DATA EVALUATION RECORD

SODIUM AZIDE

Study Type: Non-guideline; Hypotensive Action of Sodium Azide in Humans and Rats

Work Assignment No. 4-01-152 (MRID 47221401)

Prepared for Health Effects Division Office of Pesticide Programs U.S. Environmental Protection Agency 2777 South Crystal Drive Arlington, VA 22202

Prepared by Pesticides Health Effects Group Sciences Division Dynamac Corporation 1910 Sedwick Road, Building 100, Suite B Durham, NC 27713

Primary Reviewer: Michael E. Viana, Ph.D., D.A.B.T.

Secondary Reviewer: Ronnie J. Bever, Jr., Ph.D.

Project Manager: Michael E. Viana, Ph.D., D.A.B.T.

Quality Assurance: Steven Brecher, Ph.D., D.A.B.T. Signature: _______ Date: ______

Signature: ______ Date: ______

Signature: ______ Date: _____

Signature: ______ Date: _____

Disclaimer

This Data Evaluation Record may have been altered by the Health Effects Division subsequent to signing by Dynamac Corporation personnel.

SODIUM	AZIDE/107701
DODIUM	

EPA Reviewer: <u>Nancy McCarroll</u> Toxicology Branch, Health Effects Division (7509P)	Signature: _ 	
EPA Secondary Reviewer: <u>Gregory Akerman, Ph.D.</u>	Signature: _	
Toxicology Branch, Health Effects Division (7509P)		
	Date: _	
Work Assignment Manager: Myron Ottley, Ph.D.	Signature:	
Registration Action Branch 3, Health Effects Division (7	7509P) Date:	
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DATA EVALUATION RECORD

<u>STUDY TYPE</u>: Non-guideline; Hypotensive Actions in Humans and Rats

PC CODE: 107701

DP BARCODE: D327025

TEST MATERIAL (PURITY): Sodium azide (purity not provided)

SYNONYMS: Sodium trinitride; NaN₃

<u>CITATION</u>: Black, M. M., Zweifach, B. W., and Speer, F. D. (1954) Comparison of hypotensive action of sodium azide in normotensive and hypertensive patients. Department of Pathology and Clinical Pathology, New York Medical College, Flower Fifth Avenue Hospital, and Department of Biology, Washington Square College, New York University, New York, NY. Study No.: 2005-1 HA, 1954. MRID 47221401. Published: *Proc. Soc. Exptl. Biol. Med.* (1954) **85**: 11-16.

SPONSOR: Not applicable

EXECUTIVE SUMMARY: In a non-guideline study (MRID 47221401) performed to investigate the effects of (NaN₃) on lowering blood pressure in patients with diagnosed essential hypertension, NaN₃ (purity and batch/lot # not provided) in water was orally administered to both normotensive and hypertensive humans. Informed consent was not obtained. For the acute phase, 30-35 patients were studied. NaN₃ in water was administered at doses of 0.65 to 1.3 mg ($\approx 0.01-0.02$ mg/kg, assuming a 70 kg human), and blood pressure measurements were recorded at 2 to 5 minute intervals. For the chronic phase, subjects were divided into groups of 30 hypertensive patients (documented cases of elevated blood pressure, recorded "from 12 months to as long as 10 years") and 9 normotensive individuals (9 controls made up of normal healthy students and laboratory personnel as well as patients with diverse types of cancer). The effects of chronic administration were examined by oral administration of 0.3-1.3 mg (approximately 0.004-0.02 mg/kg, based on a 70-kg adult) once daily or three times daily for 5 days to over 2 years. Organ toxicity, particularly to the kidney, heart, or liver, was investigated through routine clinical examinations, and the effects of different routes of administration (oral, intravenous, or sublingual) on blood pressure were

compared. Finally, in an animal phase of testing, rats (sex, strain and number not specified), made hypertensive either by a "figure-of-eight" loop on the kidney or by a partial ligation of the renal artery 3 months prior to exposure, received intravenous (i.v.) administrations of unspecified doses of NaN₃.

