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Studies on the Alimentary Tract of the Merino Sheep in South Africa, II. Investigations on the Physiology of Deglutition, II.

By H. O. MÖNNIG, B.A., Dr.Phil., B.V.Sc., and
J. I. QUIN, D.V.Sc.,
Veterinary Research Officers, Onderstepoort.

In a previous paper on this subject the authors (1933) recorded the results of their investigations into the possibility of stimulating reflex closure of the oesophageal groove, for the purpose of dosing sheep directly into the abomasum. The bulk of the work done consisted of attempts to produce such stimulation by means of sodium salts as Wester had successfully done in the case of cattle, and to find out which factors were limiting or opposing this action of the sodium-ion in sheep. However, since the results were rather inconclusive and the main object had been that of finding a way to administer anthelminthics into the abomasum, it was decided to follow up indications of successful stimulation by a few other chemicals which had been used and to try others if necessary.

Two sheep which had been dosed with a solution containing nicotine and copper sulphate, had swallowed this into the abomasum. A repetition of this test again gave the same result. A test was then made on two sheep with nicotine alone, but this failed to produce the reflex. Before copper sulphate alone was tested a paper by Ross (1933) appeared, in which he recorded successful results with copper sulphate as stimulant. This author used 1 per cent. and 2 per cent. solutions, giving 30 c.c. of these with 10 c.c. of a red stain and he found no significant differences between the results obtained with sheep straved up to 48 hours and unstarved sheep. Of 84 sheep stimulated with 2 per cent. copper sulphate 79 swallowed into the abomasum, and similarly 11 of 12 sheep stimulated with a 1 per cent. solution.

Our results with copper salts which are given below, indicate that reflex closure of the oesophageal groove can be stimulated in this way, but that there are certain limiting factors, and it was our intention to elucidate the conditions under which the best results can be obtained. While the work is still in progress, it has reached a stage at which publication of our results is warranted, particularly also because methods of treatment against gastro-intestinal worms of sheep are now being recommended on this basis.

The sequence of the records of experiments as given below does not coincide with the chronological order in which the tests were made, but was arranged to give a systematic review of the results obtained. Moreover, these experiments were run more or less

parallel with investigations on the chemotherapy of oesophagostomiasis, frequently being influenced by results obtained in that work (see paper by Mönnig in this issue).

1. Effect of Starvation.

Sheep 1-6 were not starved. Sheep 7-14 were kept from food and water for 24 hours.

All the sheep were dosed through a funnel, to which was attached a short length of rubber tubing provided with a metal nozzle, which was placed in the mouth. The drench consisted of 30 c.c. 2 per cent. copper sulphate mixed with 10 c.c. 4 per cent. lithium carmine, or in some cases 4 per cent. erythrosin was used.

Table I.

Sheep No.		Age.	Condition.	Rumen Contents.	Result.
		Teeth.			
Unstarved	1.....	8	good	semi-solid	(50·50)
	2.....	8	,,	fluid	99·1
	3.....	8	,,	semi-fluid	(10·15)
	4.....	2	,,	,,	20·80
	5.....	8	,,	semi-solid	90·10
	6.....	8	,,	,,	10·90 (2/2)
Starved	7.....	8	,,	fluid	0·100
	8.....	8	,,	,,	5·95
	9.....	8	,,	,,	5·95
	10.....	2	,,	,,	80·20
	11.....	2	,,	,,	0·100
	12.....	2	,,	,,	5·95
	13.....	8	,,	semi-solid	100·0
	14.....	8	,,	fluid	(40·60) (2/5)

Under the heading "Result" are given the estimated percentages of the drench which reached the rumen and reticulum (on the left) and the abomasum (on the right). Sheep 3 did not swallow well. Discarding the results of sheep 1, 3 and 14, it is seen that of the unstarved group two swallowed to the rumen and two to the abomasum and of the starved group respectively two and five.

The following sheep were similarly treated, but the copper sulphate solution was administered first, followed immediately by 10 c.c. 4 per cent. erythrosin.

Table II.

