active form but as a degraded part of the protein molecule. Such a possibility might explain why most of the methods used, designed to concentrate the urinary protein, do not yield adrenotrophic activity with consistency.

Assuming that adrenotrophin is excreted in human urine, the problem of its detection might be resolved in two ways. The first approach would be to increase greatly the sensitivity of the bioassay procedure so as to permit the use of fresh urine. Were it possible to obtain positive results with a few milliliters of fresh urine, it would then be relatively simple to work out systematically a technic for the concentration and purification of the hormone from urine. However, since the present Sayers' assay procedure is already extremely sensitive (in our hands a minimum of 0.8 μg of pure adrenotrophin was capable of inducing significant L—R values) it seems quite unlikely that any new assay method sufficiently sensitive to permit the use of fresh urine will be soon available.

The alternative approach would be to continue the empirical attempts to purify and concentrate the urine in the hope that a method will be found to permit the administration of large volumes of urine without toxicity to the test animals or appreciable loss of adrenotrophic activity. As such, the method described by Cooke and associates may represent a solution.

Summary. Using a specific and sensitive assay procedure, we have tested the urine of normal persons and of patients having a variety of disease states for its adrenotrophic activity. Tests using both fresh urine and urine concentrates prepared in three different ways were carried out. Contrary to previous reports, no adrenotrophic activity could be consistently demonstrated.

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Plasma Levels of Radioactive Iodine (I^{131}) in Human Tracer Studies. (17472)

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The purpose of the studies reported here was to examine the post ingestion plasma radioiodine curves in euthyroid, hypothyroid, and hyperthyroid subjects as a first step toward analysis of the various factors regulating the levels of such plasma iodine curves.

Methods. Patients were selected after previous clinical and laboratory study had established the presence of a euthyroid, hypothyroid or hypothyroid state. All were in an untreated state. They were given 100 microcuries of radioiodine by mouth before breakfast. The dosage was calculated on the basis of the shipping tag from Oakridge Laboratories. No carrier iodine was added. Each dose was given with 50 cc of distilled water and followed by two 50 cc portions of water to wash the container and mouths of the subjects. Blood specimens were drawn at 30 minutes, 1, 3, 6, 12, 24, and 48 hours; the blood was oxalated and centrifuged at 2500 rpm for 10 minutes. Then 0.2 cc of plasma was pipetted into shallow cups containing one drop of phenolphthalein, 0.2 cc of 0.75 N NaOH and 0.2 cc of detergent (Orvus). Duplicate samples were dried under an infra-red lamp and counted with a bell type Geiger Müller tube (Cyclotron Specialties Co., Model 410-A) and counter (Technical Associates Model GS4). Duplicate specimens of reagents alone, exclusive of plasma, were checked for radio-contamination The counts were corrected for decay with reference to the day of ingestion. Eleven cases of untreated myxedema and 14 non-myxedematous cases (5 hyperthyroid and 9 euthyroid) were so studied.

Results. When the data for the entire 25

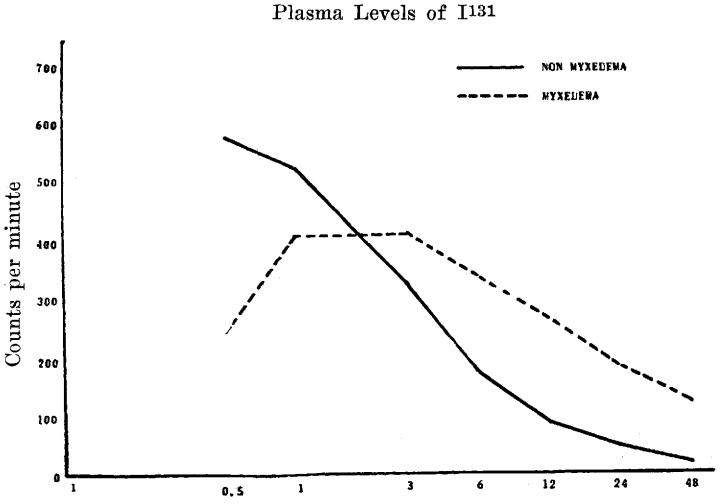

FIG. 1.
Combined plasma curves of the geometric means of the entire myxedematous and non-myxedematous groups.

patients were analyzed, two curves could be obtained, one for the myxedematous and one for the non-myxedematous patients.* Fig. 1 shows these curves; here the geometrical mean (calculated by probit analysis) of counts per minute is plotted on an arithmetical scale against time on a logarithmic scale.

The data from which these curves were obtained are shown in Table I.

