause of caseous lymphadenitis. The results described above confirm these observations: *C. pseudotuberculosis* was the only organism isolated from all abscesses cultured for bacterial examination.

No relationship could be found between severity of tick infestation and the incidence of caseous lymphadenitis. In spite of only a moderate infestation with ticks, Merino sheep usually had the highest incidence of abscesses (Table 1 and 4). Furthermore, it was found that the relatively tick-free Merino sheep on farms A and B had a much higher incidence of infection with *C. pseudotuberculosis*. (Table 6).

Further evidence of the relative unimportance of ticks as vectors of the infection is found in Tables 3 and 5. While only *C. pseudotuberculosis* could be isolated from infected lymph nodes, the mouth parts and saliva of ticks were usually contaminated with *Staphylococcus* spp. and infrequently with *Bacillus* spp., *Salmonella* spp., *Pseudomonas* spp. and *Escherichia coli*.

The two major tick species found on Karoo sheep are *Hyalomma truncatum* and *Rhipicephalus capensis*. *Ixodes rubicundus* was found on Afrikaner crossbred sheep in the Prince Albert region.

The high incidence of prescapular lymphadenitis found at the Beaufort West abattoir as well as during field observations must be regarded as highly significant and typical for this disease. Further research work in order to explain this tendency is necessary.

ACKNOWLEDGEMENTS

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## BOOK REVIEW — BOEKRESENSIE

# THE BEAGLE AS AN EXPERIMENTAL DOG

A. C. ANDERSON

Iowa State University Press, Ames, Iowa. 1970.

Pp. XIII — 601. Prys £9.70.

Die verskyning van hierdie boek is te danke aan die Amerikaanse Raad op Atoomkrag. Hulle het aan die skrywer die taak opgedra om alle beskikbare data aangaande hierdie honderas as eksperimentele dier te verwerk in die vorm van 'n referensie-boek.

Altesaam 47 navorsers (13 lede van die Universiteit van California) het meegewerk om hierdie boek moontlik te maak. Ongeveer 60 persent van die wetenskaplike gegewens, soos in hierdie boek vervat, was vantevore reeds gedokumenteer. Die res is saamgestel uit basiese data wat weens gebrek aan ruimte nie in vorige artikels ingepas kon word nie. Verder is ook spesifieke studies onderneem om gegewens te bekom wat absoluut noodsaaklik was vir die samestelling van hierdie werk.

Vier afdeling kom in die boek voor, te wete:

A. Versorging van die Beaglehond, met 4 hoofstukke. In hierdie afdeling word aspekte van behuising, bestuur, voeding en voortplanting bespreek. Die informasie in hierdie afdeling is nie slegs net eie aan die Beaglehond nie, maar het 'n wye toepassing op ander honderasse.

B. Anatomie en Fisiologie, met 12 hoofstukke. Hierdie is die mees breedvoerige afdeling. Dit behels aspekte soos groei en ontwikkeling, topografiese anatomie, die spysverteringstelsel, voortplanting en die senuweestelsel. Die skelet en die oog word in besondere detail gedokumenteer.

C. Spesiale Studies op die Beaglehond, met 6 hoofstukke. Studies in mikrobiologie, gedrag, genetika en sitogenetika word bespreek. In hierdie afdeling word daar kortliks na patologiese toestande in die Beaglehond verwys, terwyl afwykings van die oog en die nier en in besonder letsels van die aorta en kroonare breedvoerig bespreek word.

D. Spesiale Tegnieke van toepassing op die Beaglehond, verdeel in 4 hoofstukke. Kliniese ondersoek van die oog, metodiek van langtermyn eksperimentele ondersoek en die beoordeling van stremming word bespreek.

Hierdie indeling van beskikbare data is prakties slegs in die sin dat dit die maklikste manier was om diverse data te klassifiseer. Die ongelukkige gevolg van hierdie rangskikking is dat die persoon, wat spesifieke inligting aangaande 'n sekere stelsel wil nagaan, dit ontsettend maklik gaan vind. Diegene wat byvoorbeeld aspekte oor voortplanting wil naslaan sal in drie van die vier afdelings moet delf om die inligting te bekom. Eweso is dit jammer dat sekere stelsels te breedvoerig bespreek word terwyl ander nie voldoende aandag gegun word nie. Vier-en-sewentig bladsye deurspek van fotos van uitstekende gehalte word gebruik om die skelet te bespreek. In teenstelling kon daar vir die enorme veld van patologie nie eens vergelykbare ruimte afgestaan word nie.

Nieteenstaande hierdie tekortkomings, moet die verskyning van die boek as 'n stap in die regte rigting beskou word. Vir 'n geruime tyd bestaan daar 'n behoefte vir 'n leerboek van dié formaat. Beide die navorser en die praktisyn, wat in die hond belangstel, behoort hierdie boek van besondere waarde te vind, veral omdat die basiese kennis wat oor die Beaglehond versamel is ook ewe maklik vir die bestudering van ander honderasse aangewend kan word.

A.P.S.

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# *BRUCELLA MELITENSIS* STRAIN REV I AS A VACCINE FOR CATTLE

F. D. HORWELL AND* G. G. VAN DRIMMELEN**

SUMMARY

Brucella Rev 1 vaccine was used in 61 heifer calves in four dosage strengths of $10^{11}$, $10^{10}$, $10^{9}$ and $10^{7}$ living organisms. Agglutination titres of 43 of these animals were observed until maturity when 38 no longer had any significant titres. The remaining five comprised one positive and four doubtful reactors. Substantial protection against infection by *Brucella abortus* strain 544 was achieved by the smaller doses. No relationship between vaccine-induced titres and subsequent resistance to infection was observed.

## INTRODUCTION

The large number of viable S19 organisms which must be administered for the protection of cattle against infection by *Brucella abortus* often causes marked local lesions and strong, persistent serological reactions in older animals.

*Brucella melitensis* strain Rev 1 has been shown to be superior to S19 as an immunizing agent for sheep and goats even when used in much smaller doses[1]. It was anticipated that Rev 1 vaccine would impart a superior immunity when administered to heifers at considerably less than the S19 dose of $60\text{-}100 \times 10^{9}$.

A preliminary investigation into the use of Rev 1 in adult cattle revealed a number of good features which justified further trials. The strain proved safe, was not excreted, stimulated titres which were not persistent and caused less severe local reactions[2, 3]. On the basis of these findings a series of immunity tests in heifers was undertaken.

## MATERIAL AND METHODS

### *Preparation of vaccine*

The vaccine was prepared from an aerated liquid culture of *Brucella melitensis* strain Rev 1 in a yeast extract-glucose-peptone-phosphate medium, concentrated in 0,06% sodium carboxymethyl-cellulose at 4°C and freeze-dried in vials[3, 4].

### *Immunization of experimental animals*

Heifer calves born in a brucellosis-free environment were acquired as they became available and were reared in isolation. They were divided into comparable groups for vaccination at six to eight months of age. One group in each series remained unvaccinated to serve as controls.

The vaccine was administered subcutaneously in doses of $10^{7}$, $10^{9}$, $10^{10}$ and $10^{11}$ living organisms and all doses were confirmed by viability counts on the vaccine at the time of vaccination. With the exception of 18 heifers vaccinated and bred under ranching conditions, serum-agglutination titres were determined immediately before vaccination and at monthly intervals thereafter. At maturity the heifers were bred to brucellosis-free bulls.

### *Challenge of experimental animals.*

*B. abortus* strain 544, originally from Weybridge and maintained in the lyophilized state, was used as stock for culture of the exposure material. The surface growth on 48 hours-old subcultures made from selected, typical, smooth colonies on potato infusion agar was suspended in sterile 0,1% sodium carboxymethyl-cellulose solution to preserve viability immeditely before use[5]. The bacterial density of the suspensions was adjusted to the required number of organisms which was verified by bacterial counts of aliquots of the infecting material at the time of exposure. The virulence of the strain was confirmed in guinea pigs at each monthly exposure. Heifers in the later trials were exposed to re-constituted and suitably diluted freeze-dried suspensions of S544 of repeatedly confirmed viability and virulence.

*Veterinary Research Institute, P.O. Onderstepoort.
**Presently Agricultural Counsellor, Embassy of South Africa, Washington, D.C. U.S.A.

After three months' gestation, vaccinates and controls were housed in individual stalls and divided into three groups for exposure to infection. Each group comprised vaccinates representing all vaccine dosages and the necessary controls. Exposure was effected by instillation of 0,2 ml of a suspension containing the large, medium or small exposure dose of living *B. abortus* strain 544 organisms medial to the semilunar conjunctival fold.

One group was challenged by a massive exposure of $10^8$—$10^9$ organisms, another was challenged by $10^6$—$10^7$ and the remaining group by $10^3$—$10^4$ S544. Exposure was repeated monthly until birth or abortion intervened.

Abortion material and calves which died within a month of birth were examined microscopically, bacteriologically and biologically for evidence of Brucella infection. The *post partum* blood titres of the cows were determined monthly for four months.

*Serological methods*

The serum-agglutination tests were conducted according to the WHO standards by the equal-volume method in twelve tubes, commencing at a serum dilution of 1 : 2,5 and progressing by twofold, serial dilution to 1 : 5 120. The antigen used was produced from *B. abortus* strain 99 and was standardized to produce 50% agglutination in the presence of two International Units of *B. abortus* agglutinin in equal volume.

## RESULTS

Several deaths from other causes before the conclusion of pregnancy and a somewhat high rate of infertility reduced the number

Table 1: THE NUMBER OF HEIFERS AT THE CONCLUSION OF PREGNANCY

| Vaccine dose | Exposure to B. abortus S544 | | |
|---|---|---|---|
| | $10^8$—$10^9$ | $10^6$—$10^7$ | $10^3$—$10^4$ |
| $10^{11}$ | 2 | 2 | 2 |
| $10^{10}$ | 9 | 8 | 8 |
| $10^9$ | 9 | 5 | 2 |
| $10^7$ | 5 | 4 | 5 |
| Controls | 3 | 4 | 8 |

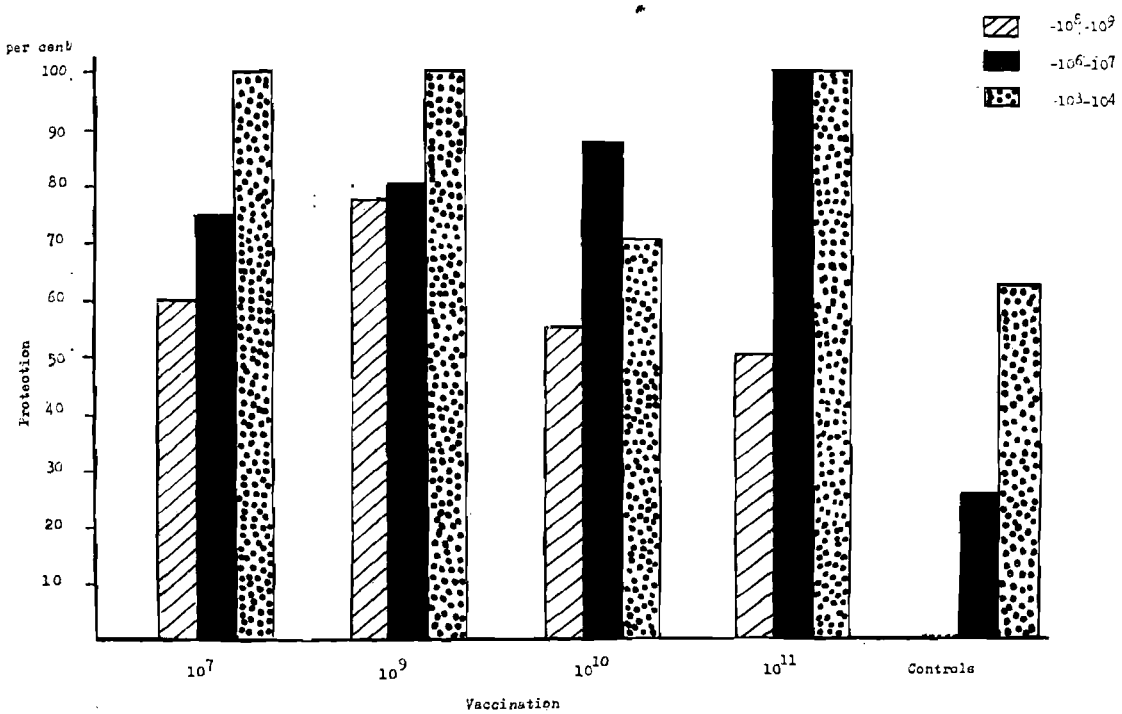


Figure 1: Histogram illustrating the protection induced by vaccination against three magnitudes of exposure

of heifers in the various categories to those given in Table 1. Of the animals vaccinated with $10^{11}$ Rev 1 only two in each exposure group survived long enough to be included in the results.

No serological responses to vaccination are available for the 18 animals reared and vaccinated under ranching conditions. Of the 43 heifers for which titres are known, one remained positive, four retained doubtful titres (1 : 20) and thirty-eight declined to negative levels.

The degree of protection induced by vaccination varied with the magnitude of the challenge but no marked difference between the four vaccine doses within each category was evident (Fig.)

There appeared to be no relationship between maximum vaccine-induced titres and resistance to infection. Four heifers with negative serological responses of $<$1 : 2,5, 1 : 2,5 and 1 : 5 and four which had significant titres of 1 : 20, 1 : 40, 1 : 80 and 1 : 1 280 aborted, indicating approximately 81% protection in both groups.

Thirty-three per cent of the vaccinates and thirty-six per cent of the controls which calved had positive *post partum* titres. Abortion was followed by positive serum-agglutination reactions in 89% of cases.

Table 2: THE RELATIONSHIP BETWEEN VACCINE-INDUCED TITRES AND PROTECTION

| Serological diagnostic level | Highest Vaccine titre | Number of animals | Abortions | Protection per cent |
|---|---|---|---|---|
| Negative | $<$1 : 2,5 | 2 | 1 | 80,9 |
| | 1 : 2,5 | 5 | 1 | |
| | 1 : 5 | 10 | 2 | |
| | 1 : 10 | 4 | 0 | |
| Suspicious | 1 : 20 | 6 | 1 | |
| Positive | 1 : 40 | 2 | 1 | 81,8 |
| | 1 : 80 | 4 | 1 | |
| | 1 : 160 | 4 | 0 | |
| | 1 : 320 | 3 | 0 | |
| | 1 : 1 280 | 2 | 1 | |
| | 1 : 2 560 | 1 | 0 | |

## DISCUSSION

The resistance of vaccinated heifers to infection by *B. abortus* during pregnancy varied considerably with the magnitude of the exposure. A high resistance was evident in vaccinates challenged by a low exposure to $10^3$—$10^4$ infecting organisms. Nevertheless, as more than 60% of the non-vaccinated controls exposed to the same infecting dose resisted infection, it is apparent that challenge by $10^3$—$10^4$ organisms was inadequate for evaluation of the protective qualities of the vaccine.