Results indicate that 13 patients (initial systolic pressures were $\geq 190 \text{ mm Hg}$), receiving an acute dose of 0.65 to 1.3 mg had an average drop of 43 mm Hg (range –30 to –65 mm Hg) in blood pressure. A marked decrease in the blood pressure of "some" hypertensive patient was reported as early as 45 to 60 seconds after treatment with 1.3 mg (0.02 mg/kg, based on a 70-kg adult). The blood pressure reduction was more pronounced in one of these patients after 8 days of treatment with 1.3 mg/3X/day. By contrast, administration of a comparable dose 3 times per day to 9 normotensive individuals (total daily dose = 0.6 mg/kg, based on a 70-kg adult) for 10 days had no sustained effect on blood pressure. We assume that no effects were also seen after 1 day of dosing.

In the chronic phase of testing, the 30 hypertensive patients, treated with 0.65 to 1.3 mg NaN₃ (at least 3X/day) for 10 days up to 2 $\frac{1}{2}$ years, showed the following signs: 5 cases showed minimal changes in blood pressure; 10 exhibited a significant fall but the diastolic pressure remained above 100 mm Hg; and 15 had persistent blood pressure levels near normal and the 3 patients, who were checked for clinical signs, showed no evidence of damage to kidneys, heart, or liver and no changes in blood pressure to normotensive levels that persisted for 14 days to 2 months after the cessation of treatment. In all hypertensive patients, while a typical response to acute administration was observed, in most patients a gradual return to hypertensive blood pressure levels was noted within 1 to 3 days following cessation of treatment. A majority of patients showed a definite improvement in subjective symptoms, including headache, chest pains, and general mental outlook.

NaN₃ administered daily for more than 1 year did not cause toxicity to the kidney, heart, or liver. Kidney function, as evidenced by the quality and quantity of urine output, blood urea nitrogen, and non-protein nitrogen, was unimpaired, and there were no changes in bowel habits or urinary function. An occasional patient complained about a transient sensation of "pounding in the head" shortly after administration of the compound. Additionally, repeated treatment with NaN₃ (for an unreported interval) resulted in an increased sensitivity to the drug for 20 patients, necessitating a daily dose reduction from 0.5 to 0.25 mg 3X/day (≈ 0.004 mg/kg, based on a 70-kg adult). Whether this was a toxic effect other than a further lowering of the blood pressure was not made clear. NaN₃ administered intravenously was effective in lowering the blood pressure of a hypertensive patient for a period of several hours. Additionally, in patients treated by sublingual administration, three drops containing a total of 0.1 mg of NaN₃ was as effective as a 0.65 mg dose administered orally.

Overall, the human data suggest that an acute total dose as low as 0.65 mg 3X/day (total daily dose = 1.95 mg or 0.03 mg/kg, based on a 70-kg adult) had a beneficial effect on patients with high blood pressure while a total dose of 1.3 mg 3X/day (total daily dose = 3.9 mg or 0.06 mg/kg, based on a 70-kg adult) had no adverse effects on normotensive individuals. Similarly, chronic doses as low as 0.25 mg (0.004 mg/kg, based on a 70-kg adult) produced beneficial effects on the blood pressure of hypertensive patients while doses of 0.01 to 0.02 mg/kg (3X/day) for periods up to

1 year had no adverse effects on kidneys, heart or liver on the basis of routine clinical studies in hypertensive patients.

In surgically-hypertensive rats, NaN₃ also produced a fall in blood pressure. However, as this dose represented a greater dose level by body weight (0.6-0.7 mg/kg for rats, compared to 0.02 mg/kg for humans), it appeared that hypertensive humans were more sensitive to the hypotensive effects of NaN₃ (\approx 30 to 35X) than surgically-hypertensive rats. Additionally, intravenous administration of comparable doses of NaN₃ to normotensive rats, either acutely or by slow infusion, had no effect on blood pressure. In contrast to other hypotensive drugs, rats which had been subjected to hemorrhage showed no deleterious effects of treatment on either blood pressure or peripheral circulation in the mesentery, and direct application of NaN₃ to the surface of the mesentery had no observable dilation action on the constricted blood vessels in the terminal vascular beds of rats subjected to hemorrhage.

