Effect of Certain Antihistaminic and Steroid Compounds on Appendical Peritonitis.* (18535)

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Since Kay and Lockwood(1) suggested the relationship between serum antiproteolytic level and the mortality of experimental appendical peritonitis, we have been looking for substances which might be effective against this disease. Ungar(2) has shown that proteolysis normally precedes the formation of histamine. For this reason, it occurred to us that various agents which might conceivably act at some point during that reaction which culminates in the release of histamine should be tried in peritonitis. We chose 4 substances, one an antihistamine Diphenhydramine Hydrochloride (Benadryl†) and 3 steroids, pregnenalone,‡ allopregnane-21-OL3, 20 dione 21 acetate (allopregnane§) and cortisone acetate‖ (Cortone).

The results of our use of these 4 compounds are here reported.

Technic. Peritonitis was produced in dogs ranging from 6 to 10 kg by the same technic as previously reported by one of the authors (Kay)(3). Postoperatively the animals were started on medication immediately and were given water to drink ad lib. No I.V. fluids were given and food was withheld for 3 days. Animals which died were autopsied immediately. Surviving animals were sacrificed on the fourteenth postoperative day and autopsied.

Dosage: Benadryl was given in doses of 5 mg per kilo every eight hours or 15 mg/kilo per day. Allopregnane was given in doses of 4 mg per kilo every 6 hours or 24 mg/kilo per day. Pregnenalone was given in doses of 20 mg per kilo every 6 hours or 120 mg/kilo per day. Cortone was given in doses of 2.5 mg per kilo every 6 hours or 10 mg per kilo per day. All medications were given intramuscularly.

Results. Ten animals were studied in each of 5 groups. In the control group the mortality was 7 out of 10. In the Benadryl group, also 7 died and 3 survived. With cortone, allopregnane, and pregnenolone, the mortality was the same in each case, 8 animals died and 2 survived. Table I below shows the day of death of each animal in each group. Animals surviving 14 days are those counted as survivals and were sacrificed on that day. The group average for days survived is recorded in the final column. There is no statistically significant difference between the groups.

Discussion. Although, we realize that a certain period of time is necessary before the steroids become effective, we believe the data reported significant because medication was begun immediately postoperatively or 12 to 24 hours before the onset of peritonitis. Furthermore it was our desire to evaluate these drugs as they might be used therapeutically rather than prophylactically. The possibility remains that the steroids might be effective if given in courses before the onset of peritonitis. During the course of our work, a report of Habif *et al.*(4) appeared which described a case of perforation of gastric ulcer which occurred following a course of ACTH. The patient showed no systemic signs of peritonitis. Our work does not refute such a possibility but suggests that the 3 steroids studied have no place in the therapy of uncomplicated experimental appendical peritonitis. The observation that these agents do not affect the mortality rate in this disease

* Aided by a grant from the Warren-Teed Products Co., Columbus, Ohio.

1. Kay, J., and Lockwood, J., *Surgery*, 1947, v21, 155.

2. Ungar, G., and Mist, S., *J. Exp. Med.*, 1949, v90, 39.

† Supplied by Parke-Davis Co.

‡ Supplied by Warren-Teed Products Co.

§ Supplied by Wyeth, Inc.

‖ Supplied by Merck and Co.

3. Kay, J., and Lockwood, J., *Surgery*, 1946, v20, 56.

4. Habif, D., Hare, C., Gloser, G., *J.A.M.A.*, 1950, v144, 996.

TABLE I. Days Survival.

Treatment	Day of death 1	2	3	4	5	6	7	8	9	10	11	12	13	14	Group avg
Control	1	5	1											3	5.6
Benadryl	2	4				1								3	5.8
Pregnenolone	1	2	3	1	1									2	5.1
Allopregnane	1	2	1	2	1			1						2	5.7
Cortisone	2	2	1		1	2								2	5.4

suggests the possibility that the observed proteolysis in peritonitis is not produced in a manner analogous to the production of fibrinolysin by specific antigens.

Conclusion. Benadryl, an antihistamine and three steroids, cortone, allopregnane and pregnenalone do not affect the course of experimental appendical peritonitis in dogs.

Received January 16, 1951. P.S.E.B.M., 1951, v76.

Effects of Methoxinine in the Mouse.* (18536)

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Roblin *et al.*(1) showed methoxinine to be a bacteriostatic agent for *E. coli* and *Staph. aureus*, and the growth inhibition caused by it to be reversed by L-, but not by D-, methionine. Shaffer and Critchfield(2) reported the alleviation, by methionine, of the toxic effects of methoxinine in rats. These latter investigators claimed that methoxinine exerted lipotropic activity, but they failed to take into consideration the effect of the caloric restriction imposed by the methoxinine. Best(3) warns that "another pitfall . . . is that of the 'pseudolipotropic' effect of a low caloric intake." In connection with other studies being carried out in this laboratory, it was of interest to study the effects of methoxinine in mice. Some of the data seemed to clarify the "apparent" lipotropic activity of methoxinine, and are reported here.

The basal diet used in these studies had the composition shown in Table I. All additions were made at the expense of sucrose. In the first experiment, young adult male mice of the Swiss strain, in groups of 4 each, were treated as shown in Table II. Male mice of the C3H strain, 5 to 6 weeks of age, in groups of 5 each,

TABLE I. Diet Composition (per kg of diet).

	g
Soy protein*	100
L-Cystine	2.5
Salts†	50
Ruffex	20
Hydrogenated vegetable oil‡	100
Lard	50
Sucrose	677.5
	mg
Thiamine	20
Riboflavin	20
Pyridoxin	20
Calcium pantothenate	40
α-Tocopherol	40
	units
Vitamin A§	67500
Vitamin D‖	5000

* Alpha-protein, The Glidden Co., Chicago, Ill.
† Hawk-Oser salt mixture.
‡ Crisco.
§ Vit. A concentrate, Nopco Chemical Co., Harrison, N. J.
‖ Drisdol, Winthrop-Stearns, New York.

* This investigation was supported (in part) by a research grant from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

1. Roblin, R. O., Jr., Lampen, J. O., English, J. P., Cole, Q. P., and Vaughan, J. R., Jr., *J. Am. Chem. Soc.*, 1945, v67, 290.

2. Shaffer, C. B., and Critchfield, F. H., *J. Biol. Chem.*, 1948, v174, 489.

3. Best, C. H., *Fed. Proc.*, 1950, v9, 506.