Challenge by $10^6$—$10^7$ S544 showed a clearly graded protection, commensurate with the size of the immunizing dose, increasing from 75% of animals vaccinated with $10^7$ to 87.5% of those which received $10^{10}$ Rev 1 organisms. The results obtained from a vaccine dose of $10^{11}$ Rev 1 (100% protection) are probably not significant, since only two animals survived long enough to be included in the results of the experiment.

The serological responses to vaccination bore no significant relationship to the degree of protection developed against *B. abortus* infection. Similar findings were reported by Cunningham [6] following vaccination of cattle with S19 and killed 45.20 adjuvant vaccine and by Alton [7] in Rev 1-vaccinated goats challenged by *B. melitensis*.

Calfhood vaccination with Rev 1 in doses of one-tenth and one-hundreth of the S19 requirement provided effective protection of 87% and 80% respectively against abortion following infection by virulent *B. abortus*. Subcutaneous injection of the vaccine produced only minor, temporary, local lesions and few persistent serum-agglutination titres of a diagnostic level.

## ACKNOWLEDGEMENT

The technical assistance of Miss H. E. Smith, Mrs. M. Mulders and Mr. J. F. Steyn is gratefully acknowledged.

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# RABIES IN OTAVI AND TSUMEB, SOUTH WEST AFRICA

J. A. VAN WYK*

SUMMARY

Some unusual clinical signs seen in an outbreak of rabies in the northern districts of South West Africa are described. In one case rabies was masked by paratyphoid and in six others by *Urginea* spp. poisoning occurring coincidentally. Such atypical features increase the danger of transmission to man. A few conditions which may be confused with rabies are described.

The possibility of short-term spread of infection through contaminated drinking troughs is suggested.

## INTRODUCTION

In a review on rabies in the northern districts of South West Africa, von Maltitz[1] described in detail an outbreak in 1948 and 1949 in which heavy losses occurred, mainly among cattle. Sometimes a number of the cattle on an affected farm developed the disease simultaneously (14 at once in one kraal) and on one farm 8% of the herd died. Jackals and dogs also died but no infected Viverridea were found.

He described the clinical disease as mainly the "mad" form of rabies, with terminal paralysis usually closely resembling typical cases of cattle suffering from botulism. Ataxia was present and straining often occurred. There was no hydrophobia, in fact cattle were sometimes observed standing near water. Furthermore, jackals were known to develop posterior paralysis in the terminal stages of the disease and large outbreaks could be caused by these jackals biting inquisitive cattle.

From 1963 to 1966 a similar rabies outbreak to that described by von Maltitz[1] occurred in the Otavi and Tsumeb veterinary area in the north of S.W.A. When the author arrived in the area in June 1963, the outbreak was in full swing in Otavi. From this date until the beginning of 1966, rabies was confirmed on 45 out of the 350 farms in the area in 40 cattle and 7 dogs. In addition, the farmers reported that approximately another 400 cattle had died from the disease.

Although the southern boundary of the Tsumeb District borders on Otavi, no cases of rabies were encountered there until July, 1964, when an outbreak occurred on a farm on this boundary. In December, 1964, rabies occurred on two farms on the eastern boundary of Tsumeb. Thereafter, cases were found on farms dispersed throughout this area but up to the beginning of 1966 rabies was confirmed histologically and/or biologically at the Veterinary Research Institute, Onderstepoort, in only 9 cattle, 2 dogs and 1 cat from 9 localities in the Tsumeb area. Undoubtely many more cases occurred in both Otavi and Tsumeb: if more than one typical case of the disease developed simultaneously on a farm, samples from one animal only were usually submitted for confirmation of the diagnosis. Any other similar cases were regarded as rabid and destroyed. If further cases occurred, farmers were urged to destroy the animals immediately and merely report the numbers killed to the author. Many atypical cases of rabies were also encountered and are described in this report.

## PATHOGENICITY

The majority of cases occurred in cattle, followed in frequency by jackals (though these cases were unconfirmed), dogs and cats.

In cattle the outbreaks of rabies often followed a characteristic pattern. Clinical signs of the disease would appear in 6 or 8 animals either simultaneously or in close successsion. In such cases investigation often revealed that a single animal had shown similar symptoms 6 to 8 weeks previously.

The jackals suspected of having had rabies, had either escaped or had been destroyed and disposed of before specimens could be collected; as a result the disease

*Present address: Section of Helminthology, Veterinary Research Institute, Onderstepoort. Formerly: State Veterinarian, Otavi, S.W.A.

was not confirmed in them. Nevertheless, a presumptive diagnosis of rabies was made if a jackal had made an unprovoked attack on people or dogs or if it had fearlessly approached dwellings and their enclosures. One case reported to the author, however, was an exception to this rule. In the Etosha Game Park, a large part of which is situated in the Tsumeb District, a jackal made an unprovoked attack on a visitor. When caught it was found to be an individual known to the game wardens for its exceptional aggressiveness. It was kept under observation but was set free when no signs of rabies developed.

No cases of suspected rabies were encountered in any member of the Viverridae during this outbreak. Specific enquiries regarding aberrant behaviour of these animals met with a negative response. This is in accordance with the findings of von Maltitz [1].

## CLINICAL SIGNS

A remarkable feature of this outbreak was the absence of viciousness in the majority of cattle and in some of the dogs infected with rabies. Some cattle were slightly aggressive but only a few were really vicious. Most of the infected cattle bellowed continuously and hoarsely (hence the Afrikaans name "bulksiekte", i.e. bellowing disease), salivated more or less profusely and were ataxic. This is the commonest form of rabies in cattle in S.W.A. and von Maltitz [1] referred to it as the "mad" form, which is a misnomer; the term should be confined to the aggressive form as described by Neitz [2] under the heading "Excitable stage: Cattle bellow, stamp with their feet and charge human beings and other animals".

Affected cattle often loiter at the watering places and attempt to drink by submerging their muzzles in the water.

## ATYPICAL CLINICAL SIGNS

(1) *Bellowing:* Some infected calves neither bellowed nor were they aggressive. They salivated and were only slightly ataxic although some of them had been ill for three days.

(2) *Postural abnormalities*

(a) *Advanced ataxia with interlocking hind limbs*

Five rabid calves on one farm developed such ataxia that their hind limbs became entwined during their attempts to run away and they fell repeatedly. Bellowing was not harsh but there was a definite change in temperament in that the animals which had been tame prior to infection became excitable and afraid of human beings. The owner stated that they had suckled until 12 hours before death.

(b) *Bounding movements*

One calf, about 4 months old, showed exaggerated nervous reactions which resulted in convulsive movements of its head and a very alert expression. It was unable to walk normally and hopped or jumped stiff-leggedly when it attempted to escape. Its hindquarters swayed while standing. Salivation was increased and it bellowed harshly.

(3) *"Pseudo-flatus" in cows*

Three cows which showed fairly typical clinical signs of rabies strained more or less continuously. Between bouts of straining, air was drawn into the vagina and/or rectum and when straining recommenced this air was forced out. These animals were seen on different farms, at different times, and the symptom was not as common as it was in the 1948/49 outbreak of rabies described by von Maltitz [1].

(4) *Docility and obedience in a dog with advanced rabies*

The large Bull Mastiff cross concerned had typical clinical signs of the dumb form of rabies [3]. Salivation, the first sign noticed by the owner, was found accompanied by inability to drink and refusal of food.. Thereupon the owner force-fed liquids (soups and water) at frequent intervals. Because the temperament of the dog, which was normally docile and obedient, was unchanged, veterinary assistance was not sought until the fifth day after commencement of the clinical signs. Despite being so weak that it had to be assisted, the dog dismounted from the owner's car and followed her into the veterinary office when she called him. It did not seem to resent being assisted.

(5) *Unusual nervous signs in a dog*

This dog was a small 10 months old Fox Terrier bitch and was under observation from the development of the first signs until the day of its death. She was a pampered pet and had little contact with other dogs.

The day the bitch came on heat for the first time, she developed the "fly-catching" signs described by Henning [3]. When

someone came close to her she gently took his hand in her mouth but did not injure him. This sign became more marked in the next two days and finally reached a point where any moving object (e.g. a door being closed) was similarly "attacked" but was not damaged in any way. Neither her owner, nor the Bantu who fed her, were ever subjected to such attacks.

Progressive signs of general malaise were now evident: partial anorexia, a tendency to sleep a great deal and a staring coat. Milk was taken rather reluctantly, and in small quantities, throughout the three day observation period. None of the other more usual clinical signs of rabies, such as fits of unprovoked viciousness, salivation or excessive barking as described by Henning [3] was present. The animal sat still for long periods and appeared to be half asleep. Then her head would nod and startle her to wakefulness.

On the third day a postural abnormality was noted. While moving around, the bitch would suddenly stop and stand with stiff legs, arched back and lowered head. She then moved backwards in short spurts, without lifting her feet from the ground. By the evening of the third day her condition had deteriorated only slightly. That night, however, she went to the neighbouring farmstead (about two miles way) and made an unprovoked attack on the farmer and his dogs, fowls and goats.

## RABIES ACCOMPANYING OTHER DISEASES

### (1) *Paratyphoid and rabies*

A 4 months old calf presented for examination had the following clinical signs of paratyphoid: hyperpyrexia, a staring hair coat, fetid diarrhoea, marked dehydration, ataxia and ocular and nasal discharge [3]. Rabies was suspected because the calf salivated profusely and bellowed hoarsely after the examination.

The diagnosis of both rabies and paratyphoid was confirmed at the Veterinary Research Institute, Onderstepoort.

### (2) *Rabies and Urginea spp. poisoning syndrome in cattle*

In six cattle rabies was diagnosed accidentally in what had appeared to be atypical cases of plant poisoning due to *Urginea* spp.

*Urginea* spp. are common in the area and appeared to have been grazed. The majority of the affected cattle died shortly after drinking water when they returned from the veld. None of the animals was examined before death but the clinical signs described by the stockman, namely, respiratory distress and death soon after drinking water, were quite typical. The lesions seen at autopsy were in agreement with those described by Steyn [4] for poisoning by *Urginea* spp., viz. cyanosis; generalized hyperaemia; pulmonary oedema, emphysema and haemorrhages; sub-endocardial and sub-epicardial haemorrhages; tympany of the small intestines and poorly demarcated, hyperaemic areas disseminated throughout the jejunum and ileum. Some of the clinical signs, however, did not agree with the above diagnosis. The animals bellowed hoarsely, salivated profusely and became vicious shortly before they died. It was assumed that the viciousness resulted from the cerebral anoxia caused by the marked pulmonary oedema found at autopsy. The brain samples, however, were positive for rabies.

Possibly the depraved appetite often associated with rabies [3] caused the infected cattle to consume large quantities of *Urginea* spp. which complicated the clinical picture.

## DIFFERENTIAL DIAGNOSIS

The following includes only those conditions which the author found difficult to differentiate from rabies.

### (1) *Meningitis and encephalitis as sequelae to dehorning*

An ox, which had recently been dehorned, was very weak, salivated profusely, was dehydrated and ataxic and moved in wide circles. Anorexia appeared to be complete. The expression was alert and the eyes were in divergent strabismus. The animal bellowed continuously and hoarsely.

At autopsy purulent encephalitis and meningitis were evident macroscopically. Histological and biological tests were negative for rabies.

### (2) *Botulism*

On two different farms, situated about 100 km apart, a number of cattle developed an atypical form of botulism which closely resembled the vicious form of rabies. The cattle salivated profusely, appeared dehydrated, walked with a markedly ataxic gait and terminally developed paraplegia. They were exceptionally alert and aggressive and even after paralysis had set in they attempted to

rise and attack anyone approaching them.

Clinical examination showed prominent lingual, abdominal and coccygeal muscle paralyses and constipation, all suggestive of botulism. At autopsy the ruminal atony, hard, impacted abomasa, constipation and distended gall bladders were also indicative of botulism. The brain samples were negative for rabies.

No further cases occurred after the diet had been supplemented with phosphate and the herds concerned inoculated with botulinus vaccine. The deaths were considered to be due to botulism, although the diagnosis had not been confirmed by laboratory tests.

Von Maltitz[1] reported that typical botulism could closely resemble the dumb form of rabies, but apparently did not encounter atypical forms of botulism as described here.

(3) *Lead poisoning*

Profuse salivation, continuous bellowing and ataxia in one calf resembled rabies. As the animal moved in wide circling movements and died within two hours, rabies was discounted. At autopsy about 50 g of battery plate lead were found in the rumen and abomasum and there was generalized cyanosis, gastro-enteritis and a blue-grey discolouration of the brain. The conclusion that death was due to lead poisoning was substantiated by the fact that tests for rabies gave negative results.

(4) *"Bone-in-the-throat" syndrome*

Osteophagia and polyphagia are very common in the Otavi and Tsumeb areas and often lead to the impaction of bones or other foreign objects in the buccal cavity of cattle. As in the case of rabid cattle, animals with foreign bodies in the buccal cavity usually cannot drink and salivate profusely and as a result become thirsty and loiter at the water troughs. Stockmen frequently mistook rabid cattle for animals with the "bone in-the-throat" syndrome, and were exposed to rabies while trying to assist them; similar observations had been made by Du Toit[5] and Snyman[6].

5) *Oesophageal obstruction*

In one cow partial oesophageal obstruction of about a day's duration gave rise to profuse salivation, dehydration and ataxia reminiscent of rabies, but the animal also developed ruminal tympany and the signs disappeared abruptly after the administration of a spasmolytic drug, followed by reduction with a probang.

(6) *Cerebral anoxia*

An ox which had been partially suffocated in a crush became very aggressive when it recovered. It charged the people around the crush and then fled into the veld. Recovery was spontaneous and complete.

## RABIES PROPHYLAXIS

Farmers were instructed to empty and disinfect drinking troughs during outbreaks of the disease in cattle, for reasons outlined under "Discussion and Conclusions".

General prophylaxis aimed at the immunization of domestic animals, combined with extermination of jackals. Most of the dogs in the Otavi and Tsumeb areas were vaccinated with the L.E.P. Flury strain live vaccine*. In addition, farmers were encouraged to inoculate cattle with the H.E.P. Flury strain live vaccine*, giving two doses at a month's interval.

