of each of the following: Coxsackie, ECHO, and poliovirus. Neutralization tests with Coxsackie Group A types 1-8, 10, 12, 14, 16, 17, and 19 were done in suckling mice, and tests with Coxsackie Group A types 9, 11, 13, 15, and 18, Coxsackie Group B types 1-5, ECHO types 1-20, and poliovirus types 1-3 were done in MAF or monkey kidney cultures. In no instance was neutralization observed.

Discussion. The properties of these agents in regard to size, ether resistance, temperature stability, CPE, recovery from fecal specimens, and isolation during summer would place them in the Enterovirus Group. The failure of these agents to produce CPE in monkey kidney cells and disease in laboratory animals suggested that these agents were different from enteric viruses currently reported. The inability of a prototype rabbit antiserum prepared from one of these isolates to neutralize known members of the enteroviruses added further evidence that they are not antigenically related.

Neutralization of virus isolates by 3 different rabbit antiserums would indicate that these agents are antigenically similar. The presence of specific antibody capable of neutralizing the prototype of this group in convalescent human serums would confirm their original presence in these patients. The spectrum of clinical illness associated with these agents will be described separately.

Summary. Agents isolated from fecal specimens in HeLa cell cultures possessed properties similar to enteric viruses. Serologic evidence indicated that these agents were not immunologically related to known members of the Enterovirus Group.

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Blocking Urinary Electrolyte Effects of Desoxycorticosterone with Progesterone in Rats.* (24471)

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Progesterone causes an increased urinary excretion of Na in Addisonian patients treated with desoxycorticosterone (DOC) possibly by competition between the 2 steroids in the kidney; progesterone was not effective in the absence of DOC treatment(1). The present report on electrolyte effects of progesterone in rats supports these findings and shows, in addition, that DOC-like property of the steroid limits blocking efficiency at large doses.

Method. Male Sprague-Dawley rats (150-200 g) were adrenalectomized and maintained with sucrose cubes and tap water overnight. Approximately 24 hours post-operatively, the animals were subcutaneously injected with 2.5 ml 0.85% NaCl solution in shoulder region, and with desoxycorticosterone acetate (DCA) in 0.1 ml Mazola oil. Other animals also received subcutaneous injection of progesterone in 0.5 ml oil. A 4-hour sample of urine was collected in metabolism cages and analyzed for Na and K concentration after dilution to 25 ml with water. Mean values of Na/K ratio were determined after analyses with Beckman flame photometer, using individual or pooled samples of urine. In this method, 12 to 48 μg of DCA cause Na reten-

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tion, some K loss and maximal reductions in the ratio of Na/K. Blocking activity was based on reversal of the Na/K effects of DCA, a less variable measurement than Na or K alone.

Results. Preliminary results from pooled data of separate tests showed ability of progesterone to block electrolyte effects of 12 μg DCA (Table I). Significant blocking of Na/K effects was obtained with 2.4 and 4.8 mg doses; in this method, the Na/K value of 0.94 is significant ($P<0.05$) with 18 rats. The effects of progesterone were interpreted as incomplete (*cf.* mean values of untreated controls) and resulting from simultaneous reversal of Na retention and K loss. Blocking was demonstrated with other dosage combinations of progesterone and DCA (Table II). When given alone at relatively large doses, the steroid mimicked DCA by producing low Na/K values; the change of mean Na/K between the 4.8 and 9.6 mg doses was significant ($P<0.05$). Progesterone appeared progressively less effective in reversing Na/K with increasing doses of 12, 24 and 48 μg of DCA (Table I and II). This observation is interpreted as a reduction in blocking efficiency of progesterone for it occurred with similar dosage ratios of progesterone/DCA and in the presence of approximately equal reductions in Na/K ratio with DCA. Loss of blocking efficiency is believed to result directly from manifestations of DCA-like action with large doses of the steroid.

