acceleration of death indicates caution in the use of this drug in the treatment of clinical endotoxin shock.

Summary. We have investigated the hemodynamics of endotoxin shock in the rat and the influence of phenoxybenzamine. Within a few minutes after injecting endotoxin there was a marked rise in portal venous pressure and a fall in both arterial pressure and mesenteric blood flow. Considerable recovery of these values toward control occurred within 30 minutes after administration of endotoxin, following which there was a gradual decline in measured parameters till death. Animals pretreated with phenoxybenzamine had lower portal and arterial pressures and mesenteric blood flow before injection of endotoxin. The magnitude and direction of the early vascular responses to endotoxin were the same as in rats not administered the adrenergic blocking agent; however, arterial pressure and mesenteric perfusion failed to recover from the early effects of endotoxin in rats receiving phenoxybenzamine. Furthermore, prior treatment with phenoxybenzamine conferred no protection against the lethality of endotoxin although it reduced the severity of the intestinal lesions.

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ACTH Stimulation and Dexamethasone Inhibition in Newcomers to High Altitude.* (31317)

FEDERICO MONCLOA, LUIS BETETA, IRMA VELAZCO AND CARMEN GOÑEZ
(Introduced by A. Hurtado)
Instituto de Investigaciones de la Altura, Universidad Peruana "Cayetano Heredia," Lima, Peru

Previous work from this laboratory has shown that sea level residents exposed to high altitude increase their cortisol secretion rate; however, the response of the adrenal cortex was not maximal(1). This may represent: 1) a not intense enough stimulation or 2) adrenal inability of a greater response. The present investigation was undertaken in an effort to answer this question, and also to study whether dexamethasone was able to prevent the transitory hyperactivity of the adrenals when sea level residents are exposed to high altitude.

Material and methods. We have studied 3 groups of young adult males, native residents of sea level. They have been observed in Lima, at sea level, and then taken by train to Cerro de Pasco, Perú (14,000 feet). The departure was at 8:00 a.m. Two hours later the train travels at altitudes over 10,000 feet.

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TABLE I. Urinary Steroids in Sea Level Natives Taken to an Altitude of 14,000 Feet Under ACTH and Dexamethasone Medication.

		17 KS	17 OHCS	17 KGS
Control	(12)	9.4 ± 1.1	7.6 ± .7	15.1 ± 1.8
ACTH—Sea level	(12)	15.3 ± 1.6	48.3 ± 5.0	88.2 ± 6.9
ACTH—High altitude	(12)	14.9 ± 1.6	52.4 ± 6.5	101.7 ±13.0
Control	(7)	11.6 ± 2.4	5.2 ± .4	16.6 ± 2.6
1st day dexamethasone, .5 mg/6 hr (sea level)	(7)	6.3 ± .9	3.1 ± .5	8.1 ± .8
2nd day dexamethasone, .5 mg/6 hr (high altitude)	(7)	5.3 ± .9	1.3 ± .3	4.5 ± .8
Control	(7)	8.5 ± .8	6.5 ± .4	15.3 ± 1.7
1st day dexamethasone, 2.0 mg/6 hr (sea level)	(7)	6.6 ± .4	5.3 ± .6	9.4 ± 1.6
2nd day dexamethasone, 2.0 mg/6 hr (high altitude)	(7)	3.5 ± .3	3.2 ± .4	3.7 ± .6

Figures are means ± S.E. Number of subjects in parentheses.

It arrives at Cerro de Pasco at about 6:30 p.m. We therefore consider that the exposure to high altitude began the day of departure at 10 a.m. The first group was formed by 12 subjects. 24-hour urine samples were collected at 3 different times: The first collection was a control taken at sea level; the second one was obtained under ACTH stimulation at sea level; and the third one when ACTH was again injected the first day of exposure to high altitude. At least 4 days elapsed between the second and the third urinary collections. The protocol of ACTH stimulation was as follows: 80 U were injected intramuscularly at 10 a.m. and 10 p.m. The compound used was an ACTH·Zn preparation (Cortocotrophin Z—Organon). The second group formed by 7 subjects was taken to Cerro de Pasco under dexamethasone administration (0.5 mg/6 hours). Medication started the day prior to the trip and continued during the first day of stay at high altitude.

There were three 24-hour urine collections: a sea level control and both days of dexamethasone administration.

The third group was identical to the second one except that the dexamethasone dose was 2.0 mg/6 hours. The doses are those proposed by Liddle(2) for his dexamethasone inhibition tests.

