ABOMASAL INFUSION OF ANTIBIOTICS IN SHEEP

1050 710

by

OLUGBEMIRO OLU AKEREJOLA

D. V. M., Ahmadu Bello University, 1971

A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Surgery and Medicine

KANSAS STATE UNIVERSITY Manhattan, Kansas

1974

Approved by:

lagor Professor

THIS BOOK CONTAINS NUMEROUS PAGES WITH THE ORIGINAL PRINTING BEING SKEWED DIFFERENTLY FROM THE TOP OF THE PAGE TO THE BOTTOM.

THIS IS AS RECEIVED FROM THE CUSTOMER.

LD 2668 T4 1974 A43 C 2 Document

ACKNOWLEDGMENTS

The author wishes to express his gratitude to Dr. J. L. Noordsy, major professor, for his guidance and assistance during the course of study. Sincere appreciation is extended to Dr. L. H. Harbers for the invaluable guidance, encouragement and assistance throughout all aspects of the training.

Acknowledgment is extended to Dr. K. Bolsen for his cooperation during the use of facilities at the Kansas State University Sheep Research Unit.

Deep appreciation is extended to all the students and staff who have in one way or the other contributed in making this study a success.

The author extends his gratitude to other members of his graduate committee, Dr. Embert Coles, Jr. and Dr. R. A. Frey, for their guidance and suggestions.

The author is most indebted to his wife Grace and children Mekamagba and Erema for their understanding, encouragement and patience necessary to make this study possible.

A special word of thanks to the Ahmadu Bello University, Zaria, and the United States Agency for International Development for the opportunity and financial assistance offered for this study.

The author heartfully dedicates this thesis to his cherished family friends Mr. Bill (E. C.) Stowe and Mrs. Audrey Stowe.

TABLE OF CONTENTS

																										Page
ACKN	OWLEI	GMENTS .		• •			•	•	•	•	•	•	•		•	•	•	•		•	•	•	3 🛶	•	•	11
INTR	ODUC	rion				•	٠	, .		•	٠	•	•	•	•	•	•	٠	•	ě	•	•	•		٠	1
Part	ı.	REVIEW OF	LITERA	TURI	E																					
	A.	Abomasal	Cannula	ition	n Te	ch	nic	ļue	s	٠	•		•	•	٠			٠	٠	•		•	•	•		3
		Studies u	sing al	omas	sa1	ca	nnı	ıla	ti	or	ı	•		•	•	•			•	•		•		•		5
	в.	Antibioti	cs in N	lutr:	itio	n	•	•	•	٠	•	. •		٠	•	•		•	•	•		•	٠	٠	•	8
	X	Mode of a	ction			•	•		•		•	•		•	•	•	•	•	٠	•	*	•				9
	X	Nutrient	sparing	g efi	Eect	•	٠	٠	•	•	•	•	*	•	•	•	•	٠		•	•	•	•	٠	•	10
	L	Vitamin s	paring	acti	Lon	•	(•)	•	÷	•	•		ě	•	•	:•:		•	•	2.●1	•			•		11
		Metabolio	effect	of	ant	ib:	iot	ic	s	•	٠	(*)	•	•	٠	•	•	٠	•		•		٠	•	•	13
		Disease c	ontrol	effe	ect	•	•	•	20	•	٠	3.	¥	ĕ	•			•	•		ě	÷:	•	: .	ě	14
	c.	Antibioti	cs and	Bloc	od C	on	sti	tu	en	its	ì	•	•	•	•	•	•	•	•	٠	•	•	•		•	17
	Lite	erature Ci	ted .			٠	•	•	•	•	•	•	٠	•	٠	٠	ě	•	•	•	•	ě	•	•	ě	20
Part	II.	A SIMPLI	FIED A	OMAS	SAL	CA	NNU	JLA	TI	ON	1	EC	CHN	II	QU I	2]	LN	Sł	ΙΕΙ	ΞP						
	Summ	ary				•	•	•	ě	•	٠	•	, É	٠	•	•	ě		•	•	÷	•	٠		٠	26
	Intr	oduction		•	• •	•	•		•		•	•	•		•	•	•	*	•	•	•	*	•	•	•	26
	Surg	ical Proc	edure			ě	•	•	•	•	•	٠	٠	ě		•		¥	•	•		ě	•	•	•	27
	Lite	rature Ci	ted .		• •	•	•	100	•			•	:•:	•	•	•	•	•	•	•	•	•	•	•	•	30
		THE EFF AND NUTRI							US	ED	Α	NI	IE	BIC	TI	C	40	1								
	Intr	oduction				•	•	•	•	٠	•	•	٠	•	٠	•	٠		•	•	•	•	•	•	•	31
	Ехре	rimental	Procedu	re		•	•	•	•	•		•	•	•		•	•			•	•	•	•	•	•	31
		Growth Tr	ial I) •		•	•		•		á•i		•	•	•	•	•	•	•	•	•	***	31
		Balance t	rial .					•	•	•	•	•	•	•	•				o.		•				•	32

																																Ĺ	Page
		Me	eth	bo	of	aı	na]	Lys	:18	3	•	•	٠	•	•	•	•	•	•	•	•	•	•	•	•	•	•	Ē	•	٠	•	÷	33
		Gr	ow	th	Tr	ia.	L	ΙI		•	•	•	•	•	•	•	•	•	•	•	***		•	•	•	::•::			•		•		34
	Res	ult	s	and	D	is	cus	isa	or	ı	٠	•	٠	٠	•	٠	٠	•	٠	•	•	٠	•	•	٠	٠	٠	•	•	•	٠	•	34
	Tabl	Les	3			•		.	•	٠		•	•	•		•	•:	•		•	•	•	: •	•	•	:•:		•	•	•		•	40
	Figu	ure	es		•	•	•	•	•	٠	٠		•	٠	•	•	•	•	٠	٠	•	•	•	•	٠	•	•		•	•	٠		45
	Lite	era	atu	re	Ci	te	đ		•	•		·	÷	•	•	ě	•	•	•	•	•	•	•	•			•		•			•	48
VITA		-					La Car		120		22	_		-	102	~	240			_	·	341	-	×	-			2		744	-	2	50

INTRODUCTION

Growth benefits received by adult ruminants from antibiotic fed at nutritional levels are minimal (Braude et al., 1953). However it has been postulated that physiological and biochemical responses of the caudal portion of the digestive tract, to an extent (beginning with the abomasum), acts similarly to that of monogastric animals (Phillipson, 1970). The beneficial effects of antibiotics addition to poultry and swine ration to promote growth has been well established. Reis and Schinckel (1964) have shown that wool growth can be increased up to 200% by passing casein directly into the abomasum of sheep. It would appear feasible that growth of internal body tissues similar to that obtained in monogastric animals could be increased if successful means were found to by-pass the rumen with antibiotics.

When plants high in cellulose content or protein sources deficient in certain amino acids as well as nonprotein nitrogen are fed to ruminants, ruminal microflora action is definitely advantageous since man digests these materials only to a limited extent, if at all. If by incorporation of a feedstuff into the ruminant diet, advantage could be taken of postruminal digestion and feed conversion ratios as presently obtained in monogastric animals could be approached, this would not only boost the much needed "red meat" in the developed countries but also enough protein intake could be stimulated in the developing countries of the world.

Thus an investigation was conducted to find a simplified means of inserting an abomasal cannula through which antibiotic would be infused to determine the effect on growth. Since there have been reports of chelating action of oxytetracycling with calcium and magnesium ions making these

inaccessible for body tissues (Smithscor, 1973; Yeh and Shils, 1966; Price et al., 1957; Weinberg, 1957), concomitant serum phosphorus and calcium balance was also determined.

Part I

REVIEW OF LITERATURE

Abomasal Cannulation Techniques

The production of openings between the various portions of the gastrointestinal tract through the skin of the abdominal wall in animals has often been used in research involving digestion and absorption. In most cases the cannulas were apparently maintained in position for a short while.

Dougherty (1955) traced the use of fistula in research from its accidental beginning in a human subject with gunshot wounds. He reported that the surgeon, Dr. Beaumont, after the surgical success in 1822 opened up the general field of gastrostomy and enterostomy. The pioneering work of Pavlov in the surgical establishment of pouches and fistulas in the digestive tract of dogs has formed a basis on which subsequent surgical procedures have been devised to enable sampling of gastric contents and introduction of substances into the tract. Earlier surgical procedures used in nonruminant animals have been described by Markowitz et al. (1937). A review of earlier work on rumen and abomasal fistulation has been given by Dougherty (1955).

Quin and van der Wath (1938) created an abomasal fistula at the mid ventral position about 8 cm posterior to the xiphoid cartilage and claimed success with this. Dougherty (1955) cited Phillipson (personal communication) as being unsuccessful in few attempts at placing cannulas in the fundus region of the abomasum but gained more success in the pyloric region. Jarret (1948) described a method of abomasal cannulation which he called a modification Witzel's method for enterostomy. He described the insertion of the whistle-tip catheter secured with a purse string suture. The catheter was

laid on the surface of the abomasum completely enclosed in serosa for a short distance. The surface of the serosa was scarified to allow adhesion to the abdominal wall while the catheter was in place. After healing, the catheter could then be removed without leakage, permitting the insertion of bigger tube for sampling purposes. Success up to a year without ill effects was ascribed to this procedure.

Ash (1962) described a procedure of omaso-abomasal re-entrant cannulation in which the proximal tube was exteriorized between the 9th and 11th rib and the distal tube was exteriorized through the abdominal wall. They encountered difficulties at placing the cannulas as well as blockage from finely ground diets.

Kondos (1967) described a method in which both ends of the tubes had end plates. The end plate to be in contact with the skin was roughened so that surgical adhesive used, could have a better contact.

A recent work was described by Driedger et al. (1970) to allow a continuous infusion of protein slurries into the abomasum. A polyester fiber mesh was glued to the cannula on the abomasal end and the abomasal wall was folded and sutured to the mesh. The cannula was run subcutaneously at the abdominal wall and exteriorized through a stab wound at a point 4-5 cm from the midline on the back. A second mesh at this end of the cannula was again sutured to the fascia of the external abdominal muscles. They did not state the length of time they were able to get the cannula to stay in place post-surgically. This also seemed to be a modification of a gastric cannulation technique described by Holtzman (1963) in his antibiotic studies with rats.

Many types of cannulas have been devised and types of materials used have also varied greatly. Ebonites were used by Quin and van der Wath (1938) and also by Phillipson and Innes (1963). This seems to be successful for the

purpose but availability of ebonite is not widespread. Dougherty (1955) chose bakelite with rubber cannula stoppered with cork that held in place with adhesive. He described a method of vulcanization of the rubber which would require some skill and could possibly be time consuming. Hull and Gregory (1951) in their work with gastric pouches in goats used silver cannulas. Perspex cannulas have been used by Chalmers et al. (1953) and Phillipson and Mitchell (1951) but these were used in duodenal cannulation. Little and Mitchell (1967) used plexiglass cannulas in their wether work. Driedger et al. (1970) used silastic silicone medical grade tubing. These would seem to be preferable for abomasal cannulation work because of their little or no tissue reactions and ease of availability.