Sheep No.		Age.	Condition.	Rumen Contents.	Result.
		Teeth			
Unstarved	15.....	2	good	semi-solid	5·95
	16.....	2	,,	semi-fluid	2·98
	17.....	2	,,	,,	10·90
	18.....	2	,,	,,	0·100 (0/4)
Starved	19.....	2	,,	,,	2·98
	20.....	2	,,	,,	0·100
	21.....	2	,,	semi-solid	5·95 (0/3)

The above results, as well of those of all the following tests in which the sheep were not starved, indicate that starvation is not an important factor in bringing about the reflex. In our previous work and also in the present series of tests it was found that fluidity of the ruminal contents favours the establishment of the reflex, and for that reason the sheep had in previous tests frequently been given a drink immediately before being treated. It had, moreover, been observed that long starvation (36-48 hours) tends to produce fluid ruminal contents, and this was also noted by Ross (1931 and 1934), whose findings, that sheep under such conditions readily swallow to the abomasum without stimulation, fully agree with our experiences.

Apart from the fact, however, that sheep suffering badly from worms, particularly *Oesophagostomum columbianum*, cannot safely be starved for lengthy periods, starvation is undesirable for other reasons which have already been discussed by one of us in previous papers (Mönnig 1929a, 1929b, and 1933). It appears, therefore, that sufficient attention has been given to this aspect of the problem and that starvation should not be practised any longer in the dosing of sheep for worms. In the following tests all the sheep were therefore allowed food and water up to the time of treatment.

2. Method of Administration.

Stiles (1901) dosed sheep with fluids through a funnel with rubber tubing and a metal nozzle, which was placed between the hind teeth, and he arrived at the conclusion that this method of drenching stimulated the animals to swallow into the abomasum, but that the position in which the sheep was held influenced the result, the most favourable position being that in which the sheep stood normally on its feet. In the above recorded tests the sheep were drenched in this way, but the results were probably not influenced by the method of administration since at least as good results were later obtained by other methods.

Table III.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
(*a*) 30 c.c. 3% $CuSO_4$ mixed	Teeth. with teaspoo	nful red lead	oxide.	
22	4	good	semi-solid	2·98
23	2	,,	,,	98·2 (1/1)
(*b*) 30 c.c. 5% $CuSO_4$ with te	aspoonful red	lead oxide.		
24	2	good	semi-solid	0·100
25	2	,,	,,	15·85 (0/2)
(*c*) 30 c.c. 3% $CuSO_4$, then r	ed lead oxide	by spoon.		
26	2	good	semi-solid	2·98
27	2	,,	,,	0·100
28	2	,,	,,	0·100
29	2	,,	fluid	(50·50) (0/3)
(*d*) Teaspoonful 5% $CuSO_4$ b	y spoon, the	n red lead ox	ide.	
30	2	good	fluid	10·90
31	2	,,	,,	0·100 (0/2)
(*e*) 20 c.c. water with red lea	d oxide.			
32	2	good	fluid	99·1
33	2	,,	semi-solid	(50·50) (1/0)

In Table III are given the results on further tests with regard to this point. The fluids were administered to sheep 22-29, 32 and 33 according to the method of Stiles.

Unfortunately sheep 33 must be discarded and the number of sheep in group (*e*) should have been larger, but the results, particularly group (*d*), as well as the results of all the following tests, show that the method of administration according to Stiles is not an important factor.

All the above results (Table I and II) seem to indicate that the reflex is stimulated very rapidly once the stimulant reaches the pharynx, but that to administer the full quantity of a drug into the abomasum it is desirable to give the drug after the stimulant and not mixed with it as the first gulp swallowed may pass into the rumen. This was further confirmed by subsequent tests and experiences. Points of importance arising from this conclusion are the time required for the reflex closrue of the oesophageal groove to occur and the duration of the reflex.

3. Rapidity of Reflex Closure.

In general it may be stated that the impression obtained in these tests is to the effect that the reflex is established immediately on stimulation, i.e. the moment a solution of the stimulant touches the mucosa of the pharynx. In order to test this point further the following sheep were dosed with a mixture of powdered copper sulphate and red lead oxide. The saliva would have to dissolve some copper sulphate before this could produce the stimulus.