These precautions appear to have been effective because the incidence of rabies decreased. None of the vaccinated cattle subsequently developed rabies. Because one or two vaccinated dogs had contracted the disease, the vaccine was subsequently transported on ice. Thereafter no further cases occurred in vaccinated dogs.

## DISCUSSION AND CONCLUSIONS

Henning[3] states that "the symptoms sometimes vary considerably in different individuals". This is to be expected as the rabies virus causes brain damage by multiplication in the central nervous system. Also, any condition which damages the same parts of the brain as the rabies virus can be expected to result in clinical signs resembling those seen in rabies.

This appears to be the first report of other diseases occurring concurrently with rabies in cattle. It emphasizes the warning by Snyman[6] that "the rabid ox is always a potential source of danger to the human being". When rabies occurs with other diseases it is masked and atypical. Therefore, all sick animals in areas where rabies is common should be examined with this possibility in mind. Even one suspicious sign should be considered as a positive indication of rabies until this is disproved.

*Onderstepoort vaccine.

The veterinary surgeon can easily be exposed to rabies under these circumstances.

The statement by Snyman[6] that the "practice in this country amongst farmers to diagnose any obscure disease as gallsickness and to dose such animals by pulling out the tongue exposes many to the dangers of rabies", is unfortunately still valid in some instances. In outbreaks of rabies every effort should be made to impress the dangers of exposure on the farmers.

Von Maltitz[1] thought that infection could occur via the buccal mucous membrane through the medium of infected licks. Correa-Giron, Allen & Sulkin[7] described the oral infection of mice with intact mucous membranes and found that the rabies virus was able to withstand the effects of the digestive juices of mice for several hours. In the present outbreak, however, no infected cattle were found at the licks. On the contrary, they were observed to loiter at the watering places and to attempt drinking by submerging their muzzles in the water. Up to 10% of animals in herds in this area have been found with buccal wounds caused by allophagia or by awns of seeds of *Aristida* spp. These considerations do suggest that infection through drinking troughs and the intact or damaged mucous membrane could be a possibility. Because sunlight rapidly kills the virus[4], only those susceptible animals which drink water soon after an infected animal would be exposed to infection. This would account for the appearance of the disease in six to eight animals simultaneously, or in close succession, six to eight weeks after the occurrence of a single case.

ACKNOWLEDGEMENTS

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## LETTER TO EDITOR — AAN DIE REDAKSIE

### ROUTINE INCISIONS FOR DETECTION OF CYSTICERCI AT MEAT INSPECTION: PRETORIA ABATTOIR

Sir,

Routine muscle incisions are apt to decrease the market value of the carcass and can be justified only if of definite value or essential in the diagnosis of cysticercosis.

A recent survey of 25,000 cattle and some 8246 pig carcases has once again confirmed the value of the routine incision into the *M. triceps brachii* as required by the South African legislation and also that of some other Southern African countries. The results are summarized in the following table:

| Cysticerci Detected in | Cattle | Pigs |
|---|---|---|
| (a) Masticatory muscles only | 2,93% | 0,072% |
| (b) **M. triceps brachii** only | 3,94% | 0,31 % |
| (c) In both (a) and (b) but nowhere else | 1,24% | 1,29 % |
| (d) In sites other than (a) and (b) | 0,27% | 0,0 % |

W. J. Wheeler.

Manager,
City Abattoir, Pretoria.

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# THE ANTHELMINTIC EFFICIENCY OF PARBENDAZOLE AGAINST GASTRO-INTESTINAL NEMATODES OF SHEEP

J. A. HART AND C. J. BOSMAN*

SUMMARY

Controlled and critical laboratory anthelmintic tests involving 183 sheep were used to assess the efficiency of parbendazole against immature and adult gastro-intestinal nematodes.

A dose rate of 30 mg/kg bodyweight was 94,1—100% effective against 3rd and 4th stage larvae, 5th stage and adult worms of the species *Haemonchus contortus*, *Ostertagia circumcincta* and *O. trifurcata*, *Trichostrongylus colubriformis*, *Gaigeria pachyscelis* and *Chabertia ovina*, and against 3rd stage and adult *Nematodirus spathiger* and 5th stage and adult *Oesophagostomum columbianum*. Fourth and 5th stage *N. spathiger* and 3rd and 4th stage *O. columbianum* were removed to the extent of 79,9—91,7%. Activity against adult *Trichuris ovis* was low.

## INTRODUCTION

The anthelmintic activity of methyl 5(6)-butyl-2-benzimidazole carbamate (parbendazole) against gastro-intestinal nematodes in a number of species of domestic animals was first reported by Actor and nine co-workers[1]. Anthelmintic efficiency against nematode parasites of sheep has since been evaluated in laboratory trials conducted in South Africa by Shone, Saayman, Erasmus & Philip[2], in Australia by Johns & Mendel[3] and in Britain by Ross[4]. These tests have confirmed the broad range of activity and high efficiency of the drug.

The present paper reports controlled and critical laboratory anthelmintic tests in which the efficacy of parbendazole against immature and adult stages of the more common gastro-intestinal nematodes of sheep was assessed.

## MATERIALS AND METHODS

The Dorper and Merino lambs used in Trials 1-7 were housed from the age of four to six weeks, together with their dams, under conditions which precluded natural infestation with gastro-intestinal nematodes. Both ewes and lambs were treated with a broad-spectrum anthelmintic on two occasions during the first 10 days of housing. The lambs were weaned at three to four months of age and a period of at least one week was allowed to elapse between weaning and the use of lambs for experimental purposes. The sheep used in Trial 9 were reared at pasture and harboured naturally acquired nematode infestations.

A 9% w/v suspension of parbendazole** was used in all experiments; the drug was administered intraruminally by stomach tube to each animal at a dose rate of 30 mg/kg bodyweight.

## ACTIVITY AGAINST IMMATURE WORMS

Anthelmintic activity against experimental immature worm infestations was studied in five experiments. The nematode species and stages in development against which efficacy was assessed in each trial are given below.

Trial 1—Activity against the 3rd stage larvae of *Haemonchus contortus*, *Trichostrongylus colubriformis* and *Oesophagostomum columbianum*.

Trial 2—Activity against the 3rd stage larvae of *Ostertagia circumcincta*, *O. trifurcata*, *Nematodirus spathiger* and *Chabertia ovina*.

Trial 3—Activity against the 4th stage and early 5th stage of *H. contortus*, *T. colubriformis* and *O. columbianum* larvae.

Trial 4—Activity against the 4th stage and early 5th stage of *O. circumcincta*, *O. trifurcata*, *N. spathiger* and *C. ovina* larvae.

Trial 5—Activity against the 3rd and 4th stage larvae of *Gaigeria pachyscelis*.

*Cooper Research Station, P.O. Box 5034, East London.

**Helmatac—Trade Mark of Smith, Kline and French (Pty) Limited, Isando, Tvl., S.A.

Table 1: EXPERIMENTAL DESIGN — TRIALS 1 AND 2

| Day | Numbers of infective larvae administered to each lamb | | | | | |
|---|---|---|---|---|---|---|
| | TRIAL 1 | | | TRIAL 2 | | |
| | H. contortus | T. colubriformis | O. columbianum | Ostertagia spp. | N. spathiger | C. ovina |
| −6 | | | 188 | | | 88 |
| −5 | | | 188 | | | 88 |
| −4 | | | 188 | | | 88 |
| −3 | 1 000 | 890 | 188 | 959 | 632 | 88 |
| −2 | 1 000 | 890 | 188 | 959 | 632 | 88 |
| −1 | 1 000 | 890 | 188 | 959 | 632 | 88 |
| Totals | 3 000 | 2 670 | 1 128 | 2 877 | 1 896 | 528 |
| 0 | Eleven lambs in each trial treated with parbendazole | | | | | |
| +6<br>+7<br>+8 | Treated and control lambs in each trial slaughtered | | | | | |

Table 2: EXPERIMENTAL DESIGN — TRIALS 3 AND 4

| Day | Numbers of infective larvae administered to each lamb | | | | | |
|---|---|---|---|---|---|---|
| | TRIAL 3 | | | TRIAL 4 | | |
| | H. contortus | T. colubriformis | O. columbianum | Ostertagia spp. | N. spathiger | C. ovina |
| −24 | | | 57 | | | 58 |
| −22 | | | 57 | | | 58 |
| −20 | | | 57 | | | 61 |
| −18 | | | 55 | | | 61 |
| −16 | | | 55 | | | 61 |
| −14 | | | 55 | | | 61 |
| −12 | 310 | 289 | 62 | 300 | 365 | 62 |
| −11 | 310 | 289 | | 300 | | |
| −10 | 310 | 289 | 62 | 300 | 365 | 62 |
| − 9 | 310 | 289 | | 300 | | |
| − 8 | 310 | 289 | 62 | 300 | 365 | 62 |
| − 7 | 310 | 289 | | 300 | | |
| − 6 | 312 | 297 | | 300 | 365 | |
| − 5 | 312 | 297 | | 300 | | |
| − 4 | 312 | 297 | | 300 | 365 | |
| Totals | 2 796 | 2 625 | 522 | 2 700 | 1 825 | 546 |
| 0 | Nine control lambs slaughtered and eleven lambs treated with parbendazole in each trial. | | | | | |
| + 3<br>+ 4 | Treated lambs in each trial slaughtered | | | | | |

*Trials 1—4*

Twenty lambs, of which nine served as untreated controls, were used in each trial. The lambs were experimentally infested with infective (3rd stage) nematode larvae, suspended in water and administered intra-ruminally by stomach tube, according to the programmes given in Tables 1 and 2. The programmes of experimental infestation were designed to ensure that the majority of the immature parasites present in the lambs was 3rd stage larvae in Trials 1 and 2 and 4th stage larvae in Trials 3 and 4 at the time of treatment with parbendazole.

Treated and control lambs were slaughtered between the sixth and eighth day after treatment in Trials 1 and 2, to allow sufficient time for the larvae administered to each animal to reach their normal habitats and for the majority to develop to the 4th larval stage. In Trials 3 and 4, the control lambs were slaughtered on the day of anthelmintic treatment and treated lambs were slaughtered between the third and fourth day after dosing.

The waterbath and technique described by Shone & Philip[5] and Reinecke[6] were used to recover immature parasites from the gastro-intestinal tract at autopsy. The abomasum, small intestine and large intestine of each animal were handled separately during the procedures involved.

The gastro-intestinal tract was removed immediately after slaughter and each of the three appropriate sections was opened and washed in 0,85% saline at 37°C. The ingesta from each were poured onto the nylon-mesh sieve of a waterbath tray containing saline and incubated in the bath for one hour at 40°C.

The mucosal and submucosal layers of the wall of each section were stripped from the serosa and homogenised in a blender (Ato-Mix, M.S.E., London) for 15 seconds at half speed. In Trials 2 and 4, the homogenised material of each section was incubated in the waterbath for three to four hours at 40°C. In Trials 1 and 3, in which the lambs were infested with *O. columbianum*, the homogenised mucosal and submucosal layers of the small and large intestines were subjected to digestion in a 1% pepsin/3% concentrated hydrochloric acid solution for approximately two hours at 40°C.

The trays were removed from the waterbath after the appropriate periods of incubation and the residues on the nylon sieves, filtrates in the trays and wall digests were washed in sieves with 400 meshes per linear inch (Endecott). Complete worm counts were made on all filtrates and wall digests. A one-tenth aliquot of each residue of the small and large intestines was examined and when this was found to be positive, the remainder of the material was screened. A one-tenth aliquot of each abomasal residue was examined and, in the case of treated sheep, the balance was screened when this was found to be positive. In the case of control animals only two or occasionally three further one-tenth aliquots were examined. Worms were counted with the aid of a stereo-microscope and the first 100—140 parasites encountered in each sample were identified, where necessary with the aid of a compound microscope.

*Trial 5*

Forty-two lambs were each infected percutaneously with 225 *G. pachyscelis* 3rd stage larvae which were concentrated in 2 ml water and applied to the skin at a site between the shoulder blades where the fleece had been closely clipped. Groups of 11 lambs were treated with parbendazole at six, 15 or 35 days after infestation. Treatments were timed to coincide with the presence of 3rd stage larvae in the lungs at six days and 4th stage larvae in the small intestine at 15 and 35 days after infestation. Treated and control lambs were slaughtered six weeks after infestation and the contents of the small intestine of each were washed in a sieve with 100 meshes per linear inch (Endecott) before macroscopic examination for *G. pachyscelis*.

ACTIVITY AGAINST ADULT WORMS

Anthelmintic activity against adult nematode infestations was assessed in four experiments. The worm species studied in each trial are given below.

Trial 6—Activity against *H. contortus* and *T. colubriformis*.

Trial 7—Activity against *O. circumcincta*, *O. trifurcata*, *N. spathiger* and *C. ovina*.

Trial 8—Activity against *G. pachyscelis*.

Trial 9—Activity against *O. columbianum* and *Trichuris ovis*.

*Trials 6 and 7*

Twenty lambs, of which nine served as controls, were used in each experiment. In Trial 6, each animal was infested with 2 900 *H. contortus* and 2 960 *T. colubriformis* 3rd stage larvae which were administered intraruminally by stomach tube in a single dose 26 days before anthelmintic treatment. In Trial 7, 2 870 *Ostertagia* spp., 2 880 *N. spathiger* and 290 *C. ovina* infective larvae were given to each animal. The larvae of *C. ovina* were administered in three equal doses on three consecutive days six weeks before anthelmintic treatment, and the *Ostertagia* spp. and *N. spathiger* larvae were given in a single dose 28 days before treatment.

Control and treated lambs were slaughtered three days after anthelmintic treat-

ment and the contents and mucosal washings of the abomasum and small intestine were washed in sieves with 325 meshes per linear inch (Endecott). A one-tenth aliquot of the material remaining on the sieve was examineed for immature and adult worms using a stereo-microscope and two further aliquots were examined when this was found to be positive. Immature worm burdens were calculated from the results of these examinations, as were the adult worm burdens when it was apparent that 600 or more mature nematodes were present. When the counts of three one-tenth aliquots indicated the presence of fewer than 600 adult worms, the balance of the material was examined macroscopically for the remaining worms.

In order to recover *Ostertagia* spp. that had remained in the abomasal wall in Trial 7, the mucosal and submucosal layers of the abomasum were homogenised as described earlier and incubated in the waterbath for three to four hours at 40°C. Total worm counts were made on wall filtrates, while a one-tenth aliquot of each wall residue was examined and two further aliquots screened when this was found to be positive. The contents of the large intestine of each lamb in Trial 7 were washed in a 100 mesh sieve and examined macroscopically for *C. ovina*.