Studies Using Abomasal Cannulation

There are several reports of postruminal administration of proteins. Cuthberston and Chalmers (1950) and Chalmers et al. (1954) reported that casein administered duodenally was better utilized by sheep than when it was administered into the rumen. Chalmers et al. (1954) also cited Dr. A. T. Phillipson as arriving at the same conclusion. Little and Mitchell (1967) compared the effects of oral versus abomasal administration of various proteins. They found that abomasal administration of casein or soybean protein produced a substantial improvement in nitrogen retention in lambs than when the protein was fed orally. Reis and Schinckel (1964) reported a considerable increase in wool growth in native sheep when cysteine, methionine and casein were abomasally infused compared to oral administration. Reis (1969) also found favorable responses with casein administration per abomasum. Schelling and Hatfield (1967) in their infusion of various amino acids found that abomasal administration of casein has similar results as other workers;

that it increased nitrogen retention as well as food consumption. When methionine and phenylalanine were infused they did not obtain any statistically significant response in nitrogen retention. They found that a mixture of argenine, histidine, lysine, methionine and phenylalanine did not give as much response as they would expect nor as much as the ten amino acid mixtures they used. But individual infusion of either lysine or glutamic acid gave a response similar to the combined effect of the five amino acids mentioned. Little, Mitchell and Porter (1968) concluded, after the administration of four different types of proteins, that the digestibility and nitrogen retention associated with the protein depends on the protein type. Highly digestible protein sources such as soybean protein or casein, infusion through the abomasum improved nitrogen retention. But if the protein used had poor amino acid balance, a decreased nitrogen balance was noted when infused abomasally. The total nitrogen retention associated with zein was highest, intermediate with soybean and lowest with casein and glycine. The latter elevated blood urea and was said to be easily degraded in the rumen. Scott et al. (1969) worked with lysine to show the value of abomasal infusion as different from oral intake. Other workers have substantiated the evidences found by the direct abomasal infusion of proteins through treatment of these protein supplements with formaldehyde to prevent degradation by rumen bacteria (Ferguson, Hemsley and Reis, 1967; Reis and Tunks, 1969). The formaldehyde treatment does not impair the partial digestibility by the sheep. Appropriate treatment thus increases the amount of protein reaching the intestine. The failure of orally administered proteins to improve animal performance or to increase plasma amino acid concentration is thought to be related to the high rate at which rumen bacteria catabolize the protein. Blaxter and Martin (1962) showed that casein was less absorbed completely

when infused into the rumen than when given abomasally. They found that rumen infusion resulted in an increase in the fermentative loss of the casein as methane and thus that the metabolizable energy of casein by abomasal infusion was more efficiently used to promote synthesis of energy containing materials in the body. They concluded that "These results with abomasal infusion are similar to those obtained in simple stomached animals. The results of our experiments suggest very strongly that the lower nutritive value of protein as an energy source for lipogenesis in ruminants compared with non-ruminants is the result of fermentative changes involving protein which occur in the rumen."

Moore <u>et al</u>. (1970) in infusing lysine to sheep found that there was a marked decrease in plasma phenylalanine than oral feeding. Plasma methionine concentration was also lower when part of the lysine was infused continuously daily than when fed but there was an increase in plasma lysines.

Papas et al. (1971) studied the effect of abomasally infused casein on feed intake. The control had an infusion of sodium sulfate. They reported a decreased intake for the control group but an increase in dry matter intake for the casein supplemented. They concluded that protein infusion has an effect on feed intake. Broderick et al. (1970) used methionine-supplemented commercial casein products infused into the abomasum of lactating cows. They reported a significant rise in milk protein content. They also observed increases in plasma amino acid when casein with methionine were infused abomasally. Plasma concentrations of leucine, isoleucine, phenylalanine, valine and total essential amino acids were elevated while a depression of glycine and total non-essential ones were observed. They thought that infusion elevated the intestinal absorption of these amino acids.

Ash (1962) used abomasal-duodenal re-entrant cannulas to study secretion outflow into the abomasum. Phillipson and Mitchell (1952) found that cobalt administered either duodenally or abomasally was concentrated in the rumen. No reference was found as regards antibiotic infusion into the abomasum.

Antibiotics in Nutrition

Oxytetracycline (Terramycin) ¹ C₂₂H₂₃O_aN₂ and Neomycin, which consists of two isomeric entities B and C containing a neamine, a diaminohexose and ribose, are obtained from <u>Streptomyces rimosus</u> and <u>Streptomyces fridiae</u> respectively (U.S. Dispensatory, 1966). The tetracycline is a derivative of polycyclic napthalene carboxamide. The crystalline bases are faintly yellow, odorless, slightly bitter compounds. They are slightly soluble in water at pH 7 (0.25-0.5 mg/ml) but forms hydrochlorides which is stable indefinitely as power. A 1% solution in distilled water shows no detectable loss of potency for at least 30 days at 25°C. Dilute solutions are stable for a similar period over the pH range of 1.0-9.0 when stored at 5°C.

It is absorbed adequately from the gastro-intestinal mucosa and after a single oral dose produces peak plasma levels of the antibiotic in 2-4 hours and persists for 6 hours. Doubling the dose does not generally double the maximum concentration in the serum but it is said that it prolongs the times during which the level remains at a given submaximal value (U.S. Dispensatory, 1966).

It is effective against rickettsiae, psitacosis lymphogranuloma víruses a number of gram negative and gram positive cocci and bacilli. Excretion is

^{1&}lt;sub>Pffizer</sub>, Inc., New York.

chiefly biliary. Distribution is generally throughout the body with highest concentrations found in the kidney, spleen, liver and lung.

Neomycin sulfate (Biosol^R)¹ is the sulfate of the neomycin product. Its absorption from the gastro-intestinal tract is limited but it is not destroyed significantly in the gastro-intestinal tract. It does not accumulate in tissues and it is rapidly excreted. A single intramuscular dose produces peak plasma levels within one hour. It has nephro and neurotoxicity properties when administered systemically.

The activity spectrum is broad, being effective against gram positive and gram negative cocci and bacilli and also mycobacterum tuberculosis. It is ineffective against anerobic bacteria. It is effective when used in combination with oxytetracycline even when the micrococci become resistant to oxytetracycline (U.S. Dispensatory and Physicians Pharmacology, 1966).

Solutions of neomycin sulfate are said to be stable over a wide range of pH values for several months and some dilute solutions are said to be stable up to two years.

Mode of Action

The discovery by Moore et al. (1946) that streptomycin and sulfasuxidine gave growth increases of 10 to 30 percent in chickens and later work by Stokstad and Jukes (1950) with chlortetracycline on growth stimulation in chicken has opened up vast research work in this field. Numerous experiments using various antibiotics in poultry, swine, cattle, sheep and other livestock nutrition and in other allied fields of science have been carried out.

 $^{^{1}}$ Biosol $^{\mathrm{R}}$ Liquid--The Upjohn Co., Kalamazoo.

The mechanism by which antibiotics stimulate growth has been discussed widely and to date there is no consensus opinion on the issue (Weiner, 1972). Various research workers have proposed theories concerning the growth promoting activity. Three basic modes of action have been proposed as summarized by Hays (1969).

Nutrient Sparing Effect

Protein sparing action: Catron et al. (1952) fed rations to pigs at different levels of protein from weaning to 200 lbs. The results showed that pigs receiving high levels of protein up to 20% without chlortetracycline supplementation gained just as much as those receiving levels of up to 8% with antibiotic supplementation. They suggest that the level of proteins required by pigs for maximum performance is less in the presence of dietary supplements of antibiotics. Black and Bratzler (1952) fed rations containing 33 mcg Vit B_{12} plus 5.5 mg streptomycin per kg. They concluded that the most striking effect of the supplementation was the increase in gain of body fat with only slight increase in gain in body nitrogen, so that the antibiotic has no effect on utilization of food protein. Burnside et al. (1951) fed rations containing 20, 16, 12% protein to pigs. The levels were lowered as the pigs reached 75 pounds and again 125 pounds. Vitamin B_{12} and chlortetracycline were mixed with the ration. The antibiotic produced no effect on the high protein fed pigs after 75 pounds. The antibiotic plus Vitamin B_{12} gave an increased hemoglobin and a total protein than when either was given alone. Hoeffer et al. (1952) studied the effect of oxytetracycline on the growth of pigs fed different levels of protein. They found no effect of

¹ Cyamimid Co.

oxytetracycline on protein requirement although the rates of growth were the same on both levels of proteins fed without antibiotics.

Carpenter (1951) observed increases in gain of suckling pigs when supplemented with chlortetracycline. The artificial milk used gave a marked response when antibiotics were added. Hogue et al. (1957) fed milk at two levels to young dairy calves. They showed that the calves given the poorer quality diet showed a better response to added chlortetracycline 11.3% as against 5.2% although the calves on the higher milk level intake gave a better growth response. They concluded that the amount of milk in the feed of the calves could influence the response to the antibiotics.

Tillman and MacVicar (1956) fed chlortetracycline at the levels of 11 mcg/gm feed and 16.7 mcg/gm of feed to sheep. The former level had no effect on digestibility but at the latter level there was a significant effect on ration digestibility on the dry matter, protein, fiber nitrogen free extract and energy. But at both levels the nitrogen retention was unaffected. This was similar to an earlier conclusion reached by Richardson et al. (1955) that chlortetracycline and oxytetracycline had no significant effect upon feed digestibility or nitrogen retained.

Vitamin Sparing Action

Several intestinal organisms synthesize vitamins and amino acids that are necessary for optimal performance of the host animals. Ross and Yacowitz (1952) found that penicillin appeared to decrease the vitamin D requirement for normal bone calcification in chicks. Mason et al. (1954) fed chicks with diets containing limiting amounts of folic acid. Chlortetracycline supplementation led to increase in growth and also increase in amounts of folic acid production as well as liver folic acid. They reported

that these increases were accompanied by the appearance of coliform bacteria in the caecum and duodenum. They attributed this to the favorable condition for the coliform and thus the production of extracellular folic acid synthesis. Anderson et al. (1952) had earlier reported that feeding diets containing penicillin increased the numbers of intestinal coliforms other than Escherichia coli. They said that such organisms would produce vitamins essential to the animal if a diet deficient in the vitamin was given. Catron et al. (1953) studied the relationship between vitamin B₁₂ and panthothenic acid requirements in pigs fed antibiotics and concluded that both vitamins had a sparing action on each other in the absence of the chlortetracycline fed. Guggenheim et al. (1953) found that chlortetracycline had a sparing action on riboflavin and panthothenic acid in rats by increasing liver concentration. The effect was noticed only when the antibiotic was administered orally. Sauberlich (1952) had earlier reported that chlortetracycline and penicillin had a sparing effect on water soluble vitamins in rats.

