Blood Pressure, Sodium Intake, and Sodium Related Hormones in the Yanomamo Indians, a "No-salt" Culture

By William J. Oliver, M.D., Edwin L. Cohen, M.D., and James V. Neel, M.D., Ph.D.

SUMMARY

The Yanomamo Indians are an unacculturated tribe inhabiting the tropical equatorial rain forest of northern Brazil and southern Venezuela who do not use salt in their diet. The group therefore presented an unusual opportunity to study the hormonal regulation of sodium metabolism in a culture with life-long extreme restriction of dietary sodium, with parallel observations on blood pressure. Blood pressures increase from the first to second decade but, in contrast to civilized populations, do not systematically increase during subsequent years of life. In twenty-four hour urine collections on adult male Indians, excretion of sodium averaged only $1 \pm 1.5 \, (\text{sd}) \, \text{mEq}$. Simultaneous plasma renin activities were elevated and comparable to those of civilized subjects placed for brief periods on 10 mEq sodium diets. Similarly, excretion rates of aldosterone equaled those of acculturated subjects on low sodium diets. The findings suggest that the hormonal adjustments to life-long low sodium intakes are similar to those achieved in acute sodium restriction of civilized man. Parenthetically, these elevated levels of aldosterone and renin were probably the norm for man during much of human evolution and suggest that the values observed in civilized controls are depressed by an excessive salt intake in contemporary diets.

Additional Indexing Words:

Aldosterone Renin

NUMEROUS OBSERVERS have reported a low frequency of hypertension among unacculturated peoples, ^{1 3} but few of these studies have been conducted close to the time of first contact. During the past seven years, we have been involved in an effort to develop improved insights into the biomedical and genetic changes and adaptations that have accompanied civilization. The principal subjects of our investigations have been the Yanomamo Indians of northern Brazil and southern Venezuela, still for the most part a relatively undisturbed tribe of inland, tropical rain forest Indians, to whom salt is unknown except where very recently introduced. When our initial examinations revealed the failure of blood

pressure to increase with age, it was decided to explore their sodium balance and determine, for the first time, some of the hormonal adjustments characteristic of a no-salt culture.

Sodium requirement

Materials and Methods

Subjects

described in detail elsewhere,4 approximately 12-15,000 Yanomamo are distributed among some 150 villages in an area of approximately 100,000 square miles. Although briefly contacted by some of the early explorers of this region, semi-permanent contacts of any of their villages with non-Indians date back only to the early 1950s when a few missionaries began to penetrate the region. At present there are some 16 small missions among the Yanomamo, as well as several government health stations. However, these are for the most part located on navigable rivers, and since the Yanomamo are not primarily a riverine people, even today there are probably Yanomamo villages yet to be visited by a non-Indian. The accumulating linguistic and genetic data indicate that the tribe has had a high degree of isolation for at least the past several thousand years.4 In 1965 they were selected as the subjects of an extensive multidisciplinary study. The data to be reported result from some seven expeditions to the tribe, beginning in 1966.

The Yanomamo material culture is extremely simple. The major staple of their diet consists of the cooking banana, *musa paradisica*, supplemented by irregular additions of game, fish, insects, and wild vegetable foods. The tribe has had no access to sodium chloride except where the substance has been introduced by Caucasians, i.e., it was not a trade item in the indigenous culture.

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From the Departments of Pediatrics and Communicable Diseases, Internal Medicine, and Human Genetics, University Hospital, University of Michigan, Ann Arbor, Michigan.

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Address for reprints: William J. Oliver, M.D., F2442 C. S. Mott Children's Hospital, Ann Arbor, Michigan 48104.

Blood Pressure

The selected subjects consisted of all available inhabitants of sixteen independent villages. In a few instances, several Indians were absent from a village on a hunting trip, but this was infrequent. Selection of the villages was determined by identifying a cross-section of widely dispersed living sites of the Yanomamo in Brazil and Venezuela, as remote as possible, but still accessible by small plane and/or boat. The resultant sampling included villages from all of the major geographic areas inhabited by the Yanomamo.

The examinations which defined the blood pressure values were part of complete physicals, exclusive of rectal and pelvic examinations, performed on 506 Indians during the expeditions of 1966, 1967, and 1968. Only the findings with repsect to the blood pressure will be reported here. Pressures were obtained from the right arm with the subjects supine, using either a Tycos Aneroid Sphygmomanometer or a Baum Mercurial Sphygmomanometer. No significant difference between the two types of instruments was discerned. For correlation with the studies upon sodium balance, blood pressures were obtained with a Tycos Aneroid Sphygmomanometer in an additional sample of these Indians in 1970 and 1972. These latter data are presented with the observations on sodium excretion.

