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RESEARCH NOTE

AN ATTEMPT TO TREAT THE LARVAL STAGE OF *TAENIA MULTICEPS* AND A RÉSUMÉ OF ITS NEURAL AND EXTRANEURAL DISTRIBUTION IN SHEEP

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ABSTRACT

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Sheep were experimentally infested with the larval stage of *Taenia multiceps*. On Day 36 post-infestation 2 animals were treated intraperitoneally with mebendazole at 40 mg/kg body mass. Mature viable coenuri were present in the cerebra of both these animals when they were killed on Day 114. From Day 36–Day 49 3 animals were treated daily *per os* with mebendazole at 100 mg/kg body mass. At autopsy 1 animal had a developing coenurus in the cerebrum while the other 2 animals were not infested. The drug thus had no effect on the development or viability of the coenuri by either of the 2 routes of administration. When a coenurus from a sheep treated intraperitoneally was fed to a cestode-free dog, 5 adult *T. multiceps* were recovered from the animal 21 days later.

The larvae of this cestode undergo some development in extraneural tissues but rarely attain a size of more than 2 mm before they die and degenerate. The pathological changes in these degenerate lesions are briefly described.

Résumé

ESSAI DE TRAITEMENT DU STADE LARVAIRE DE TAENIA MULTICEPS *ET ANALYSE DE SA DISTRIBUTION NEURALE ET EXTRA-NEURALE CHEZ LE MOUTON*

On a infesté expérimentalement des moutons avec des larves de Taenia multiceps. *Au 36e jour après l'infestation 2 animaux ont été traités intrapéritonéalement au mebendazole à raison de 40 mg par kg de poids vif; quand on les a tués au 114e jour, ils avaient tous deux des cénures mûrs et viables dans le cerveau. Du 36e au 49e jour 3 animaux ont été traités journellement* per os *au mebendazole, à raison de 100 mg par kg de poids vif; à l'autopsie un de ces animaux avait dans le cerebrum un cénure en voie de développement et les 2 autres animaux n'étaient pas infestés. Le médicament n'a donc pas affecté le développement ou la viabilité des cénures, quelle qu'ait été la voie d'administration. Aprés qu'on ait fait absorber à un chien libre de cestodes un cénure en provenance d'un mouton traité par voie intra-péritonéale,* 5 T. multiceps *adultes ont été retrouvés chez cet animal* 21 *jours plus tard.*

Les larves de ce cestode subissent bien quelque développement dans les tissus extra-neuraux mais atteignent rarement une taille supérieure à 2 mm avant de mourir et de dégénérer. On décrit brièvement les changements pathologiques qui s'observent dans ces lésions dégénératives.

INTRODUCTION

Mebendazole is effective against the larval stages of *Echinococcus granulosus, Mesocestoides corti* and *Taenia pisiformis* (Heath & Chevis, 1974) and *Taenia taeniaeformis* (Thienpont, Vanparijs & Hermans, 1974).

Taenia multiceps, which forms a coenurus in the brain of sheep, is a serious problem in some parts of the Republic of South Africa (Verster, 1966). This paper describes an attempt to treat the larval stage of the cestode and includes a discussion both of its neural and extraneural distribution in sheep and the pathological changes in degenerate extraneural lesions.

MATERIALS AND METHODS

Ten Dorper ewes, 5–5½ months of age, were each infested with 2 400 ova of *T. multiceps*. One animal (Sheep 6) died 16 days later and is included in the control group. Thirty-six days post-infestation the 9 remaining sheep were divided into 3 groups as follows:

Group A Sheep 1 and 2. Each received an intraperitoneal injection consisting of a 2,5% suspension of mebendazole in physiological saline at 40 mg/kg live mass.

Group B Sheep 3, 4 and 5. These were dosed *per os* with mebendazole* 5% m/v at 100 mg/kg live mass daily from Day 36–Day 49 inclusive.

Group C Sheep 7, 8, 9 and 10 acted as untreated controls.

Sheep 4 died on Day 72 and the 8 survivors were killed on the 114th day. Complete autopsies were carried out on the animals in Groups A and B but only the brains of those in Group C (controls) were examined.

The experimental design and results are summarized in Table 1.

TABLE 1 Experimental design and results

Sheep No.	Treatment and Lesions
Group A	*Mebendazole as a single dose at 40 mg/kg intraperitoneally. Complete autopsy*
1.....	Mature coenurus; extraneural degenerate lesions present
2.....	Mature coenurus; extraneural degenerate lesions present
Group B	*Mebendazole for 14 days at 100 mg/kg orally. Complete autopsy*
3.....	No coenurus; extraneural degenerate lesions present
4*.....	Developing coenurus; no degenerate lesions
5.....	No coenurus; extraneural degenerate lesions present
Group C	*Untreated controls. Brain only examined*
6**.....	No coenurus
7.....	Mature coenurus
8.....	Mature coenurus (10 mm diameter) which showed signs of degeneration
9.....	No coenurus
10.....	Degenerate cerebral lesions

* Died 72 days after infestation

** Died 16 days after infestation

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Results

Group A Intraperitoneal administration of Mebendazole

A single coenurus was present in the brain of each of the 2 animals. These coenuri were approximately 10 mm in diameter and contained several scolices.