Table IV.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
(*a*) Powder placed on back of	tongue (swal	lowed immed	iately).	
	Months.			
34	12	poor	semi-fluid	10·90
35	12	,,	,,	100·0
36	12	,,	,,	100·0 (2/1)
(*b*) Powder placed on tip of t	ongue (swallo	wing delayed	).	
37	12	poor	semi-fluid	0·30
38	12	,,	,,	0·100
39	12	,,	,,	1·99 (0/3)
(*c*) Powder placed into cheek	(swallowing	delayed).		
40	12	poor	semi-fluid	0·100
41	12	,,	,,	0·100
42	12	,,	,,	0·100 (0/3)

It is seen that where a slight delay in swallowing occurs—even in sheep 34 this probably was the case—the stimulus is given and the drug passes to the abomasum.

4. Duration of Reflex.

It is important to know how long the groove will remain closed in order to allow dosing into the abomasum with large quantities of

fluid or even with small doses of drugs. The time elapsing between the administration of the stimulant and the indicator, red lead oxide, was carefully timed by means of a stop-watch.

TABLE V.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
(*a*) 50 c.c. 2% $CuSO_4$ mixed	with red lead oxide.			
43	4	good	semi-solid	0·100
44	4	,,	,,	1·99
45	4	,,	,,	5·95 (0/3)
(*b*) 10 c.c. 5% $CuSO_4$, indicator after 10		*seconds.*		
46	2	good	fluid	0·100
47	2	,,	,,	2·98 (0/2)
(*c*) 50 c.c. 2% $CuSO_4$, indicator after 15		*seconds.*		
48	4	good	semi-solid	0·100
49	4	,,	,,	5·45 (0/2)
(*d*) 50 c.c. 2% $CuSO_4$, indicator after 20		*seconds.*		
50	4	good	semi-solid	5·95
51	4	,,	,,	100·0
52	4	,,	,,	5·95 (1/2)
10 c.c. 5% $CuSO_4$, indicator after 20		*seconds.*		
53	4	poor	semi-fluid	60·0
54	4	,,	semi-solid	50·30
55	4	,,	semi-fluid	60·0 (3/0)
(*e*) 50 c.c. 2% $CuSO_4$, indicator after 30		*seconds.*		
56	4	good	semi-solid	95·5
57	4	,,	,,	5·95
58	4	,,	,,	98·2 (2/1)
10 c.c. 5% $CuSO_4$, indicator after 30		*seconds.*		
59	4	poor	semi-solid	0·100
60	4	,,	solid	0·100
61	4	poor	semi-solid	60·0
62	2	good	fluid	100·0
63	2	,,	,,	0·100 (2/3)

The tests with 5 per cent. $CuSO_4$ in groups (*d*) and (*e*) were performed later than the rest, after it had been found that the stronger solution produces better stimulation under certain circumstances (see section 5 below). It may be concluded that reliable results can be obtained up to 15 seconds after stimulation, but that after 20 seconds the groove is no longer closed in all cases with the concentration of the stimulant used and taking into consideration the condition of the sheep (section 6) and the consistency of the ruminal contents.

5. CONCENTRATION OF STIMULANT.

The work done under this heading was greatly influenced by the results obtained in dosing sheep for *Oesophagostomum columbianum* under field conditions. At first 2 per cent. $CuSO_4$ was used in many of these therapeutic experiments, until it became clear that the stimulation was not satisfactory. This was followed by 5 per cent. and later 10 per cent. solutions, and the results of stimulation were checked in the degutition tests reported here. In the following tests the red lead oxide was given immediately after the stimulant.