Discussion. The major differences noted between these 2 groups of patients (myxedematous and non-myxedematous) may be listed as follows: 1. An early, high peak in the plasma radioactivity of the non-myxedematous group. 2. A later, lower peak in the plasma radioactivity of the myxedematous group. 3. A slower decrease in radioactivity during the first 48 hours in the myxedematous group. These differences appear valid; it seems unlikely that the effect of plasma volume or pre-existing iodine content of plasma would be the cause of these changes. It is more reasonable to suppose that the variations in these two curves are caused by: (a) different rates of absorption of radioiodine from the gastro-intestinal tract, (b) varying rates of excretion of radioiodine by the kidney, (c) speed of formation and storage of thyroid

TABLE I.
Plasma Radioactivity, as Counts Per Minute of the Three Groups of Patients Studied. The individual patient's curve is read horizontally under the time intervals shown.

30″	1′	3′	6′	12′	24′	48′
			Euthyroid			
398	350	218	120	62	10	0
460	372	231	129	62	19	0
518	398	291	170	71	25	0
600	446	313	172	90	18	4
635	480	363	194	91	31	7
671	530	363	231	118	45	20
704	638	443	247	128	70	24
731	676	499	248	128	121	63
860	822	636	272			
			Hyperthyroid			
280	400	148	63	18	16	42
551	417	258	125	57	57	48
555	496	321	190	136	137	195
813	911	385	225	148	183	218
		580	289	198	184	
			Myxedema			
75	212	296	252	184	91	19
88	223	319	253	197	116	31
158	272	349	291	199	117	50
275	345	373	304	202	139	121
312	384	381	393	213	163	125
315	459	396	336	220	216	167
336	465	416	346	274	247	190
347	522	432	358	307	278	199
397	541	493	368	320	325	205
400	568	541	400	385	364	278
542	592	543	565	475		

* The authors are indebted to Frederick J. Moore, M.D., for the statistical analysis of the data.

hormone, (d) re-entry of radioiodine into the blood stream in a protein bound form. How much of a role each one of the above factors might play in the ultimate derivation of the plasma curve requires further study.

While this work was in progress McConahey *et al.*[1] published the results of a similar study of serum radioactivity in hyper-, hypo-, and euthyroid individuals, after ingestion of I^{131}. They reported experiments on 31 patients divided as follows: 17 with hyperthyroidism, 9 euthyroid, and 6 myxedematous (one patient was studied twice, once while euthyroid and then after a "thyroidectomizing" dose of I^{131}). Their patients did not receive similar doses of radioiodine but rather there was a range from 0.1 to 100 millicuries of the drug. McConahey *et al.*[1] felt that there was little if any disturbing radiation effect on the plasma curves from the large doses given to some patients.

The principal finding of difference in McConahey's work from the work presented here, is the failure of our figures to differentiate hyperthyroid and euthyroid individuals. It seems reasonable to suppose that hyperthyroid individuals would show a different rate of increment and decrement of radioiodine in blood after an oral dose than would euthyroid individuals. The differences obtained here, however, were not sufficient to be used for diagnostic purposes and probit analysis of the data would not significantly separate the two groups in the time periods studied.

Summary. Curves of plasma radioactivity were determined for 25 patients after the ingestion of 100 microcuries of radioiodine. The patients were divided into 11 cases of myxedema, 5 cases of hyperthyroidism and 9 euthyroid individuals. The curves were constructed from plasma samples drawn at 30 minutes 1, 3, 6, 12, 24, and 48 hours. It was not possible to statistically separate, at these time intervals, the curves of the hyperthyroid and euthyroid individuals. The curves of the myxedematous patients, however, were significantly different from those of the non-myxedematous patients; thus the myxedematous curves show a later peak level, a lower peak level and a fall more delayed than do the curves of the non-myxedematous patients.

[1] McConahey, W. M., Keating, F. R., Jr., and Power, M. H., *J. Clin. Invest.*, 1949, **28**, 191.

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Acute Adaptation of Rats to Very Low Oxygen Pressure.* (17473)

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In a recent publication[1] the author reported evidence of depressed activity of the thyroid gland in anoxic rats. This thyroid depression may act as an adaptive change which would aid the accommodation to anoxia. Himwich[2] called attention to the evidence of Barach and others[3,4] which indicated that thyroidectomy increases the tolerance of rats to anoxia. Therefore, if anoxia were to result in a degree of functional thyroidectomy, this latter condition should increase the tolerance to more severe anoxia.

The experiments described here indicate that if normal rats are first exposed to anoxia for 2 or more hours at a low temperature, they can then withstand severe anoxia as readily as has been reported for surgically thyroidectomized rats.[3,4]

Method. The low pressure chambers were constructed from 9 liter vacuum desiccators.

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[1] Van Middlesworth, L., *Science*, 1949, **110**, 120.

[2] Himwich, H. E., personal communication, 1949.

[3] Barach, A. L., Eckman, M., Molomut, N., *Am. J. Med. Sci.*, 1941, **202**, 336.

[4] Streuli, H., *Biochem. Z.*, 1918, **87**, 359.