are small and rounded, and cells from tryptose medium are larger, more oblongate, and vacuolated. Electron micrograph studies have confirmed these observations. Fenn(2) found greater phagocytosis of larger than of smaller quartz particles, presumably because the probability of collision of particle and of cell depended on their size. The difference between phagocytosis of *E. coli* cells grown in tryptose and beef infusion media cannot be ascribed to size, since the smaller beef infusion grown organisms are more readily phagocytosed.

The foregoing experiments demonstrate that *E. coli* can be sensitized for phagocytosis by growth in beef infusion medium, and indicate that *in vitro* phagocytosis of microorganisms can be influenced by the medium in which they are cultivated. The sensitizing material cannot be washed free; 10- to 12-fold washing in saline did not decrease the phagocytosis of beef-grown *E. coli*. The absence of a sensitizing system from either the original beef infusion or from culture supernatants, and its appearance during growth, indicate its elaboration by the bacteria.

Summary. 1. The medium in which *E. coli* is grown influences its phagocytosis. Organisms grown in beef infusion are phagocytosed much more than those grown in tryptose medium. 2. The factor(s) in beef infusion is ultrafilterable and stable to autoclaving. 3. The absence of opsonin from beef infusion or from supernatant of beef infusion cultures, and the appearance of sensitization during growth, indicate formation of sensitizing substances by *E. coli* in beef infusion medium.

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Comparison of Effect of Progesterone and 11-Ketoprogesterone upon Glycosuria of Partially Depancreatized Rat. (20133)

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The 11-oxygenated steroid compounds of the adrenal cortex are more potent than their 11-desoxy analogs(1) in affecting carbohydrate metabolism. The data of the present study show that 11-ketoprogesterone has a greater diabetogenic effect in the partially depancreatized rat than does progesterone. The first demonstration that 11-ketoprogesterone is diabetogenic was in unpublished experiments by Dr. R. O. Stafford and Mr. W. P. Baker, Department of Endocrinology, The Upjohn Research Division.

Methods. Male rats of the Sprague-Dawley strain were maintained on Archer Dog Pellets until they were partially depancreatized at a weight of 275 to 280 g. After diabetes was established all of the rats were placed in metabolism cages and force-fed a medium carbohydrate diet(2) by stomach tube each morning (8:30 to 9:30 a.m.) and afternoon (4:15 to 5:00 p.m.). The technics and diet were modifications of those described by Reinecke, Ball and Samuels(3). The test substances were ground into a fine suspension in peanut oil and were administered by subcutaneous injection twice daily. The animals were kept at a temperature of 74 to 78°F. Twenty-four-hour samples of urine were collected at the same hour (8:00 to 8:30 a.m.) and preserved with toluene. Urine glucose was determined by the method of Shaffer and Williams(4). The 11-ketoprogesterone was obtained from the Department of Chemistry of the Upjohn Company, where it was prepared from 11α-hydroxyprogesterone obtained by the microbiological oxidation procedure recently developed in these laboratories(5).

Experiments and results. Exp. 1 (Fig. 1) involved 12 moderately diabetic rats which were observed during a control period of 14 days. Six rats were each treated with progesterone in doses of 1, 2, 4, 8, 16, 32, and 64

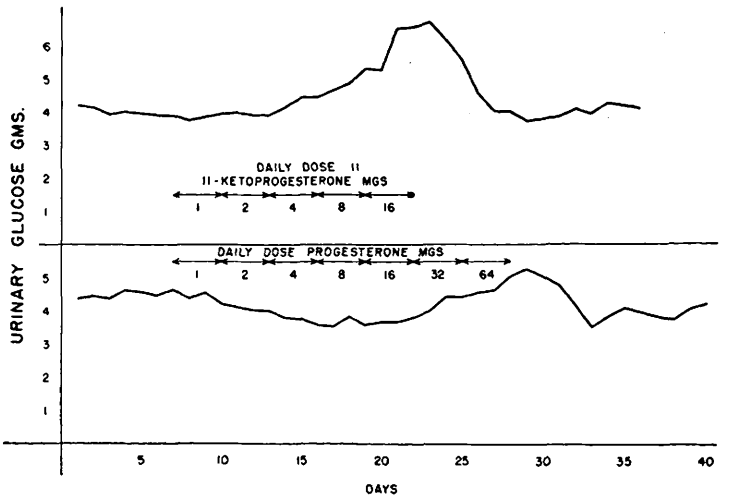

FIG. 1. A comparison of the effects of progesterone and 11-ketoprogesterone upon glycosuria. Averages for 6 rats/group.