Russoff et al. (1954) administered chlortetracycline by intramuscular injection and orally to young calves. They found that the B-vitamin content of the rumen fluid was similar for the control, the orally administered antibiotic group, and the intramuscularly injected group.

Thus conflicting views exist as regards the vitamin sparing action of antibiotics. This was well expressed by Jukes (1955) who wrote "that various investigations already described indicate that dietary antibiotics in many cases improve nutrition of animals with respect to the B-vitamins but in other cases the antibiotics are without any effect on the B-vitamin requirement. A few exceptions can be noted, especially the case of streptomycin, which appears to reduce the synthesis of biotin in the intestines."

Metabolic Effect of Antibiotics

Hays (1969) expressed this mode of action as pertaining to "the direct effect on the rate and pattern of the metabolic processes in the host animal." The effect could be termed to include the action on organisms themselves. Weinberg (1957) indicated that bacterial phosphorylation and oxidation reactions requiring magnesium ions are inhibited by tetracycline. This view was supported by Franklin (1963) who stated that chlortetracycline inhibits the transfer of amino acids of the transfer--RNA complex to the ribosomal protein in both animal and bacterial systems. In the work it was found that the antibiotic was more inhibitory in the Escherichia coli than the rat-liver system that was being used. He proposed that chlortetracycline acted as a chelating agent by reducing the magnesium ions necessary in the enzyme system and thus inhibited incorporation of leucine into the protein: Allison and Berry (1955) showed also that the feeding of chlortetracycline at the levels of 10 mg per pound of feed depressed the respiration of rumen microorganisms as well as the number of microorganisms sampled. Brody et al. (1954) also found that tetracycline inhibited fatty acid oxidation by mitochoridria, in the work done with rat liver cells. Jukes and Williams (1953) cited work done by others who found that streptomycin is involved in the oxalo-acetatepyruvate reaction. They indicate that penicillin prevents the uptake of glutamic acid by bacterial cells and chlortetracycline uncouples oxidative phosphorylation reactions. Yeh and Shils (1966) reported that tetracycline administered to rats decreased incorporation of amino acids into many tissue proteins including those of the gastro-intestinal tract. They concluded that an intramuscular injection of 250 mg/kg body weight causes impairment of fat absorption possibly by interfering with specific transfer mechanism across

the gut wall by interfering with the B-lipoprotein synthesis in the mucosal cells.

These metabolic effects might have a significant effect on the response of bacteria when the bacteriostatic actions of antibiotics are considered. But as pointed out by Hays (1969) such metabolic effects could not alone justify the growth response observed in animals at the level of supplementation of the additives.

Disease Control Effect

By far the greatest support on the mode of action of antibiotics has been attributed to the disease control effects obtained by their action. Weiner (1972) refers to Groschke who concluded in a work done in 1950 that antibiotics stimulate growth indirectly by changing the intestinal flora from undesirable to desirable types which synthesize unknown growth factors. Sorokin et al. (1972) using chick-gnobionts with monoflora of Escherichia coli studied the mechanism of oxytetracycline stimulation of growth. They observed a 10% increase in growth of chicks receiving oxytetracycline and a reduction in the number of bacilli.

Radisson et al. (1956) demonstrated that feeding of low level chlortetracycline induced increased sensitivity of intestinal bacteria to the host defense mechanism. In a later work, MacFadden and Bartley (1959) inferred that a relationship might exist between the age of calf, its development of defense mechanism and growth response to antibiotic feeding. In their experiment they found that feeding chlortetracycline aided the host defense mechanism so that by the 5th week a near maximum phagocytic activity against intestinal coliform bacteria was reached. They postulated that the improved rate of growth and feed efficiency was at least in part a result of the

effect of the antibiotic on the alteration of the virulence of the microbes due to contact and hence an increase susceptibility to host phagocytosis. This supports Radisson et al. (1956) who presented data on calves to indicate that low levels of an antibiotic may affect the normal intestinal flora in such a manner that the bacteria may become susceptible to the host defense mechanism of phagocytosis without the phagocytic activity of the leucocytes in the blood being affected.

Jukes and Williams were cited by Soule (1957) as setting forth three possible ways in which an antibiotic may favorably affect the intestinal flora and promote growth: 1) the antibiotic may inhibit or destroy organisms which produce subclinical infections; that is, they suppress organisms which produce toxic reactions and cause a slowing of growth of the host animal, 2) antibiotics may produce an increase in the number of activity of organisms which synthesize certain known or unknown vitamins or growth factors, and 3) antibiotics inhibit organisms which compete with the host for available nutrients.

Thus according to the disease control effect healthy well managed animals may respond less to antibiotic supplementation than poorly managed animals with possibly subclinical manifestation of disease. This could be as a result of thinner, healthier intestinal walls seen in antibiotic fed animals.

Braude et al. (1955) demonstrated that the intestinal wall of pigs fed diets containing antibiotics was thinner than those fed diets without the antibiotic. Coates (1955) working with chicks was also able to show that the intestinal wall of chicks responded the same way as above. Earlier Coates (1953) had also demonstrated that chicks isolated for two weeks in a semigerm-free environment, supplied with filtered air and clean water did not

respond to penicillin supplementation. Jukes (1953) however still pointed out that the growth promoting effect obtained by addition of crude preparations of Streptomyces aureofaciens in the diet of chick occurred despite the fact that the chickens were being used for assay work on Vitamin B_{12} and so were apparently healthy and kept in cages that were frequently cleaned and which were steam sterilized at monthly intervals. Nevertheless preponderance of evidence still indicates that the disease control effect contributes to the mode of action of antibiotics.

Related to the disease control theory is the proposal that there is a possibility that toxic materials produced by bacteria are removed or their production inhibited by the presence of antibiotics. Visek et al. (1959) demonstrated decreases in gastro-intestinal ureolytic activity with the administration of chlortetracycline and oxytetracycline to rats. They concluded that these antibiotics would thus affect urea metabolism and reduce toxic ammonia produced by bacteria. Harbers et al. (1963) found that the addition of barbituric acid and chlortetracycline to a casein diet in chicks increased growth and this was coincidental with the decrease ureolytic activity and ammonia concentration of the gastro-intestinal tract. Further support for this mode of action was given by Alvares et al. (1964) who found increased growth in chicks when barbituric acid and chlortetracycline were administered, but this action depended on the type of carbohydrate fed. However they concluded that the action of the antibiotic in growth stimulation was due to the suppressing of the activity of urease producing bacteria, leading to a decrease in the amount of enterotoxin produced.

Antibiotics and Blood Constituents

The effect of chlortetracycline and oxytetracycline on the blood count in mice was studied by Mirone (1953). He found no significant difference between the treated and control mice in hemoglobin level, erythrocyte, leucocyte and differential counts. These same conclusions were reached by Sheffy et al. (1952), Burnside et al. (1954) and Robinson (1954) in pigs.

Loginov (1959) studying the reflex component of the mechanism of production of blood changes by chlortetracycline reported two peaks of leucocytosis after an intramuscular injection of chlortetracycline to rabbits; the first reaching a maximum after 2 hours and the second peak after 24-48 hours. He explains that the first rise was due to "excitation of the receptor apparatus of the muscle tissue" while the second was due to the humoral action of the absorped chlortetracycline on the hematopoetic organs. Recent work by Efremov (1971) on pigs that were receiving 500 IU/kg body weight once daily for 2 months was said to have resulted in chronic hyperemia of the liver lobes with an increase in interlobular connective tissue. A dose of 2,500 IU twice during one month intramuscularly, was also reported to have caused similar changes in the liver and also a decrease glycogen synthesis and storage properties.

Sorokin et al. (1972) however reported that chick-gnotobionts with monoflora of Escherichia coli receiving oral oxytetracycline daily showed an intensification of carbohydrate and protein metabolism in internal organs and an increase in glycogen content in the muscle cells of the myocardium and liver cells with an increased reaction by lymphoid organs.

Thompson et al. (1973) reported that neomycin sulfate produces a transient decrease in serum cholesterol levels after an oral dose in germ

free pigs. They regarded the findings as indicating that the antibiotic has an effect on lipid metabolism independent of its antibiotic action.

Fisher and Faloon (1957) reported the use of neomycin sulfate to decrease blood ammonia levels in human patients with hepatic cirrhosis. This is attributed to the effect of the antibiotic in suppressing bacteria fermentation of ammonia from proteins. A decrease in serum cholesterol level in men due to administration has also been observed by Samuel and Sterner (1959) up to levels of 22% at a dose of 1.5 or 2 g per day. They thought the effect of the antibiotic might be due to its effect on intestinal bacterial flora or upon certain enzyme systems of the gastro-intestinal tract.

Stauffer et al. (1973) on their work to find the effect of tetracyclines in serum calcium found that after intravenous but not intraperitoneal injection of the antibiotic, serum calcium both total and ionized increased in the rats that were calcium deficient but was normal in "normal" rats. They proposed that the increased serum calcium could have been due to inhibition of bone mineralization or a stimulation of osteoclastic activity. Various works have been undertaken to study the effect of tetracycline on mineral metabolism particularly multivalent cations. Yeh and Shils (1966) worked with oxytetracycline and reported an impaired intestinal absorption of radioactive iron in rats. A thorough review has been done by Weinberg (1957). Based on this and other evidences that considerable number of antimicrobial compounds can and do chelate metallic cations, Albert (1953), there have been proposals that antibiotics such as oxytetracycline might be inhibited in their actions by forming complexes with cations such as calcium and magnesium (Weinberg, 1955). Conversely it has been proposed that the chelating action of oxytetracycline could bind these ions to form stable compounds and thus make calcium in feeds or orally administered inaccessible to body tissues (Smithscor, 1972).

Ahuja et al. (1971) studied the effect of chlortetracycline on the utilization of calcium, phosphorus and nitrogen in the chicken. Chickens were fed two protein levels and data was collected for the fourth and eighth weeks of feeding. They found a constant level of these minerals showing no effect of the antibiotics on the mineral level. Price et al. (1957) have also proposed a preferential adsorption theory for the mechanism of inactivation of oxytetracycline by calcium but their work was inconclusive as no measurements were made of the intracellular calcium as different from extracellular.

Similar work by Ahuja et al. (1971) in chicken has not been reported in sheep and the balance trial is proposed in this work.

