

Studies on the Alimentary Tract of the Merino Sheep in South Africa. XX.—The Failure of the Rumen Musculature to respond to Carbamylcholine Chloride when paralysed by Potassium Cyanide.

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INTRODUCTION.

QUIN and van der Wath (1938) showed that the dosing of 150 to 200 mg. of potassium cyanide to sheep, caused a prompt, though transitory, paralysis of the rumen. On the other hand carbamylcholine chloride is known to cause active stimulation of ruminal movements under normal conditions. It was therefore decided to investigate the action of carbamylcholine chloride on the rumen subsequent to paralysis by potassium cyanide.

EXPERIMENT I.

As a preliminary trial the combined effects of potassium cyanide and acetylcholine were investigated on the isolated duodenal strip of the rabbit. Examples of the results obtained are shown in figures 1 and 2.

FIG. 1.

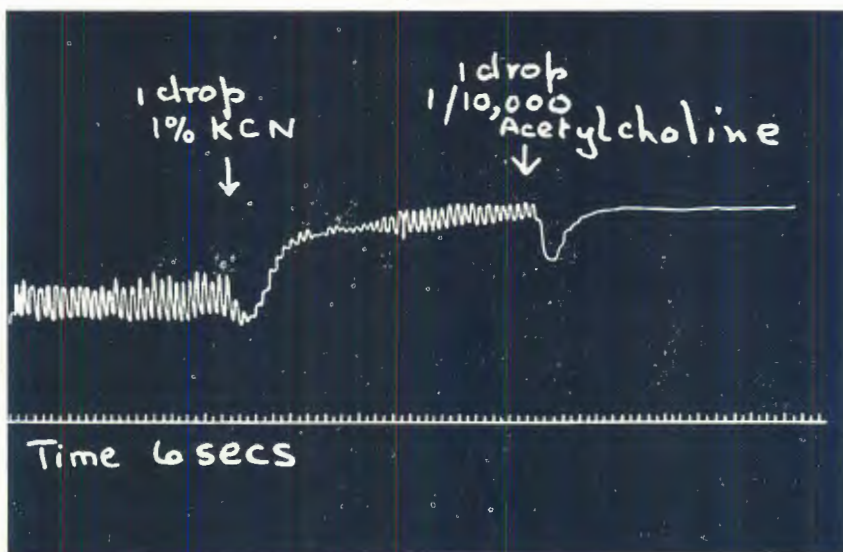
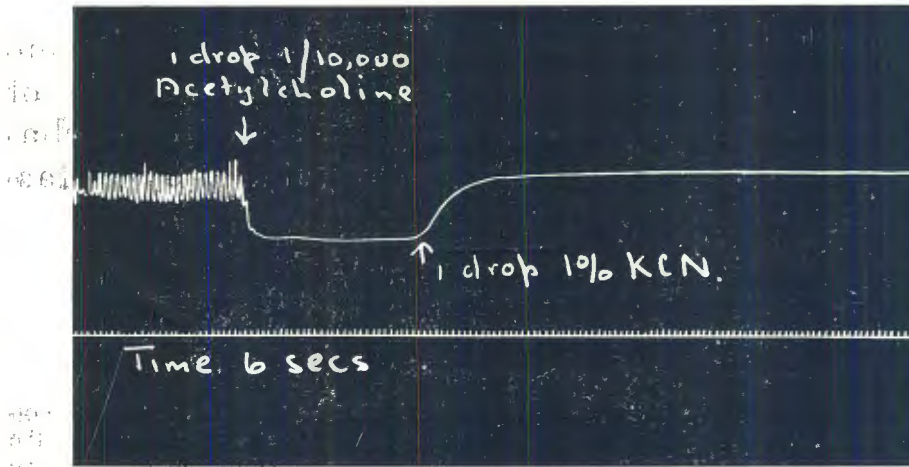


FIG. 2.



As will be seen from figure 1 the addition of one drop of 1 per cent. potassium cyanide caused prompt inhibition of the movements of the intestine. As the bath contained 100 c.c. of fluid this would represent 0.5 mgm. potassium cyanide per 100 c.c. It was found that even ten times this amount did not cause complete cessation of movement but for the purpose of the experiment total paralysis was not desired. The further addition of one drop of a 1/10,000 solution of acetylcholine caused a very weak and transitory contraction followed by complete paralysis.

In order to test the activity of the acetylcholine, a fresh strip of intestine was used and the drug added during the period of normal spontaneous contractions. The result is seen in Fig. 2.

Here the addition of the same amount of acetylcholine as used in the previous experiment caused a prompt and sustained contraction. The further addition of one drop of 1 per cent. potassium cyanide brought about complete paralysis. As this amount of cyanide did not cause total paralysis when administered before acetylcholine it would appear that the intestine under the stimulation of acetylcholine is particularly sensitive to cyanide. These experiments were repeated several times with identical results.

EXPERIMENT 2.

