Effect of albendazole on the metacestodes of *Taenia saginata* in calves[1]

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Summary. Albendazole, a benzimadazole-carbamate anthelmintic, has been shown to effectively cause destruction of the metacestodes of *Taenia saginata* in calves.

A number of benzimadazole-carbamate anthelmintics have shown activity against the metacestodes of *Taenia taeniaeformis* and *Taenia crassiceps* in mice[3-6]. However, mebendazole was not effective when used to treat experimental infections of *Taenia saginata* in calves[7].

A new benzimadazole-carbamate anthelmintic, albendazole[8], has been demonstrated to have a broad spectrum of activity against parasites of cattle, including gastrointestinal nematodes and cestodes, *Dictyocaulus viviparus* and *Fasciola hepatica*[9]. The broad spectrum activity of albendazole suggested that this drug might be effective in the treatment of the metacestodes of *T. saginata* in cattle and this report presents the results of such a study.

Materials and methods. 26 Holstein and Holstein-cross calves 2 months of age were each infected orally with 32,000 viable eggs of *T. saginata* the dose consisting of 16,000 eggs obtained from Dr G.J. Gallie (Midlothian, Scotland) and 16,000 eggs obtained from a self-induced human infection.

10 weeks after infection 11 calves were treated orally with albendazole (50 mg/kg) and 11 calves were administered a placebo (drench suspension). All the calves were killed in a 17 day period beginning 4 weeks after treatment. At necropsy the striated muscle was removed and any remaining on the bones was examined at the time of boning-out. Then the complete musculature of each calf was sliced thinly and the number of metacestodes counted. A metacestode was judged viable if it was surrounded by a mild cellular reaction with clear fluid and a white scolex within the cyst. Organisms were assessed as 'degenerating' when there was a marked cellular reaction surrounding them and when an abnormality of the size and structure of the cyst, such as a caseous centre, was evident. The results were analyzed statistically by Student's t-test.

Results. The results demonstrating the effect of albendazole on the metacestodes of *T. saginata* in cattle are presented in the table. There was a highly significant ($p < 0.001$) 86% reduction in the number of viable metacestodes found in the treated calves as compared to the placebo treated animals. The majority of the viable metacestodes in the treated group were found in a single animal (2,504 metacestodes) while the remaining 10 animals in the treated group contained an average of 115 viable metacestodes. The 11 placebo treated animals contained an average of 2,374 viable metacestodes per animal.

There was also a significant ($p < 0.005$) 52% reduction in the total number of metacestodes in the albendazole treated group of animals as compared to the placebo treated animals. Since the placebo treated animals contained a consistantly high level of infection the reduction in the number of metacestodes in the treated group of animals probably was due to a rapid resolution of the majority of the metacestodes in the treated animals and the difficulty in detecting these resolving lesions.

The majority of the dead metacestodes in the placebo treated animals were similar in size to the viable metacestodes but contained a caseous core. The dead metacestodes in the albendazole treated animals could be divided into 3 types. A minority were similar to those in the placebo treated animals. However, the majority of the dead metacestodes were present either as small (< 2 mm) white, cream or greenish granulomatous lesions or as the shell of a collapsed parasite cyst which had lost its cyst fluid.

Discussion. The results demonstrate that albendazole is effective in the treatment of metacestodes of *T. saginata* in cattle. Treatment of infected cattle with albendazole resulted in a marked reduction in the viability of the metacestodes. Also, there appeared to be a fairly rapid resolution of the majority of the dead metacestodes in the treated animals. This rapid resolution of the metacestodes would suggest that the lesions would have become inapparent if the time between treatment and slaughter had been extended.

The high and consistant levels of infection in the placebo treated group of animals are in marked contrast to the low and highly variable counts of metacestodes which are frequently apparent in cattle experimentally infected with *T. saginata*. Such consistant levels of infection are necessary

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	Control animals			Treated animals		
	Total No. cysts	No. viable cysts	Dead cysts (%)	Total No. cysts	No. viable cysts	Dead cysts (%)
	3,104	1,791	42.3	972	133	86.3
	2,398	2,225	7.2	863	0	100.0
	3,800	3,426	9.8	1,986	17	99.1
	1,779	1,424	20.0	531	2	99.6
	3,012	2,706	10.2	754	0	100.0
	4,174	3,972	5.1	3,478	42	98.8
	2,289	1,464	36.0	1,519	0	100.0
	2,277	1,887	17.1	1,090	231	78.8
	5,066	4,204	17.0	679	25	96.3
	3,649	2,787	23.6	1,167	696	40.4
	3,367	6	99.8	3,650	2,504	31.4
Total No. cysts	34,915	25,892		16,689	3,650	
Mean No. cysts per animal	3,174	2,374	26.2	1,517 ($p < 0.005$)	332 ($p < 0.001$)	84.6

if phenomena such as the resolution of the lesions are to be evaluated objectively.
The decreased viability of the metacestodes and the rapid resolution of the lesions would suggest that albendazole could be a suitable drug to use in the field to treat cysticercosis in cattle, sheep and swine.