Literature Cited

- Ahuja, A. K., N. S. Malik and J. S. Ichhponani. 1971. Effect of chlortetracycline on calcium, phosphorus and nitrogen utilization on chicks kept on normal and above normal levels of energy and protein. Indian J. Anim. Sci. 41(5):391-396, 396-400.
- Albert, A. 1953. Avidity of terramycin and aureomycin for metallic cations. Nature, London 172:201.
- Allison, M. J., and E. C. Berry. 1955. The effect of aureomycin upon the microflora of ovine rumen. South Dak. Acad. Sci. Proc. 34:23-29.
- Alvares, A. P., L. H. Harbers and W. T. Visek. 1964. Effect of barbituric acid, chlortetracycline and carbohydrates upon growth and gastro-intestinal urease activity of chicks. J. Nutr. 82:93.
- Anderson, G. W., J. D. Cunningham and S. J. Slinger. 1952. Effect of protein level and penicillin on growth and intestinal flora of chickens. Jour. Nutr. 47:175-198.
- Ash, R. W. 1962. Omaso-abomasal re-entrant cannulae for sheep. J. Physiology 164(1):4p-5p.
- Black, A., and J. W. Bratzler. 1952. The effects of a vitamin $\rm B_{12}$ supplement, vitamin $\rm B_{12}$ and streptomycin on the metabolism of the rat. Jour. Nutr. 47:159-173.
- Blaxter, K. L., and A. Martin. 1967. The utilization of protein as a source of energy in fattening sheep. Brit. J. Nutr. 16:397-407.
- Braude, R., S. K. Kon and J. W. G. Porter. 1953. Antibiotics in nutrition. Nutr. Abstr. and Rev. 23:473.
- Braude, R., M. F. Coates, M. K. Davies, G. P. Harrison and K. G. Mitchell. 1955. The effect of aureomycin on the gut of the pig. Brit. J. Nutr. 9:363.
- Broderick, G., T. Kowalczyk and L. D. Satter. 1970. Milk production response to supplementation with encapsulated methionine per Os or casein per abomasum. J. Dairy Sci. 53:1714.
- Brody, T. M., R. Hurwitz and J. A. Bain. 1954. Magnesium and the effect of the tetracycline antibiotics on oxidative processes in mitochondria. Antibiot. Chemother. 4:864.
- Burnside, J. R., R. H. Grummer, P. H. Phillips and G. Bohshedt. 1954. The influence of crystalline aureomycin and vitamin $\rm B_{12}$ on the protein utilization of growing fattening swine. J. Anim. Sci. 13:184-200.

- Burnside, J. E., R. H. Grummer, P. H. Phillips and G. Bohstedt. 1951. The effect of vitamin $\rm B_{12}$ and aureomycin when fed high, intermediate and low protein levels of swine. J. Anim. Sci. 10:1042-1043.
- Catron, D. V., A. H. Jensen, P. G. Homeyer, H. M. Maddock and G. C. Ashton. 1952. Re-evaluation of protein requirements of growing-fattening swine as influenced by feeding an antibiotic. J. Anim. Sci. 11:221.
- Catron, D. V., R. W. Bennison, H. M. Maddock, G. C. Ashton and D. G. Honeyer. 1953. Effects of certain antibiotics and vitamin B₁₂ on pantothenic acid requirements of growing-fattening swine. J. Anim. Sci. 12:51-61.
- Carpenter, L. E. 1951. Effect of APF concentrate containing aureomycin on gestating, lactating and growing swine. J. Anim. Sci. 10:657-664.
- Chalmers, M. I., D. P. Cuthberston and R. L. M. Synge. 1954. Ruminal ammonia formation in relation to the protein requirement of sheep. I. Duodenal administration and heat processing as factors influencing fate of casein supplements. J. Agric. Sci. 44:254-262.
- Coates, M. E. 1953. The mode of action of antibiotics in animal nutrition. Chem. Ad. Ind. 50:1333-1335.
- Coates, M. E., M. K. Davies and S. K. Kon. 1955. The effect of antibiotics on the intestine of the chick. Br. J. Nutr. 9:110.
- Cuthberston, D. P., and M. I. Chalmers. 1950. Utilization of casein supplement administered to ewes by ruminal and duodenal fistulae. Biochem. J. 46:17.
- Dougherty, R. W. 1955. Permanent stomach and intestinal fistulas in ruminants. Some modifications and simplifications. Cornell Vet. 45:331-357.
- Driedger, A., R. J. Condon, K. N. Nimrick and E. E. Hatfield. 1970. A new technique of abomasal and rumen cannulation. J. Anim. Sci. 30:318.
- Efremov, G. G. 1971. Effect on various doses of oxytetracycline on the gastric fundus. Nauchrye Trudy. Omskii Veterarlyi Institut 27, No. 3, 162-171, 172-175, 176-177, 181-182. [Vet. Bulletin 42(3):abstr. 1561.]
- Ferguson, K. A., J. A. Hemsley and P. J. Reis. 1967. Nutrition and wool growth. The effect of protecting dietary protein from microbial degradation in the rumen. Aust. J. Agric. Sci. 30:215-217.
- Fisher, C. J., and W. Falloon. 1957. Blood ammonia levels in hepatic cirrhosis. Their control by the oral administration of neomycin. The New England J. of Med. 256(22):1030.
- Franklin, T. J. 1963. The inhibition of incorporation of leucine into protein of cell free systems from rat liver and Escherichis coli by chlortetracycline. Biochem. J. 87:449-453.

- Guggenheim, K., S. Halevy, I. Hartman and R. Zaunt. 1953. The effect antibiotics on the metabolism of certain B vitamins. J. Nutr. 50:245-253.
- Harbers, L. H., A. P. Alvares, A. I. Jacobson and W. J. Visek. 1963. The effect of barbituric acid and chlortetracycline upon growth, ammonia concentration and urease activity in the gastrointestinal tract of chicks. J. Nutr. 80:75.
- Hays, V. W. 1969. Biological Basis for the use of antibiotics in livestock production. In proceedings to a symposium: The use of drugs in animal feeds. National Acad. Sci., Washington, D.C., pp. 11-30
- Hoeffer, J. A., R. W. Leucke, P. Thorp and R. Johnson. 1952. The effect of terramycin on the growth of pigs fed different levels of protein. J. Anim. Sci. 11:455-458.
- Hogue, D. E., R. G. Warner, J. K. Loosli and C. H. Grippin. 1957. Comparison of antibiotics for dairy calves on two levels of milk feeding. J. Dairy Sci. 40:1072.
- Holtzman, J. L. 1963. Studies on the relationship of the growth stimulatory effects of antibiotics in exchange resins to the endogenous urea turnover. Ph.D. Dissertation, The University of Chicago.
- Hill, K. T., and R. A. Gregory. 1951. The preparation of gastric pouches in the ruminant. Vet. Rec. 63:647.
- Jarrett, I. G. 1948. The production of rumen and abomasal fistulae in sheep. J. Austr. Council for Sci. and Ind. Research 20-25; 311-314.
- Jukes, T. H., and W. C. Williams. 1953. Nutritional effects of antibiotics. Pharmacol. Rev. 5:381-420.
- Jukes, T. H. <u>Antibiotics in Nutrition</u>. 1955. Antibiotics Monograph 4, Medical Encyclopedia Inc.; New York, p. 47.
- Kondos, A. C. 1967. A new method for cannulation of the abomasum in sheep. Australian Vet. J. 43(4):145-151.
- Little, C. O., and G. E. Mitchell, Jr. 1967. Abomasal vs. oral administration of proteins to wethers. J. Anim. Sci. 26:411.
- Little, C. O., G. E. Mitchell and G. D. Potter. 1968. Nitrogen in the abomasum of wethers fed different protein sources. J. Anim. Sci. 27(6): 1722-1726.
- Loginov, A. V., and Dumova. 1959. A reflex component of the mechanism of production of blood changes by chlortetracycline (biomycin) Biu Eksperim. Biol. i Med. 47(1):42-46. [Biol. Abstr. 35, No. 42209 (1960)].
- Markowitz, J. 1937. <u>Textbook of Experimental Surgery</u>. W. Wood and Company, Baltimore, pp. 115-116.

- Mason, W. J., A. E. Harper, M. E. Winje, C. A. Elvehjem, R. A. Rhodes and U. B. Sarles. 1954. A mechanism of the vitamin sparing effect of anti-biotics. J. of Nutr. 52:627.
- MacFadden, D. L., and E. E. Bartley. 1959. Mode of action of antibiotics in the nutrition of dairy calf. Relative effect of age, colostrum, and chlortetracycline feeding on susceptibility of intestinal coliform bacteria to phagocytosis. J. Anim. Sci. 18:1378-1387.
- Mirone, L. 1953. Effect of aureomycin and terramycin on growth reproduction and blood count in mice. Jour. Antibiotics and Chemicotherapy 3:600-603.
- Moore, R. R., A. Everson, T. D. Luckey, E. McCoy, C. A. Elvehjem and E. B. Hart. 1946. Use of sulfasuxdine, streptochricin and streptomycin in nutritional studies with the chick. J. Biol. Chem. 165:437-441.
- Moore, C. P., C. O. Little, G. E. Mitchell, Jr., R. A. Scott and H. E. Amos. 1970. Feeding vs. abomasal infusion of lysine in sheep. J. Anim. Sci. 31(1):249.
- Papas, A., E. E. Hatfield, A. Nimrick and F. W. Owens. 1971. Effects of abomasally infused casein on feed intake. J. Anim. Sci. 33(5):1169.
- Phillipson, T. in <u>The Physiology of Domestic Animals</u>: Ithaca, N.Y.: 7 Comstock Publishing Co., Inc. 1970 ed.
- Phillipson, A. T., and J. R. Innes. Permanent stomach fistulae in ruminants. Quart. J. Exp. Physiol. 29:333-341.
- Phillipson, A. T., and R. L. Mitchell. 1951. The administration of cobalt by different routes to lambs maintained on low cobalt diet. Brit. J. Nutr. 6:176-189.
- Price, K. E., Z. Zolli, J. C. Atkinson and H. G. Lutter. 1957. Antibiotic inhibitions. II. Studies on the inhibitory action of selected divalent cations for oxytetracycline. Antibiotic and Chemotherapy 7:689-701.
- Quin, J. I., J. Van der Wath and S. Myburgh. 1938. Studies on the alimentary tract of merino sheep in South Africa. IV. Description of experimental technique, V. The motility of the rumen under various conditions. Ondertespoort J. Vet. Sci. 11:341.
- Radisson, J. J., E. E. Bartley, T. H. Lord and M. J. Swenson. 1956. The mode of action of antibiotics in the nutrition of the dairy calf. Its effect of aureomycin administered orally to young dairy calves on the sensitivity of intestinal bacteria to phagocytosis. J. Dairy Sci. 39(10):1386-1395.
- Reis, P. J., and P. G. Schinckel. 1964. The growth and composition of wool: III. The effect of casein gelatin and sulphur-containing amino acids given per abomasum. Australian J. Biol. Sci. 17:532-547.

