10555

Effects of Sulfanilamide, Phenothiazine and Thionol in Experimental Trichinosis.*

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It is almost impossible to evaluate the efficacy of the various drugs recommended for the treatment of human trichinosis. Animal experimentation appears to be the only feasible solution to the problem of studying the effects of therapeutic agents in this disease. This paper deals with the effects of sulfanilamide, phenothiazine and thionol on experimental trichinosis in rats.

Methods. Sixteen adult white rats of the Wistar strain averaging 190 g in weight were segregated into 4 groups of 4 each. After one week of observations on the quantity of standard dry rat diet consumed by each group they were placed on diets to which known quantities of the drugs being studied had been added. They were allowed to eat this diet for 2 days in order to develop some concentration of the therapeutic agents prior to infection. After an 18-hour fast each rat was infected by a quantity of rat meat containing 2,350 encysted larvae. The number of living larvae per gram of rat meat was calculated by multiple counts on multiple digests of thoroughly minced muscle from rats according to methods previously described.[1] The strain of *Trichinella spiralis* had been originally obtained from a human diaphragm. The rats were kept in cages in which the feed cups were designed to prevent losses, so as to permit determination of the amount of food consumed each day. Water was available at all times. One group of rats on standard diet served as controls; the other 3 groups were kept on the same diet plus the drugs being studied. The various agents in powder form were thoroughly mixed with the feed in a mechanical mixer. Rat weights and food consumption were recorded twice weekly for 6 weeks. All rats were then sacrificed, their carcasses individually digested and an estimate made of the total number of larvae which had developed in the muscles of each.

*Supported in part by the Rockefeller Fluid Research Fund of the School of Medicine of Stanford University.

1 McNaught, J. B., and Pierce, G. N., Jr., *Am. J. Clin. Path.*, 1939, **9**, 52.

TABLE I.
Effects of Sulfanilamide, Phenothiazine, and Thionol on Trichinosis in Rats.

Drugs	Group* wt Initial, g	Group* wt Final, g	Total food Consumed, g	Avg daily drug intake per kilo body wt, g	No. of Larvæ recovered	Reduction in infestation, %
Controls	797	955	1,931		762,400	
Sulfanilamide	986	985	2,263	.96	343,120	55
Phenothiazine	633	746	1,512	.14	198,720	74
Thionol	751	783	1,680	.13	421,760	45

*Four rats in each group. Each rat was infected by 2350 encysted larvæ.

Controls. Four male rats were used as controls. Table I shows the pertinent data for this group which gave an intake-output ratio of 1 to 81.1 larvae. Each gram of skinned, eviscerated rat contained 1,463 larvae.

Sulfanilamide. Inasmuch as sulfanilamide has been shown to be a beneficial therapeutic agent in certain bacterial infections and since its value in parasitic diseases can be determined only by trial it seemed worthwhile to test its effectiveness in trichinosis. Powdered sulfanilamide (p-aminobenzenesulphonamide—Prontylin—Winthrop) was added to the standard diet to a concentration of 1.66%. Male rats were used in this experiment. Table I shows only 45% as many larvae recovered as in the control group. The intake-output ratio was 1 to 36.5. There were 639 larvae per gram of dressed rat.

McCoy[2] in a similar experiment on rats, infected by excysted Trichinella and receiving a dose of 125 mg of sulfanilamide daily for 16 days beginning the day after infection, found no material difference in the final larvae counts between the treated and control animals. In a second experiment his figures do show a decrease of 30% in the total count of larvae in the treated group. His conclusions were that sulfanilamide had no value in treatment of experimental trichinosis in rats. Our figures showing a decrease of 55% are possibly accounted for by the fact that we gave larger doses, continued therapy for 42 days instead of 16 days and began medication two days prior to infestation.

Phenothiazine. Phenothiazine has shown promise as an insecticide[3] and as a urinary antiseptic.[4] It has been reported to give 100% control of larvae of the horn fly, *Haematobia irritans L.*, developing in the manure when administered to cattle at the rate of 0.1 g or less

2 McCoy, O. R., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 461.

3 Smith, L. E., Munger, F., and Siegler, E. H., *J. Econ. Entomol.*, 1935, **28**, 727.

4 Thomas, J. O., DeEds, F., and Eddy, C. W., *J. Pharm. Exp. Therap.*, 1938, **64**, 280.

per kilo of body weight.[5] In view of these findings it seemed advisable to try the effects of this drug on trichinella in the gastrointestinal tract. Accordingly parasitized female rats were fed the standard dry rat diet to which .25% phenothiazine was added.

