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CLINICAL USES OF 2,3-DIMERCAPTOPROPANOL (BAL). IV. PHARMACOLOGIC OBSERVATIONS ON BAL BY INTRA- MUSCULAR INJECTION IN MAN¹

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The present report deals with a study² of the effects of 2,3-dimercaptopropanol (BAL) in humans. It was designed to explore the range of doses which may be safely administered to humans in relation to the schedules of doses which have been found effective in the treatment of Lewisite poisoning in animals.

SUBJECTS

The experiments were carried out in 9 subjects, 8 females and 1 male, 7 colored and 2 white. Their ages ranged from 18 to 49. They all had secondary or tertiary lues. One had diabetes and another hypertension, and a third, rheumatic heart disease. Three were under active antiluetic treatment; the remaining ones had not received treatment for at least several months.

PLAN

In each of 4 cases the experiments were carried out in the outpatient clinic, the patient leaving the clinic after symptoms had subsided. In each of 5 cases the patient was placed in the hospital, and was discharged on the day following the last dose. The experiment was so conducted as to eliminate anticipation or fear as a factor in the subjective symptoms.

American Reference Standard BAL was used in a 10 per cent solution in peanut oil containing 20 per cent benzyl benzoate (Hinson, Westcott and Dunning). It was injected deeply into the gluteal muscles.

In the general plan the subject was weighed and placed in bed or on an examining couch, where he remained throughout the experiment. The blood pressure, the heart rate, and in some cases

the respirations were recorded at approximately 10-minute intervals for 30 minutes prior to the injection, and at approximately 15-minute intervals for about an hour after the injection. Symptoms were recorded as they occurred until the effects had completely or nearly completely disappeared.

RESULTS

Dosage. The schedules of dosage and the results are summarized in Tables I and II. All doses were administered in terms of mgm. per kgm. of body weight. Single doses varied from 3.0 to 8.0 mgm. per kgm.; and total amounts at each injection, from 133.5 to 640 mgm. (1.3 to 6.4 ml. of the 10 per cent solution). In those cases in which more than 1 injection was given in a day, the total doses varied from 8.0 to 20.0 mgm. per kgm. The latter amounts were administered in a period of from 8 to 10 hours.

In the dosage range employed in these experiments (3.0 to 5.0 mgm.) distinct cumulation occurred when doses were given at intervals of 30 minutes. The 30-minute interval, however, greatly reduced the toxicity, since 8.0 mgm. per kgm. at one time produced severe symptoms, while the same amount given in a dose of 5.0 mgm. and 3.0 mgm. with an interval of 30 minutes, produced relatively mild symptoms in the same person.

Cumulation also occurred when the second dose was given at an interval of 2 hours. It may be fairly marked, as shown by case Li Co, in which slight symptoms from the first dose of 5.0 mgm. became very severe symptoms when the same dose was repeated in 2 hours.

A 3-hour interval between doses seemed to permit negligible cumulation, although we had only 1 case (An Ma) on this schedule. With the 4-hour interval between doses there was no cumulation.

Effects. A single dose of 3.0 mgm. per kgm. produced no symptoms. A single dose of 5.0

¹ The work described in this paper was done under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Cornell University Medical College.

² The experiments were carried out at the Hospital for Joint Diseases, New York.

mgm. per kgm. produced practically no symptoms in half of the cases (4 out of 8); and in the remaining ones, symptoms of moderate severity. After a single dose of 8.0 mgm. per kgm. the symptoms were among the most severe.

Following the injection of BAL intramuscularly, symptoms appeared in from 5 to 30 minutes. They gradually developed in intensity, reaching a plateau which lasted about 30 minutes, and then subsided gradually. In some, the entire course of symptoms lasted only about 15 minutes, while in others the symptoms persisted for as long as 2 hours.

The heart rate was usually accelerated moder-

ately during the peak of the symptoms. A rise of the blood pressure was one of the most regular effects. It was seen in 7 out of 9 cases. It was usually present after the second dose of 5.0 mgm., although occasionally after the first dose. Both the systolic and diastolic pressures rose. The increase ranged from 14 to 52 mm. Hg systolic, and from 10 to 40 mm. Hg diastolic. The course of the blood pressure change usually paralleled the symptoms. The only subject in whom the blood pressure failed to rise was the one with hypertension (An Mo). In this case the blood pressure fell. The patient started in the control period as a hypertensive in the range of 180/90, and

TABLE I

Effects of 10 per cent solution of BAL in various dosage schedules by intramuscular injection in man