- Reis, P. J., and A. M. Downes. 1969. Rate of response of wool growth to abomasal supplement of casein (sheep). J. Ag. Sci. (London) 73(3):445-452.
- Reis, P. J., and D. A. Tunks. 1969. Evaluation of formaldehyde-treated casein for wool growth and nitrogen retention. Aust. J. Agric. Res. 20:775-781.
- Richardson, D., R. P. Soule, Jr. and C. E. Aubel. 1966. Antibiotics for growing-fattening swine. 42nd Ann. Livestock Feeders Day. Cir. 320 pp. 24-38.
- Robinson, N. W. 1954. The effect of antibiotics upon feed utilization by fattening swine. M.S. Thesis, Kansas State College.
- Ross, F., and H. Yacowitz. 1954. Effect of penicillin growth and bone ash of chicks fed different levels of vitamin D and phosphorus. Poultry Sci. 33:262.
- Russoff, L. L., J. M. Russel and C. E. Hyde. 1954. Parenteral administration of aureomycin to young calves with a note on mode of action. J. Dairy Sci. 37:488-497.
- Samuel, P., and A. Steiner. 1959. Effect of neomycin on serum cholesterol level of man. Proc. Soc. Exp. Biol. and Med. 100:193-195.
- Sauberlich, H. E. 1952. Effect of aureomycin and penicillin upon the vitamin requirement of the rat. J. Nutr. 46:99.
- Schelling, G. T., and E. E. Hatfield. 1967. Effect of abomasally infused nitrogen sources on nitrogen retention of growing lambs. J. Nutr. 96:319-326.
- Scott, R. A., C. L. Streeter, C. O. Little and G. E. Mitchell. 1969. Oral and abomasal administration of lysine to wethers. Ky. Agric. Exp. Sta. Progr. Rep. 181:47-48.
- Sorokin, V. V., A. V. Nikolaeva, I. G. Shponza, A. Kozlyuk, G. S. Ponomareva and D. V. Dubrovskaya. 1972. Uanie poststimuliruyuslchego diestiviya terramitsina na gnotobiontov s monofloro: [Study of a growth-stimulus of terramycin on chick-gnotobionts with monoflora]. (Izv Al Mol) SSR Ser Biol Khim Nauk 1:54-57. [Bio. Abst. Mar. 15, 1972.]
- Soule, R. P., Jr. 1957. Effects of chlortetracycline and oxytetracycline hydrochlorides on the carcass characteristic or market pigs. Ph.D. Dissertation, Kansas State College.
- Sheff, B. E., R. H. Grummer, P. H. Phillips and G. Bohstedt. 1952. Comparison of growth responses of 2 day old pigs to streptomycin, aureomycin and crude APF alone and in combination with vitamin B_{12} . J. Anim. Sci. 11:97-102.

- Smithscor, S. F. 1972. Interaction between calcium and tetracyclines. Mod. Vet. Prac. 53:13, May.
- Stauffer, M., D. Baylink, J. Wergedal and C. Rich. 1973. Decreased bone formation, mineralization and enhanced resorption in calcium deficient rats. A. J. Physiology 225(2).
- Stokstad, E. L. R., and T. H. Jukes. 1950. Further observations on the animal protein factor. Proc. Soc. Expt. Biol. and Med. 73:523-528.
- Thompson, G. R., K. Henry, N. Edington and P. C. Trexler. 1973. Effect of neomycin on cholesterol metabolism in the germ free pig. Eur. J. Clin. Invest. 2:365-371. [Biol. Abstr. 27579.]
- Tillman, A. D., and R. W. MacVicar. 1953. The effect of aureomycin upon growth, digestion and ration constituents, rectal temperature and urine volume of sheep (Abs.). J. Anim. Sci. 12:955-956 (Nov.).
- U.S. Dispensatory and Physicians Pharmacology. 26th Ed. 1966. B. Lippin-cott Co., Philadelphia and Toronto.
- Visek, W. J., J. M. Baron and D. M. Switz. 1959. Urea metablism and intestinal ureolytic activity of rats fed antimicrobial agents. J. Pharm. & Expt. Therap. 126(4):359.
- Weiner, H. 1972. Antibiotic supplementation of animal feeds. Pfizer Inc., New York.
- Welch, H. 1953. About the chemically descriptive general terms for aureomycin (chlortetracycline) and terramycin (oxytetracycline). Antibiotics and Chemotherapy 3:659-662.
- Weinberg, E. D. 1957. The mutual effects of antimicrobial compounds and metallic cations. Bact. Rev. 21:46.
- Weinberg, E. D. 1955. Further studies on metallic ions reversal of oxytetracycline. Reactivation of drug inactivated cells by Mg++. In Antibiotic Annual 1954-1955, New York, Medical Encyclopedia, Inc. 169-173.
- Yeh, S. D. J., and M. E. Shils. 1966. Effect of tetracycline on intestinal absorption of various nutrients. Proc. Exp. Bio. and Med. 123:367-370.

Part II

A SIMPLIFIED ABOMASAL CANNULATION TECHNIQUE IN SHEEP

Summary

A method is described by which an abomasal cannula was introduced and maintained in place for a period of five months in sheep. Following normal surgical preparations a rubberized cannula with a mushroom head, having a shaft approximately 25-30 cm long was inserted on the right abdominal wall, approximately 7 cm from the ventral midline. The cannula was placed in the abomasum midway between the lesser and greater curvature about 15 cm from the pylorus with the mushroom head held in place by a purse string. The shaft of the tube was exteriorized about 8 cm dorso-lateral to the paramedian incision, secured to the skin by a synthetic suture. Abomasal drainage through the tube was prevented by use of clamp.

Introduction

Many types of abomasal cannulation techniques have been used in sheep. Quin and van der Wath (1938), Jarrett (1948), Dougherty (1955), and Phillipson and Innes (1930) reviewed the literature involving rumen and abomasal cannulations used. Several surgical modifications and cannulae materials have since been introduced that simplify surgery and impose versatility (Kondos, 1967; Hart, 1972). Dridger et al. (1970) described a method by which the cannula can be placed subcutaneously and the tube brought out at the dorsal aspect of abdominal wall. Essentially any cannula fitted should be such that permits easy infusion of fluid into the abomasum without leakage. It should also

permit relative ease in the use of the cannula and its manipulation without an untowards effect on the patient.

Surgical Procedure

Food and water were withheld from sheep for 12-24 hours prior to surgery.

The patient was sedated with 5 ml of magnesium-chloral hydrate solution 1

intravenously while in dorsal recumbency.

Normal surgical preparation included clipping the operative area which was the paramedian ventral aspect of the abdomen about 15 cm square bounded by the ventral abdominal midline and the sternum. The area was scrubbed once with soap and water, rinsing well and then scrubbed three times with a germicidal detergent solution. Local nerve blockage was obtained by the infiltration of 10 ml of 2% lidocaine hydrochloride into the tissue to be incised. An alcoholic quaterinary ammonium compound was applied to the surgical area. Sterile gloves, mask and cap were used by the surgeon. The entire area was draped with sterile cloth.

An incision of approximately 10 cm in length was made through the skin, musculature and peritoneum on the right side about 7 cm from the ventral midline, extending from close to the last rib towards the ilium. The abomasum was exposed, the pylorus located and the organ brought to the surface. A purse string suture making a circle about 1.5 cm in diameter was made through

Mag-Chloral Relaxant--Haver Lochart Lab., Kansas City.

²Betadine--The Purdue Frederick Company, Yonkers, N.Y.

³2% Lindocaine HC1 U.S.P.--McGaw Laboratories [Div. of American Hospital Supply Corporation].

⁴ Ioprep.

the abomasal wall using #2 chromic catgut where the cannula was to be inserted. The suture was approximately 15 cm from the pylorus and midway between the greater and lesser curvatures of the abomasum. Tissue forceps were applied in two places around the periphery of the purse string and the area was exteriorized to prevent leakage into the peritoneal cavity. An incision was made and the cannula was then inserted to the cuff of the cannula. The cannula consists of a rubber tubing having a mushroom head from which the shaft of the tube 25-30 cm long begins. The lower side of the mushroom head had 4 holes each approximately 5 mm in diameter. The purse string was tied tightly around the cuff. A few interrupted sutures were taken through the walls of the tube to the abomasum. Occasional difficulty was encountered in inserting the cannula if the incision on the abomasum was too small but by using a hemostat to squeeze the mushroom head, the tube insertion was made easier. A stab wound was made and the other end of the tube exteriorized about 8 cm dorso-lateral to the paramedian incision. The abomasal wall was placed in contact to the peritoneum. The end of the tube was clamped to prevent abomasal drainage.

The peritoneum was sutured with a continuous suture of #2 medium chromic catgut. The muscle layers were sutured with continuous row of #2 medium chromic catgut and the skin sutured with synthetic sutures using either a lock type stitch or horizontal mattress suture.

The tubes were then taped to the abdominal wall to facilitate antibiotic infusion with an 18 gauge 4"-needle. When the cannula was removed or when it fell out accidentally fibrous tissue that formed around the tract prevented obliteration so that the orifice could be enlarged permitting insertion of other tubes.

Post-operative care included holding each lamb in the clinic for 3 to 4 days after which they were removed to the KSU Sheep Research Station. During hospitalization rectal temperatures were recorded at 24 hour intervals. Feed was made available after surgery and no additional medication was administered.

Recovery from surgery was prompt. The patient remained in perfect health without leakage of abomasal contents and normal body temperatures were observed.

Literature Cited

- Dougherty, R. W. 1955. Permanent stomach and intestinal fistulas in ruminants. Some modifications and simplification. Cornell Vet. 45: 331-357.
- Dridger, A., R. J. Condon, K. N. Nimrick and E. E. Hatfield. 1970. A new technique of abomasal and rumen cannulation. J. Anim. Sci. 30:318.
- Hart, R., and J. T. Williams. 1972. A technique for chronic catheterization of sheep abomasum. Res. Vet. Sci. 13:496-497.
- Jarrett, I. G. 1948. The production of rumen and abomasal fistulae in sheep. J. Austr. Council for Sci. and Ind. Res. 20-25, 311-314.
- Kondos, A. C. 1967. A new method for cannulation of the abomasum in sheep. Australian Vet. J. 43(4):145-151.
- Phillipson, A. T., and J. R. M. Innes. 1939. Permanent stomach fistulae in ruminants. Quart. J. Exp. Physiol. 29:333-341.
- Quin, J. I., J. Van der Wath and S. Myburgh. 1938. Studies on the alimentary tract of merino sheep in South Africa. IV. Description of experimental technique. V. The motility of the rumen under various conditions. Ondertespoort J. Vet. Sci. 11:341.