Excretion of Creatinine, Sodium, Potassium, and Chloride

On four different occasions, in two different years (1970 and 1972), a total of 44 plastic containers of two liter capacity were distributed early in the morning to males with the standard instructions: void now, then save all samples until the next morning, void into the container just before bringing the samples in. Additional containers were available if needed. Subjects were weighed and blood pressures measured at the time the containers were distributed; a few escaped weighing and measurements of blood pressure. Most subjects were adults, but a few teenagers were included. Urine volumes were measured when the specimens were returned, and aliquots transferred to suitable containers, containing thymol crystals. These were refrigerated in styrofoam chests containing ice until reaching the laboratory. Samples were frozen until analyzed. Two of the collection sites were remote villages, two were at missions where the missionaries were not providing salt. The collections were complicated by the rather difficult conditions under which the field work was conducted, as well as the free and unfettered nature of the Yanomamo psyche, which found it difficult to take seriously the concept of a 24 hr urine.

Control subjects consisted of members of the expedition who ingested a normal diet augmented by table salt ad lib. Similar samples were obtained from these subjects.

Blood Samples

Blood samples were obtained in these ambulatory subjects between 8 and 10 a.m. upon completion of the urine collections. For renin, blood was collected in EDTAcontaining Vacutainers and promptly centrifuged in a handdriven instrument. The harvested plasma was placed in styrofoam chests containing ice, and maintained cold until reaching the laboratory where samples were frozen until measurements of plasma sodium and chloride.

assayed. Aliquots of these plasma samples were used for

Sodium and potassium were determined by flame photometer, chloride by the titratometric method utilizing the Buchler-Cotlove Chloridometer. 6 Creatinine was determined by the method of Hare.7 The inclusion of measurements of creatinine was deemed necessary as a rough index of the completeness of each sample. It is known that creatinine excretion per kilogram of body weight, while relatively constant, varies considerably.8 For young adult male Caucasians, values range from 8.7 to 32.3 mg/kg/24 hr.9 There are no comparable data for subjects of this study who usually weigh between 44 and 52 kg. On the basis of the literature regarding the variability of creatinine excretion, 24 hr collections containing less than 500 mg of creatinine were considered to be incomplete. To substantiate that conversion of creatinine to creatine had not occurred in the samples before determination of creatinine, measurements of creatine were made in a representative group of samples upon receipt in the laboratory. No measurable conversion to creatine was found.

Urinary aldosterone excretion rate was measured utilizing a radioimmunoassay for aldosterone. 10 Plasma renin activity was determined by the method of Cohen et al. 11 Specimens were drawn and processed as described above. In order to correct for the contribution of generation of Angiotensin I that occurred between the time of collection and processing, or any nonspecific effects upon initial binding that could have been present in these particular plasmas, all samples were assayed directly for Angiotensin I prior to incubation at 37°C. These blank values were significantly higher $(0.67 \pm 0.43 \text{ ng/ml})$, than values determined in normal North American Caucasians ingesting a 10 mEq Na diet for three days $(0.157 \pm .025 \text{ ng/ml})$, and probably represent generation of Angiotensin I following collection and during processing. These blank values were subtracted from the values obtained following incubation. Normal values for plasma renin activity measured in two hour continuously ambulatory (8-10:00 a.m.) males and females (age 22-62 years) are 4.3 ± 0.5 ng/ml/hr (general diet) and 17.7 ± 2.20 ng/ml/hr (10 mEq Na $^+$ diet for three days) $(N = 24)^{11}$

Results

Blood Pressure

In table 1 are presented the mean systolic and diastolic blood pressures by decade of life and by sex for the 506 subjects in the first series of studies. As has usually been observed, both systolic and diastolic pressures increase from the first to second decades of life. However, in contrast to the usual finding in civilized populations, blood pressure does not continue to increase thereafter but even seems to decline slightly. The variability in blood pressure has been partitioned into that determined by the regression on age, that determined by the variability of group means, and the residual. To this end, the change in blood pressure with age (exclusive of the first decade) has been treated as a simple linear function of the form:

$$\hat{\overline{\mathbf{x}}}_{i} = \overline{\mathbf{x}} + \mathbf{b} (\mathbf{A}_{i} - \overline{\mathbf{A}})$$

^{*}We are greatly indebted to the following physicians for their participation in these examinations: Drs. Powell Baker, Lowell Weitkamp, Miguel Lavrisse, and Charles Patten.