Table I shows that this group yielded only 26% as many larvae as did the control group, thus indicating that phenothiazine in the quantities and manner given furnished 74% protection from experimental trichinosis in rats. There apparently were no ill effects from the continued use of this drug. The total dose of phenothiazine was only a tenth of the total dose of sulfanilamide.

There was a final yield of 493 larvae per gram of dressed rat and an intake-output ratio of 1 to 21.1.

Following completion of this study our attention was called to the report of Harwood, Jerstad, and Swanson[6] on the beneficial results following the use of phenothiazine for the removal of ascarids and nodular worms from swine.

Thionol. It has previously been shown[4] that the bactericidal properties of urine following oral administration of phenothiazine are to be attributed to thionol, an oxidation product of phenothiazine. It therefore seemed advisable to compare the efficacy of this compound with the parent substance, phenothiazine. The thionol used was prepared from phenothiazine by a simple process of oxidation recently described.[7]

Four parasitized female rats were fed the standard dry rat diet containing .25% thionol. Table I shows that this group yielded 55% as many larvae as did the control group, thus indicating that thionol in the quantities given furnished 45% protection from trichinosis and was far less efficacious than phenothiazine. There was a final yield of 974 larvae per gram of dressed rat and an intake-output ratio of 1 to 44.8.

An interesting observation in these experiments concerns the maintenance of weights of the animals and their food consumption. All groups lost weight the first 2 weeks of infestation because of their diminished food intake during the acute stage of the disease. All except those on sulfanilamide had returned to their original weights by the end of the third week and some showed up to 20% gain by the close of the experiment. More grams of food were consumed per gram of rat in the group on sulfanilamide than in any other group

[5] Knipling, E. F., *J. Econ. Entomol.*, 1938, **31**, 315.

[6] Harwood, P. D., Jerstad, A. C., and Swanson, L. E., *J. Parasitol.*, Supplement, 1938, **24**, 16.

[7] DeEds, F., and Eddy, C. W., *J. Am. Chem. Soc.*, 1938, **60**, 1446.

yet these rats just succeeded in attaining their original weights by the final week. This suggests that some factor in sulfanilamide did not permit the normal utilization of the diet in trichinous rats. McCoy noted that infected rats lost considerably more weight under sulfanilamide therapy than control rats and also more than other rats which were given the same amount of drug but were not infected with Trichinella. There is a possibility in our experiment that there was some loss of food among the shavings of the rat cage in the case of sulfanilamide due to dislike for the food. It is interesting that although the control rats carried a heavier parasitic infestation than any other group they made the greatest gain (20%) over their original weight. The rats on phenothiazine made a gain of 18%.

Conclusions. (1) A rather large amount of sulfanilamide, 0.96 g per kilo of body weight daily, used over a period of 6 weeks reduced the number of trichinella encysting in the muscles of rats by 55%. (2) The continuous use of phenothiazine, in a dosage approximately one-tenth that of sulfanilamide, over a period of 6 weeks reduced the severity of trichinous infection in rats by 74% and warrants further experimentation. (3) Thionol is of little use in reducing the severity of trichinous infestation in rats.

10556

Phosphorus Metabolism in Leukemic Blood.

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The fact that radioactive phosphorus is chemically like ordinary phosphorus and is "tagged," has made it valuable in following the exchange of phosphorus in biological systems.[1] The present study is concerned with the absorption, distribution, and excretion of labelled phosphorus (P^{32}) in 2 patients suffering from chronic myelogenous leukemia. The mixture of P^{31} (inactive) and P^{32} (radioactive) atoms were converted into Na_2HPO_4 and administered orally in an isotonic solution of this salt.

The first patient studied was a case of untreated chronic myelogenous leukemia, in fair clinical condition. The white blood count

[1] Lawrence, J. H., Artificial Radioactivity and Neutron Rays in Biology and Medicine, *Handbook of Physical Therapy*, Am. Med. Assn., 1938.