Part III

EFFECT OF ABOMASALLY INFUSED ANTIBIOTIC ON GROWTH AND NUTRIENT BALANCE IN SHEEP

Introduction

Several theories have been proposed for the mode of action of antibiotics in livestock production. One of the most widely accepted theories is the nutrient sparing effects. Monson et al. (1954) found that adding an antibiotic to a chick diet low in folic acid increased the folic acid levels in the liver. Murley et al. (1951) reported a greater increase in blood sugar levels in chlortetracycline fed calves than the controls. Russoff et al. (1954) administered chlortetracycline intramuscularly and reported that the rumen had been bypassed by the antibiotic. From their results they postulated that the rumen was not where growth was stimulated since the drug was not demonstrable in the saliva. A similar work by Hester et al. (1954) supported such a proposal. Russoff et al. (1954) also observed larger size of bone and carcass of chlortetracycline fed calves than the controls, implying that there was an increase in osteosseous tissue deposition.

The present investigation was to find out the effect of abomasally infused oxytetracycline/neomycin sulfate mixture on growth, feed efficiency, calcium, phosphorus and nitrogen balance in sheep.

Experimental Procedure

Growth Trial I

Twelve Hampshire-Rambouillet crossbred lambs (six males, six females) averaging 29 kg, aged 4 months, were obtained from commercial sources. They

were dosed with an anthelminthic on arrival and kept on a basal alfalfasorghum grain-soybean meal pelleted ration.

Animals were allotted to 4 groups of 3 lambs each. The lambs were fed in a 2 x 2 factorial arrangement of treatments in a completely randomized design. Three groups (2 cannulated, 1 control-uncannulated) received the basal diet (Table 2, Ration 1), the other uncannulated group received the same pelleted (3/16") basal diet supplemented with antibiotic (Table 1, Ration 2). Feeding was ad libitum for 45 days with average daily feed intake determined every three days.

One cannulated group received abomasal infusion of antibiotic daily at 3:30 p.m. at 40 mg/lb of the average daily feed intake. Equivalent quantities of physiological saline solution were administered abomasally to the other cannulated group at the same period daily. Blood samples were drawn from the jugular veins of all lambs with separate disposable polyethylene syringes on the first day of experiment and every 7 days thereafter. Initial weights were determined at the start of experiment, every 7 days thereafter and on the 45th day.

The criteria of response were hemoglobin, hematocrit (packed cell volume), erythrocytes, leukocytes, total blood proteins, inorganic calcium and phosphorus of blood plasma.

Balance Trial

At the end of 45 days the lambs were randomly placed in individual metabolism stalls (Thyfault and Harbers, 1972). Each lamb received 600 gms of their allotted diet twice daily for a 7-day adjustment period and 7-day collection period. On the third day of the adjustment period, 1 lamb was off feed, was removed but died 4 days later. Abomasal infusions of antibiotic

and physiological saline solutions continued at 3:30 p.m. to the same lambs receiving them as in the growth trial. A measured quantity of water was provided ad libitum twice daily to each lamb. Previously offered unconsumed feed and water were removed at each feeding. The quantity of feed and water refused were determined and subtracted from amount offered to determine intake. A water sample (25 ml) was taken at each water supply, mixed in a polyethylene bottle and each day's sample stored for analysis.

Fecal evacuations from each lamb were removed daily, weighed, and 5% of total weight placed in individual polyethylene bags then frozen immediately after collection. Total daily volume of urine from each lamb was determined in polyethylene graduated cylinder and 10% of the total daily output placed in acid washed bottles. Twenty-five ml of 50% reagent-grade concentrated hydrochloric acid was added to prevent ammoniation. Blood samples (10 mls) were obtained from the jugular vein with disposable polyethylene syringes on the first day and the 7th day of balance trial. Each sample was centrifuged for 10 minutes at 2,000 rpm and refrigerated for later analysis.

At the end of digestion trial the fecal samples from each lamb and feed for the collection period were composited, then dried in a forced draft oven at 55°C for 5 days. They were ground in a Wiley mill and stored in air tight containers for analysis.

Method of Analysis

Proximate analysis were conducted according to A.O.A.C. (1970) methods (Table 3). Calcium analysis was performed with an atomic absorption spectrophotometer. Samples of blood were removed, thawed and 1 ml

¹Jarrell-Ash 82-500.

deproteinated with 1 ml of 48% trichloroacetic acid in 3 mls of distilled H₂O. Calcium concentrations were determined in 1% strontium chloride. Samples of urine, wet ashed, were similarly diluted using automatic pipetting device and concentration determined in 1% strontium chloride. Phosphorus concentration was determined by spectrophotometry using colorimetric methods (Fiske and Subbarow, 1925).

Growth Trial II

A 30-day growth trial was conducted after the balance trial to evaluate the effect of oral administration of oxytetracycline/neomysulfate in the abomasally cannulated sheep. The group infused with antibiotic in growth Trial I and the uncannulated group on Ration 2 were fed ad libitum Ration 2. The cannulated group receiving infusion of physiological saline solution and the control remained on Ration 1. Infusion of antibiotic and saline solutions were stopped. Animals were weighed at the start of the growth trial, every seven days thereafter and on the 30th day.

Results and Discussion

Growth trial I. Data on performance of lambs are summarized in Table 3. Feed consumption shows slight differences which were not statistically significant. Average feed intake was slightly higher in the group receiving antibiotic infusion than the controls and the group receiving oral antibiotic. This supports the findings reported by Jordan (1954) that lambs receiving antibiotic in a pelleted ration required less feed per unit gain than the controls in his experiment. Daily gain and feed efficiency was lower in the group receiving antibiotic infusion though not at a statistically significant level. The decreased efficiency may be related to changes induced in the

gastro-intestinal tract by the infused antibiotic. Lassiter (1955) indicated that although not much data had been presented to show changes that occur in the intestinal tract as a result of antibiotic feeding, it does not mean that possible changes in the flora do not occur by the feeding. In our experiment the group receiving antibiotic infusion had an increase in abomasal pH to 3.5 as measured by pH meter after three days of routine infusion procedure. Similar increases in rumen pH have been observed in calves on antibiotic supplementation by Chance et al. (1953) and Mann et al. (1954).

Growth Trial II. Data obtained in the second growth trial are shown in Table 4. Feed consumption values differ slightly between the cannulated and the uncannulated groups. The group receiving antibiotic infusion in Trial I show a higher feed intake than those orally fed in Trial I. The daily gain shows differences which are not statistically significant. The average daily gain is the same for the two groups on antibiotic. This shows an improvement in performance by the cannulated group than when they were receiving the antibiotic by infusion in growth Trial.I. Russoff et al. (1953) demonstrated that oral administration of chlortetracycline improved average daily gain better than by intramuscular injections. Richardson et al. (1953) also reported no advantageous growth promoting effect by subcutaneous or intramuscularly injected chlortetracyclines in calves over oral feeding. The present studies seem to confirm the superiority of oral compared to the abomasal route although the performance is not statistically significant. However, the number of animals used in each group in these trials were apparently too few to give a basis for statistically significant differences.

¹ Beckman pll meter.

A longer postsurgical adaptation period might be needed since the response to antibiotic administration in the second growth trial might be due to adaptation rather than route of administration per se.

Balance trial. The results of the balance study are presented in Table 5. Effect of antibiotic on the digestibility of dry matter, energy, organic matter, protein, ether extract and nitrogen-free extract was found not to be statistically significant among the various treatment groups. This agrees with the work by Tillman and MacVicar (1956) who found that chlortetracycline had no effect on ration digestibility at levels of 11 mcg/gm of feed. Slight differences were found in the protein and dry matter digestibility between the antibiotic fed group and the other groups indicating a slight depression of these nutrients by oral antibiotic. Keith and Lehrer (1955) noted that feeding of antibiotic tends to depress digestibility of feed especially crude fiber and protein. They cited Hester et al. as showing that antibiotic moves rapidly through the gastric system to the intestine. This might account for the low nutrient digestibility associated with feeding of antibiotics. Crude fiber digestibility in the group receiving oral antibiotics was significantly lower (P < .05) than in the other treatment groups. This might be due to the depression of cellulolytic microorganisms by the antibiotic. Evans et al. (1955) reported a statistically significant decrease in crude fiber digestibility on feeding chlortetracycline to lambs. Evans et al. (1957) also reported a decreased crude fiber digestibility with chlortetracycline supplementation to their wether lambs at all levels of supplementation used except at 1 mg per pound of feed. Munch-Peterson and Armstrong (1958) found a decreased crude fiber digestibility in sheep on oral tetracycline which they also attributed to the decrease in the number of rumen microorganisms. Our

studies show that abomasal administration of antibiotic apparently does not affect the crude fiber digestibility in these lambs.

The nitrogen balance results (Table 5) indicate a higher nitrogen intake in the groups receiving antibiotics which may be related to a higher average feed intake observed in the group. Differences between the controls and the groups receiving antibiotic are observed in the values for retained nitrogen, percent nitrogen, retained of intake, percent absorbed of nitrogen retained, although the differences are not statistically significant. These values show that the antibiotic administration increases loss of nitrogen although improving efficiency of feed utilization and average daily gain. The gain may reflect a more efficient fat metabolism and fat deposition as seen in the values for back fat thickness in Table 4. The orally antibiotic fed group had a marked back fat deposition and the group receiving abomasal infusion of antibiotic having a comparatively higher back fat thickness over those receiving saline solution. The differences are not statistically significant. Hartsook and Johnson (1953) reported a similar oxytetracycline effect on rats. They found that the efficiency of fat utilization was increased while nitrogen utilization decreased.

Calcium and phosphorus balance. Table 6 shows the results obtained in the mineral balance trial. Phosphorus intake shows a statistically significant difference (P < .05) between the group receiving oral antibiotic and the other groups. This may be due to a higher feed consumption during the period. The group also shows a higher phosphorus retention, although the difference is not statistically significant. The data indicate that a high percentage of the absorbed phosphorus was retained by all the groups without significant differences among the groups.

Fecal calcium appears to be slightly higher among the group receiving oral antibiotics although not statistically significant. This may be due to antibiotic interference with absorption of the calcium as indicated by Yeh and Shils (1966) who reported that tetracycline administration to rats may interfere with absorption of divalent and multivalent ions thereby causing rapid excretion of the antibiotic-ion complex formed. Statistically significant differences (P < .05) were noted in the percent calcium retained of intake in the cannulated groups in relation to the uncannulated groups. The higher retention of calcium indicates that surgical cannulation caused changes in the serum calcium in the lambs. A 2-way analysis of variance of the calcium and phosphorus balance data shows that antibiotic administration by oral or intra-abomasal route does not significantly effect any changes in the balance of these ions. A similar result was obtained by Ahuja et al. (1971) in their work with chlortetracycline in chickens. However, measurements of the blood ionic calcium levels in an experiment with this same design carried out over a prolonged period might give a better basis on which conclusions can be made on the effect of antibiotic on blood calcium and phosphorus in sheep.