TABLE VI.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
(*a*) 10 c.c. 0·1% $CuSO_4$.	Teeth.			
64	6	good	semi-solid	100·0
65	6	,,	,,	0·100
66	6	,,	,,	60·30 (2/1)
(*b*) 10 c.c. 0·25% $CuSO_4$.				
67	6	good	semi-solid	0·100
	Months.			
68	6	,,	,,	0·100
69	Young lamb	,,	empty	0·100 (0/3)
(*c*) 10 c.c. 0·5% $CuSO_4$.	Teeth.			
70	6	good	semi-solid	0·100
71	6	,,	,,	0·100 (0/2)
(*d*) 10 c.c. 2% $CuSO_4$.				
72	4	good	solid	10·90
73	4	,,	semi-solid	(40·60)
74	4	,,	,,	0·100
75	4	medium	,,	70·30
76	4	good	semi-fluid	70·30
77	4	,,	semi-solid	0·100
78	4	,,	,,	100·0
79	4	,,	,,	0·100
80	4	,,	,,	(50·50)
81	4	poor	,,	100·0
82	4	,,	,,	100·0 (5·4)
(*e*) 10 c.c. 5% $CuSO_4$.				
83	4	good	solid	20·80
84	4	,,	semi-solid	5·95
85	4	,,	,,	10·70
86	4	,,	solid	0·100
87	4	,,	fluid	0·100
88	4	,,	semi-solid	0·100
89	4	,,	semi-fluid	0·100
90	4	,,	fluid	0·100
91	4	,,	semi-fluid	0·100
	Months.			
92	12	poor	,,	0·100
93	12	,,	,,	0·100
94	12	,,	fluid	0·100
95	12	,,	,,	0·100
96	12	,,	,,	0·100
	Teeth.			
97	8	very poor	semi-solid	0·100
98	8	,,	semi-fluid	0·100
99	8	,,	,,	95·5 (1/16)
(*f*) 3 c.c. 10% $CuSO_4$.	Months.			
100	12	poor	semi-fluid	0·100
101	12	,,	,,	0·100
102	12	,,	fluid	0·100
103	12	,,	,,	0·100
104	12	,,	,,	0·100 (0/5)
5 c.c. 10% $CuSO_4$.	Teeth.			
105	8	very poor	semi-solid	0·100
106	8	,,	,,	0·100
107	8	,,	,,	0·100 (0/3)
2·5 c.c. 10% $CuSO_4$.				
108	8	very poor	semi-fluid	0·100
109	8	,,	semi-solid	100·0
110	8	,,	solid	0·100
111	8	,,	semi-solid	0·100
112	8	,,	,,	0·100
113	8	,,	,,	0·100
114	8	,,	,,	5·95
115	8	,,	semi-fluid	(2·10) (1/6)

The 0·1 per cent. solution is apparently too weak. A 0·25 per cent. or 0·5 per cent. solution may give quite good results if all other factors are favourable, and this will also be the case with a 2 per cent. solution, but the results obtained with the latter were on the whole very disappointing, particularly with sheep in poor condition (Nos. 81 and 82). The 5 per cent. solution gave much more satisfactory results. The 10 per cent. solution was tested only on poor sheep and the results are very promising even with as small quantities as 2·5 c.c.

It may be difficult to draw definite conclusions from the above results since the numbers of sheep used are still small and the results may not be very convincing. However, if one considers also the results under the other headings and particularly the field experiences in dosing against *Oesophagostomum columbianum*, it becomes quite clear that there are certain other controlling factors and that, if these are favourable, a 2 per cent. solution will produce the reflex, but if these factors are unfavourable a 5 per cent. or even a 10 per cent. solution is necessary.

The chief controlling factors appear to be age and condition of the sheep and consistency of the ruminal contents. The last point has already been discussed. Young sheep can undoubtedly be more easily stimulated than older sheep, but what is much more important is the observation made in the field tests referred to, namely that sheep badly infested with a worm like *Oesophagostomum columbianum* or which for some other reason are in very poor condition, sluggish and numb, are very unsatisfactory subjects to stimulate. It stands to reason that their nervous reflexes are not as lively as are those of sheep in reasonably good condition. The article on therapy of oesophagostomiasis in this issue will show the marked difference in the results obtained after stimulation with 10 per cent. and with weaker solutions.

Unfortunately this knowledge was gained at a relatively late stage of the work and it will be noticed that the tests in other sections suffered from lack of knowledge on this point. The results all round could have been more definite if variations due to the concentration of the stimulant had not been present.

6. Condition of Sheep.

In order to obtain an idea of the percentage of successes that may be obtained, a test was made at a local abattoir on sheep which were being slaughtered there and, since these sheep were all in good condition and fairly excited, the results will be interesting as confirmation of the conclusions arrived at in section 5 above and in contrast to other tests reported below in this section.

The sheep slaughtered at the abattoir had been allowed to graze and drink until the previous evening and were then brought into a bare paddock. Early in the morning they were taken in lots of about 30 to small pens adjoining the slaughter hall. Here they were caught one by one and dragged into the hall, some coming in on their sides or backs, only a small minority on their feet. Just inside the door they were dosed with 10 c.c. 2 per cent. $CuSO_4$

immediately followed by red lead oxide and this was done in whatever position the sheep happened to be at the time. Immediately after having been dosed, the sheep were killed and the stomachs were examined later. Of 143 sheep dosed 32 had not swallowed before they were killed. Of the remaining 111, 108 swallowed into the abomasum. The ruminal contents were fluid or semi-fluid. There were 25 persian lambs, of which 24 swallowed into the abomasum, and the other sheep were of different ages but mostly full-mouth, some being presians or cross-breeds but the majority merinos. The position in which the sheep were held at dosing did not appear to have any effect at all.