Based on the above information, a NOAEL for hypertensive patients could not be established; however, a NOAEL of 0.06 mg/kg for normotensive individuals was determined.

This study is classified acceptable/non-guideline.

<u>COMPLIANCE</u>: Signed and dated Data Confidentiality, GLP Compliance, and Quality Assurance statements were not provided; however, the study was performed prior to the adoption of Good Laboratory Practice standards. Furthermore, this study was never intended to be submitted to the Agency for review.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Sodium aside (NaN ₃)
	Description:	Not provided
	Batch #:	Not provided
	Purity:	Not provided
	Compound stability:	Not provided
	CAS #of TGAI:	26628-22-8
	Structure:	
		$-N^+ \equiv N$
		N N

2. Vehicle: water

B. PROCEDURES AND STUDY DESIGN

Na

- 1. <u>Background and purpose</u>: In a previously published scientific article¹, it was noted that in cancer patients with co-existing hypertension, acute administration of NaN₃ caused a temporary lowering of blood pressure toward normotensive levels, while the blood pressure of normotensive individuals was not appreciably changed. Therefore, the purpose of this study was to use NaN₃ as a tool for investigating hypertensive disease in man and experimental animals. Additionally, it was theorized that repeated administration of NaN₃ is considered to be a highly toxic compound (lethal range = 10 mg/kg subcutaneously); however, a much lower oral dose (0.01-0.02 mg/kg) produces a decrease in blood pressure in humans.
- 2. Information on patients: A total of 35 patients (nine normotensive [systolic pressures <140 mm Hg]; 26 hypertensive) were monitored for the effects of acute oral administration on blood pressure. Chronic observations were made on a group of 39 patients (nine normotensive [diastolic pressures <90 mm Hg]; 30 hypertensive) that received NaN₃ orally over periods from five days to 2 1/2 years. In addition to the above studies, one hypertensive patient was dosed intravenously, and three hypertensive patients were dosed sublingually. The normotensive patients included normal healthy controls (students and laboratory personnel) as well as cancer patients. Patients with elevated blood pressures were documented cases of essential hypertension, recorded from 12 months to 10 years after diagnosis. Additionally, several patients suffering from renal parenchymatous damage were included (further information was not provided). Informed consent was not obtained, as it was stated that the patients were unaware of "the nature of the drug or the change to be expected" following dosing.

¹ Black, M. M., Kleiner, I. S., and Bolker, H. Cancer Res. (1947) 7, 818.

Also, the effects of NaN_3 on blood pressure was examined in rats (strain and source not provided) that were made hypertensive for a three-month period by either a figure-of-eight loop on the kidney or by a partial ligation of the renal artery.

- 3. Dosage preparation and administration: For acute administration, doses of either 0.65 or 1.3 mg (approximately 0.01-0.02 mg/kg, assuming a 70 kg human) were dissolved in one-half or one-quarter of a glass of water; later, doses were dissolved in one teaspoon of water. For chronic administration, 0.3-1.3 mg (approximately 0.004-0.02 mg/kg; volume not provided) was administered once daily or three times daily for 5 days to up to more than 2 years. Also, NaN₃ was administered intravenously at a concentration of 3 μ g/mL in a 5% glucose solution, and sublingually at a concentration of 0.1 mg in three drops (further information not provided).
- **C.** <u>**OBSERVATIONS</u>:** Blood pressure measurements were made by the conventional inflated cuff procedure, with the patient in a sitting position. Several readings were obtained prior to the administration of the drug, after basal conditions had been established. The lowest of three blood pressure determinations was taken as the basal pretreatment level. It was stated that repeated blood pressure readings rarely differed by more than 15 mm Hg for the systolic values. Following the acute administration of NaN₃, measurements were made at 2-to 5 minute intervals, until the pressure had either returned to its original level or had stabilized at a new level. For chronic administration, reproducible blood pressure values (at least three to four readings) were obtained under standard basal conditions in the sitting position, after the patient had been allowed to rest for 5 minutes. Blood pressure was routinely recorded from 4 to 12 hours after the last dose of NaN₃ had been taken.</u>
- D. <u>DATA ANALYSIS</u>: No description of statistical analyses of the data was provided.

