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Effects of Serum Uric Acid and Parotid Flow Rate on Concentration and Secretion Rate of Uric Acid in Parotid Fluid.* (31097)

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A prime objective of this laboratory is the development of additional capabilities in biomedical monitoring by the use of parotid fluid. Such endeavor is intimately related to the use of this fluid in the diagnosis of disease, an area in which a measure of success has been attained(1-3). Uric acid measurements, generally carried out on serum or urine, are extremely important in a diagnostic sense. Increased levels of this end product of purine metabolism are seen in association with increased nitrogen retention and increased urea, creatinine, and other nonprotein nitrogen constituents of blood.

The present study is a primary effort in evaluating parotid fluid uric acid as a possible diagnostic measurement. It explores the relationship between uric acid values in serum and parotid fluid and determines the effect of flow rate on parotid fluid uric acid. The flow rate level is very low and the range is narrow since no exogenous stimulants were employed. The correlation coefficients are of the between-subject type since only one saliva sample was provided by each subject.

Materials and methods. Subjects were 508 males between the ages of 17 and 22 years. Each was found fully qualified for unrestricted military duty by recent medical examination. Times of arising and retiring, physical exertion, intake of food and liquids, as well as environmental and emotional exposure were very similar for all participants. This was a barracks-dwelling group of USAF enlistees with all of the homogeneity that this implies. Each subject had resided in this environment and ingested the basic military ration for at least 3 weeks prior to participation.

Subjects fasted overnight and a 2-hour parotid fluid collection period began at approximately 7:30 a.m. No exogenous stimulants were employed, this being an attempt to obtain, as nearly as possible, the resting secretion of the gland. Subjects were seated comfortably in a quiet portion of the temperature-controlled laboratory and a parotid sampling device(4) was placed over the right Stensen's duct with an absolute minimum of manipulation. Extraneous interferences were prohibited and close supervision assured that each subject remained awake and alert. Parotid saliva was collected in graduated tubes and volume was read to the nearest 0.05 ml. A single venous blood sample was drawn from each participant at approximately 9:30 a.m.

Uric acid content of both parotid fluid and serum was measured on the Technicon AutoAnalyzer by a sodium cyanide-phosphotungstic acid procedure in which the blue color of the reaction is read at 660 mμ in a 15 mm light path. Such a procedure includes in serum approximately 10% chromogen that cannot be acted upon by uricase.

Results. The relationship between serum and parotid fluid uric acid concentrations is shown in Fig. 1. For the group of subjects with the lowest serum uric acid level (less than 4.01 mg/100 ml) the parotid fluid con-

* The opinions expressed in this paper are those of the author and do not necessarily reflect official USAF policy.

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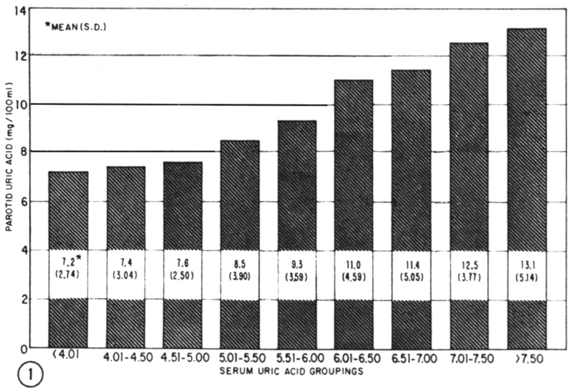

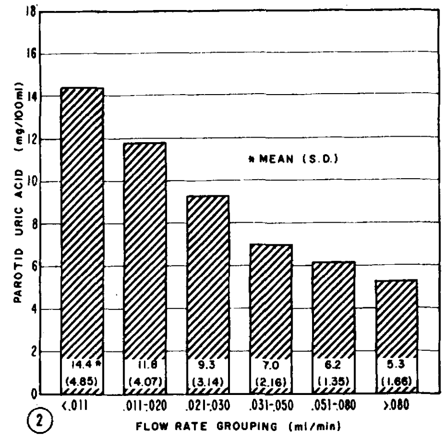

FIG. 1. Parotid fluid uric acid levels as related to serum concentration.
FIG. 2. Parotid uric acid in mg/100 ml for flow rate groups (n = 508).

centration was also the lowest (7.2 mg/100 ml). In groups containing increasingly more uric acid in the serum, there was a corresponding progressive increase in parotid fluid uric acid content. The correlation coefficient between these 2 variables for all 508 subjects (r = .398) was significantly different from zero at the .01 level. A similarly significant coefficient (r = .336) was found for serum uric acid and parotid fluid uric acid secretion rate in micrograms per minute. The mean for serum uric acid for all 508 participants was 5.70 mg/100 ml, while for parotid fluid uric acid concentration the mean was 9.52 mg/100 ml, and that for parotid secretion rate was 2.47 μg/minute. Frequency distributions for uric acid concentration are presented in Table I.