Urinary 17-ketostreoids (17 KS), 17,21-dihydroxy-20-ketosteroids (17 OHCS) and 17-ketogenic steroids (17 KGS) were measured by the methods used in previous work from this laboratory(3).

Results and comments. Table I summarizes the results of these experiments. The data obtained with ACTH indicate that the adrenal cortex of the subjects studied is capable of the same degree of response either when the stimulation is performed at sea level or during acute exposure to a low oxygen tension environment ($P>0.20$ in all instances). At high altitude, the response to ACTH stimulation is significantly higher than the one obtained by simple exposure(1,4) suggesting that hypoxic stimuli alone were not sufficient to provoke a maximal response of the adrenal cortex. This also indicates that the adrenal cortex of newcomers is still capable of further response, at least with high doses of ACTH. If that is the case with lower doses remains to be studied. In acute exposure to high altitude 17 KS have been found normal or even decreased(1,4). The fact that 17 KS were normally raised when ACTH was given at high altitude favors the possibility that the lack of response in the absence of exogenous ACTH is due to a concomitant decrease in excretion of testicular androgens(5). The results indicate that when dexamethasone is given the hypoxic stimuli are easily blocked. This is well shown by the significant fall in the 17 KS and 17 KGS ($P<0.01$ in all instances). The data on 17 OHCS when the

dexamethasone dose was 2.0 mg/6 hours may be partly reflecting drug excretion in the urine.

The present work suggests that the transitory adrenal hyperactivity occurring during exposure to the hypoxia and other stimuli present at this level of altitude can be either increased or depressed. Such results are of interest when we consider the possibility that the adrenals may play a role in improving tolerance to acute oxygen deficiency.

Summary. The response to ACTH stimulation and to dexamethasone inhibition was studied in young adult males acutely exposed to an altitude of 14,000 feet. The results indicate that the adrenal cortex can be further stimulated with exogenous ACTH during the first day of exposure to an environment of low oxygen tension. Dexamethasone administration was started the day before the trip to high altitude and depressed the excretion of urinary steroids despite the hypoxic stimulus.

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Enzyme Activities in the Preincubation Media from Adrenal Tissue Incubations.* (31318)

CHARLES TSANG† AND ANDRÉS CARBALLEIRA (Introduced by J. S. L. Browne)
Department of Investigative Medicine, McGill University, Montreal, Canada

The preincubation period was first introduced by Saffran and Bayliss(1), who noted that after preincubation adrenal slices produced less corticoids than the non-preincubated tissue in the absence of ACTH. Later, Schönbaum *et al*(2) reported the detection of NADP-dependent dehydrogenases in the incubation or preincubation medium from rat adrenal quarters. Recently we have obtained evidence that the preincubation media from bovine or rat adrenal tissue are capable of metabolizing added labelled pregnenolone or progesterone. These findings may have considerable interest with regard to steroidogenesis *in vitro*.

Material and methods.‡ Fresh bovine adrenal glands obtained at a local abattoir were transported to the laboratory in ice-cold Krebs-Ringer bicarbonate solution (pH 7.4) containing 200 mg% glucose (KRBG). After removal of surrounding fat, the method of Stachenko and Giroud(3) was followed to separate the zona glomerulosa (Z.G.) from the zona fasciculata (Z.F.) with the Stadie-Riggs microtome. Slices of the whole cortex were also used. In the latter case, the gland was cut at right angles to its surface, and the

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† Present address: Endocrine Research Laboratory, Montreal Children's Hospital, Montreal, Canada.

‡ ^{14}C- or 3H-labelled precursors were obtained from New England Nuclear Corp. NAD (nicotinamide adenine dinucleotide, NADP (nicotinamide adenine dinucleotide phosphate, monosodium salt), G-6-P (glucose 6-phosphate, disodium salt) were purchased from Sigma Chem. Co. Other trivial names used in the text: Pregnenolone (3β-hydroxy-pregn-5-en-20-one); 11β hydroxyprogesterone or 11β-OH-P (11β-hydroxy-pregn-4-ene-3,20-dione); 11-deoxycorticosterone or DOC (21-hydroxy-pregn-4-ene-3,20-dione); 17α-hydroxyprogesterone or 17α-OH-P (17α-hydroxy-pregn-4-ene-3,20-dione); 11-keto-progesterone (pregn-4-ene-3,11,20-trione), compound S (17α, 21-dihydroxy-pregn-4-ene-3,20-dione).