*Trials 8 and 9*

Twenty-one critical anthelmintic tests were conducted using 11 lambs harbouring experimentally established adult *G. pachyscelis* infections and 10 lambs with naturally acquired *O. columbianum* and *T. ovis* burdens. The total faecal output of each animal was collected for three days after treatment and washed in a 44 mesh sieve. The material remaining on the sieve was examined macroscopically for nematode parasites. Animals were slaughtered on the fourth day after treatment and complete counts were made of the numbers of worms remaining in the appropriate regions of the intestinal tract.

## RESULTS AND DISCUSSION

The results obtained in Trial 1—5 on the efficacy of parbendazole at a dose rate of 30 mg/kg bodyweight against immature gastro-intestinal nematodes are shown in Tables 3—5.

Treatment was 97,7—99,9% effective against 3rd stage larvae of *H. contortus O. circumcincta* and *O. trifurcata, T. colubriformis, N. spathiger* and *C. ovina,* while 94,1% of six-day-old 3rd stage larvae of *G. pachyscelis* were removed. Third stage *O. columbianum* larvae were, however, slightly more resistant and 82,5% efficacy was obtained against these.

Parbendazole was also highly active against 4th stage and early 5th stage larvae of *H. contortus, Ostertagia* spp., *T. colubriformis* and *C. ovina,* 95,4—100% of which were removed. Against 4th and 5th stage larvae of *N. spathiger,* treatment was 84,2 and 91,7% effective respectively. Complete clearance of 4th stage larvae of *G. pachyscelis* aged 15 days was obtained and 98,6% efficacy was recorded against 35-day-old 4th stage larvae. Treatment was highly effective against 5th stage *O. columbianum* larvae, but 4th stage larvae were less susceptible and 79,9% were removed.

It is possible that the 5th stage *Ostertagia* spp. and *N. spathiger* larvae burdens recovered from treated lambs in Trial 4, at least in part resulted from development of 4th stage larvae to the 5th stage during the three to four-day period between treatment and

Table 3: TRIALS 1 AND 2— ANTHELMINTIC ACTIVITY AGAINST THE THIRD LARVAL STAGE OF **H. contortus, T. colubriformis, O. columbianum, Ostertagia spp., N. spathiger** and **C. ovina**

| Trial No. | Species | NUMBERS OF WORMS RECOVERED AT AUTOPSY | | | | Efficacy (%) |
|---|---|---|---|---|---|---|
| | | Control | | Parbendazole 30 mg/kg | | |
| | | Mean | Range | Mean | Range | |
| 1 | **H. contortus** | 1 496 | 1 350—1 603 | 7 | 0— 35 | 99,5 |
| | **T. colubriformis** | 1 383 | 1 235—1 714 | <1 | 0— 1 | 99,9 |
| | **O. columbianum** | 634 | 502— 805 | 111 | 55—187 | 82,5 |
| 2 | **Ostertagia spp.** | 1 083 | 906—1 493 | 25 | 7— 53 | 97,7 |
| | **N. spathiger** | 848 | 681— 981 | <1 | 0— 1 | 99,9 |
| | **C. ovina** | 232 | 183— 292 | 4 | 0— 7 | 98,3 |

Nine control and eleven treated lambs in each trial.

Table 4: TRIALS 3 AND 4 — ANTHELMINTIC ACTIVITY AGAINST THE FOURTH LARVAL AND EARLY FIFTH STAGES OF

**H. contortus, T. colubriformis, O. columbianum, Ostertagia spp., N. spathiger and C. ovina**

| Trial No. | Species | NUMBERS OF WORMS RECOVERED AT AUTOPSY | | | | Efficacy (%) |
|---|---|---|---|---|---|---|
| | | Control | | Parbendazole 30 mg/kg | | |
| | | Mean | Mean Range | Mean | Range | |
| 3 | **H. contortus** | | | | | |
| | 4th stage | 827 | 695— 952 | <1 | 0— 2 | 99,9 |
| | 5th stage | 313 | 226— 496 | <1 | 0— 1 | 99,9 |
| | **T. colubriformis** | | | | | |
| | 4th stage | 797 | 471—1 012 | <1 | 9— 2 | 99,9 |
| | 5th stage | 266 | 121— 393 | 0 | — | 100 |
| | **O. columbianum** | | | | | |
| | 4th stage | 189 | 156— 213 | 38 | 23— 66 | 79,9 |
| | 5th stage | 85 | 8— 128 | <1 | 0— 2 | 99,4 |
| 4 | **Ostertagia spp.** | | | | | |
| | 4th stage | 745 | 633— 968 | 34 | 5—176 | 95,4 |
| | 5th stage | 111 | 72— 182 | 5 | 0— 18 | 95,5 |
| | **N. spathiger** | | | | | |
| | | 89 | 8— 143 | 0 | — | — |
| | 4th stage | 745 | 664— 846 | 118 | 5—232 | 84,2 |
| | 5th stage | 156 | 49— 253 | 13 | 0— 37 | 91,7 |
| | **C. ovina** | | | | | |
| | 4th stage | 319 | 263— 368 | <1 | 0— 1 | 99,9 |
| | 5th stage | 43 | 12— 80 | 0 | — | 100 |

Nine control and eleven treated lambs in each trial.

Table 5: TRIAL 5 — ANTHELMINTIC ACTIVITY AGAINST THE THIRD AND FOURTH LARVAL STAGES OF **G. pachyscelis**

| No. of lambs | Age of infection at treatment (days) | Number of worms recovered at autopsy Mean | Range | Efficacy (%) |
|---|---|---|---|---|
| 9 | Control | 22 | 7—34 | — |
| 11 | 6 | 1,3 | 0— 5 | 94,1 |
| 11 | 15 | 0 | — | 100 |
| 11 | 35 | <1 | 0— 2 | 98,6 |

slaughter. The numbers of 5th stage worms recovered, however, were extremely low and the results, particularly those relating to efficacy against 4th stage larvae, cannot have been affected to any significant extent by such development.

The results obtained in Trials 6—9 on efficacy against adult worm infections are given in Tables 6 and 7.

Treatment was 100% effective against *H. contortus, Ostertagia* spp., *T. colubriformis, G. pachyscelis, C. ovina* and *O. columbianum,* and 96,8% efficacy was obtained against *N. spathiger.* Activity against adult *T. ovis,* however, was low and in 10 critical anthelmintic tests efficiency ranged from nil to 48%.

In Trials 1—4, it was found that significant numbers of 4th and early 5th stage larvae of *H. contortus* and *Ostertagia* spp. frequently failed to migrate from homogenised abomasal wall material during the periods of incubation in the waterbath. Counting immature worms in aliquot samples of this material proved extremely time consuming, and it is considered that acid-pepsin digestion of the mucosal and submucosal layers of the abomasum would be more suitable for the recovery of histotrophic stages. In Trials 2 and 4, however, it was found that virtually all immature *N. spathiger* and *C. ovina* migrated from homogenised mucosal and submucosal layers of the small and large intestines.

Table 6: TRIALS 6 AND 7 — ANTHELMINTIC ACTIVITY AGAINST FIFTH STAGE AND ADULT **H. contortus, T. colubriformis, Ostertagia** spp., **N. spathiger and C. ovina**

| Trial No. | Species | NUMBERS OF WORMS RECOVERED AT AUTOPSY | | | | Efficacy (%) |
|---|---|---|---|---|---|---|
| | | Control | | Parbendazole 30 mg/kg | | |
| | | Mean | Range | Mean | Range | |
| 6 | **H. contortus** | | | | | |
| | 4th stage | 59 | 7— 150 | 0 | — | — |
| | 5th stage + adult | 1 430 | 930—1 923 | 0 | — | 100 |
| | **T. colubriformis** | | | | | |
| | Adult | 1 711 | 1 527—1 903 | 0 | — | 100 |
| 7 | **Ostertagia** spp. | | | | | |
| | 4th stage | 65 | 0— 102 | 1 | 0— 4 | — |
| | 5th stage + adult | 1 421 | 1 189—1 595 | 0 | — | 100 |
| | **N. spathiger** | | | | | |
| | 4th stage | 129 | 17— 617 | 10 | 0— 37 | — |
| | 5th stage + adult | 1 782 | 853—2 123 | 57 | 0—285 | 96,8 |
| | **C. ovina** | | | | | |
| | 5th stage + adult | 170 | 151— 193 | 0 | — | 100 |

Nine control and eleven treated lambs in each trial.

Table 7: TRIALS 8 AND 9 — ANTHELMINTIC ACTIVITY AGAINST EXPERIMENTAL ADULT **G. pachyscelis** AND NATURAL ADULT **O. columbianum** AND **T. ovis** INFESTATIONS

| Trial No. | Species | No. of critical tests conducted | Total No. of worms expelled | Total No. of worms at autopsy | Range in burdens of individual sheep | Efficacy (%) Overall | Range |
|---|---|---|---|---|---|---|---|
| 8 | **G. pachyscelis** | 11 | 421 | 0 | 9— 61 | 100 | — |
| 9 | **O. columbianum** | 10 | 2 234 | 0 | 4—378 | 100 | — |
| | **T. ovis** | 10 | 136 | 560 | 10—158 | 19,5 | 0—48 |

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# TRIALS WITH RAFOXANIDE

## 1. *FASCIOLA GIGANTICA* IN CATTLE IN ANGOLA

A. J. SNIJDERS*, J. P. LOUW* AND F. M. H. SERRANO**

SUMMARY

Rafoxanide† (3,5-diiodo-3′-chloro-4′- (p-chlorophenoxy)-salicylanilide) was dosed at rates ranging from 2,5 to 20 mg/kg liveweight against *Fasciola gigantica* in field infestations in cattle. All dosage rates used were highly effective and no signs of toxicity were observed.

SUMÁRIO

Foram realizados ensaios com o rafoxanide† (3,5-diiodo-3′-cloro-4′- (p-clorofenoxi-salicilanilida), em bovinos infestados pela *Fasciola gigantica* em condições naturais.

Este anti-helmíntico revelou uma grande eficácia para as formas adultas de *Fasciola gigantica*, principal agente patogénico da Distomatose no continente africano.

A acção terapêutica foi obtida nas doses de 2,5 a 10 mg por q.p.v. nao tende os animais apresentade qualquer sinal de toxicidade na dose de 20 mg por q.p.v.

### INTRODUCTION

The search continues for anthelmintics effective against parasitic trematodes of cattle.

The activity of a new compound, rafoxanide (3,5-diiodo-3′-chloro-4′- (p-chlorophenoxy)-salicylanilide) has been described against *Fasciola hepatica* [1-6]. Following an anthelmintic trial in a natural infestation of *F. hepatica* in sheep in South Africa, a field trial was arranged to treat *Fasciola gigntica* in cattle in Angola. The latter is described as the common liver fluke of domestic stock of Africa [7] and is a major problem in cattle on the central plateau of Angola, where it also restricts the introduction of sheep in some areas.

### MATERIALS AND METHODS

*Environment:* The farm Fazenda Cuito, of the Companhia Agricola e Pecuaria de Angola, at Huambo, Angola, is 42 000 hectares in extent, approximately 1 800 metres above sea level with an average annual rainfall of 1 600 mm. Rain occurs mainly from October to May with a peak in February to March. The mean temperature is 19°C, maximum 24 to 25°C. The country is broken by hills and flats and the predominant grass is *Hyparrhenia* spp.

*Animals:* Aged bulls and cows of various breeds including indigenous stock, Africander, Aberdeen Angus, Charolais crosses and Brown Swiss were identified by numbered ear-tags and examined for infestation with *Fasciola* spp., using a simple faecal sedimentation technique. The animals were in poor condition.

Infested animals were weighed and treated in the order that they were presented in the race, with the exception that the ten heaviest animals were kept as controls for carcass salvage purposes as well as to reduce the amount of experimental material used. Some of these control animals were treated orally with the inert vehicle for rafoxanide.

*Treatment:* The drug rafoxanide was used as a 3,03% w/v preformed suspension. Treatment was administered intraruminally by hypodermic syringe and cannula, or orally, designed to provide 2,5 5,0 10,0 and 20,0 mg/kg liveweight. The cattle receiving the two higher dosage rates were treated orally.

*Autopsy:* Animals were slaughtered from 11 to 14 days after treatment. Livers were collected and initially the rumens were examined for amphistomes. Initially, the intestines were also collected for nematode examination.

At the laboratory, the livers were cut into 1 to 2 cm slices and all visible fluke

*MSD (PTY) LTD., 142 Pritchard Street, P.O. Box 7748, Johannesburg.
**Instituto de Investigação Veterinária de Angola, C.Postal 7, Nova Lisboa, Angola.
†"RANIDE". Reg Trade Mark of MSD (Pty.) Ltd., Merck, Sharp & Dohme International, Division of Merck & Co. Inc., Rahway, N.J., U.S.A.