Table 7 shows serum calcium and phosphorus changes observed during two successive weeks (3rd and 4th weeks) of growth (Trial I). The serum calcium shows a general decrease in value among the noncannulated group and a general increase among the cannulated group. This is a reflection of the increased calcium retention in the calcium balance shown in Table 6. No trend was observed in the serum phosphorus. An increase being noted in both the cannulated and uncannulated groups. Data on serum samplings are too few and show wide individual animal variation that conclusive deductions cannot be made. But all fall within the range of the mean.

Blood parameters. Figures 1 and 2 show the trend in blood changes in hemoglobin concentrations, total leucocyte count, hematocrit and total protein. Our results indicate that antibiotic infusion or oral administration does not produce any significant changes on any of the blood parameters different from the controls for the period of measurement. This finding is similar to the report by Russoff et al. (1954) who studied the effect of chlortetracycline in calves and found that the antibiotic had no effect on hemoglobin percentage, packed cell volume and white blood count. In Figure 1 a sharp decrease is observed in hemoglobin concentration of the control group on the 14th day. This rises to the pre-experimental level on the 21st day. This correlates with the rapid increase in total blood protein on the 14th day and a corresponding decrease on the 21st day indicating a possible hemoconcentration at this period. Similar changes were observed for the same group in the total leucocyte count and hematocrit as shown in Figures 2 and 3. The findings are unrelated to the experimental treatment.

Table 1. Design of experiment for growth trial.

		Antibiotics				
		+	-			
		Animal no.	Animal no.			
		7313 (10)	7329 (7)			
	+	No tag(11)	7319 (8)			
ıla		7350 (12)	7310 (9)			
Cannula		Animal no.	Animal no.			
		7370 (4)	7331 (1)			
	=	7325 (5)	7344 (2)			
		7387 (6)	7333 (3)			

Table 2. Percentage composition of basal diet.

Item	Perce	entage
	Ration 1	Ration 2
Soybean oil meal	5.0	5.0
Ground grain sorghum	39.0	39.0
Dehydrated alfalfa	50.0	50.0
Molasses	5.0	4.9
Salt	0.5	0.5
Ammonium chloride	0.5	0.5
Antibiotic ¹ 20/20		.1

 $^{^{1} {\}tt Oxytetracycline\ hydrochloride/neomycin\ sulfate.}$

Table 3. Performance data of lambs during growth Trial I.

	Treatment						
Item	l No antibiotic No cannula	2 Antibiotic ^a No cannula	3 No antibiotic Cannula	4 Antibiotic Cannula			
No. of lambs	3	3	3	3			
Time on feed, days	45	45	45	45			
Initial weight, kg	32.50	32.95	31.06	31.82			
Final weight, kg	40.60	42.12	39.47	37.01			
Daily gain, kg	.18	.20	.19	.12±0.52 ^b			
Daily feed intake	1.25	1.20	1.13	1.27			
Efficiency of feed u zation (gain/feed),		16.65	16.81	9.4			

^aNoncannulated animals received antibiotic orally in feed; abomasally cannulated animals were given a solution of antibiotics by cannula once daily.

Table 4. Performance data of lambs during growth Trial II.

	Treatment						
Item	1 No antibiotic No cannula	2 Antibiotic No cannula	3 No antibiotic Cannula	4 Antibiotic Cannula			
No. of lambs	3	3	2ª	2 ^b			
Time on feed, days	29	29	29	29			
Initial weight, kg	41.97	43.48	38.86	41.14			
Final weight, kg	45.98	49.92	44.32	47.50			
Daily gain, kg	0.14	0.22	0.19	0.22±0.43			
Daily feed intake, kg	0.93	1.12	1.79	1.44			
Efficiency of feed ut zation (gain/feed), %		19.64	10.61	15.27			
Back fat thickness, c	em ^c 0.22	0.30	0.15	0.20			

 $^{^{\}mathrm{a}}$ One animal died of acute serufibrinous bronchiopneumonia.

bStandard error of mean.

bOne animal was off feed for several days and was removed from group.

^cMeasured by sonar ray using live animal.

dStandard error of mean.

Table 5. Effect of abomasal infusion and orally fed antibiotics on nutrient digestibility and nitrogen balance in lambs. Mean value with the standard error of difference for three animals/group.

	Treatment							
Digestibility,	1 No antibiotic No cannula	2 Antibiotic No cannula	3 No antibiotic Cannula	4 Antibiotic Cannula	SE			
Energy	74.19	68.29	73.52	74.26	0.03			
Dry matter	77.56	73.03	76.30	77.34	10.54			
Organic matter	79.64	74.87	79.12	79.53	0.89			
Protein	72.80	62.70	71.08	73.76	1.28			
Crude fiber	49.03 ^a	29.52 ^b	51.77 ^a	50.08 ^a	3.15			
Ether extract	70.31	56.24	65.96	67.70	1.86			
Nitrogen free extract	86.13	83.28	85.29	85.82	0.58			
Nitrogen baland								
Intake	24.72	26.57	25.26	27.11	0.55			
Fecal	6.79	8.07	7.35	7.90	0.42			
Absorbed	17.93	18.50	17.91	19.21	0.82			
Urine	10.56	13.24	10.47	10.08	0.54			
Retained	7.34	5.26	7.45	4.86	0.51			
Intake N retained, %	29.48	19.75	29.84	18.02	2.00			
Absorbed N retained, %	40.48	27.75	41.86	28.77	2.59			

a-bRows with differing superscripts significantly different (P < .05).

Table 6. Effect of abomasal infusion and orally fed antibiotics on calcium and phosphorus balance in lambs. Mean value with the standard error of difference for three animals/group.

	Treatment						
Calcium gm/day	1 No antibiotic No cannula	2 Antibiotic No cannula	3 No antibiotic Cannula	4 Antibiotic Cannula	SE		
Intake	9.71	10.63	10.38	10.96	0.24		
Fecal	7.40	8.41	6.44	7.06	0.35		
Urine	0.061	0.077	0.059	0.038	0.009		
Retained	2.07	1.85	3.89	3.86	0.32		
Intake Ca retained, %	21.41 ^a	19.95 ^a	37.81 ^b	35.41 ^b	3.08		
Absorbed Ca retained, %	91.03	95.23	98.56	98.94	1.62		
Phosphorus bala							
Intake	2.96	3.62	3.00	3.21	0.10		
Fecal	2.21	1.90	2.24	2.13	0.15		
Urine	0.13	0.24	0.10	0.20	0.03		
Retained	0.62	1.48	0.66	0.87	0.14		
Intake phosphoretained, %	cus 20.94	40.88	22.00	27.10	3.90		
Absorbed phosph retained, %	norus 82.66	86.04	86.84	80.55	2.34		

 $^{^{\}mathrm{a-b}}$ Rows with differing superscripts significantly different (P < .05).

Table 7. Changes in serum calcium and phosphorus over a 2-week period in lambs.

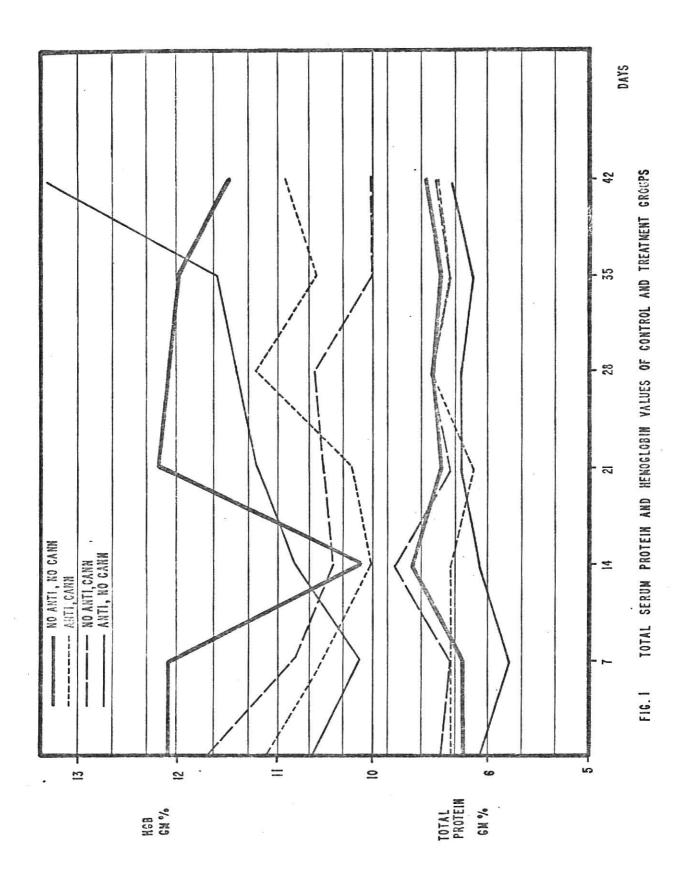
Serum calcium values (mg/g) Week 1 Week 2							
Animal no.	Non- cannulated No antibiotic	Animal no.	Cannulated No antibiotic	Animal no.	Non- cannulated No antibiotic	Animal no.	Cannulated No antibiotic
1	11.6	7	11.0	1	10.5	7	12.7
2	11.7	8	11.3	2	12.1	8	11.4
3	12.4	9	11.3	3	10.9	9	9.9
	No cannula antibiotic		Cannulated antibiotic		No cannula antibiotic		Cannulated antibiotic
4	12.9	10	11.7	4	10.9	10	11.2
5	12.0	11	11.5	5	10.2	11	11.2
6	12.8	12	11.5	6	8.7	12	12.1

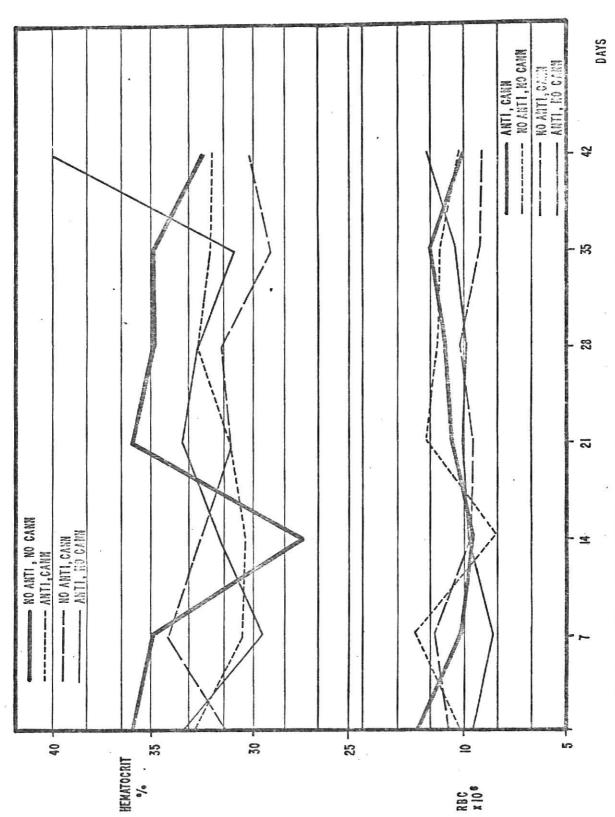
	Serum	phosphorus	values	(mg/g)		
Week 1					Week	2

