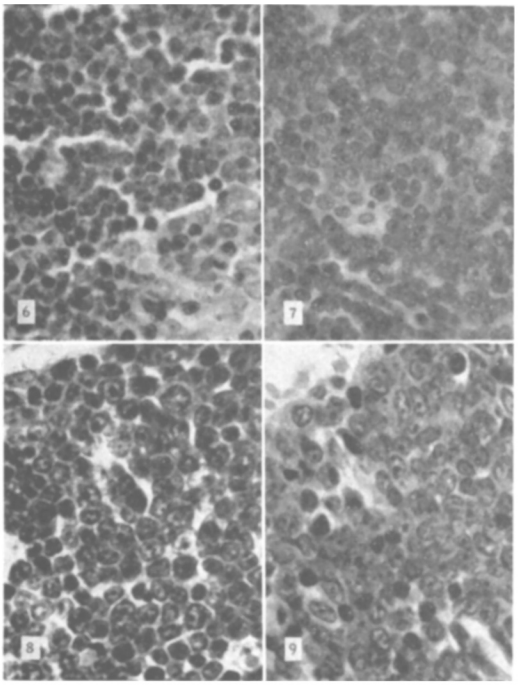

From the thymus of AK/Z mice

FIG. 6. Virus-inj. 58-day-old mouse. Bio-assay negative. × 550.

FIG. 7. Virus-inj. 65-day-old mouse. Bio-assay negative. × 550.

FIG. 8. Virus-inj. 68-day-old mouse. Bio-assay positive. × 550.

FIG. 9. Virus-inj. 73-day-old mouse. Bio-assay positive. × 550.

tion was somewhat below 100%. Some thymuses, which were judged to be leukemic "in situ", were not transplantable. 4. Bioassays indicate the presence of virus in non-leukemic thymuses of virus-injected mice. 5. It is concluded that the pathogenesis of virus-induced thymic lymphoma is similar to that of "spontaneous" lymphoma in the high leukemic strain but occurs at an earlier age.

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Steroids and Carbohydrate Metabolism in the Domestic Bird.* (26369)

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Cortisone has frequently been used as a standard reference compound in the study of glucocorticoid activity in the mammal. In such studies, cortisone has invariably been ranked close to hydrocortisone in activity although slightly less potent(1-3). While numerous investigators have reported a high potency for hydrocortisone in the bird(4-7), few have attempted to compare the activity of hydrocortisone and cortisone. In some instances, cortisone has been utilized in studies in the bird(8,9), but no comparison with hydrocortisone was undertaken. Previous results from this laboratory have indicated that cortisone, in contrast with hydrocortisone, possesses little glucocorticoid activity in the bird(7). In addition, Stamler(4) reported a failure to induce hyperglycemia in the chick with cortisone at doses which were effective with hydrocortisone.

In view of an apparent lack of knowledge concerning the relative effectiveness of vari-

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ous adrenal corticoids on carbohydrate metabolism of the bird it was felt that a comparison of certain steroids should be made with respect to their action upon blood glucose and liver glycogen in the chicken.

Materials and methods. Adult White Leghorn hens were used in the studies on blood glucose. The birds were kept in individual wire cages under conditions of constant temperature, humidity and light throughout period of experimentation. Food and water were supplied *ad libitum*. In each experiment birds were given daily intramuscular injections for periods of 14 days. The hormones were suspended in saline and Tween 80 and injected in a volume of 0.2 or 0.4 ml. Stilboestrol was given in oil solution. Blood glucose determinations were made according to the method of Nelson and Somogyi (10 and 11) on day one (before the initial injection) and on various days thereafter. Blood was obtained from the non-fasted bird by cardiac puncture.

Day-old Arbor Acres White Rock Vantress chicks were used in the glycogen study. The birds were placed in chicken brooders and kept there until placed on experiment. Chicks weighing between 300 and 600 g were starved for 24 hours prior to killing. All hormones were suspended in saline and Tween 80 and injected intramuscularly in a volume of 0.2 ml per injection. The total dose of hormone was divided into 4 equal injections spaced at 2 hour intervals. The birds were decapitated 2 hours following final injection and a sample of liver quickly removed and frozen in a dry ice-ether mixture. Frozen samples were weighed on a torsion balance and digested in hot 30% KOH. Glycogen concentration was determined by the anthrone procedure(12).