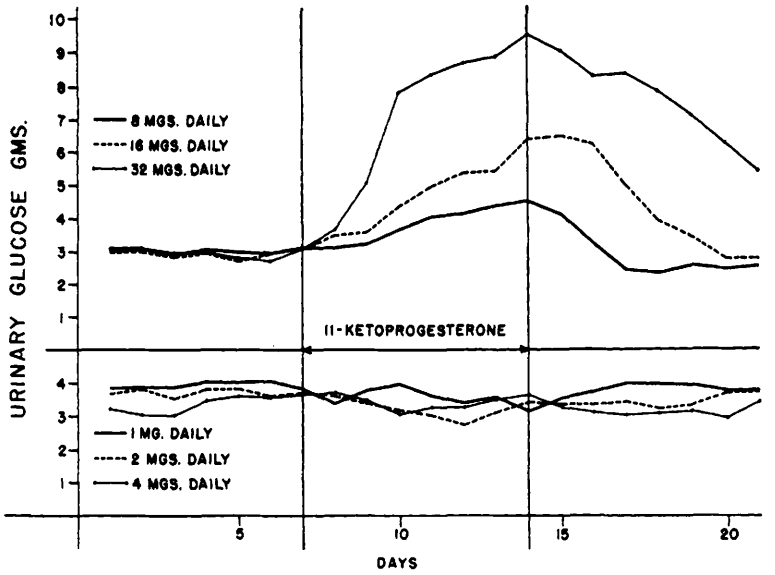

FIG. 2. The effect of different doses of 11-ketoprogesterone upon glycosuria. Averages for 6 rats/group.

mg daily for 3 days per dose. Six rats were each treated with 11-ketoprogesterone in doses of 1, 2, 4, 8, and 16 mg daily for 3 days per dose. When the injections were stopped all of the rats were observed during a final control period of 14 days. During the administration of progesterone in doses of 2 to 16 mg daily there was a small decrease in the average level of glycosuria. At a dose of 64 mg per day there was some rise in the average level of glycosuria. During the administration of 11-ketoprogesterone in doses of 1 to 4 mg daily there was no significant change in the level of glycosuria, but the injection of 8 to 16 mg daily caused a marked increase of the glycosuria of each rat. Equal doses of progesterone were ineffective.

Exp. 2 (Fig. 2) involved 36 moderately diabetic rats which were observed during a control period of 14 days, injected with 11-

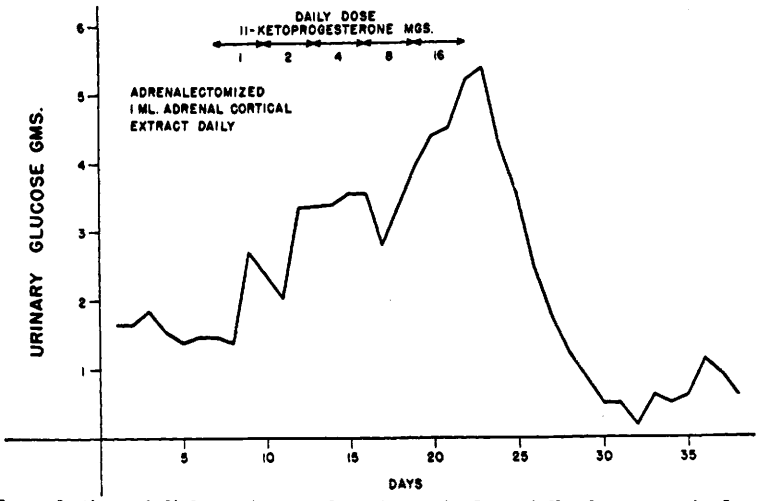

FIG. 3. Exacerbation of diabetes in an adrenalectomized-partially depancreatized rat given 1 ml daily of adrenal cortical extract during the experiment.