II. RESULTS

A. <u>Acute administration</u>: Oral administration of NaN₃ to hypertensive patients resulted in a rapid fall in blood pressure. It was stated that for "some" hypertensive patients, decreased blood pressure was observed 45 to 60 seconds after administration of 1.3 mg. Generally, although the actual fall in systolic pressure was considerably greater than the change in diastolic pressure, the diastolic pressure more often approached normal values than did the systolic. The fall in blood pressure was not accompanied by any significant changes in pulse or respiration rates. Flushing of the face was not observed. The majority of patients did not develop orthostatic hypotension, even following exercise. Further, exercise during the acute hypotensive phase did not cause any significant elevation in pressure; rather, most patients exhibited an additional lowering of diastolic pressure (5-10 mm Hg).

The hypotensive action of NaN₃ appeared to be more closely related to the magnitude of the original blood pressure rather than to the dose administered. In 13 patients whose initial systolic pressures were equal or greater than 190 mm Hg, the acute drop in pressure averaged 43 mm Hg (range \downarrow 30-65 mm Hg). In contrast, in nine relatively normotensive individuals whose systolic pressures were below 140 mm Hg, the acute drop in pressure

averaged 4 mm Hg (range $\uparrow 12$ to $\downarrow 22$ mm Hg). Accordingly, the highest dose showing no effects in relatively normotensive individuals was 1.3 mg 3X/day (0.06 mg/kg/day, based on a 70-kg adult). A similar relationship was observed on diastolic pressure. No apparent refractoriness to the drug developed with repeated administration; comparable and even greater falls in blood pressure were noted when the compound was administered acutely as many as ten to twelve times to the same patients at intervals of several days to several weeks.

- **B.** <u>Chronic administration</u>: The data for the hypertensive patients receiving chronic treatment with NaN₃ was presented as Table I in the study report, and is included as an Appendix. It was stated that the administration of up to 1.3 mg of NaN₃ three times daily for 10 days had no sustained effect on blood pressure in normotensive individuals. In the 30 hypertensive patients, treated with 0.65 to 1.3 mg NaN₃ (at least 3X/day) for 10 days or 2 $\frac{1}{2}$ years, the following signs were shown: 5 cases showed minimal changes in blood pressure; 10 exhibited a significant fall but the diastolic pressure remained above 100 mm Hg; and 15 had persistent blood pressure levels near normal and the 3 patients, who were checked for clinical signs, showed no evidence of damage to kidneys, heart, or liver and no changes in bowel habits or urinary function after 1 year. Additionally, in five of the patients, treatment resulted in a fall in blood pressure to normotensive levels that persisted for 14 days to 2 months after the cessation of treatment. It was stated that in these five patients, persistent hypertension had been documented for periods of at least 2 years. It was also stated that in all hypertensive patients, while a typical response to acute administration was observed, in 22 of 26 patients a gradual return to hypertensive blood pressure levels was noted within 1 to 3 days following cessation of treatment. A majority of patients showed a definite improvement in subjective symptoms, including headache, chest pains, and general mental outlook.
- **C.** <u>Toxicity</u>: Three patients taking NaN₃ daily for more than 1 year were examined for signs of organ toxicity to the kidney, heart, and liver by routine clinical studies. It was stated that kidney function was unimpaired, as evidenced by the quality and quantity of urine output, blood urea nitrogen, and non-protein nitrogen, and there were no changes in bowel habits or urinary function. No hepatic or cardiac toxicity was reported. It was also stated that an occasional patient complained of a transient sensation of "pounding in the head" shortly after administration of the compound. In 20 patients, repeated treatment with NaN₃ resulted in an increased sensitivity to the drug, necessitating a reduction in the daily dosage from 0.5 to 0.25 mg (0.004 mg/kg, based on a 70-kg adult) three times daily. Whether this was a toxic effect other than a further lowering of the blood pressure was not made clear (only 1 patient listed in Table 1 showed evidence of increased sensitive manifested as a further lowering of blood pressure).
- **D.** <u>Route of administration</u>: Several studies were performed to investigate the decrease in blood pressure with regards to route of administration. NaN₃ administered intravenously $(3.0 \ \mu\text{g/mL})$ at a dose rate of 10 $\mu\text{g}/10$ minutes lowered from 190/110 mm Hg to 150/85 mm Hg for a period of several hours. Additionally, three hypertensive patients were treated by

