Activity of Certain Drugs Against the Fringed Tapeworm

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Information concerning Thysanozoon reticuloides; the fringed tapeworm of sheep, is unfortunately out of proportion to its common occurrence in the western states.

The life cycle of this parasite remains unknown, despite the fact that parasitologists are devoting considerable effort toward detection of an intermediate host and other details of the life history. Meanwhile, any attempt to control the worm will necessarily be directed toward the selection of an efficacious and specificicide.

Ryff et al. 1 have reported favorably concerning the activity of his 1-chloro-2-hydroxyphenyl-1-methane against the fringed tapeworm, and in a later paper 2 they have given optimum dosage levels. This compound is synonymous with 2,2'-methylenebis (4-chlorophenol) and 2,2'-dihydroxy-5,5'-di-chlorodiophenylmethane. In addition, compound G-55 is a pharmacological grade, and parahexane 3 is a feed grade containing specified amounts of utapullos etc.

The critical treatment trials reported herein involve the drug mentioned above and two others, with respect to activity against the fringed tapeworm. They were undertaken for the purpose of helping to formulate an intelligent answer to the many inquiries from West Texas ranchmen regarding treatment for the fringed tapeworm.

A Thysanozoon should meet the following qualifications in order to merit recommendation for use on West Texas ranges: (1) efficacy approaching 100 per cent without toxic manifestations and with one treatment, since the worm apparently produces no symptoms in this area and the only known benefit from the treatment derives indirectly from the packers; (2) activity against the worm without benefit of fasting, which is often costly and will not be practiced by most ranchmen; (3) low cost and comparability with phenothiazin or other verminicides used for stomach worms, since separate drenching for tapeworms is not economically feasible at the present time.

Methods and Materials

The sheep used in these trials were Ramboonies 1 to 25 years old and weighing 60 lb to 125 lb. They were maintained on pasture under normal range conditions and were penned for only a few hours at a time for the selection of animals for treatment. Those selected for treatment at any given time were required to be in good health and to have positive fecal samples on the day of treatment. Thysanozoon proglottids histologically adheres to the moist surface of the food pellets and if not devoured are eliminated without recourse to microscopic examination.

Dosage rates for tetramisole 4 and 2,2'-methylenebis (4-chlorophenol) 5 are shown in tables 1 and 2, based on brief observations. Two other drugs were used: 2,2'-methylenebis (4-chloro-iso-propylphenol) 4 and 4,4'-iso-isopropylidenedi (4-chlorophenol). 6

All medicaments were put in hard gelatin capsules and administered by boling. Immediately after treatment, the sheep were placed in a concrete stall equipped with a removable worm floor (fig. 1). Incidentally, this floor has proved to be superior in several respects to the wooden slats floors previously used for parasite studies. It is constructed of an angle iron frame and removable expanded metal having diamond-shaped openings approximately 0.5 in. long and 0.5 in. wide. Observations regarding post-treatment symptomatology were made during the treatment recovery interval, which varied from two weeks to 14 hours.

Results

Results are given in tables 1 and 2 for tetramisole and 2,2'-methylenebis (4-chlorophenol). Since dosage rates great enough to produce severe securing gave insufficient evidence of activity against Thysanozoon by 4,4'-iso-isopropylidenedi (4-chlorophenol) and 2,2'-methylenebis (4-chlorophenol) tetramisole was used. The dosage rates of 1.5 and 3.0 per cent were used in this study.

Controls were not used in these trials in the strict sense of the word, i.e., a control animal was not slaughtered at the time each treated animal was destroyed. The reason for this is that the success of successful treatment was determined to be complete elimination of the worm from infected sheep. Since we know of no instances which indicate that fringed tapeworms are shed spontaneously, as is the case with Moniezia, this procedure seemed justifiable. However, in order to provide an estimation of the extent of infection, 20 sheep from the same flock were destroyed at intervals during the study. This indicated that 92.9 per cent were infected and that in the infected animals the number of worms ranged from 2 to 38, with an average of 28 per animal.