Table: **F. gigantica** RECOVERED AT AUTOPSY, 11 TO 14 DAYS AFTER TREATMENT WITH RAFOXANIDE

| Animal No. | Weight (kg) | Dose (ml) | Fasciola gigantica: Alive: Immediately visible | Alive: After incubation | Dead | Total |
|---|---|---|---|---|---|---|
| **Control group (Placebo)** | | | | | | |
| 3 673 | 540 | 135 | 49 | 4 | 0 | 53 |
| 158 | 630 | — | 47 | 8 | 0 | 55 |
| 161 | 530 | — | 21 | 3 | 0 | 24 |
| 3 699 | 561 | 150 | 126 | 6 | 0 | 132 |
| 159 | 595 | — | 48 | 6 | 0 | 54 |
| 124 | 510 | — | 35 | 0 | 0 | 35 |
| 145 | 506 | 135 | 78 | 3 | 0 | 81 |
| 156 | 554 | — | 80 | 11 | 0 | 91 |
| 154 | 516 | — | 63 | 1 | 0 | 64 |
| 157 | 561 | — | 16 | 1 | 0 | 17 |
| **Rafoxanide — 2,5 mg/kg (intraruminal)** | | | | | | |
| 142 | 455 | 36,5 | 0 | 0 | 0 | 0 |
| 153 | 252 | 20 | 0 | 0 | 0 | 0 |
| 123 | 308 | 25 | 0 | 0 | 0 | 0 |
| 195 | 349 | 28 | 0 | 0 | 2 | (2) |
| 199 | 317 | 26 | 3 | 0 | 1 | 3(1) |
| 200 | 330 | 26 | 2 | 1 | 0 | 3 |
| 197 | 332 | 27 | 0 | 0 | 0 | 0 |
| 20 | 301 | 24 | 0 | 0 | 0 | 0 |
| 194* | 443 | 37 | 5 | 0 | 6 | 5(6) |
| 193 | 371 | 30 | 0 | 0 | 0 | 0 |
| **Rafoxanide — 5,0 mg/kg (intraruminal)** | | | | | | |
| 137 | 325 | 52 | 0 | 0 | 0 | 0 |
| 150 | 288 | 46 | 0 | 0 | 1 | (1) |
| 2 988 | 276 | 44 | 0 | 0 | 0 | 0 |
| 132 | 339 | 54 | 0 | 0 | 0 | 0 |
| 122 | 247 | 40 | 2 | 0 | 0 | 2 |
| 130 | 355 | 36 | 0 | 0 | 0 | 0 |
| 118 | 521 | 84 | 0 | 0 | 1 | (1) |
| 121 | 389 | 62 | 0 | 0 | 0 | 0 |
| 3 831 | 248 | 40 | 0 | 0 | 0 | 0 |
| 34 | 313 | 50 | 0 | 0 | 0 | 0 |
| **Rafoxanide — 10 mg/kg (per os)** | | | | | | |
| 147 | 283 | 94 | 0 | 0 | 0 | 0 |
| 162 | 280 | 93 | 0 | 0 | 0 | 0 |
| 135 | 462 | 154 | 0 | 0 | 0 | 0 |
| 119 | 248 | 83 | 0 | 0 | 0 | 0 |
| 17 | 234 | 78 | 0 | 0 | 0 | 0 |
| **Rafoxanide — 20 mg/kg (per os)** | | | | | | |
| 9 202 | 290 | 193 | 0 | 0 | 0 | 0 |
| 155 | 244 | 163 | 0 | 0 | 0 | 0 |
| 151 | 425 | 283 | 0 | 0 | 3 | (3) |
| 3 571 | 305 | 203 | 0 | 0 | 2 | (2) |
| 9 165 | 282 | 188 | 0 | 0 | 0 | 0 |

*Very severe fibrosis
( ) = Dead flukes

removed and stored for counting. The gall-bladders from livers with no visible fluke were retained and the bile and epithelial scrapings examined for fluke eggs.

The liver slices were incubated in a 0,9% salt solution on a mesh screen with 0,5 cm apertures, shaped to fit into galvanized trays. These trays were immersed in water kept at 42°C in a large water bath. The slices were removed after one hour, washed and squeezed manually, and the remaining material in the tray washed onto sieves with 317 $\mu$m apertures. The contents of these sieves were collected and examined microscopically. The number of liver fluke present was determined by counting oral suckers recovered.

## RESULTS

The treatment schedule and fluke recoveries at autopsy are summarised in the table.

All the controls were infested with *F. gigantica* and the population consisted of gravid and non-gravid flukes. All livers had some degree of cholangitis. Macroscopically some of the treated livers had a normal parenchyma but portions of the bile ducts were fibrotic or even calcareous.

The presence of dead flukes was not related to the dosage rate. The gross morphology of dead flukes, their colour, shape and lack of movement made them easy to distinguish from live ones. It is highly probable that only some of the dead flukes were recovered and recognized.

Figure: Dead **F.gigantica** (left) and fluke (alive) collected 11 days after treatment.

*F. gigantica* eggs were present in all the gall-bladders from livers from which no fluke were recovered and which appeared

relatively normal. The egg shells were empty and without morulae nor any cells. By contrast, the eggs recovered from the gall-bladders of livers containing both live and dead flukes had normal and ghost eggs.

Rafoxanide suspension was completely effective against adult *F. gigantica* at a dosage level of 10 mg/kg liveweight or more. At 5 mg/kg two live flukes were found in ten animals. At 2,5 mg/kg the largest number of flukes was recovered from an animal with severe fibrosis of the liver. Even in this animal the drug was active as indicated by the recovery of 6 dead flukes out of a total of 11 (Animal 194, Table).

Rafoxanide suspension had no appreciable effect on adult amphistomes in the rumen. Because the nematode infestations were either very low or variable in the three controls examined, no further examination for these parasites was carried out.

Despite the poor condition of the animals, no obvious toxicity was encountered at doses up to 20 mg/kg liveweight. Animal 253, treated at the rate of 2,5 mg/kg, had generalized tuberculosis with extensive liver involvement.

## DISCUSSION AND CONCLUSIONS

The results of anthelmintic trials with rafoxanide in infestations of *F. hepatica* in sheep have been reported [2-6]. The results of the present experiment indicate its efficacy on *F. gigantica* in cattle.

Rafoxanide at dosage rates of 2,5 to 20 mg/kg was highly effective against adult *F. gigantica*. This activity was not affected by chronic cholangitis and calcification, nor by severe cirrhosis (Animal 194, Table).

In three of the treated groups, dead flukes were encountered at autopsy 11 to 14 days after treatment. This did not affect the ultimate conclusions, since they were easily distinguishable from live flukes. Subsequent work in sheep has shown that dead fluke may be recovered even 31 days after treatment, although degenerative changes in some flukes can be seen as early as two days after treatment (unpublished data). It is recommended that animals should not be killed within 10 days of treatment to facilitate interpretation of results.

In the current trial a therapeutic ratio of at least eight was obtained since a dosage rate of 2,5 mg/kg was highly effective against adult fluke and no toxic symptoms were observed at 20 mg/kg liveweight. Rafoxanide was thus not only a highly effective, but also a safe remedy against *F. gigantica* under the conditions of this experiment.

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# TRIALS WITH RAFOXANIDE*

## 2. EFFICACY AGAINST *FASCIOLA GIGANTICA* IN CATTLE

A. J. SNIJDERS, I. G. HORAK AND J. P. LOUW†

SUMMARY

Calves were infested with 200 metacercariae of a laboratory strain of *Fasciola gigantica* and treated with rafoxanide at varying intervals after infestation.

In the first experiment dosages of up to 11,25 mg/kg administered *per os* were only partially effective against fluke 57 days days of age. When the fluke were 113 days old, a dosage rate of 3,75 mg/kg was almost completely effective.

In the second experiment calves were treated either 56 or 98 days after infestation. No difference in efficacy was apparent between oral or intraruminal routes of administration of 10 to 20 mg/kg and these dosage rates were highly effective against 56 day old fluke. Dosage rates of 3,75 and 7,5 mg/kg were almost completely effective against 98 day old *F. gigantica*. In addition 7,5 mg/kg was 90% effective against 4th stage larvae and adults of *H. placei*.

Ten calves infested with 200 metacercariae of *F. gigantica* and treated at 45 mg/kg showed no ill effects.

### INTRODUCTION

The discovery of the chemical compound, rafoxanide, (3,5-diiodo-3'-chloro-4'-(p-chlorophenoxy)-salicylanilide) for the treatment of liver fluke in sheep was described by Mrozik and thirteen co-workers [1]. Subsequent workers confirmed the activity of this compound against various ages of *Fasciola hepatica* in sheep [2, 3, 4].

We have established and maintained a strain of *F. gigantica* in *Lymnaea natalensis* and have used this parasite in our trials since it is the most prevalent liver fluke in Africa [5].

The results of a trial with rafoxanide against a field infestation of *F. gigantica* in cattle have been described [6]; this has been followed by the presently described laboratory trials.

### MATERIALS AND METHODS

*Experiment I*

Fifty-three weaner calves, six to eight months old, were purchased in an area where liver fluke does not occur and transported to the laboratory where they were kept in a paddock free from a natural source of *F. gigantica* infestation.

Each animal was infested with 200 metacercariae of *F. gigantica*, harvested 19 to 38 days previously on cellophane strips, from artificially infested *L. natalensis*.

*Section 1 (F. gigantica 57 days old at treatment):* Twenty-five calves were assigned to five numerically equal groups comparable as to sex and liveweight. Four of these groups were treated when the flukes were 57 days old. Rafoxanide was used as a 3,035% w/v suspension and administered *per os* at dosage rates of 5,0, 7,5, 11,25 and 45 mg/kg. One group was retained as untreated controls. In addition, one calf was killed as a viability control and two were slaughtered on the day of treatment to determine the number and size of the flukes.

Fifteen treated calves and five controls were slaughtered 18 to 21 days after treatment while the five calves treated at 45 mg/kg were retained for observation.

At autopsy all visible flukes were recovered after cutting the livers into slices 0,5 cm thick. The slices were placed on a coarse 5 mm mesh Endecott screen fitted into round containers with saline and incubated at 42°C in a waterbath for two hours. The slices were then macerated and incubated for a further two hours. The filtrates were examined microscopically;

*"RANIDE": Reg. Trade Mark of MSD (PTY) LTD, Merck Sharp & Dohme Internasional, Division of Merck & Co. Inc., Rahway, N.J., U.S.A.

†MSD Research Centre, P.O. Box 7748, Johannesburg.

complete flukes and those portions with ventral suckers only were counted.
*Section 2 (F. gigantica 113 days old at treatment):* Twenty-five calves were assigned to five equal groups on sex and liveweight.

Twenty were treated with a 3,035% w/v suspension of rafoxanide at dosage rates of 2,5, 3,75, 5,625 and 45,0 mg/kg liveweight 113 days after infestation. The compound was administered ruminally using a trochar and cannula. Five calves were retained as untreated controls.

The group treated at 45 mg/kg was kept for observation while the other calves were killed 10 to 12 days after treatment.

At autopsy the fluke were recovered as before and counted macroscopically against a black background.

*Experiment II*

Sixty-seven calves between six and ten months old were obtained in a fluke-free area and transported to the laboratory. The calves were treated with thiabendazole** to remove existing nematode burdens.

Each of the calves was infested with 200 metacercariae of *F. gigantica* collected on cellophane strips. Fifty-six days later three groups of five calves each were treated *per os* with rafoxanide (2,5% w/v suspension) either 10, 15 or 20 mg/kg liveweight while three comparable groups were treated intraruminally at the same dosage rates. All the treated calves and five controls were slaughtered 14 to 15 days later. At autopsy, flukes were recovered from the liver and counted as described in Experiment I.

The remaining 32 calves were each infested with 200 third stage infective larvae of *Haemonchus placei* on five occasions to provide worms from 14 to 28 days old at treatment. Treatment with rafoxanide 2,5% w/v suspension took place when the *F. gigantica* infections were 98 days old and 11 calves were treated intraruminally at 3,75 mg/kg and 11 calves at 7,5 mg/kg liveweight while the remaining 10 calves served as untreated controls.

The infestation dates and procedures are summarized in the experimental design in Table 1.

Table 1: INFESTATION AND TREATMENT PROCEDURES OF EXPERIMENT II

| Day | Procedure |
|---|---|
| 0 | Infest 67 calves with 200 metacercariae of **F. gigantica** |
| +56 | Treat 5 calves each at 10, 15 or 20 mg/kg **per os**<br>Treat 5 calves each at 10, 15 or 20 mg/kg intraruminally |
| +70–75 | Slaughter 30 treated calves and 5 untreated calves |
| +73 | Infest 32 calves with 200 **Haemonchus placei** |
| +77 | Infest 32 calves with 200 **Haemonchus placei** |
| +80 | Infest 32 calves with 200 **Haemonchus placei** |
| +84 | Infest 32 calves with 200 **Haemonchus placei** |
| +98 | Treat 11 calves with rafoxanide at 3,75 mg/kg intraruminally<br>Treat 11 calves with rafoxanide at 7,5 mg/kg **per os**<br>Slaughter 10 controls |
| +111–113 | Slaughter 22 treated calves |

## RESULTS

*Experiment I*

The treatment schedule and fluke recoveries are summarized in Table 2 and 3.

Dosage rates of 11,25 mg/kg and less *per os* were only partially effective against 57 days old *F. gigantica*. When the flukes were 113 days old, rafoxanide had good activity at 2,5 mg/kg and was highly effective at 3,75 mg/kg liveweight.

No signs of toxicity were seen in both groups treated at 45 mg/kg liveweight.

*Experiment II*

The fluke recoveries *post mortem* are summarized in Table 4 and 5.

Rafoxanide at 10 to 20 mg/kg liveweight, administered either intraruminally or *per os*, was highly effective against 56 day old *F. gigantica*.

The dosage rate of 3,75 mg/kg administered intraruminally was highly effective

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Table 2: **EXPERIMENT I** — TREATMENT AND WORM RECOVERIES **POST MORTEM** OF **F. GIGANTICA** TREATED WHEN 57 DAYS OLD

| Animal No. | Dosage rate mg/kg | Days after treatment | F. gigantica | |
|---|---|---|---|---|
| | | | Live | Dead |
| 387 | Control | 16 | 110 | 0 |
| 389 | ,, | 15 | 123 | 0 |
| 393 | ,, | 15 | 136 | 0 |
| 384 | ,, | 14 | 99 | 0 |
| 385 | ,, | 14 | 133 | 0 |
| Ave | — | — | 120 | 0 |
| 242 | 5,0 | 16 | 71 | 11 |
| 353 | 5,0 | 15 | 77 | 0 |
| 386 | 5,0 | 15 | 50 | 14 |
| 372 | 5,0 | 14 | 117 | 1 |
| 392 | 5,0 | 14 | 59 | 13 |
| Ave | — | — | 75 | 8 |
| 240 | 7,5 | 17 | 17 | 0 |
| 364 | 7,5 | 16 | 6 | 5 |
| 368 | 7,5 | 16 | 14 | 1 |
| 370 | 7,5 | 14 | 36 | 14 |
| 390 | 7,5 | 14 | 68 | 0 |
| Ave | — | — | 28 | 4 |
| 243 | 11,25 | 17 | 45 | 0 |
| 363 | 11,25 | 16 | 44 | 0 |
| 378 | 11,25 | 16 | 8 | 6 |
| 379 | 11,25 | 15 | 49 | 8 |
| 382 | 11,25 | 15 | 20 | 43 |
| Ave | — | — | 33 | 11 |
| 248, 357, 391, 244, 355 | 45,0 | **Observation** | | |
| | | No overt signs of toxicity observed. All survived for six months. | | |

Table 3: **EXPERIMENT I** — TREATMENT AND WORM RECOVERIES **POST MORTEM** OF **F. GIGANTICA** TREATED WHEN 113 DAYS OLD

| Animal No. | Dosage rate mg/kg | Days after treatment | F. gigantica |
|---|---|---|---|
| 367 | Control | 13 | 103 |
| 375 | ,, | 13 | 101 |
| 365 | ,, | 13 | 109 |
| 234 | ,, | 13 | 127 |
| 371 | ,, | 14 | 110 |
| Ave | — | — | 110 |
| 235 | 2,5 | 14 | 13 |
| 238 | 2,5 | 14 | 0 |
| 394 | 2,5 | 14 | 10 |
| 358 | 2,5 | 14 | 0 |
| 374 | 2,5 | 14 | 70 |
| Ave | — | — | 19 |
| 239 | 3,75 | 14 | 4 |
| 376 | 3,75 | 15 | 7 |
| 397 | 3,75 | 15 | 0 |
| 236 | 3,75 | 15 | 5 |
| 366 | 3,75 | 15 | 0 |
| Ave | — | — | 3 |
| 246 | 5,625 | 13 | 0 |
| 377 | 5,625 | 14 | 0 |
| 369 | 5,625 | 13 | 0 |
| 395 | 5,625 | 13 | 0 |
| 373 | 5,625 | 13 | 0 |
| Ave | — | — | 0 |
| 247, 361, 380, 245, 381 | 45,0 | **Observation** | |
| | | No overt symptoms of toxicity observed. All survived for six months. | |

against 98 day old *F. gigantica*, but only 65% effective against 4th stage larvae and adults of *H. placei*, while at 7,5 mg/kg rafoxanide was highly effective against both parasites.

