In a more recent publication Long and Bliss[7] also found that the unsubstituted thiazol derivative was equal to, or slightly superior to, sulfanilamide and to sulfapyridine in its bacteriostatic action upon cultures of *E. coli* and *B. proteus* in broth.

Conclusions. On the basis of *in vitro* studies sulfathiazol and sulfamethylthiazol have been found to be somewhat more effective than sulfapyridine, sulfaphenylthiazol and sulfanilamide in their *in vitro* effects upon bacteria representative of the colon-typhoid-dysentery group. In general, the unsubstituted thiazol derivative appears to be the most active compound, being followed in decreasing order of effectiveness by sulfamethylthiazol, sulfapyridine, sulfaphenyl thiazol and sulfanilamide.

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Changes Produced by Desoxycorticosterone Overdosage in the Rat.*

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Kuhlmann, *et al.*,[1] found recently that dogs chronically treated with very high doses of desoxycorticosterone acetate show definite signs of damage and reveal blood chemical changes which appear to be the opposite of what is seen in adrenal insufficiency. Thus they noted " . . . . a striking decrease in serum potassium, a slight increase in serum sodium, a slight decrease in serum protein and non-protein nitrogen . . . . ". In this connection it appears of interest to mention our experiments in the rat which indicate that treatment with as high a dose as 10 mg of desoxycorticosterone acetate daily given for 20 days fails to produce any externally visible signs of damage and that, contrary to expectations, the blood chlorides prove to be consistently low. Meanwhile we have no explanation for the fact that although desoxycorticosterone prevents hypochloremia in the adrenalectomized rat, chronic overdosage with this

7 Long, P. H., and Bliss, E. A., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 324.

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1 Kuhlmann, D., Ragan, C., Ferrebee, J. W., Atchley, D. W., and Loeb, R. F., *Science*, 1939, **90**, 496.

TABLE I.
Changes in Blood Chemistry and Adrenal Weight Induced by Desoxycorticosterone Overdosage.

Treatment	No. and sex of animals		Body wt	Blood chloride	Blood glucose	Adrenal wt
Desoxycorticosterone acetate						
2 mg in 0.1 cc oil/day for 20 days	6	♂	157 (124-185)	380 (338-396)	99 (92-107)	40 (26-58)
	6	♀	100 (74-135)	335 (326-349)	86 (71-103)	36 (30-52)
Oil controls						
0.1 cc/day for 20 days	6	♂	159 (142-172)	429 (425-431)	95 (83-103)	35 (29-44)
	6	♀	108 (73-145)	430 (420-443)	95 (88-107)	42 (38-53)
Desoxycorticosterone acetate						
10 mg in 0.4 cc oil/day for 20 days	6	♂	159 (147-174)	380 (369-404)	70 (67-79)	19 (15-21)
	6	♀	122 (103-131)	381 (374-410)	86 (75-96)	22 (19-28)
Oil controls						
0.4 cc oil/day for 20 days	6	♂	167 (147-178)	430 (421-456)	82 (75-92)	38 (33-43)
	6	♀	116 (106-131)	447 (438-456)	78 (71-92)	53 (48-65)
Desoxycorticosterone acetate						
10 mg in 0.4 cc oil/day for 20 days	6	♂	150 (140-159)	334 (322-351)	85 (71-96)	20 (17-22)
Cholesterol controls						
10 mg in 0.4 cc oil/day for 20 days	6	♂	150 (140-160)	400 (380-416)	86 (71-96)	40 (35-43)

compound decreases the blood chloride concentration in normal animals. Our experiments clearly indicate, however, that this is the case. The blood chlorides were determined by the Van Slyke method and are expressed in mg of NaCl/100 cc of blood. Blood sugars (Hartmann-Shafer-Somogyi's method) are expressed in mg of glucose/100 cc and the adrenal weight in mg. White Wistar rats were used for all experiments. Desoxycorticosterone was administered once daily by subcutaneous injections in peanut oil, the last injection being given 24 hours before autopsy. All animals were fasted for 24 hours before the determinations. In Table I, which summarizes our findings, the average values are given with the range of variations in brackets.

As the table indicates, the blood chlorides are significantly decreased in each case while the blood sugar does not appear to be affected. The absence of hypoglycemia indicates that overdosage with desoxycorticosterone acetate does not elicit all the symptoms of adrenal insufficiency. Gross estimations of the blood volume of our animals show that a decrease in the amount of the circulating blood—also characteristic of adrenal deprivation—likewise fails to occur in case of desoxycorticosterone overdosage. We mention this particularly because, contrary to the statement of Kendall,[2] who claimed that desoxycorticosterone and its acetate cause no significant adrenal atrophy—and thereby differ from corticosterone and compound E—we noted in agreement with our previous findings[3] that the adrenals became very atrophic. It should be stated, however, that Kendall used relatively small doses of desoxycorticosterone and that from his findings, it appears that corticosterone and his compound E are even more active in causing adrenal involution.

Summary. Experiments on the rat indicate that chronic treatment with desoxycorticosterone acetate in daily doses of up to 10 mg does not lead to any significant external signs of damage but causes marked hypochloremia and adrenal atrophy. Since the blood sugar and blood volume is not significantly influenced by this treatment, the hypochloremia cannot merely be regarded as a sign of general adrenal insufficiency resulting from the atrophy of the adrenal cortex unless one assumes that the compound interferes specifically with the chloride regulating function of these glands. It should be emphasized, however, that even such doses of desoxycorticosterone acetate which do not suffice to cause significant adrenal atrophy produce definite hypochloremia.

2 Kendall, Edward C., *Proc. Am. Soc. Biol. Chem.*, New Orleans, 1940.

3 Selye, Hans, *Canad. Med. Assn. J.*, 1940, **42**, 113.