sublingual administration. It was stated that three drops containing a total of 0.1 mg of NaN₃ given sublingually was as effective as 0.65 mg administered orally.

E. <u>Animal experiments</u>: In surgically-hypertensive rats, a dose of as little as 0.1 mg of NaN₃ produced a fall in blood pressure lasting for 30-45 minutes. However, as this dose represented a greater dose level by body weight (rat weight of 150-180 g yields a dose level of 0.6-0.7 mg/kg, compared to 0.01-0.02 mg/kg for humans), it appeared that humans were more sensitive (\approx 30-35X) to the hypotensive effects of NaN₃ than surgically-hypertensive rats. Additionally, it was stated that intravenous administration of comparable doses of NaN₃ to normotensive rats, either acutely or by slow infusion, had no effect on blood pressure. In contrast to other hypotensive drugs, rats, which had been subjected, to hemorrhage until a blood pressure of 40 mm Hg was observed showed no deleterious effects of treatment on either blood pressure or peripheral circulation in the mesentery. Also, direct application of NaN₃ (0.01-0.5 mg) to the surface of the mesentery had no observable dilation action on the constricted blood vessels in the terminal vascular beds of rats subjected to hemorrhage.

III. DISCUSSION AND CONCLUSIONS

- A. <u>INVESTIGATORS' CONCLUSIONS</u>: Doses of 0.65-1.3 mg of NaN₃ administered orally had a rapid hypotensive effect, which persisted from 10-15 minutes post-dosing. When given chronically to hypertensives (0.6-1.3 mg three to four times daily for up to 2 years), NaN₃ produced a sustained lowering of the blood pressure toward normotensive levels. Repeated administration of the drug resulted in a greater hypotensive effect following equivalent doses and/or a progressively more sustained period of normotensive blood pressure levels. The observations indicated that a substantial difference existed in the relative sensitivity of hypertensive and normotensive individuals to the hypotensive effects of NaN₃. Intravenous injection of the drug to rats subjected to hemorrhage had no dilating effects on the constricted blood vessels in the exteriorized mesentery. NaN₃ (0.5 mg/100 g body weight) lowered the blood pressure of hypertensive rats. The observation that NaN₃ in hypertensive individuals rarely lowered the elevated blood pressure below normotensive levels suggested a general non-specific action of the drug on all vascular beds.
- **B.** <u>**REVIEWER COMMENTS:**</u> Oral administration of NaN₃ to hypertensive patients resulted in a rapid fall in blood pressure. In "some" hypertensive patient, decreased blood pressure was observed 45 to 60 seconds after administration of 1.3 mg (approximately 0.02 mg/kg, assuming a 70 kg human). Generally, although the actual fall in systolic pressure was considerably greater than the change in diastolic pressure, the diastolic pressure more often approached normal values than did the systolic. The fall in blood pressure was not accompanied by any significant changes in pulse or respiration rates. Flushing of the face was not observed. The majority of patients did not develop orthostatic hypotension, even following exercise. Further, exercise during the acute hypotensive phase did not cause any significant elevation in pressure; rather, most patients exhibited an additional lowering of diastolic pressure (5-10 mm Hg).

The hypotensive action of NaN₃ appeared to be more closely related to the magnitude of the original blood pressure rather than to the dose administered. In 13 patients whose initial systolic pressures were equal or greater than 190 mm Hg, the acute drop in pressure averaged 43 mm Hg (range \downarrow 30-65 mm Hg). In contrast, in nine relatively normotensive individuals whose systolic pressures were below 140 mm Hg, the acute drop in pressure averaged 4 mm Hg (range \uparrow 12 to \downarrow 22 mm Hg) at a daily dose of 3.9 mg (1.3 mg X 3 dosings or 0.06 mg/kg, based on a 70-kg adult). A similar relationship was observed on diastolic pressure. No apparent refractoriness to the drug developed with repeated administration; comparable and even greater falls in blood pressure were noted when the compound was administered acutely as many as ten to twelve times to the same patients at intervals of several days to several weeks.