Discussion. Demonstration of DCA-blocking activity by progesterone confirms the findings of Landau *et al.* in man(1). Inability of the steroid alone to elicit Na/K changes that would oppose DCA action rules out physiological antagonism as a mechanism of its inhibitory effects. As a contrast, that progesterone produced a DCA-like effect suggests an affinity for similar receptor sites in target tissues and the possibility of competition with DCA as discussed by Landau *et al.*(1). The potency of progesterone in rats, as determined by doses required for 50% block of 12 μg of DCA,† is estimated to be a small fraction of the activity described for steroidal lactones (2). Rosemberg also described a minimal activity for progesterone in similar animals(3). At large doses, the DCA-like property in our study and in others(4-9) appears to be an important factor that limits blocking efficiency of the compound. Thus, the steroid possesses unique electrolyte effects by inhibiting and mimicking the action of another steroid; this combination of effects in a compound is not uncommon in study with non-steroids(10,11).

TABLE I. Blocking Urinary Electrolyte Effects of Desoxycorticosterone Acetate with Progesterone.

Treatment/rat			Mean urinary values		
DCA, μg	Progesterone, mg	No. test animals	Na	K	Na/K
		65	6.07	2.80	2.21
12		66	2.30	4.17	.59
"	1.2	35	2.98	3.50	.88
"	2.4	19	3.52	3.44	1.08
"	4.8	23	3.54	3.06	1.15

Na and K values = mM/l concentration after dilution of sample/rat to 25 ml.

TABLE II. Action of Progesterone in Blocking Urinary Na/K Effects of Desoxycorticosterone Acetate.

Treatment/rat		
DCA, μg	Progesterone, mg	Mean urinary Na/K*
24		.46
"	2.4	.89
"	4.8	.88
"	9.6	.97
	4.8	1.15
48		.50
"	4.8	.69
"	9.6	.77
"	19.2	.75
	9.6	.82

* Changes in mean Na/K value of ± 0.24 required for least significant difference ($P<0.05$); No. test rats/treatment = 9-10.

Summary. Progesterone partially blocked the effects of desoxycorticosterone acetate (DCA) on the urinary ratio of Na/K in adrenalectomized rats by simultaneously reversing Na retention and K loss. Progesterone alone at large doses caused DCA-like reductions of the Na/K ratio. Tests of various dosage combinations with DCA suggest that blocking efficiency of progesterone is limited by its DCA-like property. The compound appears to be a competitive inhibitor

† This degree of blockade corresponds to reduction of Na/K effect from 12 to 6 μg DCA, or to change in Na/K response from 0.59 to approximately 1.0.

of DCA and a unique example of a steroid with blocking and DCA-like effects in rats.

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Effect of Certain Flavonoids on the Pituitary-Adrenal Axis.* (24472)

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Oral administration of a number of flavonoids to animals and humans has been shown to result in the urinary excretion of a variety of hydroxy aromatic acids(1,2,3). This finding suggested that, through the medium of their metabolites, flavonoids might influence the pituitary-adrenal axis in a manner comparable to that reported for salicylic acid and related compounds(4,5). The present report concerns an investigation of this possibility with the flavonoids quercetin, dihydroquercetin, and eriodictyol.

Methods. Albino rats from a colony maintained in this laboratory since 1931 were used. Young rats were weaned at about 21 days of age, weighed individually, and sexes segregated. Overweight and underweight rats were discarded. When selected rats were not more than 4 weeks old they were fed for 1 to 4 weeks a basal diet with or without addition of a flavonoid. The basal diet had the following percentage composition: corn meal 73, casein 10, linseed oil cake meal 10, alfalfa meal 2, cod liver oil 3, bone ash 1.5, and sodium chloride 0.5. The quercetin was prepared by acid hydrolysis of the rhamnoside quercitrin(6), and eriodictyol was prepared from dihydroquercetin‡ by the method of Pew(7). At end of feeding period all control and experimental rats were sacrificed, body weights and thymus weights determined, and all organs examined for evidence of gross changes. Comparable experiments were performed with groups of rats which had been adrenalectomized or hypophysectomized. Adrenalectomized rats were placed on the diets immediately after operation and supplied with 0.9% sodium chloride in the drinking water. Hypophysectomized rats were placed on the diets 4 days after operation.

Results. The data on fresh thymus weights, expressed as per cent of body weight for rats receiving quercetin, dihydroquercetin, or eriodictyol, and their respective controls are summarized in Table I. The smaller thymus weights of flavonoid-fed rats as compared with their respective controls are clearly significant. In the case of quercetin, where the largest number of rats was used, an analysis of the individual data, with construction of

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‡ Dihydroquercetin was supplied by Oregon Forest Products Lab., Corvallis.