The extent of diarrhea following treatment was objectionable in all but the mild cases. Successful feeders and sheep look with much disfavor upon treatments which soften feces beyond the "fallen" stage, and dozes which do this are not likely to be widely used in sheep-producing areas.

The trials with 2,2'-methylenebis (4-chlorophenol) and tetramisole seem to confirm the findings of Ryff et al. with respect to optimum dosage levels, but in addition revealed some instances: experiment 24-158, 1-549, and 1-349 of apparent toxicity. fig. 1.

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Fig. 1—Removable screen floor made of ret-rolled, expanded metal reinforced with angle iron and pipe.
TABLE 1—Dosage Rates for Tentorial and Brief Observations on Results of Its Use

<table>
<thead>
<tr>
<th>Dosage rate</th>
<th>Species No.</th>
<th>Treatment—mortality interval</th>
<th>Necropsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>4:8 gm. per lb.</td>
<td>3:39</td>
<td>Moderate diarrhea &amp; impotence</td>
<td>3 hr.</td>
</tr>
<tr>
<td>2:54</td>
<td>Moderate diarrhea</td>
<td>12 hr.</td>
<td>1 H. Thymosins (4)</td>
</tr>
<tr>
<td>1:58</td>
<td>Moderate diarrhea</td>
<td>3 hr.</td>
<td>1 H. Thymosins (5)</td>
</tr>
<tr>
<td>1:08</td>
<td>Moderate diarrhea</td>
<td>3 hr.</td>
<td>1 H. Thymosins (5)</td>
</tr>
<tr>
<td>0:25</td>
<td>Moderate diarrhea</td>
<td>3 hr.</td>
<td>1 H. Thymosins (5)</td>
</tr>
</tbody>
</table>

*In accordance with directions printed on animal label.

**For 10 gm. at 10 gm. for each additional 5 lb. of body weight.

TABLE 2—Dosage Rates for 2:2-Methylethinyl 4-Chlorophenol and Brief Observations on Results of Its Use

<table>
<thead>
<tr>
<th>Dosage rate</th>
<th>Species No.</th>
<th>Treatment—mortality interval</th>
<th>Necropsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>0:04 Gen. per lb.</td>
<td>1:19</td>
<td>Moderate diarrhea</td>
<td>0 hr.</td>
</tr>
<tr>
<td>0:32 Gen. per lb.</td>
<td>0:67</td>
<td>Moderate diarrhea &amp; impotence</td>
<td>2 hr.</td>
</tr>
<tr>
<td>0:34 Gen. per lb.</td>
<td>0:69</td>
<td>Nausea &amp; impotence</td>
<td>120 hr.</td>
</tr>
<tr>
<td>0:39 Gen. per lb.</td>
<td>0:31</td>
<td>Moderate diarrhea &amp; impotence</td>
<td>72 hr.</td>
</tr>
<tr>
<td>0:25 Gen. per lb.</td>
<td>0:19</td>
<td>Moderate diarrhea &amp; impotence</td>
<td>72 hr.</td>
</tr>
<tr>
<td>0:25 Gen. per lb.</td>
<td>0:21</td>
<td>Mild diarrhea</td>
<td>96 hr.</td>
</tr>
<tr>
<td>0:25 Gen. per lb.</td>
<td>0:27</td>
<td>Moderate diarrhea</td>
<td>72 hr.</td>
</tr>
<tr>
<td>0:25 Gen. per lb.</td>
<td>0:28</td>
<td>Mild diarrhea</td>
<td>96 hr.</td>
</tr>
</tbody>
</table>

2 and 3). The gall bladders of these specimens were enlarged about three times and the mucous surfaces were inflamed, ulcerated, and, in some areas, necrotic. The first 2 of these specimens revealed localized fibrinous peritonitis. In specimen 1-519 the peritonitis had become diffuse. (Although a matter of speculation, the peritonitis appeared to have originated from the gall bladder.) None of the 3 had resumed eating at the time of autopsy. All remaining animals of the flock from which they were taken are still in excellent health, and none of the sheep treated with ineffective dosage levels exhibited any such pathological changes.