In patients receiving NaN₃ chronically, it was stated that the administration of up to 1.3 mg of NaN₃ three times daily for ten days (total daily dosing of 0.06 mg/kg, based on a 70-kg adult) had no sustained effect on blood pressure in normotensive individuals. In the 30 hypertensive patients, treated with 0.65 to 1.3 mg NaN₃ (at least 3X/day) for 10 days or 2 $\frac{1}{2}$ years, the following signs were shown: 5 cases showed minimal changes in blood pressure; 10 exhibited a significant fall but the diastolic pressure remained above 100 mm Hg; and 15 had persistent blood pressure levels near normal and the 3 patients, who were checked for clinical signs, showed no evidence of damage to kidneys, heart, or liver and no changes in bowel habits or urinary function after 1 year. Additionally, in five of the patients, treatment resulted in a fall in blood pressure to normotensive levels that persisted for 14 days to two months after the cessation of treatment. It was stated that in these five patients, persistent hypertension had been documented for periods of at least two years. It was also stated that in all hypertensive patients, while a typical response to acute administration was observed, in 22 of 26 patients a gradual return to hypertensive blood pressure levels was noted within one to three days following cessation of treatment. A majority of patients showed a definite improvement in subjective symptoms, including headache, chest pains, and general mental outlook.

Three patients taking NaN₃ daily for more than one year were examined for signs of organ toxicity to the kidney, heart, and liver by routine clinical studies. It was stated that kidney function was unimpaired, as evidenced by the quality and quantity of urine output, blood urea nitrogen, and non-protein nitrogen, and there were no changes in bowel habits or urinary function. No hepatic or cardiac toxicity was reported. It was also stated that an occasional patient complained about a transient sensation of "pounding in the head" shortly after administration of the compound. In 20 patients, repeated treatment with NaN₃ resulted in an increased sensitivity to the drug, necessitating a reduction in the daily dosage from 0.5 to 0.25 mg (0.004 mg/kg, based on a 70-kg adult) three times daily. However, whether this was a toxic effect other than a further lowering of the blood pressure was not made clear (only 1 patient listed in Table 1 showed evidence of increased sensitive manifested as a further lowering of blood pressure).

Several studies were performed to investigate the decrease in blood pressure with regards to route of administration. NaN₃ administered intravenously $(3.0 \ \mu g/mL)$ at a dose rate of 10

 μ g/10 minutes lowered from 190/110 mm Hg to 150/85 mm Hg for a period of several hours. Additionally, three hypertensive patients were treated by sublingual administration. It was stated that three drops containing a total of 0.1 mg of NaN₃ given sublingually was as effective as 0.65 mg administered orally.

In surgically-hypertensive rats, a dose of as little as 0.1 mg of NaN₃ produced a fall in blood pressure lasting for 30-45 minutes. However, as this dose represented a greater dose level by body weight (rat weight of 150-180 g yields a dose level of 0.6-0.7 mg/kg, compared to 0.01-0.02 mg/kg for humans), it appeared that humans were more sensitive (\approx 30 to 35X) to the hypotensive effects of NaN₃ than surgically-hypertensive rats. Additionally, it was stated that intravenous administration of comparable doses of NaN₃ to normotensive rats, either acutely or by slow infusion, had no effect on blood pressure. In contrast to other hypotensive drugs, rats, which had been subjected, to hemorrhage until a blood pressure of 40 mm Hg was observed showed no deleterious effects of treatment on either blood pressure or peripheral circulation in the mesentery. Also, direct application of NaN₃ (0.01-0.5 mg) to the surface of the mesentery had no observable dilation action on the constricted blood vessels in the terminal vascular beds of rats subjected to hemorrhage.