Results. Blood sugar and general changes. Hydrocortisone induced a marked and rapid hyperglycemia at the effective dosages of 2.5 to 10 mg per day (Fig. 1). The rise in blood sugar occurred in 24 hours and was accompanied by a marked polyuria, often within 2 to 4 hours after initial injection of the hydrocortisone. Marked polydypsia became apparent after 2 to 3 days of treatment. In general, the peak in the hyperglycemic response was reached in 1 to 3 days and was maintained throughout the treatment. All blood glucose levels returned to normal within 2 to 5 days after cessation of treatment.

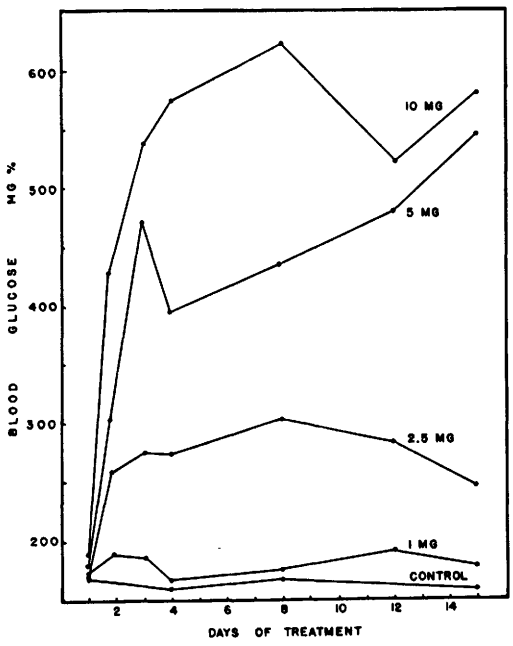

FIG. 1. Hyperglycemia in the hen following daily inj. of 1.0 to 10 mg hydrocortisone for 2 wk.

Only hydrocortisone and corticosterone produced a highly significant hyperglycemia of 300 mg % or more over the 14 day period of treatment (Table I). While 1 mg hydrocortisone induced a slight rise from 174 to 202 mg % blood glucose, 2.5 mg elevated blood glucose to a maximum value of 335 mg % and 10 mg elevated the sugar level to 651 mg %. Likewise, 5 mg corticosterone elevated the blood sugar level to 448 mg %.

In contrast to these results, neither cortisone nor desoxycorticosterone induced a comparable response when given at dosage levels as high as 40 to 50 mg per day. Cortisone showed a very slight hyperglycemic response in that blood sugar rose from 166 to 221 mg % and desoxycorticosterone caused a rise from 150 to 227 mg %. Stilboestrol failed to induce any hyperglycemic response at dose levels of 1 to 2 mg. Testosterone caused a decrease in blood sugar levels from 164 to 125 mg % at a daily dose of 20 mg, and from 190 to 161 mg % at a daily dose of 40 mg.

TABLE I. Blood Glucose Response to Various Hormones in the Hen.

Treatment	No. of birds	Blood glucose, mg/100 ml Initial	Maximum	Minimum
Control	10	170	175	154
Hydrocortisone				
1 mg	7	174	202	159
2.5 "	8	171	335	195
5 "	9	181	546	303
10 "	4	190	651	440
Corticosterone, 5 mg	5	159	448	241
Cortisone				
10 mg	3	190	203	177
20 "	6	174	199	161
40-50 "	15	166	221	161
Desoxycorticosterone acetate, 40 mg	5	150	227	179
Testosterone				
20 mg	6	164	169	125
40 "	4	190	166	161
Stilboestrol, 1-2 mg	5	181	193	168

However, when blood glucose values in the androgen-treated birds were corrected for increase in hematocrit, no significant differences were obtained in blood sugar levels following treatment with testosterone.

Stilboestrol and DCA produced no overall change in body weight. However, DCA caused a marked fluctuation in body weight throughout period of treatment. Changes of over 10% were seen within periods of 3 or 4 days. Testosterone produced a slight gain in weight throughout the experimental period. However, this was followed by a sharp weight depression upon termination of treatment. Cortisone and corticosterone at the doses used and hydrocortisone at doses above 2.5 mg caused body weight depression.

Oviposition was depressed by all hormones used except stilboestrol. Of the other hormones cortisone had the least depressing action.