Table 1
Blood Pressures Obtained in the Yanomamo Indians

	No of	Syste	olic	Diastolic	
Age	subjects	Mean	SD	Mean	SD
Males					
0-9	59	93.2	8.9	58.6	9.2
10-19	63	107.5	9.6	66.9	8.6
20-29	5 8	108.4	8.6	69.1	7.3
30-39	30	105.9	8.9	69.4	5.7
40-49	27	106.6	7.6	67.1	6.8
50+	7	100.0	8.2	63.7	8.1
Females					
0-9	60	95.7	12.0	61.6	8.0
10-19	72	104.9	9.7	64.5	10.8
20-29	62	99.8	10.0	62.6	6.6
30-39	32	99.5	10.5	62.9	6.3
40-4 9	19	97.6	11.4	62.2	16.8
50 +	17	105.7	17.7	64.1	7. 3

where $\hat{\overline{x}}_i$ = estimated pressure for a specific age class, \bar{x} = mean pressure for entire population, \bar{A} = mean age for entire population, A_i = mean age of age class.

The results for males and females are presented separately in table 2. Although the slope of the regression is negative in all four analyses, significance is not achieved in any case. There is significant (unexplained) variability of the age group means about the predicted mean in the case of female systolic pressure, occasioned primarily by the group older than 50 years. We conclude that although at this stage of the study we are not entitled to speak of a decline of blood

pressure with age, it is clear that the increase with which we are so familiar in civilized populations is not observed. The data are subject to the usual reservation with a population in which mortality rates are high throughout adult life¹² that there might have been a selective elimination of those with higher blood pressures, but this seems an unlikely explanation.

Urinary Excretion of Sodium, Potassium, Chloride and Creatinine

Analyses of aliquots from the 44 male subjects revealed highly variable 24 hr creatinine values. Utilizing the criterion that 24 hr collections containing less than 500 mg of creatinine were incomplete, 26 of the 44 samples from Indians and all eight from the controls were adjudged to be complete. On a per kilogram basis, the lowest creatinine excretion for the Indian subjects was 11.0 mg, within the range accepted as normal.9 The results of the analysis for weight, urine volume, and creatinine are shown in table 3 and for Na⁺, K⁺ and Cl in table 4. Results for the minerals are expressed both as mEq/L and per 24 hr. The findings with respect to controls fall well within the accepted range of normal, either on a per liter or 24 hr basis. 13 The relatively small volume of urine excreted by the controls, especially as compared to the smaller Indian, possibly reflects the observed tendency of the members of the expedition to perspire more than the naked Indian, even after acclimatization of several weeks, as well as unmeasured

Table 2

The Results of an Analysis of the Regression of Blood Pressure on Age in Yanomamo Males and Females

Category	Source of variation	Sum of squares	Degrees of freedom	Mean squares	F
Male, systolic	Slope of regression	233.70	1	233.70	2.97
(b =0951)	Variation of group means about regression	283.15	3	94.38	1.20
	Within group	14171.77	180	78.73	
	Total	14688.62			
Female, systolic	Slope of regression	194.23	1	194.23	1.62
(b =0766)	Variation of group means about regression	1515.32	3	505.11	4.21*
	Within group	23611.29	197	119.85	
	Total	25320.84			
Male, diastolic	Slope of regression	2.60	1	2.60	0.05
(b =0100)	Variation of group means about regression	350.98	3	116.99	2.07
	Within group	10157.80	180	56.43	
	Total	10511.38			
Female, diastolic	Slope of regression	33.30	1	33.30	0.36
(b =0317)	Variation of group means about regression	146.66	3	48.89	0.53
	Within group	18188.94	197	92.33	
	Total	18368.90			

^{*}Significant at 0.01 level.

Table 3

Body Weight, Twenty-four Hour Urine Volume and Excretion of Creatinine in Yanomamo Indians and Control Subjects

Subjects	Weight (kg)	Urine volume (ml)	Creatinine mg/24 hr (mean ± sp)	Creatinine coefficient (mg/kg/24 hr)
Indians $(N = 26)$	48.41* ±4.46	1000.88 ± 398.82	932.70 ±367.60	19.3
Controls $(N = 8)$	72.67 ± 6.10	665.87 ± 211.47	$1768.94 \\ = 470.07$	22.1

 $[*]Mean \pm sp.$

differences in intake. The excreted creatinine/kg/24 hr is well within the range of normal⁹ as is the $Na^+:K^+$ ratio of $2.74.^{13}$

