

Chemotherapy of Gnathostomiasis

Principal Investigator: Professor Svasti Daengsvang, Med. D.*

Assistant Investigators: Boonsri Sermwatsri¹
Pichit Youngyi, B.Sc.¹
Dhawe Guname, B.Sc.¹
Phaibul Sirichahwal, B.Sc.²
Paisal Yingyourd, B.Sc.²
Rapee Machimasatha, B.Sc.²

OBJECTIVE: The objective of this study is to determine the effect of multiple subcutaneous doses of Ancylos Disophenol (2, 6-diiodo-4-nitrophenol) on the immature and larval stages of G. spinigerum in the definitive hosts (dogs and cats). Since immature worms are the stages responsible for human gnathostomiasis, the study has pertinence to human as well as domestic animal infections.

DESCRIPTION: In the last Annual Progress Report (1969) a study of the chemotherapy of mature adult G. spinigerum infections in the stomach of 7 cats was reported. The adult worms were successfully removed by one subcutaneous injection of Ancylos, but the larval stages in the tissue seemed to resist the drug. A study of the effect of the same chemotherapeutic agent on the larval stages and immature adults migrating in the tissue of various organs of dogs and cats by more than one subcutaneous dose of the drug has now been initiated. The study was undertaken on 5 adult animals (3 dogs and 2 cats) 1 to 3 months after being infected transcutaneously with different numbers of advanced third-stage larvae. The drug given at a dosage of 0.1 ml per pound body weight according to the directions given by the manufacturer for treatment of canine hookworm. The experimental animals were sacrificed and examined for the presence of the worms in the tissues of various organs 7-15 days after the last dose of the drug was given.

PROGRESS: 1969: A negative adult female dog (#15) weighing 15 lbs was successfully inoculated in 45 minutes with 100 advanced third-stage larvae (97% successful penetration via skin). Thirty-three days later the animal was given 3 subcutaneous doses of 1.5 ml each of Ancylos at 7-day intervals. Autopsy one week after the last dose of the drug showed 5 living immature males and females in the muscles of the chest (1 female), back (1 female), abdominal wall (1 male), the peritoneal fat (1 female) and right lung (1 male). In addition, there were 7 living unencysted advanced third-stage larvae; one each in the flesh of back, anterior abdominal wall, right front leg, peritoneum, diaphragm and the wall of the small intestine and the rectum. Twelve dead immature worms were found in the muscles of the anterior abdominal wall (3 males, 2 females), back (2 females), right front leg (1 female), right hind leg (1 female), left lung (1 male) and liver (1) and left lung (1). Sex could not be determined in two worms.

Dog #16 was treated with 6 subcutaneous injections of Ancylos at one-week intervals. The first dose of 1.6 ml was given about 3 months after successful skin penetration with 47 G. spinigerum larvae in 1/2 hours (89.0% successful penetration); 5 doses of 1.2 to 1.7 ml of the drug according to the animal's weight were then given regularly at one week intervals. The animal was sacrificed 18 days after the sixth dose and an autopsy showed 1 living immature adult male G. spinigerum located in the tissue at the junction of the esophagus and the stomach measuring 10.7 x 1.0 mm with 7 cephalic hooklet rows. Ten growing larvae measuring 5.0-6.7 mm x 0.6 mm were found in the diaphragm; 8 were degenerate and 2 were alive with active movement when removed from the tissue. No adverse effects of the drug were noted and there was little change in body weight recognized during the course of treatment.

* Retroactive in previous reports.

1 Worked for some months during the year before resignation for further education.

2 Replacement for 1.

Dog#17 was also scheduled to be given 6 subcutaneous doses of Ancylosol beginning about 1 1/2 months after being transcutaneously infected with 63 larvae (100% successful penetration). This animal unfortunately died of unknown causes 5 days after being subcutaneously injected with the third dose of 2.3 ml of the drug. During the course of treatment (about two weeks) the animal became anorexic and its body weight was reduced by about 6 lbs on the day of its death. On autopsy 2 days after its death, 11 growing larvae of the worm were found in the diaphragm; 6 showed much degeneration of the esophagus and intestine but the other 5 larvae were still alive. The measurements made on 10 larvae were 4.5-6.0 mm x 0.5-0.6 mm, slightly longer and larger than when applied to the skin.

The findings in these three treated dogs suggest that 3 to 6 doses of the chemical kills many larvae and immature worms located in the tissue when the treatment is started 1-3 months after infection.

Cat#85 was penetrated by 49 larvae in 2 hours (rate of successful penetration, 96%) Beginning 31 days after infection, the animal was treated with 4 doses of Ancylosol. The first dose was injected subcutaneously (0.5 ml) and subsequent doses were given at 7-day intervals. Fourteen days after the last treatment (67 days after skin penetration) an autopsy showed a total of 5 living advanced third-stage larvae of the worm in the muscles of the back (1) abdominal wall (1), left hind leg (2) and diaphragm (1). The rate of recovery of living worms was still 10%.

Cat#94 was exposed to a total of 54 larvae in 1/2 hour (successful rate of penetration, 95%). It was given 6 subcutaneous doses of Ancylosol at 7-day intervals beginning on 18 July 1969, one month after the infection, and ending on 3 September. On autopsy 15 days after the last dose of the drug on gnathostomes were found in the tissues; no macroscopic changes were noted in the organs examined. The animal remained normal during the course of treatment. Thus, in this cat, 6 subcutaneous doses of Ancylosol apparently cured the animal of the infection by larval stages located in the tissues. The results of the study on the chemotherapy of G. spinigerum in cats and dogs is summarized in Table 1. The study is to be continued.

SUMMARY: Multiple subcutaneous doses of Ancylosol Disophenol (2, 6-diiodo-4-nitrophenol) were used in this study of the chemotherapy of G. spinigerum infections in dogs and cats. A dosage of 0.1 ml per pound of body weight was given at weekly intervals beginning 1 to 3 months after exposure of the experimental animals. In 3 dogs, both living and dead larvae were recovered following as many as 6 subcutaneous injections of the drug.

One of 2 cats was negative for gnathostome larvae after 6 doses. These results are inconclusive and further investigation is under way.

Table 1. Chemotherapy of *G. spinigerum* larval and immature stages infecting 5 definitive hosts (3 dogs and 2 cats) by multiple subcutaneous doses of Ancylool Disophenol (2, 6-diido-4-nitrophenol) on the basis of 0.1 ml per pound of body weight per dose at 7-day intervals.

Animal No.	No. third-stage larvae penetrated thru skin/ per cent	Age of the worm in host before treatment (days)	Total weekly doses of Ancylool	Autopsy findings 7-15 days after treatment		Remarks
				No./stages of worm	Organs found infected	
Dog#15	100 (97%)	33 (1 month)	3	5 living immature	muscles of chest, back, abdomen. Lung and peritoneum.	sacrificed 7 days after the last dose
Dog#16	47 (89%)	93 (3 months)	6	12 dead immature 7 living larvae	peritoneum, diaphragm, intestinal wall flesh of back, abdomen, leg and lung	sacrificed 2 weeks after the last dose
Dog#17	63 (100%)	46 (1 1/2 months)	3	1 living immature male 2 living larvae 8 dead larvae	esophagus and stomach junction, diaphragm	died 5 days after the third dose of unknown causes
Cat#85	49 (96%)	31 (1 month)	4	11 growing larvae (6 dead)	diaphragm	sacrificed 14 days after the last dose
Cat#94	54 (95%)	30 (1 month)	6	5 living larvae negative	abdominal wall, leg, back, diaphragm None	sacrificed 15 days after the last dose