Table II presents serum uric acid means for the 508 subjects divided into 6 flow rate groups. An analysis of variance was performed on these data and parotid flow rate was not found to be significantly related to serum uric acid concentration. The correlation coefficient between these two variables (r = .026) confirmed this lack of significant relationship.

The effect of parotid flow rate on parotid fluid uric acid was very definite. As parotid flow rate increased the parotid fluid uric acid concentration decreased in stepwise fashion (Fig. 2). This difference between flow rate groups was highly significant (F = 66.856; P<.001) and the correlation coefficient between flow rate and parotid fluid uric acid concentration (r = —.524) was significantly different from zero at the .01 level. When the parotid fluid uric acid values were converted to secretion rate in μg/min and studied in relation to parotid flow rate, the correlation assumed a positive rather than a negative na-

TABLE I. Frequency Distributions for Serum and Parotid Fluid Uric Acid for 508 Subjects.

Serum uric acid (mg/100 ml)	No. of subjects	Parotid fluid uric acid (mg/100 ml)	No. of subjects
<3.51	2	<3.00	1
3.51–4.00	19	3.01– 5.00	50
4.01–4.50	40	5.01– 7.00	110
4.51–5.00	80	7.01– 9.00	114
5.01–5.50	77	9.01–11.00	82
5.51–6.00	98	11.01–13.00	60
6.01–6.50	87	13.01–15.00	37
6.51–7.00	56	15.01–17.00	22
7.01–7.50	28	17.01–19.00	16
>7.50	21	19.01–21.00	6
		21.01–23.00	5
		23.01–25.00	4
		>25.00	1

TABLE II. Serum Uric Acid Values for Parotid Flow Rate Groups.

Parotid flow rate groups (ml/min)	Serum uric acid (mg/100 ml)	
	Mean	S.D.
<.011	5.57	.98
.011–.020	5.76	1.13
.021–.030	5.75	1.08
.031–.050	5.56	.89
.051–.080	5.59	.93
>.080	6.05	1.16

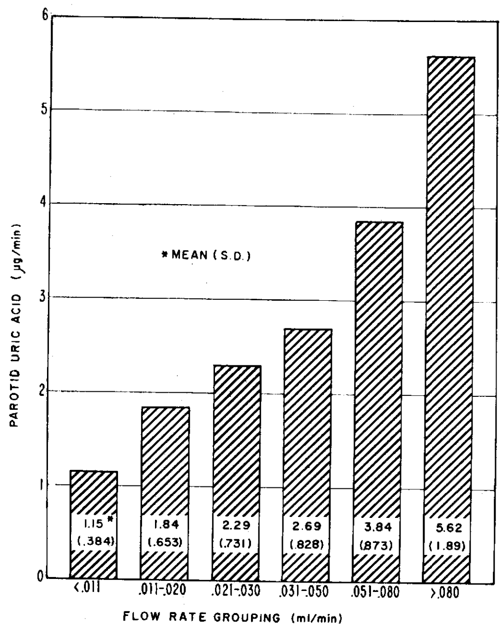

FIG. 3. Parotid uric acid in μg/min for flow rate groups (n = 508).

ture. As parotid flow rate increased the parotid fluid uric acid secretion rate increased progressively. This positive relationship (Fig. 3) was highly significant ($F = 154.096$; $P < .001$) and the correlation coefficient between these 2 variables ($r = .796$) was significantly different from zero at the .01 level).

Discussion. The presence of uric acid in saliva has long been established(5-12). Possible systemic implications of salivary uric acid levels have also received attention. Lowenstein and Gies(7) found that saliva uric acid promptly registered variations in endogenous uric acid metabolism. They also found an almost immediate rise in saliva uric acid after muscular exertion and a definite relationship between the amount of uric acid found in saliva and the quantity eliminated simultaneously in the urine of normal people on an ordinary diet.