Turning now to the data on the Indians, we note first the very small amount of sodium per liter and the striking reversal of the usual Na+:K+ ratio. Such values are simply not observed in spot samples from members of civilized populations, except under conditions of extreme therapeutic restriction of salt.14.15 The average excretion of creatinine for the 26 samples from Indians, selected as described, is 19.3 mg/kg/24 hr. This is sufficiently close to accepted values as well as to the values found in the controls to suggest that these are intact 24 hr collections. The data on Na⁺:K⁺, and Cl thus appear valid and indicate average 24 hr excretions of 1 mEq of Na+ and 152 mEq of potassium with a 24 hr value for Na+ excretion of 0.1 mEq being the lowest we observed, as is the Na+:K+ of 0.066. It should be noted that even if our collections were deficient by 50% — most unlikely in view of the creatinine values — the mean 24 hr Na+ values would still be only 2 mEq.

The belief that the described data for 24 hr urinary $Na^+:K^+$ are not unique for a selected sample population of these Indians but reflect the usual state of balance, is supported by a series of analyses of random spot urine samples obtained during the two expeditions. For 45 spot samples obtained on adult males, the mean concentration of urinary sodium was $2.0 \pm 4.8 \, \text{mEq/L}$ and of potassium $106.7 \pm 45.9 \, \text{mEq/L}$, yielding a $Na^+:K^+$ of 0.019. For 21 spot samples on 21 adult females, many of whom were lac-

tating and/or pregnant, the mean concentration of urinary sodium was 1.0 ± 1.7 mEq/L and of potassium 144.8 ± 63.0 mEq/L, resulting in a Na⁺:K⁺ of 0.007.

Simultaneous plasma sodium concentrations of ten randomly selected Indian males averaged 140 mEq/L; three controls averaged 142 mEq/L. For chloride, plasma concentrations were 106 mEq/L for both the Indian subjects and the controls. Hemolysis, although minimal, prevented valid measurement of plasma potassium.

Urinary Aldosterone and Plasma Renin Values

Of the 11 subjects who submitted acceptable 24 hr urine specimens and for whom plasma renin samples were assayed, all demonstrated aldosterone excretion in excess of the upper limit of normal obtained for Caucasians on a general diet, i.e., $17.3 \,\mu g/24 \, hr$ (table 5). Furthermore, the values were within the range, or exceeded the range, seen in normal people following short term low sodium diets. Similarly, all plasma renin values were within or exceeded the range seen in normal ambulatory North Americans ingesting short term $10 \, \text{mEq}$ sodium diets $(2.9-33.0 \, \text{ng/ml/hr})$.

Discussion

The principal contribution of this study is to our understanding of the hormonal response to severe, chronic salt restriction. It is recognized that the observations establishing the severity of this salt restriction lack the precision to be obtained in a clinical research unit. Field conditions were rather difficult. Neither sodium intake nor loss other than through urine could be measured. Nevertheless, it seems clear that the very low 24 hr sodium excretion observed in most of our subjects — of the order of 1 mEq — must correspond to sustained sodium intakes lower than any previously recorded for man. Expressed in absolute terms, several individuals excreted as little as 2 mg of sodium per 24 hours, a remarkable physiological feat.

That blood pressure should remain low throughout life under these conditions is scarcely surprising in view of the observations of others in field studies, ^{1 3} as well as the established clinical effects of salt restriction

Table 4

Urinary Excretion of Sodium, Potassium and Chloride in Yanomamo Indians and Control Subjects

Subjects	mEq Na+		$mEq K^+$		mEq Cl-	
	Liter $(mean \pm sd)$	24 hr (mean ± sp)	Liter (mean ± sp)	24 hr (mean ± sp)	$\begin{array}{c} \text{Liter} \\ \text{(mean } \pm \text{sd)} \end{array}$	$\begin{array}{c} 24 \text{ hr} \\ \text{(mean } \pm \text{sd)} \end{array}$
Indians	0.97	1.02	158.97	152.16	15.26	13.70
(N = 26)	± 1.22	= 1.51	± 57.64	± 74.51	= 9.76	\pm 7.16
Controls	152.94	104.35	58.81	38.66	152.45	102.31
(N = 8)	± 68.68	± 64.11	± 9.92	± 11.23	± 70.99	± 59.82

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Table 5							
Urinary Excretion of Sodium, Potassium, Chloride and Aldosterone Compared with Plasma Renin Activity and Blood Pressure in Yanomamo Indians and Control Subjects							