In view of these results a series of experiments were undertaken on sheep with permanent ruminal fistulae. In the first type of trial the normal ruminal movements were recorded after which potassium cyanide was introduced through the fistulae. When inhibition of the rumen was evident the sheep was injected subcutaneously with carbamylcholine chloride. Typical results are shown in Figs. 3 and 4.

As will be seen from Fig. 3 the introduction into the rumen of 200 mgm. potassium cyanide caused partial paralysis of the rumen within five minutes. Carbamylcholine chloride (0.125 mgm.) was then injected subcutaneously. Within 15 minutes the rumen was completely paralysed as seen in the third tracing. The

FIG. 3.

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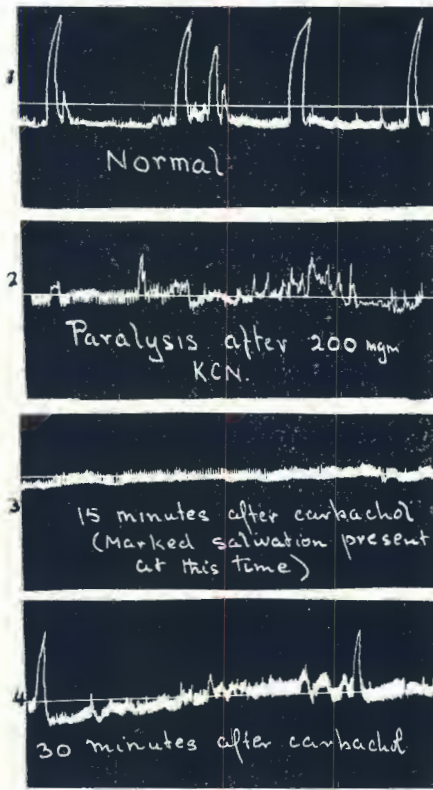
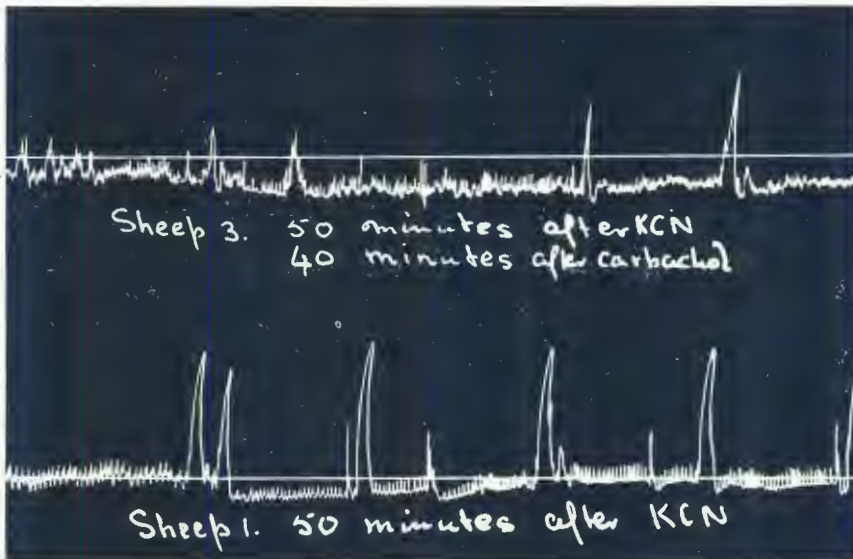


FIG. 4.



fact that marked salivation was present at this time proved that the carbamylcholine was active. Ruminal movements reappeared some 30 minutes after the injection or 35 minutes after the administration of the cyanide. From previous experience this could have been expected without any treatment as the ruminal paralysis after a single dose of potassium cyanide is transitory.

It was found that the injection of carbamylcholine chloride five minutes after the administration of potassium cyanide not only increased the severity but also the duration of the resultant ruminal paralysis. For instance three sheep kept on a ration of lucerne hay showed resumption of ruminal movements in 10 to 20 minutes after the administration of 150 mgm. of potassium cyanide. A few days later the same three sheep were given the same dose of potassium cyanide but were also injected with 0.25 mgm. carbamylcholine chloride subcutaneously 10 minutes later. Under these conditions the ruminal paralysis lasted for 40 to 60 minutes.

This effect is well shown in Figure 4.

In order to demonstrate the activity of the carbamylcholine a second series of trials were carried out in which this drug was injected before the administration of the potassium cyanide. The results are shown in Fig. 5.

As will be seen from Fig. 5 the injection of 0.125 mgm. carbamylchloride caused marked stimulation of the rumen after 15 minutes. The subsequent administration of 100 mgm. potassium cyanide was followed by complete paralysis.

In these experiments it was found that the rumen could be paralysed by smaller doses of cyanide when under stimulation by carbamylcholine than normally. This is in accordance with the findings on the rabbit duodenum.