It was noted that the livers of treated calves had considerably fewer lesions than those of the untreated controls.

## DISCUSSION

The large liver fluke, *F. gigantica*, has been described as the common liver fluke of domestic stock in Africa [5]. It is highly pathogenic for sheep and in our laboratory more than 90 metacercariae often cause death at about 80 days after infestation in sheep up to 18 months of age. It is also commonly found in cattle and causes lesions indistinguishable from those of *F. hepatica*. The infectivity of *F. gigantica* for cattle is reflected by average recoveries in the control in these experiments of more than 50% in terms of metacercariae administered.

The results obtained in these trials are in general agreement with those obtained by other workers using *F. hepatica* [1-4]. The dosage rate of rafoxanide required for effective control decreases with the age of the fluke. When the fluke were 57 days old, in Experiment I, a dosage rate of 11,25 mg/kg was

Table 4: **EXPERIMENT II** — TREATMENT AND WORM RECOVERIES **POST MORTEM** OF **F. GIGANTICA** TREATED WHEN 56 DAYS OLD

| Calf No. | Treatment | F. gigantica | | Calf No. | Treatment | F. gigantica | |
|---|---|---|---|---|---|---|---|
| | | Alive | Dead | | | Alive | Dead |
| 437 | 10 mg/kg per os | 10 | 0 | 10 | 10 mg/kg intrarum. | 3 | 0 |
| 21 | | 10 | 3 | 32 | | 10 | 5 |
| 436 | | 1 | 0 | 56 | | 3 | 0 |
| 406 | | 3 | 0 | 411 | | 1 | 0 |
| 425 | | 4 | 0 | 431 | | 2 | 0 |
| Mean | | 6 | | | | 4 | |
| 8 | 15 mg/kg per os | 1 | 0 | 31 | 15 mg/kg intrarum. | 1 | 1 |
| 30 | | 1 | 0 | 55 | | 2 | 0 |
| 410 | | 0 | 0 | 57 | | 0 | 0 |
| 427 | | 3 | 1 | 440 | | 0 | 11 |
| 442 | | 1 | 0 | 443 | | 0 | 1 |
| Mean | | 1 | | | | <1 | |
| 13 | 20 mg/kg per os | 0 | 0 | 409 | 20 mg/kg intrarum. | 1 | 0 |
| 41 | | 0 | 0 | 413 | | 1 | 0 |
| 48 | | 0 | 0 | 414 | | 0 | 0 |
| 408 | | 0 | 2 | 416 | | 0 | 4 |
| 424 | | 0 | 0 | 433 | | 0 | 0 |
| Mean | | 0 | | | | <1 | |
| 26 | Untreated Controls | 77 | 0 | | | | |
| 435 | | 77 | 0 | | | | |
| 19 | | 100 | 0 | | | | |
| 4 | | 103 | 0 | | | | |
| 22 | | 96 | 0 | | | | |
| Mean | | 91 | | | | | |

Table 5: EXPERIMENT II — WORM RECOVERIES **POST MORTEM** OF **F. GIGANTICA** AND **H. PLACEI** FROM CATTLE TREATED INTRARUMINALLY WITH RAFOXANIDE

| Untreated Controls | | 3,75 mg/kg | | 7,5 mg/kg | |
|---|---|---|---|---|---|
| F. gigantica | H. placei* | F. gigantica** | H. placei* | F. gigantica** | H. placei* |
| 109 | 195 | 0 | 93 | 0 | 8 |
| | | 0 | 72 | 0 | 14 |
| 98 | 131 | 16 | 135 | 0 | 4 |
| 90 | 156 | 0 | 45 | 0 | 4 |
| 141 | 369 | 1 | 106 | 0 | 1 |
| 80 | 178 | 0 | 68 | 0 | 10 |
| 85 | 210 | 0 | 107 | 0 | 118 |
| 105 | 218 | 0 | 39 | 0 | 6 |
| 83 | 193 | 0 | 62 | 0 | 4 |
| 135 | 198 | 0 | 56 | 0 | 41 |
| 145 | 239 | 0 | 27 | 0 | 15 |
| Mean 107 | 209 | 2 | 73 | 0 | 20 |
| % Reduction | | 98 | 65 | 100 | 90 |

*Fourth stage larvae and adult worms
**98 Days old at treatment

only 72,5% effective while 3,75 mg/kg was almost completely effective against 113 day old fluke. In Experiment II, dosage rates of 10 mg/kg administered either orally or intraruminally were almost completely effective against 56 day old fluke, while 3,75 mg/kg was 98% effective against 98 day old fluke.

None of the cattle treated at 45 mg/kg showed any ill effects, providing a favourable ratio of therapeutic to toxic dose.

*Haemonchus placei* often occurs in association with *F. gigantica*. The high efficacy of rafoxanide against both parasites at 7,5 mg/kg liveweight should be important in those enzootic areas.

The regression of liver lesions in treated calves was similar to that observed by other workers in cattle and sheep[4,6]. This is an important factor in the salvage of livers for human or animal consumption.

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## BOOK REVIEW — BOEKRESENSIE

# DISEASES OF SWINE

H. W. Dunne, Editor

Third edition. Iowa State University Press, Ames, Iowa. 1970 pp XIII + 1144. South African price: R19.85.

This welcome new edition of what has deservedly become the definitive textbook on every aspect of pig disease, has been very greatly expanded and revised to reflect the tremendous advances in this field since the second edition of 1964. Twenty-two new contributors have added to the text and no less than five additional chapters discuss recent research of interest to practitioner and specialist alike (adeno-viruses; gastric ulcers; perirenal oedema; aflatoxins and gnotobiotic pigs). Twelve chapters have been largely rewritten, while several others have undergon considerable expansion.

Valuable new information is presented on important subjects such as mycoplasmosis, colibacillosis, atrophic rhinitis, muscle disorders and typical mycobacteria. A particularly useful chapter reviews the pathogenesis of embryonal resorption and foetal death, including the effects of the so-called Smedi enteroviruses and serves to emphasize the evergrowing importance of all aspects of sow productivity in the economics of production.

The chapter on non-infectious sterility and artificial insemination could well be expanded to furnish additional information regarding such subjects as implantation and semen diluents. Another area where fuller coverage is desirable, is the newer information concerning the aetiology and treatment of exudative epidermitis. These, however, are minor criticisms, but to them may be added a plea for greater reference to the non-American literature in the future, although the bibliography found at the end of each chapter lists a large proportion of the literature up to 1969. The cross-referenced index is reasonably adequate.

The book is beautifully produced and printed, with a generous number of excellent tables, figures and colour plates. It provides a vast amount of information in compact form and must be considered as indispensable to all whose interests require an up-to-date reference work on pig pathology, reproduction and production.

R.K.L.

Jl S. Afr. vet. med. Ass. 42 (3): 259-261 1971

# THE EFFICACY OF AMDAX (R) AGAINST GASTRO-INTESTINAL PARASITES OF CATTLE

S. STAMPA*


## SUMMARY

The anthelmintic, Amdax (R)**, an organo-phosphorus compound, was tested for its efficacy and toxicity in calves. At 5—10 mg/kg the drug was highly and consistently effective against *Haemonchus* and *Trichuris* spp. It was moderately, although somewhat irregularly, effective against *Ostertagia, Trichostronglylus* and *Cooperia* spp. Efficacy against *Nematodirus* spp. was only reached at dosages in excess of 10 mg/kg. As 100 mg/kg was well tolerated, the drug can be accepted as safe.


## INTRODUCTION

An earlier paper[1] dealt with the efficacy of Amdax against gastro-intestinal parasites of sheep. A dosage of 0,36 g active ingredient was recommended for sheep of all sizes. At this rate the drug controls *Haemonchus contortus,* the main summer parasite in grassveld regions. In addition, it is moderately effective against *Ostertagia* and *Trichostrongylus* spp. in lambs receiving 15—22 mg active ingredient per kg bodyweight.

The present investigation is concerned with the efficacy of Amdax against gastro-intestinal parasites of cattle.

## MATERIALS AND METHODS

A sugar-coated granulate containing 3,6% Amdax was used in all but two trials, in which a similar 5% formulation was employed. The drug was readily swallowed by calves that were dosed. Critical anthelmintic tests[2] were performed on 11 calves with a mixed, naturally acquire dworm infestation. Six additional tests were done with calves using the worm egg counting technique[3], involving a total of 45 treated animals and 45 untreated controls. The efficacy was established by the following formula:

$$E = 100 - \frac{(a \times c)}{(b \times d)}$$

a — mean number of worm eggs per gram (epg) of faeces of the treated group before dosing,

b — mean number of epg of the treated group two weeks after dosing,

c — mean number of epg of the control group before dosing.

d — mean number of epg of the control group two weeks thereafter.

The McMaster epg counting technique was used, counting 12 chambers of 0,15 ml for each faecal specimen of each animal. The proportion of eggs to be assigned to the different worm species was calculated from differentiations of third stage larvae on a percentage basis. The larvae were harvested from faecal cultures of each animal tested.

## RESULTS

These are summarized in tables 1, 2 and 3.

None of the animals in the efficacy trials showed any ill effects from dosing. As it is difficult to administer much larger dosages of Amdax granulate, toxicity trials were done with products containing a higher percentage of the same active ingredient. The results of this test are summarized in table 4.

## DISCUSSION

The results of the worm egg counting tests confirm those of the critical tests, with the exception of the genus *Nematodirus.* The drug's efficacy against the latter was variable in tests with either technique. The large sampling error normally incorporated in the worm egg counting technique apparently is

*Faculty of Agriculture, University of Fort Hare, P.O. Port Hare.

**"Amdax". Registered Trade Mark of Farbenfabriken Bayer. It contains, according to the producer, 5% w/w naphthalophos: O'O diethyl- O (naphthalozimide) phosphate.

Table 1: EFFICACY OF AMDAX AGAINST ADULT PARASITES OF CATTLE
RESULTS OF CRITICAL TESTS

| Calf No. | Dose mg/kg | Haemonchus | Ostertagia | Trichostrongylus | Cooperia | Nematodirus | Oesophagostomum | Trichuris |
|---|---|---|---|---|---|---|---|---|
| 468 | 5 | 100 | 78,0 | 40,6 | 44,7 | 0 | — | — |
| 51 | 7,5 | — | 98,9 | 92,9 | 100 | 58,5 | — | 100 |
| 742 | 7,5 | — | 99,4 | — | 100 | 22,8 | — | 100 |
| 480 | 10 | — | 86,1 | 24,2 | 44,0 | 3,4 | 0 | 100 |
| 445 | 10 | 100 | 58,2 | 19,6 | 36,4 | 3,0 | 0 | — |
| 437 | 10 | 100 | 67,2 | 52,6 | 89,7 | 18,0 | — | 100 |
| 567 | 14,3 | 100 | 84,2 | 100 | 95,3 | 81,3 | — | — |
| 270 | 14,8 | — | 95,0 | 96,4 | 100 | 100 | — | 100 |
| 236 | 15,0 | — | 99,7 | 100 | 100 | 96,2 | — | 100 |
| 515 | 15,0 | — | 62,2 | 76,0 | 14,8 | — | — | — |
| 575 | 21,2 | 100 | 68,9 | 94,4 | 90,8 | 100 | — | — |

Table 2: NUMBER OF ANIMALS IN WHICH WORM BURDENS WERE REDUCED BY PERCENTAGES SPECIFIED

I. 5—10 mg/kg Amdax

| Reduction | Haemonchus | Ostertagia | Tricho-strongylus | Cooperia | Nematodirus | Oesophago-stomum | Trichuris |
|---|---|---|---|---|---|---|---|
| Less than 60% | 0 | 1 | 4 | 3 | 5 | 2 | 0 |
| 60— 80% | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| 80—100% | 3 | 3 | 2 | 3 | 0 | 0 | 4 |

II. 14,3—21,2 mg/kg Amdax

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Less than 60% | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| 60— 80% | 0 | 1 | 1 | 0 | 1 | 0 | 0 |
| 80—100% | 2 | 3 | 4 | 4 | 3 | 0 | 2 |

Table 3: RESULTS OF WORM EGG COUNTING TRIALS WITH AMDAX. MEAN PERCENTAGE REDUCTION OF WORM EGG COUNTS TWO WEEKS AFTER DOSING

| Test number<br>No. of animals<br>Dosage mg/kg | 1<br>8<br>6,0—8,7 | 2<br>10<br>7,2—10,2 | 3<br>12<br>7,6—12,0 | 4<br>5<br>12,5 | 5<br>7<br>12,9—16,6 | 6<br>3<br>25,0 |
|---|---|---|---|---|---|---|
| **Haemonchus** | 89,6 | 100 | 92,1 | 100 | 100 | 100 |
| **Ostertagia** | 0 | 45,0 | 71,0 | 65,3 | 74,0 | — |
| **Trichostrongylus** | — | 55,4 | 68,1 | 83,3 | 98,1 | — |
| **Cooperia** | 54,4 | 51,8 | 40,4 | 95,0 | 90,6 | 100 |
| **Oesophagostomum** | 0 | 5,3 | 0 | 22,7 | 94,2 | 100 |
| **Bunostomum** | 98,5 | 0 | — | 0 | 71,3 | 0 |
| **Nematodirus** | — | — | 0 | 71,7 | 91,5 | — |

reduced by only using mean counts of groups of test animals.

The efficacy against the gastro-intestinal parasites of cattle tends to be higher than that observed in sheep. The drug was highly and consistently effective at all dosages against adult *Haemonchus* and *Trichuris* spp. It was moderately effective, although somewhat erratic, against adult *Ostertagia, Trichostrongylus* and *Cooperia* spp. and at higher dosage rates also against *Nematodirus* spp.