These results were certainly satisfactory and both the condition of the sheep as well as the consistency of the ruminal contents were favourable. The sheep had been grazing on young, succulent grass the previous day.

Four sheep in poor condition were driven into the post-mortem hall at Onderstepoort and an attempt was made to excite them by hitting them with a white towel and chasing them about before they were dosed, but they did not pay much attention to these efforts. They were stimulated with 10 c.c. 2 per cent. $CuSO_4$ and then given the usual level teaspoonful of red lead oxide.

TABLE VII.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
116	4	poor	solid	100·0
117	4	,,	,,	90·10
118	4	,,	semi-solid	90·10
119	4	,,	,,	0·100 (3/1)

Here the condition as well as the consistency of ruminal contents, at least in sheep 116 and 117, were unfavourable and the result was accordingly unsatisfactory.

7. ACIDITY OF RUMINAL CONTENTS.

It had been noticed that the ruminal contents of some sheep have a strong acid smell and that this is usually the case when the contents are on the solid side, particularly in sheep that had received a ration of grain in their food. In order to determine whether such acidity might counteract the stimulant, four sheep (*a*) were given 50 c.c. 5 per cent. sodium bicarbonate solution before the stimulant (10 c.c. 5 per cent. $CuSO_4$) and indicator were administered, four others (*b*) were dosed only with water instead of bicarbonate and another four (*c*) only with stimulant and indicator. All the sheep had been given a ration of dry hay and maize for some days previously.

TABLE VIII.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
(*a*) 120	4	poor	semi-solid	0·100
121	4	,,	,,	0·100
122	4	,,	,,	(10·0)
123	4	,,	semi-fluid	0·100 (0/3)
(*b*) 124	4	,,	semi-solid	0·100
125	4	,,	,,	(10·10)
126	4	,,	semi-fluid	0·100
127	4	,,	,,	0·100 (0/3)
(*c*) 128	4	,,	semi-solid	(50·50)
129	4	,,	,,	100·0
130	4	,,	semi-fluid	0·100
131	4	,,	,,	0·100 (1/2)

Unfortunately the ruminal contents were not solid. The results do not indicate that there is anything in favour of the alkali, but possibly the 50 c.c. of fluid given in cases of (*a*) and (*b*) may have had a favourable effect.

8. ASTRINGENCY OF STIMULANT.

Since it was not clear why copper sulphate produced the stimulus, the tests under this and the next two headings were made to gain some knowledge with regard to this question. It is known that copper sulphate solutions are strongly astringent, and therefore other astringents were tested.

TABLE IX.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
(*a*) 10 c.c. 5% Ferric chloride, then indicator.				
132	4	medium	semi-solid	100·0
133	4	,,	,,	(30·30)
134	2	good	fluid	0·100
135	2	,,	,,	5·95
136	2	poor	semi-solid	10·90
137	2	,,	,,	10·50
138	2	,,	,,	0·100 (1/5)
(*b*) 10 c.c. 5% Sodium alum, then indicator.				
139	2	good	fluid	(50·50)
140	2	,,	,,	0·100
10 c.c. 10% Sod. alum, then indicator.	Months.			
141	12	poor	semi-fluid	100·0
142	12	,,	,,	(50·50)
143	12	,,	,,	(50·50) (1/1)
(*c*) 10 c.c. 10% Tannic acid, then indicator.	Teeth.			
144	2	poor	semi-fluid	(50·50)
145	2	,,	,,	90·10
146	2	,,	,,	95·5 (2/0)

Although the results of group (*a*) look satisfactory the metallic-ion may have had an influence (see below, section 10); the results with alum are indefinite, while tannic acid does not give the indication that astringency is the important factor. In all cases strong solutions were used, the sheep were mostly young and the ruminal contents of favourable consistency, so that, although some of the sheep were poor, better results would have been expected with the use of copper sulphate. The results, however, are admittedly not quite convincing, and the tests should be repeated.