Examination of fecal material collected under the screen failed to reveal any complete worms or even chains of proglottids. This suggested disintegration such as shown by Craigie and Kleckner in the case of dogs treated with di-phenanthrene.70 Efforts to determine compatibility of these compounds with phenolphthalein were postponed due to the toxic effects noted.

Severity of diarrhea with ineffective levels of the two other compounds precluded testing them at higher levels.

CONCLUSIONS

Under the conditions imposed by these treatment trials, preparations containing 2:2-methylethinyl (4-chlorophenol) as the active ingredient were efficacious in removal of the fringed tapeworm, *Thyanna*.
Physiological Studies of Ejection in Ruminants
The modern conception of how it is that it is due to a failure of the ejection mechanism and is not due to excess gas formation is a substantial reliance on the study of the ejection reflex and the factors which affect it. This was done mainly by forced expiration and recording of intrathoracic pressure (Onderstepoort J. Vet. Res., in press).

Ejection is a complex, coordinated reflex involving the reticulum, rumen, cardiac orifice, and esophagus. It consists essentially in the movement of free gas from the dorsal rumen forward and downward to the esophagus. This is accomplished by:

1) A wave of contraction of the ruminal musculature which starts in the posterior sac and moves forward. This usually follows on, but is distinct from, the backward cycle of contractions designed to mix the ingesta.

2) Opening of the cardiac orifice by relaxation of the reticulum. The efficiency of this phase depends on the degree of filling of the rumen.

3) Opening of the cardiac orifice is brought about by contraction of the pillars of the rumino-reticular fold. The main stimulus for ejection is gas pressure in the posterior dorsal sac of the rumen.

Factors affecting the reflex are:

A) Mechanical
1) Obstruction of the esophagus
2) Frustration of the ingesta
3) Overeating increases the difficulty of moving the gas over the empty rumen. Elevation of the hind quarters has a similar effect, while elevation of the forequarters has no effect on ejection. Animals with a nonfunctional reticulum were particularly susceptible to overeating.

B) Alkalosis inhibits the reflex by a central action
C) Section of the right vagus nerve of the vagus nerve, which supplies the reticulum and abomasum, caused chronic tympany due to inhibition of reticular activity and abomasal digestion. Section of the left dorsal branch diminished evacuation efficiency temporarily by decreasing the strength of ruminal contractions.

D) Distention of either the abomasum or the reticulum inhibits the reticulum and therefore reduces the efficiency of ejection by interfering with gastric clearance of the reticulum.

E) Drugs and Poisons
1) Causing hypothermia
2) Poisonous and smelly inorganic gases inhibit contractions with consequent inefficiency of evacuation. Burden weights were increased by forced and instillation and direct recording of intrathoracic pressure (Onderstepoort J. Vet. Res., in press).

Ejection is a definite phase in the digestion and intelligence approach to the handling of disease problems in this animal. Before changes can be recognized in the normal picture, the normal must be known, and for this reason these preliminary studies were made on 12 healthy chinchillas.

Blood counts were made by collecting a sample directly from a nick in one of the larger ear veins and smears were made to effort at arriving at a more accurate average. Erythrocyte and leukocyte counts were duplicated each time a count was made, as well as smears for a differential. Red and white cell counts were not averaged and recorded unless they were reasonably close. Red cells had to be within 500,000 and white cells within 1,000 per cubic millimeter, respectively, to be used. Differential counts were made by staining with Wright's stain and counting 500 cells to get an average percentage.

A Preliminary Report on the Blood Picture of the South American Chinchilla

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The demand for more accurate and reliable methods of diagnosis and treatment of the South American chinchilla. The clinical laboratory has this time also for making a differential white cell count. Samples were taken nearly as possible at the same time of day at weekly intervals for twelve weeks in an effort to arrive at a more accurate average.

Erythrocyte and leukocyte counts were duplicated each time a count was made, as well as smears for a differential. Red and white cell counts were not averaged and recorded unless they were reasonably close. Red cells had to be within 500,000 and white cells within 1,000 per cubic millimeter, respectively, to be used. Differential counts were made by staining with Wright's stain and counting 500 cells to get an average percentage. The hemoglobin content was determined by using the sodium carbonate method of Karr on the Coleman junior clinical speci-
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