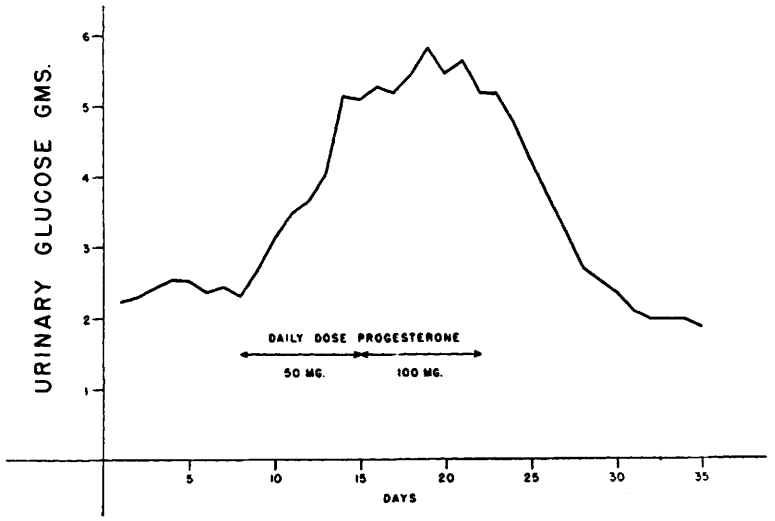

FIG. 4. Exacerbation of diabetes by large doses of progesterone. Average for 6 rats.

ketoprogesterone for 7 days and observed during a final control period of 7 days. Doses of 1, 2, 4, 8, 16, and 32 mg daily were tested on 6 rats per dose. Doses of 1, 2, and 4 mg daily were either ineffective or caused a slight suppression of glycosuria in some of the rats. Doses of 8, 16, and 32 mg daily caused exacerbation of diabetes to an extent which was related to the size of dose. When the injections were stopped the glycosuria fell to pre-injection levels.

Exp. 3 involved 3 adrenalectomized-partially depancreatized rats, each of which was maintained on 1 ml (1 glycogen unit) of adrenal cortical extract per day. Following a control period of 14 days each rat was injected with 11-ketoprogesterone in doses of 1, 2, 4, 8, and 16 mg daily for 3 days per dose. At the end of the injection period the rats were observed during a final control period of 15 days. The injection of 11-ketoprogesterone caused a rise in the level of urinary glucose to an extent that was proportional to the dose. The results are illustrated in Fig. 3.

Exp. 4 (Fig. 4) involved 6 mildly diabetic rats which were observed during a control

period of 14 days, injected with progesterone in daily doses of 50 mg for 7 days and 100 mg for 7 days, and observed during a final control period of 14 days. These doses of progesterone caused significant exacerbation of the glycosuria.

Discussion. Very large doses of progesterone are diabetogenic in the partially depancreatized, force-fed rat. The diabetogenicity of this hormone is enhanced by 11-oxygenation. The diabetogenic action of 11-ketoprogesterone is evident in the absence of the adrenal glands, thereby invalidating the hypothesis that it must be converted to an adrenal cortical hormone by the adrenal cortices before it is biologically active.

Progesterone and 11-ketoprogesterone are each capable of causing partial atrophy of the adrenal glands. The hypothesis was considered that it should be possible to cause some degree of adrenal cortical insufficiency by the administration of these compounds. Since there is a striking amelioration of diabetes in the adrenally insufficient rat we looked for signs of suppression of glycosuria in these experiments. There was a small decrease in the level of glycosuria in some of the rats given 2 to 16 mg daily of progesterone. This small change may or may not have represented suppression of adrenal cortical function. There was no significant suppression of glycosuria by any dose of 11-ketoprogesterone.

Summary. Partially depancreatized force-fed rats were injected with 1 to 100 mg per day of progesterone and 1 to 32 mg per day of 11-ketoprogesterone. Very large doses of progesterone caused exacerbation of the diabetes and 11-ketoprogesterone was found to be significantly more potent in this respect. The diabetogenicity of 11-ketoprogesterone is manifest in either the presence or absence of the adrenal glands.

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Hematologic Studies on Dogs Receiving Low Doses of Total Body Irradiation.* (20134)

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Most studies on the effect of either total or fractional body irradiation on the hematopoietic system have been performed with the application of relatively large doses. The use of such doses produced a multiplicity of changes which probably obscured some of the more basic effects. Therefore, the alteration in the level of circulating granulocytes was not considered to be a satisfactory indicator of the cellular activity in the bone marrow. Accordingly, a detailed study of both bone marrow and peripheral blood cell patterns was made to ascertain the effect of low doses of total body irradiation in both situations.

Method and material. As experimental animals, one- to 2-year-old thoroughbred cocker spaniels and beagle dogs, male and female, weighing from 7 to 11.3 kg were used. These animals were subjected to a total body irradiation of 100 roentgen, given either in single or divided doses. The allocation of the animals to the different groups is shown in Table I. Three cc of cephalic venous blood was drawn into an oxalated 5 cc syringe and transferred at once to a clean test tube. Red and white counting pipets were immediately loaded and counts made in a Neubauer counting chamber. Kingsley stained peripheral blood smears were

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