9. Other Copper Salts.

In order to make sure that it is the Cu-ion which is the active stimulent other copper salts were tested. These, it must be noted, however, all give astringent solutions.

Table X.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
(*a*) 10 c.c. 5% $Cu(NO_3)_2$, then	indicator.			
147	2	poor	semi-fluid	2·98
148	2	,,	,,	(0·0)
149	2	,,	,,	0·100
150	2	,,	,,	0·100 (0/3)
10 c.c. 2% $Cu(NO_3)_2$, then	indicator.			
151	4	poor	semi-solid	0·100
152	6	,,	semi-fluid	40·60 (0/2)
(*b*) 10 c.c. 5% copper acetate,	then indicator.			
153	2	poor	semi-fluid	0·100
154	2	,,	,,	0·100 (0/2)

Sheep 152 may have to be disregarded. Otherwise it seems fairly clear that other copper salts will give the reflex.

10. Other Metals.

Table XI.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
(*a*) 30 c.c. 3% $AgNO_3$, then	indicator.			
153	6	good	semi-solid	10·90
154	6	,,	,,	0·100
155	6	,,	,,	0·100
156	2	poor	,,	(10·30)
157	2	,,	,,	100·0
10 c.c. 1% $AgNO_3$, then	indicator.			
158	2	poor	semi-solid	10·90
159	2	,,	,,	5·95
160	2	,,	,,	95·5 (2/5

TABLE XI (*Continued*).

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
(*b*) 10 c.c. 3% $CdSO_4$, then indicator.				
161	6	good	semi-solid	0·100
162	6	,,	,,	100·0
163	6	,,	,,	95·5 (2/1)
(*c*) 10 c.c. 3% $ZnSO_4$, then indicator.				
164	6	good	semi-solid	0·100
165	6	,,	,,	10·60
166	6	,,	,,	0·100
10 c.c. 1% $ZnSO_4$, then indicator.				
167	6	good	semi-solid	100·0
168	6	,,	,,	100·0
169	6	,,	,,	·5·95 (2/4)
(*d*) 10 c.c. 3% $NiCl_2$, then indicator.				
170	2	poor	semi-solid	100·0
171	2	,,	,,	70·30 (2/0)
(*e*) 10 c.c. 3% $Al_2(SO_4)_3$, then indicator.				
172	2	poor	semi-solid	100·0
173	2	,,	,,	99·1 (2/0)
(*f*) 10 c.c. 3% $BaCl_2$, then indicator.				
174	2	poor	semi-solid	100·0
175	2	,,	,,	100·0 (2/0)
(*g*) 10 c.c. 3% Sodium acetate, then indicator.				
176	2	poor	semi-solid	(30·10)
177	2	,,	,,	100·0 (1/0)
(*h*) 10 c.c. 3% $FeSO_4$, then indicator.				
178	6	good	semi-solid	100·0
	Months.			
179	9	,,	,,	(50·50)
180	9	,,	,,	100·0
181	9	,,	,,	30·70 (2/1)

According to the periodic table the metals Zinc and Silver are the most closely related elements to Copper, and it is interesting to see that these two have also given the best stimulus. However, no definite conclusion can be drawn from these small numbers of animals and possibly the valency of the metals may have to be taken into account—compare the results with ferric and ferrous salts (Tables IX and XI). At any rate, nothing better than the Copper salt was found, and that was the information required at the moment for practical purposes.

11. DRUGS AFTER $CuSO_4$.

It was important now to determine whether certain drugs, administered after the stimulant, might not counteract the stimulant or for some other reason cause the oesophageal groove to open..

In all the groups except (*a*) the substance tested was administered immediately after stimulation with 10 c.c. 5 per cent. $CuSO_4$.

TABLE XII.

