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FOLLOWING ORAL HYDROCORTISONE DOSAGE

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Aerospace Medical Division (AFSC)
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FOREWORD

This report was prepared by the following personnel at the USAF School of Aerospace Medicine:

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ABSTRACT

A single 20-minute parotid fluid sample was collected prior to, and six 20-minute samples were collected subsequent to the oral administration of 50 mg. of hydrocortisone to 30 healthy young adult males. Blood was drawn before dosage and 2 hours thereafter. The following conclusions were drawn:

The serum free 17-OHCS increase after dosage was highly significant. Hydrocortisone did not exert a significant effect on parotid fluid flow rate.

A highly significant increase in parotid fluid free 17-OHCS levels was found in the 40- to 60-minute sample. A significant response was elicited in all subjects within 2 hours.

This technical documentary report has been reviewed and is approved.


ROBERT B. PAYNE
Colonel, USAF, MSC
Chief, Operations Division

CORTICOSTEROIDS IN HUMAN PAROTID FLUID FOLLOWING ORAL HYDROCORTISONE DOSAGE

1. INTRODUCTION

The oral administration of hydrocortisone, as well as certain of its synthetic analogs, produces significant increase in parotid fluid free 17-hydroxycorticosteroid (17-OHCS) levels 2 hours after dosage (1). No information is available as to the time required for these increases in steroid concentration first to become evident.

The present study was designed to determine the amount of time required for parotid fluid free 17-OHCS levels to increase significantly after oral hydrocortisone dosage and to follow this steroid response over a 2-hour period.

2. MATERIALS AND METHODS

Subjects were 30 systemically healthy males between 17 and 22 years of age. Times of arising and retiring, diet, and environmental exposure were very similar for all participants. All participants had fasted for at least 12 hours.

A venous blood sample was collected from each subject between 7:30 and 8:00 a.m. and parotid fluid collection was instituted immediately thereafter. A parotid collection device (2) was placed over the orifice of the right duct and each subject was provided three size-32 pure gum rubber bands as masticatory stimulants. A 10-minute accommodation period was allowed and the sample discarded. A 20-minute control parotid fluid sample was then collected; each subject was given 50 mg. of hydrocortisone by mouth, and six additional 20-minute parotid fluid samples were collected from each participant. A second

blood sample was collected 2 hours after drug dosage. Each subject thus provided two blood samples and seven parotid fluid samples for analysis.

Parotid fluid volume was read to the nearest 0.05 ml. in graduated collection tubes. The free 17-OHCS concentration of both serum and parotid fluid was determined by the method of Peterson et al. (3), which employs the Porter-Silber (4) reaction of phenylhydrazine-sulfuric acid with 17,21-dihydroxy-20-ketosteroids. Statistical analyses were performed on the data for parotid fluid flow rate and for parotid fluid and serum free 17-OHCS.

3. RESULTS AND DISCUSSION

The means for parotid fluid flow rate varied from .534 (S.D., .260) ml./min. for the control sample to .588 (S.D., .320) ml./min. for the 0- to 20-minute postdrug sample. Means for the five subsequent samples were .564 (S.D., .273), .567 (S.D., .279), .563 (S.D., .276), .563 (S.D., .277), and .571 (S.D., .282) ml./min., respectively. There was no significant effect of hydrocortisone on parotid flow rate.

Parotid fluid free 17-OHCS means, both before and after dosage, are shown in figure 1. The mean of 2.73 $\mu\text{g.}/100$ ml. for the 0- to 20-minute time interval was not significantly different from the control mean of 2.57 $\mu\text{g.}/100$ ml. The mean of 4.51 $\mu\text{g.}/100$ ml. for the 20- to 40-minute samples was significantly different from the control mean but only at the .05 level. The difference between the means for the later samples and the control mean was highly significant. The number of subjects with increased parotid fluid free 17-OHCS

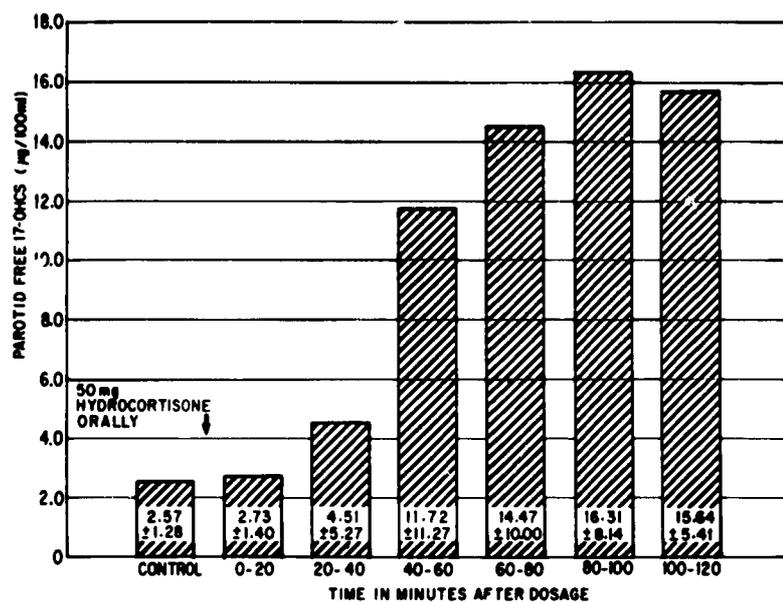


FIGURE 1

Parotid fluid free 17-OHCS for 30 subjects given 50 mg. hydrocortisone orally.