Toxicity trials revealed a very wide margin of safety (table 4).

Table 4: TOXICITY TRIALS WITH AMDAX

| No. of Calves | Dosage rate mg/kg | Results |
|---|---|---|
| 61 | 50 | No ill effects |
| 179 | 50—59 | No ill effects |
| 137 | 53—89 | No ill effects |
| 12 | 75 | One calf suffered from temporary diarrhoea, others no ill effects |
| 36 | 100 | Ten calves suffered from temporary diarrhoea, others no ill effects |
| 7 | 125 | No ill effects |
| 3 | 150 | No ill effects |

## CONCLUSION

A dosage of not less than 10 mg/kg is recommended for the treatment of calves against internal parasites. A heaped dessertspoon 3,6% Amdax contains 0,75 g active ingredient and would be sufficient for calves up to 75 kg (165 lbs) liveweight. This dosage would still be safe for very small calves. An animal of 35 kg (77 lbs) would only receive 20 mg/kg. In the case of the 5% Amdax formulation, a heaped dessertspoon would be sufficient for calves up to 90 kg (200 lbs) liveweight. The same dosage would amount to 29 mg/kg for a calf of 35 kg (77 lbs) liveweight, which is still well within the safety margin.

## ACKNOWLEDGEMENTS

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# LETTER TO EDITOR — AAN DIE REDAKSIE

## PRELIMINARY OBSERVATIONS ON REPRODUCTIVE FAILURE IN SOWS

Sir,

Since starting to investigate the role played by viruses in causing reproductive failures in our pig population some interesting results have been obtained.

The SMEDI syndrome—still-birth, mummification, embryonal death and infertility—can be caused by several infectious and non-infectious factors and it is often difficult to reach a definite diagnosis. Losses can be so high that pig breeding becomes uneconomical.

During our present investigation we have concentrated mainly on the SMEDI A, B and C as well as the T80 virus groups.

The preliminary results of a serological survey, so far carried out only on pig farms with reproductive problems, indicate clearly the presence of high level antibodies to three of the four virus groups. Antibodies to SMEDI and T80 viruses are present in about 80% of the sera tested, whereas antibodies to SMEDI B virus are present in a smaller proportion of sera. It also appears that a similar situation may exist in Rhodesia.

SMEDI B virus has been isolated from foetuses obtained from two farms with a high incidence of mummification, abortions, still-births and weak piglets, as well as other forms of reproductive failure. On these two farms certain aspects of management and nutrition of the breeding herd were considered to be unsatisfactory.

Studies to establish the degree of pathogenicity of such isolates under South African conditions will have to be undertaken and more data and material from the field will have to be obtained and examined.

A. Pini.

Virology Section, Onderstepoort. In co-operation with S. K. Bakker and P. V. A. Davies, Pig Research Section, Onderstepoort.

# Get the jump on mastitis... before your patient can say "Mooo"

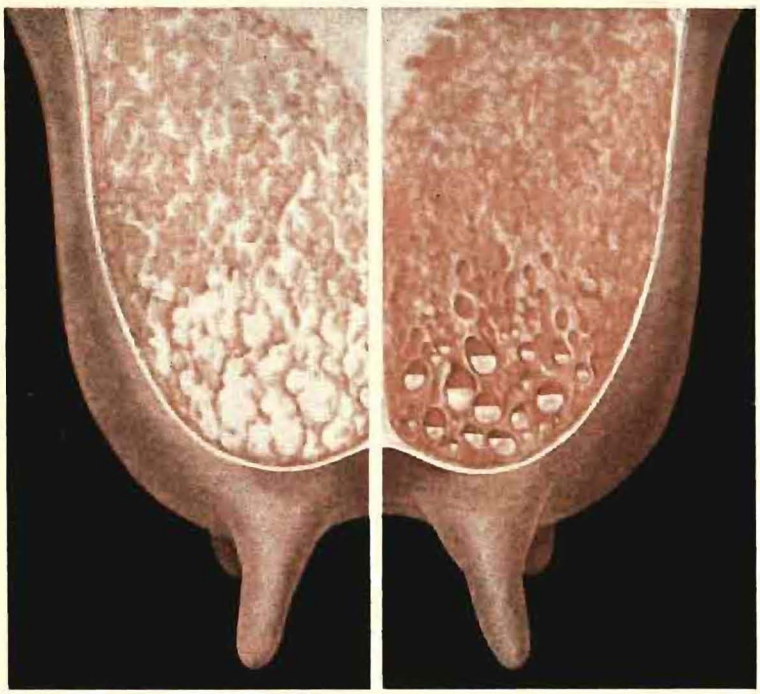

Illustration shows how new Metibiotic Mastitis Foam, when injected, completely fills the quarter of the udder.

Contrast this with the way ordinary oily remedy only fills the teat and cistern, failing to reach upper rear quarter.

## New METIBIOTIC is a self-propelled foam. Only a foam can fill the whole quarter. And then hang on to do its work!

There are dozens of fine antibiotics for mastitis. But conventional methods of infusion after milking leave the agents undispersed and floating in the teat and gland cistern. Medication usually fails to reach the infected upper udder for a complete milking cycle.

**New Metibiotic aerosol-powered mastitis foam** reaches the top of the udder instantly. Metibiotic also contains Tween, emulsifying and dispersing agent which carries the antibiotic to conventionally hard-to-reach collecting ducts and alveoli.

**No "milk-out" before treatment.** In conventional treatment much of the medicating agent is frequently "milked-out" before reaching infected tissue. Metibiotic's instant dispersing action puts the entire dosage to work before "milking-out" can occur.

**Tested formula, reduces tissue damage.** Active ingredients include two proven antibiotics (penicillin G procaine 100,000 units, dihydrostreptomycin 300 mg.) and one corticosteroid (prednisone acetate U.S.P. 4 mg.) to control infection and soothe inflammation. Treatment is faster, tissue damage smaller. Cost is low.

## NEW METIBIOTIC

**Warning:** Milk taken from animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food.

**Packaging:** Single dose containers, box of 12.

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Jl S. Afr. vet. med. Ass. 42 (3): 263-264 1971

# CORDYLOBIA INFESTATION IN THE YELLOW MONGOOSE *CYNICTIS PENICILLATA* (CUVIER)

INGOLF ZUMPT*

SUMMARY

For the first time in Southern Africa the Yellow Mongoose, *Cynictus penicillata* (Cuvier), was found infested with *Cordylobia anthropophaga* (Blanchard). The larvae of this fly reach maturity in this mongoose and the animal therefore acts as a natural host. This new focus of codylobiasis has apparently become established only recently and a further spread is to be expected.

## INTRODUCTION

The epidemiology of infestations with larvae of the "Tumbu fly", *Cordylobia anthropophaga* (Blanchard) (Diptera; Calliphoridae) in man and animals in Southern Africa has recently been discussed by F. Zumpt [1, 2].

Wild rats and mice of the genera such as *Aethomys, Arvicanthis, Cricetomys, Praeomys, Rattus, Saccostomus,* and *Tatera* act as primary hosts. They are highly susceptible to this infestation and often, if not regularly, die after the maggots have reached maturity and left the skin lesions. Various carnivores, including the domestic dog, humans and wild primates, and rarely small antelopes are also to be regarded as secondary hosts [1]. The course of infestation is more or less inhibited by immunological reactions, with only a relatively low percentage of the invading larvae reaching maturity, or all dying after a very short time, as for instance in the domestic pig. Nevertheless, several of these secondary hosts may play an important role in the epidemiology of the disease. Because of the larger area they inhabit or by temporary migrations, they can spread the parasite and cause new foci of infections in primary hosts, which had been free so far. In this respect, the domestic dog is of great importance, a fact that has been stressed by Zumpt [2].

## MATERIAL AND METHODS

In the Veterinary Investigation Centre at Mafeking, yellow mongooses, caught in the neighbouring area are kept for experimental purposes. They are housed in wire cages with soil and semi-hollow termite heaps as shelters. Only exceptionally do yellow mongooses dig their own burrows, as they usually use those of the Cape bristly ground squirrel, *Xerus inauris* (Zimmerman), with which they live in close association. On the 4th February, 1970 it was found that of six captive mongooses, two had died and two were in a very weakened condition and had to be killed. The *post mortem* examination showed that one of these animals had 19 "boils" and the other 13. By gentle pressure, a maggot from each "boil" was recovered and some of them isolated on dry sand, the rest were preserved in 70% alcohol.

The two affected animals were extremely emaciated and dehydrated. The preferential sites wese the lower limbs and the root of the tail; only a few "boils" were found on the back and the abdomen. The two remaining mongooses were in good condition and had only two and five skin lesions respectively. Six more captive *Cynictis penicillata* yielded between three and nine larvae. "Boils" were seen to be scratched and constantly licked. On the 23rd February, four male and five female flies hatched, all in perfect condition. The identification of the flies, as well as of the larvae confirmed that an infection of *Cordylobia anthropophaga* was concerned.

A survey was carried out from the 4th February to the 28th March, 1970, in order to detect infestations in mongooses in the field. Of 61 specimens, two had old lesions, most of them in a healed state. They were again situated on the lower limbs. These infestations were apparently of mild nature and the animals were in a reasonably good

*Regional Veterinary Investigation Centre, P/Bag 5020, Stellenbosch.

condition. Ground squirrels have not yet been found infested.

Since 1967, a great number of mongooses has constantly been examined during investigations into their role in the epidemiology of rabies, but no cordylobia infestations had been found until February, 1970. Since then, two dogs with cordylobia lesions have been detected in the Mafeking area. So far, no human cases have come to light, but they may certainly be expected.

## DISCUSSION

The discovery of natural infestations by *C. anthropophaga* in the yellow mongoose in the Mafeking area is of great interest. It is recorded here for the first time. Blacklock & Thompson[3] recorded a "mongoose" in Sierra Leone as host, but they did not give the scientific name, and also the West African striped ground squirrel, *Xerus erythropus* (Geoffroy), has been found infested, but until now these groups of animals have not been named as hosts of *Cordylobia anthropophaga* in Southern Africa.

Has this fly only recently invaded the Mafeking area and is a new focus of cordylobiasis coming into existence? This could well be so. Infested dogs may have introduced the parasite from the warmer parts to the north and east of the area, and the infestation may have become established in the local mongooses and probably also in the Muridae, in which, so far, it has not been detected. The yellow mongoose has now been shown to act as a reservoir of the infestation.


## ACKNOWLEDGEMENTS

I am indebted to my father in more ways than one and to the Director, Veterinary Services (Field) for permission to publish this article.


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# BOOK REVIEW — BOEKRESENSIE

## ANIMAL GROWTH AND NUTRITION

E. S. E. Hafez and I. A. Dyer, Editors

Lea & Febiger. Philadelphia, 1969.

This is a well presented publication consisting of the combined efforts of twenty contributors. It is written in a form easy to read and suitable for use as an advanced student reference. It deals primarily with thought-provoking concepts and includes references, examples and mathematical formulae and models which adequately illustrate the theories presented. It cannot claim to handle any specific aspect exhaustively but within its 402 pages it contains a substantial volume of facts and concepts to make the edition a good reference and a highly desirable publication for a postgraduate research worker.

Four main categories are given consideration in this book:

1. Prenatal growth and foetal nutrition.
2. Postnatal growth, taking into consideration genetics, climate, environment, feed intake, growth regulators and anomalies of growth patterns. Aging, diseases and parasite bias are also discussed.
3. Body composition with attention to muscle, bone, fats and the epidermis.
4. Nutritional requirements for growth with emphasis on basic nutrition dealing with energy, protein, minerals, vitamins, water metabolism and mathematics of growth.

The individual papers are well illustrated with efficient diagrams, tables, formulae and black and white photographs. Liberal detailed references follow each section, facilitating further study.

This book can be recommended without reserve to advanced students of nutrition.

P.A.B.

Jl S. Afr. vet. med. Ass. 42 (3): 265-267 1971

CASE REPORT GEVALVERSLAG

# THE CLINICAL DIAGNOSIS OF OESOPHAGEAL INVAGINATION OF THE STOMACH IN THE DOG

P. ALCANTARA*

SUMMARY

A case of oesophageal invagination of the stomach in a Dalmatian pup is described. Indications of diagnostic symptoms are given.

## HISTORY

A Dalmation dog, aged 2 months, was referred to the Department of Surgery of the Faculty of Veterinary Medicine of the University of Lourenço Marques.

This animal had been vomiting frequently for about one month; four days before admission the owners had noticed that the vomited material included brownish blood, which was attributed to the ingestion of foreign bodies. The patient had had occasional diarrhoea and sometimes the faeces had been blood-stained. No treatment of any kind had been attempted before admission.

## CLINICAL DATA

The clinical examination disclosed an intense paleness of the oral and conjunctival mucosae, signs of severe dehydration, abdominal pain and a temperature of 38,6°C. The PCV was 21 per cent.

The radiological examination of the digestive tract showed several small opaque foreign bodies along the rectum and small intestine and a dilatation of the intrathoracic oesophagus at the cardia (Fig. 1). The administration of a barium meal (50 ml) and another radiograph 15 minutes after the meal confirmed the dilatation of the thoracic oesophagus, although the contrast medium had not attained the most caudal portion of the dilatation, nor the cardia (Fig. 2).

A tentative diagnosis of achalasia of the oesophagus was made. It was assumed that an acute haemorrhagic gastro-enteritis had been caused subsequently by the ingestion of acerate foreign bodies. It was also assumed that the dog was infes.ed with intestinal worms, namely *Ancylostoma* spp., *Toxocara* spp. and *Toxascaris leonina,* an almost constant finding in young dogs in Lourenço Marques.

Accordingly, 0,6 ml "Ancylol" was administered subcutaneously and 150 ml Ringer's solution and 150 ml 5 per cent dextrose solution in water intravenously. Blood was not available at the moment, but a blood transfusion was requisitioned for the next day in an attempt to improve the patient's condition.

The dog died during the night.

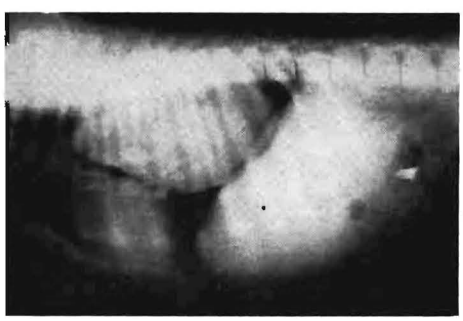

Fig. 1. Radiograph of case.