Sheep No.	Age.	Condition.	Rumen Contents.	Result.
	Teeth.			
(*a*) 0·5 c.c. 40% nicotine sulp	hate + 0·5	Gm $CuSO_4$ +	30 c.c. water	+ Pb_3O_4.
182	4–8	medium	semi-solid	0·100
183	4–8	,,	,,	0·100
814	4–8	,,	,,	0·100 (0/3)
(*b*) 5 c.c. CCl_4 + 10 c.c. liquid	paraffin +	Pb_3O_4.		
185	4–8	medium	semi-solid	10·90
186	4–8	,,	,,	30·70
187	4–8	,,	,,	10·90 (0/3)
(*c*) 5 c.c. C_2Cl_4 + 10 c.c. liqui	d paraffin +	Pb_3O_4.		
188	4–8	medium	semi-solid	0·100
189	4–8	,,	,,	0·100
190	4–8	,,	,,	100·0 (1/2)
Many more cases have sin	ce been treat	ed in this wa	y with good	results.
(*d*) 50 c.c. 20% $MgSO_4$ + Pb_3	O_4.			
191	6	good	semi-solid	100·0
192	6	,,	,,	0·100
193	6	,,	,,	0·100 (1/2)
(*e*) 100 c.c. 10% Jalap + Pb_3	O_4.			
194	6	good	semi-fluid	0·100
195	6	,,	,,	0·100
196	6	,,	semi-solid	0·100 (0/3)
(*f*) ½ teaspoon calomel + ½ t	easpoon Pb_3O	$_4$.		
197	6	good	semi-solid	0·100
198	6	,,	,,	0·100 (0/2)
(*g*) 50 c.c. ol. lini + Pb_3O_4.				
199	6	good	semi-solid	0·100
	Months.			
200	6	,,	,,	0·100 (0/2)
	Teeth.			
(*h*) teaspoonful As_2S_3 powder.				
201	6	good	semi-solid	90·10
202	6	,,	,,	10·90 (1/1)
(*i*) 30 c.c. 3% Lugol's iodine	+ Pb_3O_4.			
203	6	good	semi-solid	10·90
204	6	,,	,,	0·100 (0/2)
(*j*) 30 c.c. 1% Tarter emetic	+ Pb_3O_4.			
205	6	good	semi-solid	0·100
206	6	,,	,,	0·100 (0/2)
(*k*) 30 c.c. 1% Gentian violet	+ Pb_3O_4.			
207	6	good	semi-solid	0·100
208	6	,,	,,	0·100 (0/2)
(*l*) 30 c.c. water at 40° C. +	Pb_3O_4.			
209	6	good	semi-solid	0·100
210	6	,,	,,	10·90 (0/2)
30 c.c. water at 50° C. +	Pb_3O_4.			
211	6	good	semi-solid	0·100
212	6	,,	,,	0·100 (0/2)
(*m*) 3 hard tablets each 9 mm. wards the edges. Tablets spat out.	in diameter, not shown in	4·5 mm. thick in centre result were not found in s		and tapering to- heep, probably
213	6	good	semi-solid	0·2
214	6	,,	,,	0·3
215	6	,,	,,	0·2
216	6	,,	,,	1·0
217	6	,,	,,	0·3 (1/4)
(*n*) 1 gelatine capsule 100 mg.	filled with P	b_3O_4.		
218	6	good	semi-solid	1·0
219	6	,,	,,	1·0
220	6	,,	,,	1·0 (3/0)

The results show that the oesophageal groove is firmly closed and that ordinary drugs will not cause it to open. Even small tablets are frequently swallowed through—a point which should be further investigated and which may be of great value in therapeutic work—but that large bodies such as a gelatine capsule measuring 25 by 8 mm. will still pass to the rumen.

12. Rate of Passage of Drugs through Alimentary Tract.

It was next attempted to find at what rate drugs administered into the abomasum would pass through the intestine since this point is of some importance in therapy against worms in the colon. The work done up to the present is not yet very informative, but the following results may be given.

Eight sheep were dosed with 10 c.c. 5 per cent. $CuSO_4$ followed by a teaspoonful of red lead oxide.

(*a*) Killed after 1 hour:—

Sheep 221, 4t., poor, powder in abomasum and duodenum.
Sheep 222, 4t., poor, powder in abomasum only.

(*b*) Killed after 3 hours:—

Sheep 223, 4t., poor, powder in forestomachs.
Sheep 224, 4t., poor, powder in abomasum and down to 18 feet anterior to ileo-caecal valve.

(*c*) Killed after 5 hours:—

Sheep 225, 4t., poor, powder in abomasum and down to ileo-caecal valve.
Sheep 226, 4t., poor, powder in abomasum and down to beginning of ansa spiralis of colon.

(*d*) Faeces analysed for lead at intervals. Dosed 11.0 a.m.