Liver Glycogen. Hydrocortisone acetate, corticosterone and 11-dehydrocorticosterone induced significant deposition of glycogen in the fasting chick (Table II). Significant increases in the liver glycogen values were obtained with 25 μg of hydrocortisone acetate, 200 μg of corticosterone and 4 mg of 11-dehydrocorticosterone. Since the regression lines for these 3 compounds were somewhat comparable (Table II), it was possible to obtain an estimate of relative potency. If hydrocortisone is assigned an activity of 100, then corticosterone can be shown to possess an activity of 12.5 and 11-dehydrocorticosterone an activity of 1. On the other hand, neither cortisone acetate nor 11-desoxy-17-hydroxycorticosterone produced significant deposition of liver glycogen at doses as high as 16 mg. Thus, neither cortisone acetate nor 11-desoxy-17-hydroxycorticosterone were active in deposition of liver glycogen at dosages that were 640 times the effective dose of hydrocortisone.

Discussion. The present investigation has reaffirmed the observation that the bird is sensitive to glucocorticoid activity(4-7). Contrary to the findings of Brown, Brown and Meyer(8) who used cortisone, the dosage of hormone required to elicit a physiological change in the bird does not appear to be greater than that in the mammal if hydrocortisone is used as the glucocorticoid. Ol-

TABLE II. Liver Glycogen Response to Various Steroids in the Chick.

Treatment	No. of birds	Liver glycogen mg/100 g liver	Slope of curve
Control	59	248	
Hydrocortisone acetate			
25 μg	10	356 ± 29.6	4.1
50 "	10	662 ± 63.7	
100 "	9	738 ± 79.6	
200 "	11	888 ±124.3	
400 "	10	732 ± 41.6	
800 "	10	991 ±100.5	
Cortisone acetate			
4 mg	10	280 ± 35.5	.92
8 "	7	325 ± 56.4	
16 "	10	326 ± 41.4	
Corticosterone			
200 μg	10	348 ± 27.2	3.9
400 "	9	466 ± 50.6	
800 "	8	741 ± 67.0	
11-dehydrocorticosterone			
2 mg	10	296 ± 51.6	4.9
4 "	10	544 ±102.0	
11-desoxy-17-OH-corticosterone			
8 mg	10	246 ± 23.0	.88
16 "	10	290 ± 33.5	

son, Thayer and Kopp(1) using 440 μg of hydrocortisone found a liver glycogen deposition of 730 mg per 100 g of liver in the adrenalectomized rat. In the present study a total dose of 200 μg produced a glycogen deposition of 900 mg per hundred grams of liver. While the 2 experiments are not entirely comparable the results tend to indicate that the bird is no less responsive to glucocorticoids than the mammal.

The point that many investigators have failed to note is the fact that cortisone is virtually inactive as a glucocorticoid in the bird. Thus, the observation of Brown *et al.* must be restricted to cortisone. Certainly enormous doses of this hormone are required to elicit a physiological change in the bird. However, a failure to respond is not obtained for all glucocorticoids. Indeed, hydrocortisone and corticosterone are highly active in the bird. Therefore, it is important that studies involving the use of glucocorticoids in the bird employ corticoids which are physiologically active in the bird. This failure of the chick to respond in a manner comparable to that seen in the mammal has also been noted for the progestogens(13).

The depressant activity of testosterone upon blood glucose levels in the hen has previously been demonstrated(14). It appears that this effect is not a result of direct interference in carbohydrate metabolism of the bird but is, rather, an indirect effect resulting from an increase in hematocrit induced by treatment with testosterone.

Summary. The effects of a series of steroids on the carbohydrate metabolism of the bird were studied using blood glucose and liver glycogen as endpoints. The highly active compounds in the hyperglycemic reaction were hydrocortisone and corticosterone and the active compounds in the liver glycogen test were the above two plus 11-dehydrocorticosterone. Cortisone was inactive in both tests and 11-desoxycorticosterone acetate was tested only in the hyperglycemia reaction and was inactive. If hydrocortisone is assigned an activity of 100 in the glycogen test, then corticosterone shows an activity of 12.5 and 11-dehydrocorticosterone an activity of 1. In direct contrast to the mammal, cortisone is inactive in the bird. Testosterone appears to lower blood glucose but this apparently is a result of an increase in red blood cell number rather than an absolute drop in glucose present in the blood. Stilboestrol had no effect on blood glucose levels.

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Interaction of Myxoviruses with Human Blood Platelets *in vitro*. (26370)

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The interaction of myxoviruses with red blood cells has been the subject of extensive investigation. The kinetics of adsorption, its requirements of cations and the kinetics of elution are known(1). The distribution and chemical identity of the virus receptors