In conclusion, NaN₃ administered orally at a dose of 1.3 mg (equivalent to 0.02 mg/kg) three times daily for up to more than 2 years lowered blood pressure and did not result in any observable adverse effects in humans. A NOAEL for hypertensive patients was, however, not observed in this study. Nevertheless, a NOAEL of 0.06 mg/kg for normal subjects was recorded.

This study is classified acceptable/non-guideline.

- C. <u>STUDY DEFICIENCIES</u>: The following deficiencies were observed:
 - The source, purity, and batch/lot # of the test compound should have been provided.
 - The total number of patients observed was low.
 - Informed consent was not obtained.
 - A greater number of patients should have been studied for organ toxicity.
 - It was not stated if patients of both sexes were included in the study.

APPENDIX

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ana di si seco	TA	BLE I. Effect	of Sodium	Azide o	n Blood I	Pressure of Hypertensives.
		0	TR1	load mere		
	-	Duration	Pre-	Post-	treatment	1
latient	Dose (m	g) (days)	ticatment	Acute	Chtoni	e Remarks
О. D.	1.3, q.d.	ភ	270/340	200/110) 187/11	2 Discontinued because of screre epis- taxis
N.P.	13, ti.	1 7	205/110	140/ 90) 180/105	5
\$2. F.	.7, q.d.	. ī	176/108	376/108	3 162/ 95	57.
Ģ . F.	4, 1.1.6	ł. 7	186/ 90	140/ 80	155/88	
M. R.	1.3, "	10	205/110	145/ 90	195/ 95	
ÊS.	.65, q d.	10	220/140	<u> </u>	165/140	 B.P. varied during day; renal paren- chymatous damage
Ç.M.	1.8, by i. injq.c	10	150/ 90	115/ 75	115/ 75	
15. († .	1.3, idem	10	165/116	140/ 92	130/ 95	
6 C.	65, t.i.d	. 10	195/108	155/ 85	140/ 90	
D.E	1.0, 7	14	210/140	161/ 85	155/ 76	
Li W	.65,	1.7	210/120	1827110	178/100	
ЫL.	1.3. "	17	215/185	149/102	210/130	Range versing trunching demago
JÍS:	65. "	18	10/130	158/195	175/105	wonar barenen inutous duntage
SIW	1.3. "	21	250/105	205/ 95	250/105	1 de angend arteriogoloragie
BA	նո 2	÷1	186/104	115/ 89	190/100	R D personal T and most the
	any que	. u.	100/304	1107 00	1207 00	ment
GII	1.3, tid.	21,	200/120	160/110	160/100	Previously treated with apresoline un- successfully
A L	65, "	21	160/112	143/ 75	145/ 85	-
HIS.	.65, "	21	210/110	160/ 90	160/90	B.P. remained normal for 14 days post- treatment
B.C.	65, "	30	195/110	140/110	185/ 95	
3 S.	"6ā, "	30	180/110	740/ 90	140/ 90	B.P. remained at low level for several weeks after drug
м. _I К.	1.3, "	3()	260/105	200/ 80	260/100	
<u>а</u> <u>ж</u> .	.5, "	30.	182/100	135/ 84	145/ 95	Sympathectomy 7 yr previous
/.Q.	.5, "	60	170/115	140/ 90	150/ 95	
L S.	13, "	60	280/128	195/ 95	234/110	
4. W.	65, "	90	198/110	144/ 92	160/ 90	
r R i	.65, "	250	195/110	150/ 85	135/ 80	Off medication 2 mo-B.P. unchanged
r. Ş. 🖓	65, "	275	175/110	145/ 90	130/ 90	
₹. <u>K</u>	1.3, "	365	200/120	125/ 88	155/100	
e Mi :	1.3, "	1.5 yr §	220/125	190/100	175/ 90	B.P. remained at low level for 4 mo after drug withdrawal
* N ,	.65, "	2.5 yı 1	180/100	120/ 70	160/105	3 yr postsympathectomy-showed in- creased sensitivity to azide, 0.3 mg drops B.P. to 70/40