Subjects	Na+ mEq/24 hr	$^{ m K^+}_{ m mEq/24~hr}$	Cl- mEq/24 hr	Aldosterone excretion $(\mu g/24 \text{ hr})$	Renin activity (ng/ml/hr)	Blood pressuret
Indians						
1622*	3.44	152.64	7.06	76.9	7.92	102/60
1631	.53	234.36	6.05	155.4	3.93	98/72
1668	.30	128.00	5.44	59.9	8.68	88/52
1671	.33	150.00	6.38	74.3	19.97	104/60
1690	.31	175.74	9.31	65.8	11.36	94/40
1691	.38	114.03	7.56	49.8	7.96	94/60
1699	.71	194.36	12.56	27.3	10.21	90/50
16104	.90	390.72	15.18	164.9	7.98	98/50
16116	.61	178.56	16.37	42.0	53.79	102/50
16119	.42	194.65	29.58	62.9	8.91	122/60
16120	6.76	291.10	22.58	40.5	3.43	120/52
Mean = sp	1.34	200.38	12.55	74.52	13.10	
	± 2.01	± 80.17	± 7.80	± 44.94	± 14.17	
Controls						
E.M.	208	75	241.9	3.8	2.52	120/80
H.S.	254	54	233	3.5	9.61	142/82
W.O.	193	$\overline{52}$	201	1.0	1.46	122/78
A.B.	142‡	44‡	171.9‡	_	6.19	120/82

^{*}Expedition identification number for individual subjects.

on blood pressure. 14, 15 However, in the case of the Yanomamo, we wish to avoid simplistic explanations concerning the effects of salt. The Yanomamo are seldom obese and rarely demonstrate weight gain with advance in age. Furthermore, they are physically a highly active people with an overtly aggressive life style very different from that of present western culture. 5 A role for other factors in these findings regarding blood pressure cannot be excluded.

MacFarlane¹⁷ and Prior et al. ¹⁸ have documented increments in resting blood pressure with acculturation (which included increased salt intake) for the Chimbu Melanesians of the central highlands of New Guinea and the Melanesians of the Cook Islands, respectively. Inasmuch as the area inhabited by the Yanomamo is now yielding to the inroads of civilization, the present report could serve as the point of departure for a prospective study drawing on a broader set of parameters than previous investigations.

Acute stimulation of the renin-angiotensin system in normal people ingesting low sodium diets has been well documented. ¹⁹ Chronic stimulation of the system in normals²⁰ and hypertensives²¹ ingesting benzothiadiazine drugs has also been reported. The effects of chronic, severely restricted sodium intake upon the renin-angiotensin-aldosterone system have not been reported. Therefore, this study is unique in that it involves subjects with life-long low levels of

sodium intake. It is likely that chronic elevation of aldosterone secretion is involved in the homeostatic mechanisms affecting sodium balance in these people. That renin is similarly involved seems very likely in view of the high prevalence of elevated values for renin in these same subjects.

It is well known that potassium is a direct stimulus for aldosterone secretion^{22, 23} and it is possible that it has played a significant role in maintaining the impressive elevation of aldosterone secretion in these potassium-loaded subjects. However, it should be noted that chronic potassium loading has not affected suppression of the plasma renin in these subjects. Therefore, it would appear that the stimulus of sodium deficiency supercedes that of potassium suppression upon renin activity in people on chronic low sodium-high potassium intakes. As a result, two stimuli for increased aldosterone secretion remain chronically active.

The chronic elevation of renin without hypertension once again emphasizes the importance of the level of body sodium in affecting hypertension in man. In fact, the elevation of renin in these subjects is appropriate for a low level of body sodium and may be important in maintaining normal blood pressure. ²⁴ Chronic elevation of aldosterone secretion must play a continuing role in the renal conservation of filtered sodium in these people. It could also be important either alone or in association with other corticosteroids

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[†]Blood pressures obtained with subjects in the sitting position.

[‡]Concentration in mEq/L on spot sample only.

in the mobilization of sodium from bone to maintain effective plasma volume during periods of potential crisis, such as hemorrhage, gastrointestinal electrolyte loss, pregnancy, and lactation.^{25 28} Studies by our group are in progress to ascertain the normal characteristics of adult females in this society who are chronically stressed, in relation to sodium balance, by continuous lactation and/or pregnancy.

In the overview, the data presented in this study, combined with those previously reported, ^{1 3} suggest that the customary quantities of salt in contemporary diets far exceed the amount necessary to maintain sodium balance and result in depressed levels of the sodium-related hormones, renin and aldosterone. These observations on an unacculturated people provide further support for Dahl's conclusion that in civilized societies "salt *appetite* is not to be equated with salt *requirement*."²⁹

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