Sheep 227, 4t., poor, first traces in faeces after 5 hrs. (4 p.m.), strong after 22 hrs. (9.0 a.m. next day).
Sheep 228, 4t., poor, nothing in faeces 4 p.m., strong after 22 hrs.

Another six sheep were dosed as follows: 229-231 given 10 c.c. 1 per cent. $CuSO_4$ followed by a teaspoonful copper arsenate, 232-234 given 10 c.c. 5 per cent. $CuSO_4$ followed by the same drug. The sheep were dosed at 4.30 p.m., 11.10.34, and the presence of copper was determined in the faeces at intervals. In the record of results − indicates absence of copper, (+) a trace, + small quantity, + + large quantity, 0 no faeces passed.

Sheep.	12.10.34. 9.0 a.m.	10.30 a.m.	2 p.m.	4 p.m.	13.10.34. 9.0 a.m.
229.....	(+)	0	0	+	+
230.....	—	0	0	0	0
231.....	—	+	+	0	+
232.....	(+)	0	++	0	++
233.....	—	(+)	0	++	++
234.....	—	(+)	0	0	+

It is, of course, not known which of these sheep had swallowed the drug into the abomasum.

The results appear to indicate that the drug passes out of the abomasum in small quantities over a period of several hours, that the first amount may pass the ileo-caecal valve about 5 hours after treatment and that it remains in the colon for several hours, usually not being passed in the faeces before 15 hours have elapsed since the time of treatment, the bulk being passed from about the 22nd hour. It must, however, be expected that marked variations may occur, depending on the nature of the drug itself, the food eaten by the sheep and the general digestive conditions in the alimentary tract at the time of treatment, for instance the degree of acidity of the abomasal contents. In therapeutic work on *Oesophagostomum columbianum*, in which the results have been observed on several hundred sheep, it was found that the first worms may be passed from about 15 hours after treatment, while the majority are passed after that time and sometimes for a period up to five days, but this does not necessarily mean that the drug remains in the colon all that time.

13. The Danger of Administering Drugs into the Abomasum.

This article would not be complete without a warning against the dangers involved in administering drugs into the abomasum. The mucosa of this organ is remarkably tender, apparently much more so than the gastric mucosa of non-ruminants, and it is consequently very easily corroded by drugs which come in contact with it in a concentrated form. In therapeutic tests it was found that this danger is not by any means negligible. For instance, sheep dosed with 1 gm. sodium fluosilicate after copper sulphate all died and showed a localised necrosis surrounded by an inflamed area in the abomasal mucosa. Also some farmers who had heard about the method of administration and administered various remedies for *Haemonchus contortus* in this way, lost considerable numbers of sheep through remedies which they had previously used successfully.

Summary and Conclusions.

(1) A solution of copper sulphate stimulates reflex closure of the oesophageal groove in sheep so that drugs subsequently administered will pass into the abomasum.

(2) Preliminary starvation has no favourable influence, unless the sheep are starved for such a long period that the ruminal contents become fluid, in which case the latter condition is favourable. Starvation is, however, contra-indicated for reasons which are discussed.

(3) The method of administration and the position in which the animal is held are of no importance.

(4) The reflex is established immediately after the stimulant touches the mucosa of the pharynx.

(5) The groove remains closed for 15 seconds, sometimes longer, after stimulation.

(6) Other conditions being favourable, the stimulus can definitely be produced by a 0·25 per cent. copper sulphate solution. Unfavourable factors are advanced age, poor condition and dryness of ruminal contents. In it shown that a 10 per cent. solution is necessary to overcome the counteracting effects of these adverse factors.

(7) It has not been definitely proved whether acidity of the ruminal contents is an unfavourable condition, but there are indications that this is not the case.

(8) Copper salts other than the sulphate produce the reflex, but it has not been definitely proved that the stimulus may not be due to astringency of the stimulant.

(9) There are indications that the related metals zinc and silver may also produce the reflex.

(10) Various drugs administered after the stimulant did not reverse the reflex. Small pills may be swallowed into the abomasum after stimulation but larger objects (small capsules) are not.

(11) Preliminary tests indicate that a drug administered into the abomasum may reach the colon in about five hours and that it may be passed in the faeces from about the 15th hour.

(12) Since the abomasal musosa is very tender, care must be exercised in administering drugs in the way indicated.

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