Sheep 1 had several small focal caseous lesions disseminated in the myocardium, skeletal muscles and musculature of the diaphragm, tongue and oesophagus. These lesions were identical with those that had been encountered earlier in many other cases of experimentally-produced infestation with the parasite and may be very numerous in situations both within and without the central nervous system if the infective dose contains large numbers of ova (Tustin & Verster, 1960, unpublished observations). They represent the tissue response of the host to live and/or dead immature coenuri. In this animal the lesions varied in size and shape: some were irregularly spherical and about 1–5 mm in diameter, while others were somewhat elongated and appeared as irregular tracts 1–3 mm wide and up to 10 mm long. Each lesion consisted of a core containing yellowish-white, partially calcified necrotic material which was surrounded by a narrow zone of fibrous connective tissue. There were 3 identical lesions in the myocardium and 1 in the tongue of Sheep 2.

The coenurus from Sheep 1 was fed to a dog which had been reared under cestode-free conditions. Five *T. multiceps* were recovered from the terminal portion of the ileum when this dog was destroyed and examined 21 days later.

Group B. Oral administration of Mebendazole

Sheep 4, which died on Day 72 of gangrenous pneumonia, had a single coenurus in the right hemisphere of the cerebrum.

No coenuri were found in the brains of Sheep 3 and 5. In Sheep 3 there were 3 lesions in the myocardium and 2 lesions in the tongue identical with those in the myocardium and other extraneural organs of Sheep 1. In Sheep 5 a single such lesion was present in the tongue.

Group C. Controls

Sheep 6 died of haemonchosis on Day 16, and there were no lesions caused by *T. multiceps* either in the brain or in any of the other organs.

The brain of Sheep 7 contained a single live coenurus about 10 mm in diameter. A coenurus of similar size was present in the brain of Sheep 8 but the cyst wall had a yellowish discoloration which was believed to be due to degeneration. The nervous tissue surrounding this parasite showed a comparatively intense zone of inflammation and encephalomalacia. There was an old small lesion caused by the death and degeneration of a young coenurus on the ventral surface of the cerebrum of Sheep 10. There were no coenuri or lesions in the brain of Sheep 9.

Discussion

The effect of mebendazole on the larval stages of different cestodes depends on the route of application, dosage, species and age of the parasite, and on the species of the intermediate host.

Orally administered mebendazole is effective against the larvae of *E. granulosus* in mice (Kammerer & Judge, 1976) and in pigs (Pawlowski, Kozakiewicz & Zatonski, 1976); of *Mesocestoides corti* in mice (Heath, Christie & Chevis, 1975); of *Taenia hydatigena* in pigs (Hörchner, Langnes & Oguz, 1976), and in sheep (Heath & Lawrence, 1978); of *Taenia ovis* in sheep (Heath & Lawrence, 1978); of *Taenia pisiformis* in rabbits (Heath *et al.*, 1975; Hörchner *et al.*, 1976), and of *Taenia taeniaeformis* in mice (Thienpont *et al.*, 1974). It is less effective by this route against the larvae of *E. granulosus* in sheep (Heath & Lawrence, 1978) and of *E. multilocularis* in mice (Campbell, McCracken & Blair, 1975). The intraperitoneal route of administration is effective only against the larvae of *T. taeniaeformis* in mice (Borgers, De Nollin, Verheyen, Vanparijs & Thienpont, 1975) and of *T. pisiformis* (Heath *et al.*, 1975), while subcutaneous administration is effective against *E. granulosus* and *M. corti* in mice and *T. pisiformis* in rabbits (Heath *et al.*, 1975), but not against *E. granulosus* in sheep (Heath & Lawrence, 1978).

The coenuri recovered from Sheep 1, 2 and 4 showed no signs of degeneration and that from Sheep 1 was infective when it was fed to a dog. The ineffectiveness of this drug when given either orally or intraperitoneally may well be due to the blood brain barrier which prevents the passage of certain substances from the blood to the brain. Perhaps treatment with mebendazole combined with a drug which can penetrate this barrier may be as destructive of the coenuri in the central nervous system as mebendazole is of many of the cestode larvae mentioned above.

Heath *et al.* (1975) state that the drug is more effective when the larval stage is actively growing (e.g., the tetrathyridia of *M. corti* in mice). The cystic stage of *T. multiceps* in the brain of sheep grows rapidly for the first 90–100 days, after which the rate of growth, though decreasing considerably, does not cease (Tustin & Verster, 1960, unpublished observations). The cysts in these sheep were at the stage of rapid growth at the time of treatment but the drug was either ineffective or did not penetrate the blood brain barrier.

The distribution of hexacanth embryos of the parasite via the blood stream is a haphazard phenomenon and only those which reach the central nervous system develop to maturity. There are, however, certain extraneural tissues of the intermediate host, particularly striated muscular and renal tissues, in which they can develop up to a certain stage before dying. In these extraneural sites the young larvae never attain a diameter of more than about 2 mm. Of the muscles, the cardiac, diaphragmatic and masticatory muscles are the most frequently and most heavily involved. When the parasite is deposited in an organ or tissue, it frequently migrates outside the blood vessels for up to about 15 mm, leaving a tract filled with necrotic debris behind it. When the parasite dies, as it inevitably does in extraneural situations, a more severe inflammatory reaction occurs until all traces of it disappear. Subsidence of the reaction and resorption of the exudate then slowly occur.

In general, the live mature larval stages of many tapeworms, including the one under review, provoke only a mild inflammatory reaction in their immediate vicinity. Should they die, however, a severe inflammatory response invariably occurs. The response in the brain surrounding the coenurus with the discoloured wall in Sheep 8 was considerably greater, viewed both macroscopically and microscopically,

than is usually the case in live cysts. This evidence supports the contention that the cyst was indeed dead and degenerating.

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