of 3 days raises the adrenal cholesterol concentration above that of control animals. This is particularly striking with a total dose of 5 mg of the adrenotropic preparation. It is to be noted that the increases in cholesterol concentration are greater when calculated on the basis of animal body weight. This is due to the fact that adrenal hypertrophy is occurring under the influence of the hormone, and cholesterol is being deposited in the new adrenal tissue in a concentration at least as great as that present in the adrenal gland before stimulation.

The results in Table I suggest that the adrenotropic hormone is concerned with the regulation of metabolic changes in the adrenal gland involving cholesterol. In view of the fact that the active principles of the adrenal cortex are also steroids, it is possible that variations in the cholesterol content of the adrenal also reflect changes in concentration of steroid hormones. This suggestion finds support in evidence of increased function of the adrenal cortex following adrenotropic hormone administration, as measured by liver glycogen changes[6] and in the report[7] that adrenotropic hormone increases the resistance of hypophysectomized and normal rats to cold, starvation and anoxia.

It may be added that the cholesterol concentration of the adrenals of 45-day-old hypophysectomized rats has been found to be elevated in comparison to the cholesterol levels in the adrenals of unoperated animals of the same age. Cholesterol data similar to those which are reported have also been obtained by employing 2 mg of an adrenotropic hormone fraction prepared from whole sheep pituitary glands by a procedure essentially that described by Li, Simpson and Evans.[7]

Summary. Pituitary adrenotropic hormone produces a distinct lowering of the adrenal cholesterol level 3 hours after injection of 2 mg into 24-day-old male rats; repeated injections over a period of 3 days results in an increase in adrenal cholesterol concentration above that of control animals.

[6] Grattan, J. F., and Jensen, H., *J. Biol. Chem.*, 1940, **135**, 511.

[7] Li, C. H., Simpson, M. E., and Evans, H. M., *Science*, 1942, **96**, 450.

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Excretion of Keto Acids and Hydroxyphenyl Compounds in Pernicious Anemia.

MARIAN E. SWENDSEID, IRVING F. BURTON AND FRANK H. BETHELL. (Introduced by Cyrus C. Sturgis.)

From the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan, Ann Arbor.

It has been found in this laboratory that the urinary excretion values for keto acids of patients with untreated pernicious anemia in relapse show a marked decrease when liver extract is administered by intramuscular injection. Since there are several indications that tyrosine metabolism may be disturbed in pernicious anemia, it was of interest to measure the urinary hydroxyphenyl compounds in this disease in order to determine whether or not their excretion values could be correlated with those of the keto acids. Previous experiments by Becher[1] have shown a rise in blood phenols in pernicious anemia and, in contrast, Volterra[2] observed a low excretion of volatile phenols in the urine in untreated pernicious anemia and a greatly increased excretion of these compounds after liver therapy.

Twenty-four-hour urine samples were collected in acid and analyzed for keto acids by

[1] Becher, E., Litzner, S., and Täglich, W., *Z. klin. Med.*, 1926, **104**, 195.

[2] Volterra, A., *Schweiz. med. Wochschn.*, 1939, **69**, 627.

TABLE I.

Urinary Excretion Daily Values for Keto Acids and Hydroxyphenyl Compounds in Pernicious Anemia.

	Keto acids expressed as pyruvic acid in mg per 24 hr.				Hydroxyphenyl compounds expressed as tyrosine in mg per 24 hr			
	Relapse		Remission		Relapse		Remission	
Patient	Range	Avg	Range	Avg	Range	Avg	Range	Avg
W.H.	228-177	202	107-94	99	741-444	584	292-242	278
H.U.	158-107	135	63-56	60	799-427	513	290-270	280
S.H.	153-103	138	97-68	76	428-308	400	260-201	219
C.O.	135-124	127	93-74	82	682-362	442	287-240	256

the method of Penrose and Quastel[3] and for hydroxyphenyl compounds by the Medes modification of the method of Folin and Ciocalteu.[4] Analyses were made on 4 patients with pernicious anemia before and after liver therapy and, for comparison, on 10 patients receiving the same hospital diet who were apparently healthy except for traumatic injuries.

The analyses on the comparison group gave values for urinary keto acids expressed as pyruvic acid, ranging from 73 to 100 mg per 24 hours with an average of 82 mg. For urinary hydroxyphenyl compounds expressed as tyrosine, the values range from 150 to 230 mg per 24 hours with an average of 195 mg.

The data for the pernicious anemia cases are shown in Table I. At least 4 twenty-four-hour collection specimens were employed in determining the average and range values.

These results indicate that patients with untreated pernicious anemia have an increased excretion of keto acids and hydroxyphenyl compounds, but that after therapy the excretion levels are similar to those of healthy individuals. In every instance, the hydroxyphenyl compounds parallel the keto acids in their excretion values. This would suggest that the keto acid which is excreted in increased amounts in untreated pernicious anemia is an hydroxyphenyl compound. However, since, in both cases, the methods used determine a group of chemically related compounds, this finding does not preclude the possibility that other keto acids or other compounds with hydroxyphenyl groups are involved. Experiments designed to clarify these relations are in progress. The fall in excretion levels of both the keto and hydroxyphenyl compounds in pernicious anemia after institution of therapy is simultaneous with the beginning of the reticulocyte response and precedes any other change in the cellular components of the blood.

These findings point the way to a more detailed consideration of the metabolism of keto and hydroxyphenyl compounds in pernicious anemia.

[3] Penrose, L., and Quastel, J. H., *Biochem. J.*, 1937, **31**, 266.

[4] Medes, G., *Biochem. J.*, 1917, **26**, 917.