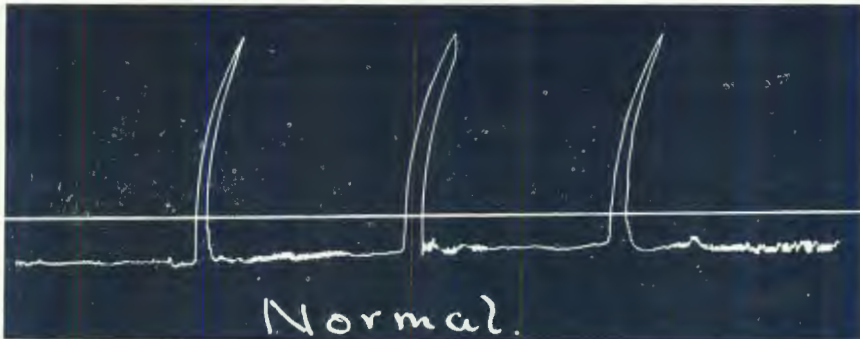
THE DANGER OF CARBAMYLCHOLINE CHLORIDE IN PRUSSIC ACID POISONING.

On physiological grounds the use of carbamylcholine chloride in cases of prussic acid poisoning might be highly dangerous. Prussic acid acts as an inhibitor of respiratory enzymes and causes respiratory and circulatory failure. Carbamylcholine causes inhibition of the heart and vaso-dilation with consequent retardation of the circulation. The two drugs would therefore be expected to combine in causing respiratory and circulatory failure. This was found to be the case in the present investigations.

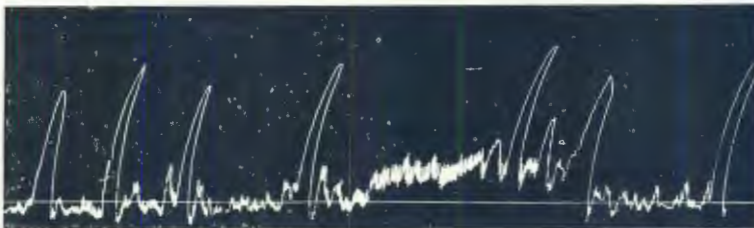
The first sheep in the series was given 100 mgm. potassium cyanide with no visible effects. A further 100 mgm. after ten minutes caused partial inhibition of the ruminal movements and slight hyperpnoea with no distress. The animal was then injected with 0.25 mgm. carbamylcholine chloride subcutaneously and within two minutes it showed very severe respiratory distress and collapsed in convulsions. It was treated immediately with sodium thiosulphate both into the rumen and intravenously but without any success. It was then given 25 mgm. of atropin subcutaneously and within two minutes showed signs of recovery. Within half an hour it was normal.

The doses of both prussic acid and carbamylcholine used were too small for either alone to have caused the acute reaction described. The severe reaction can only have been due to their combined effects.

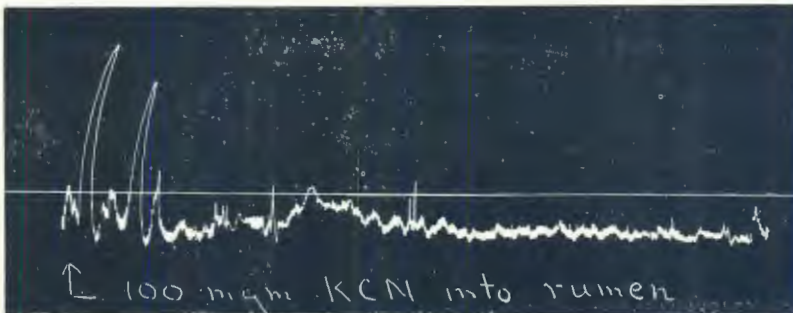
FIG. 5.



(a) Normal.



(b) 15 Minutes after carbochol.



(c) Paralysis after KCN.

DISCUSSION.

The above findings show that the use of carbamylcholine chloride in the treatment of ruminal stasis due to prussic acid poisoning is not only ineffective but dangerous. Care should be taken to exclude prussic acid poisoning as the cause of ruminal stasis before such treatment is applied.

STUDIES ON THE ALIMENTARY TRACT OF MERINO SHEEP IN SOUTH AFRICA.

SUMMARY.

1. It was found that acetylcholine did not restore motility to the isolated rabbit duodenal strip inhibited by prussic acid.

2. Similarly ruminal paresis induced by prussic acid could not be successfully treated with carbamylcholine chloride. In fact such treatment caused an increase in the severity and duration of the ruminal stasis.

3. Carbamylcholine and prussic acid combine in causing respiratory and circulatory failure.

REFERENCES.

- QUIN, J. I. AND VAN DER WATH, J. G. (1938). Studies on the alimentary tract of the merino sheep in South Africa V. The motility of the rumen under various conditions. *Onderstepoort Jl.* Vol. 11, No. 2, pp. 361-370.