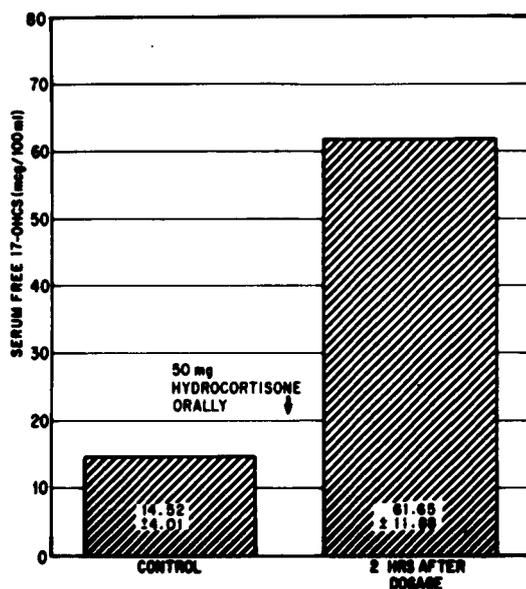


FIGURE 2

Serum free 17-OHCS for 30 subjects before and 2 hours after 50 mg. hydrocortisone orally.

levels was calculated for each time interval. At intervals 0 to 20, 20 to 40, 40 to 60, 60 to 80, 80 to 100, and 100 to 120 minutes, significant steroid increases were found for 0, 13.3, 46.6, 76.6, 93.3, and 100.0% of participants, respectively. Using probit analysis, estimate was made of the time required for the subjects to demonstrate a significant response. An interval of 27.3 minutes was estimated for a 10% subject response; a 50% subject response required 54.3 minutes, and a 90% response time was calculated as 81.3 minutes.

Means for serum free 17-OHCS before and after dosage are shown in figure 2. The pre-treatment mean of 14.52 (S.D., 4.01) µg./100 ml. compared quite favorably with our recently reported (5) baseline mean of 14.82 (S.D., 3.91) µg./100 ml. found for 1,000 directly comparable subjects at the same time of day. Two hours after hydrocortisone dosage, the serum mean had undergone a highly significant increase to 61.65 (S.D., 11.88) µg./100 ml.

The findings of the present study confirm the previous observation that, at 2 hours after hydrocortisone dosage, significant increases in both serum and parotid fluid free 17-OHCS are present. Further, when parotid fluid samples were collected at 20-minute intervals within this 2-hour period, a highly significant increase in the mean for steroids in this fluid was seen in the 40- to 60-minute sample. A significant increase in parotid fluid 17-OHCS was elicited in all subjects, but the time required for this response varied greatly between subjects. It is not possible to estimate the proportion of this intersubject variation that might be due to differences in gastric emptying time and intestinal absorption.

Since this study was not designed to induce stimulation of the adrenal cortex, no conclusions can be drawn concerning the relative increase of steroids in blood and parotid fluid as they might be affected by alterations in cortical activity. Rather, the results point out that, under the conditions of this study, there is a rapid reflection of blood steroid changes in parotid fluid. Studies are now in progress in which ACTH is being administered to systemically healthy subjects and to persons with diagnosed or suspected disorders of the adrenal cortex. The goal is a simple clinical test for adrenal disease which does not involve multiple blood sampling.

ADDENDUM

Since the completion of this study the authors have been privileged to study a case of Cushing's syndrome, apparently due to adrenal hyperplasia. A control parotid fluid sample was collected; the patient was given 40 units of gel ACTH intramuscularly, and parotid fluid was again collected at 60 and at 120 minutes after injection. The free 17-OHCS concentration in each of these three samples was 5.6, 21.9, and 27.1 $\mu\text{g./100 ml.}$, respectively. This response far exceeded that seen in any of our normal subjects studied under comparable conditions. For example, in 18 normal males, the preinjection mean for parotid fluid free 17-OHCS was 4.1 $\mu\text{g./100 ml.}$, this figure increasing to 10.3 $\mu\text{g./100 ml.}$ 2 hours after the administration of 40 units of ACTH intramuscularly (Shannon et al. *J. Clin. Endocr.* 19:1477 (1959)). The maximal concentration found for any subject was 16.0 $\mu\text{g./100 ml.}$ No data are available for 1-hour postinjection levels in normal subjects for comparison with the remarkably high value of 21.9 $\mu\text{g./100 ml.}$ found for the patient exhibiting Cushing's syndrome.

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<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-63-12. CORTICOSTEROIDS IN HUMAN PAROTID FLUID FOLLOWING ORAL HYDROCORTISONE DOSAGE. Apr. 63, 3 pp. incl. illus., 5 refs.</p> <p>A single 20-minute parotid fluid sample was collected prior to, and six 20-minute samples were collected subsequent to the oral administration of 50 mg. of hydrocortisone to 30 healthy young adult males. Blood was drawn before dosage and 2 hours thereafter. The following conclusions were drawn:</p>	<p>1. Dental sciences</p> <p>2. Parotid fluid</p> <p>I. AFSC Task 775602</p> <p>II. Shannon, I. L., Katz, F. H.</p> <p>III. In ASTIA collection</p>	<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-63-12. CORTICOSTEROIDS IN HUMAN PAROTID FLUID FOLLOWING ORAL HYDROCORTISONE DOSAGE. Apr. 63, 3 pp. incl. illus., 5 refs.</p> <p>A single 20-minute parotid fluid sample was collected prior to, and six 20-minute samples were collected subsequent to the oral administration of 50 mg. of hydrocortisone to 30 healthy young adult males. Blood was drawn before dosage and 2 hours thereafter. The following conclusions were drawn:</p>
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