Animal no.	Non- cannulated No antibiotic	Animal no.	Cannulated No antibiotic	Animal no.	Non- cannulated No antibiotic	Animal no.	Cannulated No antibiotic
1	9.59	7	7.92	1	10.5	7	9.41
2	9.54	8	7.92	2	9.54	8	8.81
3	8.68	9	10.1	3	7.40	9	10.0
	No cannula antibiotic		Cannulated antibiotic		No cannula antibiotic		Cannulated antibiotic
4	8.76	10	4.58	4	13.0	10	7.85
5	6.72	11	8.37	5	12.1	11	8.26
6	8.63	12	8.76	6	14.8	12	10.9

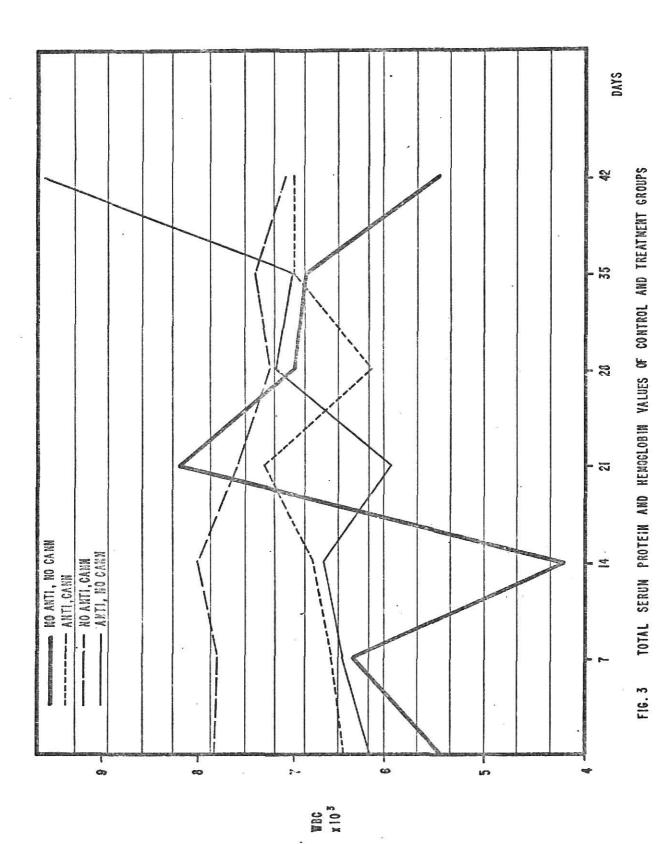
THIS BOOK CONTAINS NUMEROUS PAGES WITH DIAGRAMS THAT ARE CROOKED COMPARED TO THE REST OF THE INFORMATION ON THE PAGE. THIS IS AS RECEIVED FROM

CUSTOMER.





TOTAL SERUM PROTEIN AND HENCELOBIN VALUES OF CONTROL AND TREATMENT GROUPS F16. 2



Literature Cited

- Ahuja, A. K., N. S. Malik and J. S. Ichhponani. 1971. Effect of chlortetracycline on calcium, phosphorus and nitrogen utilization on chicks kept on normal and above normal levels of energy and protein. Indian. J. Anim. Sci. 41(5):391.
- A.O.A.C. 1970. Official Methods of Analysis (8th Ed.). Washington, D.C.
- Chance, C. M., C. K. Smith, C. F. Huffman and C. W. Duncan. 1953. Antibiotics in rumen digestion and synthesis. III. The effect of aureomycin on rumen microorganisms with special reference to the streptococci and coliform groups. J. Dairy Sci. 36:743.
- Evans, J. L., R. B. Grainger and C. M. Thompson. 1955. Effects of various levels and prolonged supplementation of chlortetracycline (aureomycin) upon roughage digestion in sheep. J. Anim. Sci. 14:1202.
- Evans, J. L., R. B. Grainger and C. M. Thompson. 1957. The effect of different levels and prolonged supplementation of chlortetracycline upon roughage digestion by sheep. J. Anim. Sci. 16:110.
- Fiske, C. H., and Y. Subbarow. 1925. The colorimetric determination of phosphorus. J. Biol. Chem. 66:375, 1015.
- Hartsook, E. W., and B. C. Johnson. 1953. Effects of dietary terramycin and methionine supplements on fat and protein gains in weanling rats. J. Nutr. 51:205.
- Hester, H. H., Jr., F. T. Landagora and L. L. Rusoff. 1954. The distribution of aureomycin in the body of dairy calves showing a growth response when the antibiotic is administered orally or intramuscularly. J. Anim. Sci. 13:988.
- Jordan, R. M. 1954. Lamb responses to antibiotic and pelleted rations. J. Anim. Sci. 13:55.
- Keith, T. B., and W. P. Lehrer. 1955. Growth responses of lambs fed three levels of roughage and chlortetracycline and aurofac 2A. Idaho Agr. Expt. Sta. Res. B. 31. 8 p.
- Lassiter, C. A. 1955. Antibiotics as growth stimulants for dairy cattle. A review. J. Dairy Sci. 38:1102.
- Mann, S. O., F. Masson and A. E. Oxford. 1954. Effect of feeding aureomycin to calves upon the establishment of microflora and microfauna. Brit. J. Nutr. 8:246.
- Monson, W. J., A. E. Harper, M. E. Winje, C. H. Elvehjem, R. A. Rhodes and U. B. Sarles. 1954. A mechanism of the vitamin sparing effect of anti-biotics. J. of Nutr. 52:627.

- Munch-Peterson, E., and J. Armstrong. 1958. The influence of orally administered oxytetracycline on the rumen bacteria of sheep. Australian J. Exp. Biol. 36:77.
- Murley, W. R., R. S. Allen and N. L. Jacobson. 1951. The effect of aureomycin on feed nutrient utilization by young dairy calves. J. Anim. Sci. 10:1057.
- Richardson, C. W., M. Ronning, E. R. Berousek and C. L. Norton. 1953. The effect of aureomycin upon the growth of dairy calves when administered orally, subcutaneously and intramuscularly. J. Dairy Sci. 36:593.
- Russoff, L. L., J. M. Fussell, C. E. Hyde and R. M. Crown. 1953. Oral supplementation versus intramuscular injection of aureomycin to young calves. J. Dairy Sci. 36:593.
- Russoff, L. L., C. E. Hyde, R. M. Crown, J. M. Fussell and L. S. Gall. 1954. Parenteral administration of aureomycin to young calves with a note on mode of action. J. Dairy Sci. 37:488.
- Russoff, L. L., F. T. Landagora and H. H. Hester. 1954. Effect of aureomycin on certain blood constituents (Hb, Packed RBc, Ca, P, RBC and WBC), body temperatures, weights of organs and tissues, and thickness of small intestine. J. Dairy Sci. 37:654.
- Thyfault, H. A., and L. H. Harbers. 1972. A versatile sheep metabolism unit. Lab. Practice 21:813.
- Tillman, A. D., and R. MacVicar. 1956. Aureomycin studies in sheep. Okla. Agr. Expt. Sta. Misc. P. MP. 45:9.
- Yeh, S. D., and M. E. Shils. 1966. Effect of tetracycline on intestinal absorption of various nutrients. Pro. Exp. Bio. and Med. 123:367.

VITA

Olugbemiro Olusola Akerejola was born on August 14, 1945, in Ogori,
Nigeria, where he completed his elementary education. He attended St. Paul's
College, Zaria, for his secondary education from 1959-1963 and King's College,
Lagos, for his higher school certificate education from 1964-1965. He
received his Doctor of Veterinary Medicine degree from Ahmadu Bello University, Zaria, in June 1971. He worked as a Lecturer at the Faculty of
Veterinary Medicine, Ahmadu Bello University, Zaria, Nigeria, from 1971-1972.
He enrolled at the Graduate School, Kansas State University, in August 1972.
He was married to Grace Jamgbadi on December 27, 1969. They have two sons,
Erema Mekabomo and Mekamagba Bamanosibina.

ABOMASAL INFUSION OF ANTIBIOTICS IN SHEEP

by

OLUGBEMIRO OLU AKEREJOLA

D. V. M., Ahmadu Bello University, 1971

AN ABSTRACT OF A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Surgery and Medicine

KANSAS STATE UNIVERSITY Manhattan, Kansas Experiments were conducted to study the effects of abomasal infusion of antibiotics on performance and nutrient balance in sheep. An attempt was made to develop a simplified abomasal cannulation technique that facilitates infusion of fluid without side effects on the sheep.

Surgery was performed and a rubberized cannula with a mushroom head inserted into the abomasum. The shaft of the cannula was exteriorized approximately 15 cm from the ventral midline and sutured to the skin.

Infusion of fluid was by the use of an 18 gauge 4"-needle.

Animals were allotted to 4 groups of 3 lambs each. The control, which were uncannulated, and two cannulated groups were on basal diet without antibiotic supplementation. One of the cannulated group received antibiotic (oxytetracycline/neomycin sulfate) infusion while the fourth group were uncannulated and received the basal diet with oral antibiotic supplementation.

Average feed intake was slightly higher in the group receiving antibiotic infusion but had lower feed efficiency and lower average daily weight gain than the other groups. When the group receiving abomasal antibiotic infusion were placed on oral antibiotic, they showed an improved performance similar to the uncannulated group receiving oral antibiotic, indicating the superiority of oral route to abomasal route in the administration of the antibiotic.

Effect of antibiotic on the digestibility of energy, organic matter, ether extract and nitrogen free extract were found not to be statistically significant among the various treatment groups. Slight differences were found in the protein and dry matter digestibility between the antibiotic fed group and the other groups.

Nitrogen balance results indicate a higher nitrogen intake in the groups receiving antibiotics but no statistically significant differences were found in the values for percent retained nitrogen of intake, percent absorbed of nitrogen retained.

Values for back fat thickness were found to be slightly higher in the groups receiving antibiotic than those not on antibiotic.

Phosphorus intake shows a statistically significant difference (P < .05) between the group on oral antibiotics and the other groups.

Fecal calcium appears to be slightly higher in the group receiving oral antibiotics. Statistically significant differences (P < .05) were noticed in the percent calcium retained of intake in the cannulated groups.

No statistically significant differences were observed in serum calcium and phosphorus among the various groups. The data indicate that antibiotic infusion or oral administration does not produce any significant changes in hemoglobin concentrations, total leucocyte count, hematocrit and total protein.