

This Week's Citation Classic

Nelson D H & Samuels L T. A method for the determination of 17-hydroxycortico-steroids in blood: 17-hydroxycorticosterone in the peripheral circulation. *J. Clin. Endocrinol. Metab.* 12:519-26, 1952. [Dept. Biochemistry, Univ. Utah Coll. Med., Salt Lake City, UT]

Cortisol or 17-hydroxycorticosterone is found to be present in the peripheral circulation of man. A method is described for the measurement of this steroid in blood. [The **SC[®]** indicates that this paper has been cited over 270 times since 1961.]

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"Early in 1949 I came as a postdoctoral fellow into the laboratory of Leo T. Samuels, head of the department of bio-chemistry, University of Utah College of Medicine. Samuels' laboratory was heavily involved in studying the synthesis and metabolism of the androgenic steroids. He thought that it would be of interest to also look at the corticosteroids and thus the task assigned to me on arrival in the laboratory was to evaluate methods for the estimation of the corticosteroids. Each of those available proved to be nonspecific and the results obtained were highly variable. I was enough of a novice in the field of endocrinology that it came as a surprise to me that no one had identified the major corticosteroid secreted by the adrenal cortex and thus I took as my first task identification of the major steroids secreted by the gland. After many trials and errors we were able to demonstrate that 17-hydroxycorticosterone was the major corticosteroid in the adrenalvenous blood of dogs.¹ This was accomplished using a lipid extraction followed by chromatographic separation and measurement by ultraviolet absorption of the steroids present in blood coming from a can-nulae placed in the adrenal veins of dogs. Application of this technique to peripheral blood failed to demonstrate any steroids due to the much lower levels of the hormone present.

"At about this time Porter and Silber

described a new color reaction with some specificity for the dihydroxyacetone structure found in the 17, 21-dihydroxy-20-ketone of cortisol. Their initial applications of this procedure had also failed to demonstrate measurable hormone in peripheral blood.² Using much larger quantities of blood and paper chromatography which recently had become available, we then demonstrated cortisol in the peripheral blood of man. As we now knew the hormone that was present and approximate amount we combined our extraction and chromatography procedure, which had been successful in the isolation of cortisol from blood, with a micromodification of the color reaction of Porter and Silber and were able to measure cortisol in the peripheral blood of man. This procedure was then employed by us and others to measure cortisol in blood including normal levels, demonstration of diurnal variation, and response to ACTH and other physiologic stimuli. We introduced the term '17-hydroxycorticosteroid' to indicate that the color reaction was not totally specific for cortisol, although this was by far the major steroid in the circulation measured by the procedure. This method was replaced by a simplified application of the Porter-Silber reaction which did not require chromatography, a protein binding assay, and radioimmunoassays.

"The many citations of the paper are probably due to the fact that this was not only the first reproducible method for the measurement of '17-hydroxycorticosteroids' in peripheral blood or plasma but also the first demonstration that cortisol was the major circulating corticosteroid, and establishment of the amounts present in the circulation. We have always been pleased that although the methodology was somewhat primitive by modern standards, the levels of cortisol in blood measured by this method were essentially the same as those which continue to be measured by other procedures."

1. **Nelson D H, Reich H & Samuels I. T.** Isolation of a steroid hormone from the adrenal-vein of dogs. *Science* 111:578-9, 1950.
2. Porter C C & Silber R H. A quantitative color reaction for cortisone and related 17, 21-dihydroxy-20-ketosteroids. *J. Biol. Chem.* 185:201-7. 1950.