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The level of action of 2,4-D on transcription

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Summary. In mature cells, 2,4-D retards transcription when it is applied before ^{3}H-uridine incorporation. But transcription is accelerated when it is applied after feeding with ^{3}H-uridine. It has been suggested that the action of 2,4-D on transcription is only at the level of initiation.

It has been shown[2,3] that 2,4-D accelerates replication as well as histone synthesis in nuclei of mature tissue. Retarding effect of 2,4-D on transcription in endomitotic nuclei has been demonstrated[4], though normally they show heavy uridine uptake[5]. In the previous communication[4], the result of treatment of 2,4-D applied along with ^{3}H-uridine, was reported. In this case, it was observed that the endosperm and the root cells showed much lower uridine incorporation, as compared to the controls where 2,4-D was not applied in those tissues. It was later thought that the entry of uridine in the tissue might have been influenced by the presence of 2,4-D along with uridine. In that case, the observed low rate of transcription might have been due to the lesser uptake of uridine rather than to the retarding effect of 2,4-D.

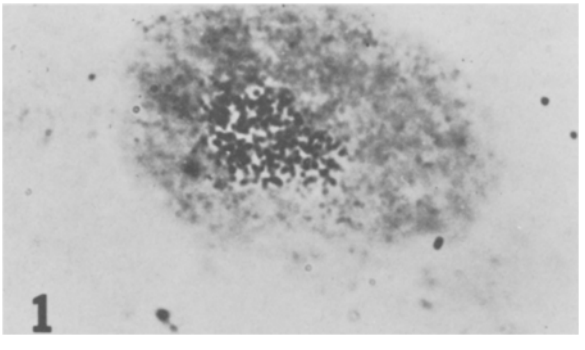

Fig. 1. The nucleus fed with ^{3}H-uridine prior to 2,4-D application showing heavy uridine incorporation.

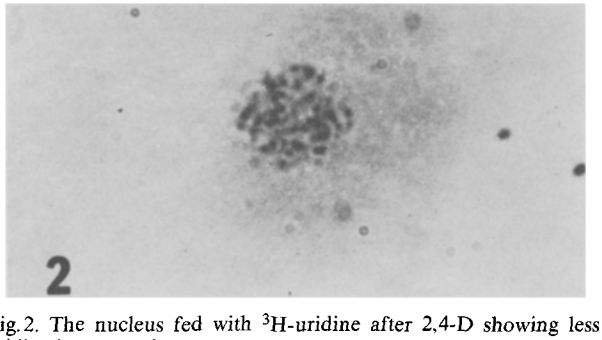

Fig. 2. The nucleus fed with ^{3}H-uridine after 2,4-D showing less uridine incorporation.

In order to ascertain precisely the accelerating or retarding effect (if any) on transcription, this experiment was planned involving application of 2,4-D before and after treatment with uridine, in mature nuclei of root cells.
Material and methods: For root cells, rooted bulbs of *Allium cepa* and for endosperm, inflorescence stalk bearing fertilized ovary of *A. tuberosum* were taken. The experiments were set up in 2 sets. In the 1st set, bulbs and inflorescence stalks immersed initially in 5 µCi uridine (sp. act. 500 mCi/mM) for 24 h were followed by treatment in 0.01% 2,4-D solution for the next 24 h. In the 2nd set, 0.01% 2,4-D was applied for the initial 24 h, followed by feeding with 5 µCi uridine for the 2nd 24 h. The material was then thoroughly washed in running water, fixed in acetic ethanol and stained in Feulgen solution. The mature cells of the root and endosperm were squashed on a clean slide. Stripping film autoradiography with Kodak AR10 film was adopted, and the observations were carried out on 100 nuclei from roots and endosperm cells of the same age.
Results and discussion: The mature nuclei of root cells and endosperm show an interesting effect of 2,4-D on uridine uptake and consequently RNA synthesis. The uptake was found to be very heavy when the tissue was treated with uridine prior to the application of 2,4-D (figure 1). The incorporation was found to be significantly low in similar mature nuclei when 2,4-D was applied before feeding with uridine (figure 2). The 2nd set of results clearly suggest that transcription is affected in mature tissue following 2,4-D application. It is likely that 2,4-D accumulates in the tissue during initial phase and exerts its retarding effect on transcription indicated by low uridine incorporation. Heavy uptake of uridine in tissue fed with labelled precursor prior to 2,4-D treatment suggests that the process once initiated cannot be retarded by 2,4-D. This is indicated also in control set up[4] without any 2,4-D treatment, where a quantitatively equal incorporation was found. The action of 2,4-D on transcription may possibly lie at the level of initiation of RNA polymerase activity. Once transcription is initiated, 2,4-D is unable to exert its retarding effect.

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