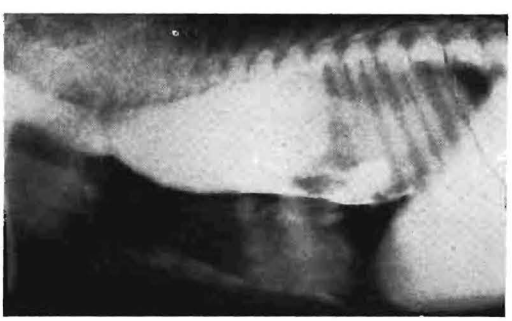

Fig. 2. Radiograph 15 minutes after barium meal.

*Faculdade de Veterinária, Universidade de Lourenço Marques. Moçambique.

## POST MORTEM EXAMINATION

The thoracic portion of the oesophagus, between the diaphragm and the cranial third of the thoracic cavity, was dilated, having assumed the shape of a cylinder with a diameter of about 10 cm. A longitudinal incision of the oesophagus directly over its dilated portion exposed its contents: the characteristic folds of the gastric mucosa were clearly visible. Study of this ectopic tissue confirmed that the dilated oesophagus contained the entire stomach, which had been invaginated. since regressive changes and signs of mechanical stasis were just detectable.

Passive congestion of the abdominal organs and vicarious compression of the thoracic contents where also noticeable (Figs. 3, 4).

## DISCUSSION

Oesophageal invagination of the stomach occurs occasionally as an agonal phenomenon in the dog and is not correlated with the cause of the death [1]. Its occurrence as a sequel to oesophageal disease or repeated

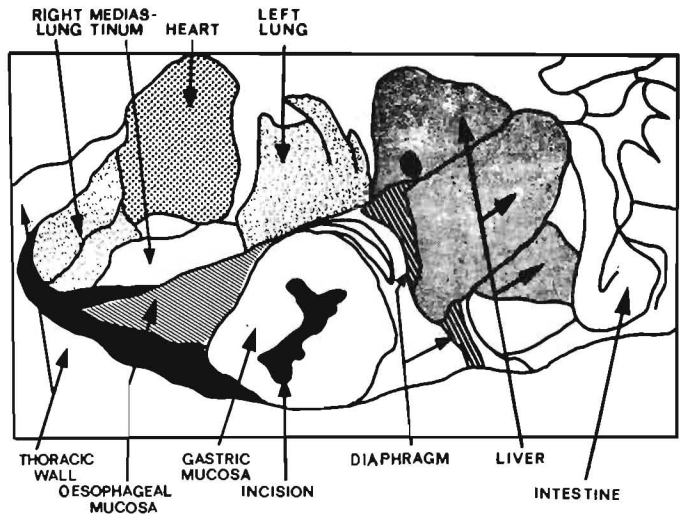


Fig. 3. Viscera exposed.

Fig.4. Key to fig. 3.

The gastric mucosa was in contact with the oesophageal mucosa and the gastric serosa lined a newly formed cavity, which contained the spleen and about five cm of duodenum. An acute inflammatory process of the gastric mucosa was evident.

The invagination was relatively recent, vomiting is less common, as can be inferred from the few cases reported [2, 3]. In the present instance the oesophageal invagination of the stomach was probably produced by repeated and violent attempts at vomiting, following an acute gastritis.

The initial failure to diagnose the condi-

tion deserves some comment. Reviewing the radiographs obtained from this case, we believe that at least a suspicion of the truth could have emerged, since a) the dilated portion of the oesophagus was clearly seen in fig. 1; b) the radiograph, obtained after the barium meal had been administered, suggested the presence of something filling the most caudal portion of oesophagus (Fig. 2). The association of these facts with the presence of semi-digested blood in the vomited material would strongly suggest possible gastric invagination.

## CONCLUSIONS

Based upon the retrospective study of a case of oesophageal invagination of the stomach in a dog, the author suggests the following basis for the clinical diagnosis of this condition:

1. Symptoms of oesophageal obstruction.
2. Dilation of the terminal portion of the oesophagus, with increased radiodensity of the corresponding area.
3. Identification of gastric juice in the vomited material (acid pH, partly digested contents).
4. Abdominal pain, more intense over the epigastric area.
5. Oesophagoscopic examination, whenever possible, should confirm the diagnosis by the identification of the gastric mucosa bulging inside the oesphagus.


## ACKNOWLEDGEMENTS

The author is indebted to Dr. Armando Castelo Branco Gonçalves, who referred the case to him, and to Dr. J. L. Nunes Petisca, who performed the *post-mortem* examination.


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# BOOK REVIEW — BOEKRESENSIE

## REPRODUCTION AND BREEDING TECHNIQUES FOR LABORATORY ANIMALS

E. S. E. Hafez, Editor

Lea and Febiger, Philadelphia, 1970. — 162 Illustrations and 46 plates

The extensive use of laboratory animals in research today exemplifies the need for a better understanding of their basic reproductive physiology and behavioral patterns. Dr. Hafez has succeeded admirably in this book in bringing together several well-known authorities who present a vastly diversified field in a concise and lucid way. Whether one is intimately involved with laboratory animal units, or only called on for advice intermittently, this book will be found of great value.

The volume is divided into two parts. The first contains aspects of comparative reproductive physiology, while the second deals with modern methods of breeding and handling of the most commonly kept laboratory animals, including rodents, carnivores, lagomorphs and primates. Relevant data in most cases are set out in table form, making for easy reference.

The appendices contain useful data on breeding records, anaesthesia, euthanasia; legal aspects of animal care; space requirements; centres for breeding stocks, as well as information on films on reproductive biology.

The selected bibliography at the end of each chapter provides an adequate source for further delving.

The volume is well presented with the professional production we have come to expect from the publishers.

R.I.C.

# REFRESHER COURSE

## MODERN ASPECTS OF ANIMAL BREEDING, MANAGEMENT, NUTRITION AND DISEASE PREVENTION

14—18 June 1971

A most successful refresher course under the above title was organized by the Department of Zootechnology of the Faculty of Veterinary Science from 14-18 June, 1971. Seventy participants, hailing from as far as Rhodesia and Moçambique, attended. Twenty four lectures were given, in many cases followed by practical demonstrations. Of the eighteen speakers, nine were members of the Faculty, and nine were guest speakers. The discussions were animated and productive. The three social functions were well attended and much appreciated. Twenty letters of appreciation were received subsequently; one stated: "It was the best congress I have ever attended and it gives you much credit." Numerous requests were received for a similar course to be held again.

The following papers were presented:—

1. Introduction and genetical terminology. D. R. Osterhoff, O.P.
2. Introduction and nutritional terminology. P. A. Boyazglu, O.P.
3. Ethology and its application in modern farming. I.S. McFarlane, O.P.
4. Qualitative and quantitative inheritance. D. R. Osterhoff, O.P.
5. Compiling balanced rations. P. A. Boyazoglu, O.P.
6. Feeding the dairy cow. F. van der Merwe, Stellenbosch.
7. A.I. in modern breeding plans. D. R. Oosterhoff, O.P.
8. The future of A.I. in South Africa. A. B. la Grange, Irene.
9. Fertility problems in the dairy herd. R. I. Coubrough, O.P.
10. Modern design within animal production techniques. I. S. McFarlane, O.P.
11. Climatological research at Mara (Afrikaans). J. Bonsma, Pretoria.
12. Breeding beef cattle. G. O. Harwin, Pietermaritzburg.
13. Beef cattle nutrition. P. K. van der Merwe, Johannesburg.
14. Immunity and vaccines. C. Cameron and P. G. Howell, O.P.
15. Beef production and quality. J. Lombard, Pietermaritzburg.
16. Beef production in feedlots. J. van Marle, Vereeniging.
17. Animal transportation. G. D. Sutton, O.P.
18. Modern aspects of veld management. J. O. Grunow, Pretoria.
19. Winter and drought feeding of sheep. B. D. H. van Niekerk, Johannesburg.
20. Sheep farming management and disease control. (Afrikaans). K. van der Walt, O.P.
21. Modern breeding plans in pigs. D. R. Oosterhoff, O.P.
22. Feeding of pigs. (Afrikaans). M. Griessel, Vereeniging.
23. Horse nutrition. P. A. Boyazoglu, O.P.
24. Function and confirmation in producing animals. I. D. McFarlane, O.P.

A limited number of copies of the proceedings has been duplicated and bound. Copies are obtainable at R6.00 each from:

The Head,
Department of Zootechnology,
Faculty of Veterinary Science,
P.O. Box 12580,
Onderstepoort.

BOOK REVIEW BOEKRESENSIE

# FERTILITY AND INFERTILITY IN THE DOMESTIC ANIMALS

J. A. LAING, EDITOR

Second edition. Baillière, Tindall & Cassell, London. 1970.

pp. 480. Price 120 S.

"No normal state requires wider understanding than fertility and no abnormal condition has a more varied background than infertility." The first sentence in the preface to this long awaited second edition very succinctly emphasizes the difficulties which are encountered in covering so comprehensive a field. The fact that Prof. Laing has sought the collaboration of other colleagues has led to a marked increase in the value of the work as a text in this discipline.

While agreeing wholeheartedly with the reasons for omitting chapters on the physiological control of reproduction in the female—a number of standard textbooks are now readily available—I would be inclined to believe the fifth chapter on artificial insemination could have been omitted for the same reason.

Five chapters discuss the aberrations occurring in the six most common domestic animals, whereas only one chapter of 35 pages elaborates on the abnormalities and diseases of the male genitalia. Information on the characteristics of dog semen is a notable omission in chapter four.

These criticisms are of minor importance when the presentation, organisation and illustrations of material presented, are taken into consideration. The line drawings, especially of the genital organs, and of the stages of pregnancy, are clean and meaningful.

This book can be highly recommended to colleagues and students alike.

J.S.v.H.

BOOK REVIEW BOEKRESENSIE

# THE CONTROL OF BOVINE MASTITIS

F. H. DODD AND E. R. JACKSON, EDITORS

Unwin Brothers Ltd. The Gresham Press, Old Woking, Surrey, England, 1971.

Pp. 130.

This extremely interesting booklet represents a collection of papers providing students of the subject with a comprehensive and up-to-date review of economics, bacteriology, pathogenesis, hygiene, animal husbandry and other aspects relative to the control of the problematical disease complex known as bovine mastitis.

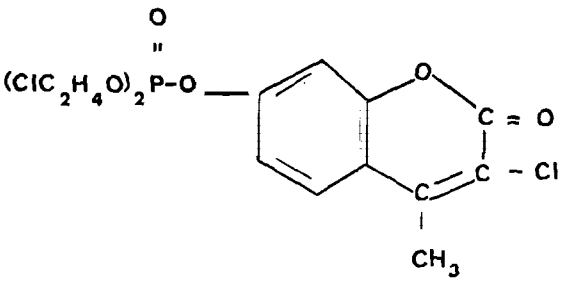
One is compelled to congratulate the researchers involved for the admirably concerted efforts made to establish a scientific basis for the control of mastitis and the clear although frequently very concentrated fashion in which the numerous findings are compiled.

The data presented are best summarized by citing directly: "Great improvements in udder health can be made by the individual efforts of farmers and veterinary surgeons; but the concept of an overall basis of mastitis control in the country as a whole represents the real challenge. The benefits from such a comprehensive system would be very great . . ."

The booklet is not a "may be" but a "must" for those concerned with mastitis.

W.H.G.

# HALOXON




is 'n

## COOPER ONTDEKKING

Dit is 'n OXON van 'n

HALOGENEERDE ORGANIESE FOSFAAT,

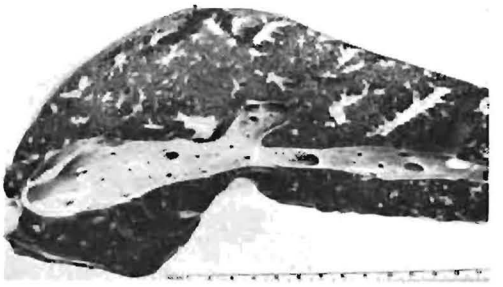
is onoplosbaar in water, verwek net 'n onbeduidende maat van cholienesterase-vermindering in die bloed, is baie veilig.

# LOXON

is 'n hoogsdoeltreffende en veilige middel veral teen perde-, skaap-, bok-, en bees-rondewurms met 'n terapeutiese indeks van 4 tot 25 afhangende van die dieresoort.

J. 4790

# FEATURE PAGE — TREFFERBLAD



## STAGGERS SYNDROME IN EXPERIMENTAL HYPERERGIC (?) SCHISTOSOMIASIS

A worm-free Africander × S. Devon ox was infested with 7,5 cercariae of **Schistosoma mattheei** per kg live mass at 9 months of age. After 18 months it was challenged by 90 cercariae per kg biomass. Four months later the following signs developed: marked loss of weight, periodic straining, knuckling over at the hind fetlocks, a tendency to lean with the head against the fence, sunken eyes with alternative wild and somnolent expression, foaming at the mouth and eating its own excreta. It was killed **in extremis** six days later. At autopsy an advanced periportal fibrosis was found, similar to that described by Symmers in human bilharzia. Six control oxen died almost two months after a single infestation with 90 cercariae per kg biomass. Only the usual signs of acute schistosomiasis were seen, without the noticeable periportal fibrosis.

Submitted by: J. A. van Wyk and R. C. Bartsch, Veterinary Research Institute, Onderstepoort.

Photography: A. M. du Bruyn.

## STOOTSIEKTE-SINDROOM BY EKSPERIMENTELE HIPERERGIESE (?) SCHISTOSOMIASE

'n Wurmvrye Afrikaner × S. Devon-os is op 9 maande ouderdom met 7,5 serkarië van **Schistosoma mattheei** per kg lewende massa besmet. Na 18 maande is hy met 90 serkarië per kg lewende massa gedaag. Vier maande later ontstaan die volgende siektetekens: opvallende gewigsverlies, periodieke persing, vooroorswik van die agterste kootgewrigte, 'n neiging om met die kop teen die heining te leun, ingesonke oë met afwisselende verwilderde en vakerige voorkoms, skuim by die bek en vreet van sy eie ontlasting. Na ses dae is hy **in extremis** geslag. Nadoods is daar 'n uitgesproke periportale fibrose van die lewer gevind, soortgelyk aan die deur Symmers by menslike bilharzia beskrywe. Ses kontroleosse het bykans twee maande na eenmalige besmetting met 90 serkarië per kg lewende massa met gewone tekens van akute schistosomiase beswyk, sonder opvallende periportale lewerfibrose.

Ingestuur deur: J. A. van Wyk en R. C. Bartsch, Navorsingsinstituut vir Veeartsenykunde, Onderstepoort.

Fotografie: A. M. du Bruyn.