Lewis and Updegraff(8) calculated the salivary uric acid concentration to be approximately 30% of the blood level. In a later publication(10) this figure was found to be 40.1%. Morris and Way(11) studied blood and saliva from patients with blood uric acid concentration ranging up to more than twice the normal level. In most pathological cases studied the uric acid in saliva was diminished markedly, often even to the point of disappearance. Dodds(12) reported that saliva uric acid concentration was equal to 55% of the blood concentration and that no constant relationship, except that salivary levels were much lower, could be found. Zipkin, Hawkins, and Mazzarella(13) found a significant decrease in uric acid content of paraffin stimulated parotid saliva collected from rheumatoid arthritis patients. It was pointed out, however, that this might be a salicylate induced decrease.

The results of the present study point out a definite correlation between serum and parotid fluid uric acid levels and demonstrate promise that saliva analyses might be substituted for blood measurements. It is significant that subjects with high uric acid levels in serum also tended to have high levels in unstimulated parotid fluid but this does not answer the question of whether or not, within an individual, salivary uric acid levels undergo concomitant changes as the serum concentration is modified. Studies are in progress involving patients with high blood uric acid levels undergoing hemodialysis on the artificial kidney and normal subjects being administered uricosuric drugs.

Lowenstein and Gies(7) found that flow rate exerted a definite influence on saliva uric acid levels. Nash and Morrison(14) noted very little change in saliva uric acid content when flow rate was increased by the mechanical stimulation of chewing paraffin. Morris and Jersey(9) recommended the use of resting saliva for uric acid analysis and pointed out the hazards of employing exogenous stimulants. They compared resting whole saliva uric acid concentration to saliva collected with various stimulants. Paraffin increased flow by 429% and increased uric acid content by 63%; acetic acid elevated flow by 560%, uric acid by 71%; pilocarpine increased flow by 502%, uric acid by 183%; atropine decreased flow by 88%, and decreased uric acid concentration by 66%. It was concluded that uric acid, more than any other constituent, represented the actual cellular activity and that it might well serve as an index of gland metabolism.

The highly significant effect of flow rate on parotid fluid uric acid found in the present study must be interpreted with care. It can be concluded only that subjects with high flow rates tended to have low uric acid concentrations while those with low flow rates generally had much higher uric acid levels.

The results of the present study indicate that the longer a given portion of parotid fluid remained in the ducts (the lower the flow rate) the higher the concentration of uric acid became. Reabsorption of water could serve as an explanation for change if reabsorption balanced secretion or if neither reabsorption nor secretion of uric acid took place in the ducts. A more appropriate explanation is that both reabsorption and secretion do occur and that in the extremely low flow rate range the secretion process is of prime importance. The degree of reabsorption, if present, is subject to speculation. A convenient explanation is that the reabsorption of urate is either total or that it is limited to a specific capacity. Thus, while saliva traverses one portion of the duct system, uric acid is removed from the flow fluid and, during the remainder of its time in the ducts, uric acid is secreted into the saliva by ductal cells. With reabsorption bringing uric acid to a relatively common concentration the level of this constituent in the exiting fluid would then become dependent upon the length of time that the fluid spends in the secreting portion of the duct system. The higher flow rates would thus produce lower concentration while the slowly exiting fluid would contain a higher level. Experiments are in progress to test the tenability of this concept.

Summary. Parotid fluid was collected without exogenous stimulation from 508 healthy young adult males. The mean uric acid concentration in serum was 5.70 mg/100 ml and that for parotid fluid was 9.52 mg/100 ml. A significant correlation ($r = .398$) was found between serum and parotid fluid uric acid concentrations. Parotid flow rate was negatively correlated ($P < .001$) with uric acid concentration ($r = -.524$) but positively correlated ($P < .001$) with the secretion rate (μg/min) for uric acid ($r = .796$). A tentative explanation of uric acid transport in the parotid system is offered. Reabsorption, probably in the proximal portion of the duct system, brings uric acid to a relatively common concentration by a total or limited capacity process and uric acid is secreted into the saliva by cells of other ductal segments. Final concentration thus depends upon the length of time the fluid spends in the ducts—the longer the time (the lower the flow rate), the higher the uric acid concentration. This concept is being tested.

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