Case	Date	Dose of BAL		Interval since last dose	Effect on			Symptoms				
		per kgm.	Total		Heart rate	B. P. (mm. Hg.)		Intensity 0 to 4+	Onset	Duration*		
						S	D					
Cl Wa	4/18	3.0	177.3	30 min.	0	0	0	0	10	43		
	4/21	5.0	295.0		0	0	0	0				
	5.0	295.0	+8		+32	+18	++					
El De	4/20	5.0	400.0	30 min.	0	0	0	±	18	131		
	4/21	3.0	240.0		0	+32	+38	+				
		8.0	640.0		+30	+28	+14	++++			8	52
Et Wo	4/19	5.0	245.0	32 min.	+8	0	0	+	25	30		
		3.0	141.0		+20	+30	+32	++++			5	59
Ma Jo	4/18	3.0	133.5		0	0	0	0				
Id Vi	4/29	5.0	320.0	2 hrs. 4 hrs.	+14	+26	+20	++	30	70		
		5.0	320.0		+24	+32	+36	++++	17	40		
		5.0	320.0		+24	+30	+24	++++	15	50		
An Mo	5/1	5.0	320.0	2 hrs. 4 hrs. 4 hrs.	0	-12	0	0	12	46		
		5.0	320.0		0	-44	-38	++				
		5.0	320.0		0	+8	+12	+			30	21
		5.0	320.0		0	-16	0	0				
Li Co	5/3	5.0	300.0	2 hrs. 4 hrs. 4 hrs.	+12	+14	+20	+	30	80-		
		5.0	300.0		0	+52	+40	++++	15-	29		
		5.0	300.0		+12	+16	+12	+	25	15		
		5.0	300.0		0	0	0	±	14			
An Ma	5/4	5.0	284.0	2 hrs. 3 hrs. 3 hrs.	0	+10	+14	0	33	15		
		5.0	284.0		0	+42	+28	±				
		5.0	284.0		0	+36	+26	+			15	30
		5.0	284.0		-14	-12	-8	0				
Is Bl	5/5	5.0	293.0	2 hrs. 4 hrs. 4 hrs.	+24	+14	+38	++	17	27		
		5.0	293.0		+24	+40	+28	++++	7	37		
		5.0	293.0		+16	0	+14	++	16	50		
		5.0	293.0		+28	+10	+10	+	26	28		

* In most instances mild and vague symptoms continued after the last observation and wore off gradually. S (systolic); D (diastolic).

TABLE II
Symptoms produced by BAL in man

Case	Date	Dose of BAL	Interval since last dose	Symptoms									
				Nausea	Vomiting	Salivation	Eye	Pain	Anxiety	Unrest	Paresthesias	Local pain	Warmth
Cl Wa	4/18	3.0	30 min.	0	0	0	0	0	0	0	0	0	0
	4/21	5.0		0	0	0	0	0	0	0	0	0	0
		5.0		0	0	0	+	++	+	++	+	0	0
El De	4/20	5.0	30 min.	±	0	0	0	0	0	0	0	0	0
		3.0		+	0	+	0	+	0	+	+	+	+
	4/21	8.0		++++	+	+	0	++++	++++	++++	+	0	0
Et Wo	4/19	5.0	32 min.	0	0	0	0	0	0	0	+	+	0
		3.0		0	0	++++	0	+	++++	++++	+	0	+
Ma Jo	4/18	3.0		0	0	0	0	0	0	0	0	0	0
Id Vi	4/29	5.0	2 hrs. 4 hrs.	+	++	+	0	++	++	++	+	0	0
		5.0		++	+	++	0	++++	++	++++	++++	+	0
		5.0		++	++	+	0	++++	+	++++	0	+	0
An Mo	5/1	5.0	2 hrs. 4 hrs. 4 hrs.	0	0	0	0	0	0	0	0	0	0
		5.0		0	0	++	0	0	0	0	++	0	0
		5.0		0	0	+	0	0	0	0	+	0	0
		5.0		0	0	0	0	0	0	0	0	0	0
Li Co	5/3	5.0	2 hrs. 4 hrs. 4 hrs.	0	0	+	0	+	0	0	0	+	0
		5.0		++++	0	0	0	++++	0	++++	+	0	0
		5.0		0	0	0	0	+	0	0	0	0	0
		5.0		0	0	+	0	0	0	0	0	0	0
An Ma	5/4	5.0	2 hrs. 3 hrs. 3 hrs.	0	0	0	0	0	0	0	0	0	0
		5.0		0	0	0	0	0	0	0	±	0	0
		5.0		0	0	0	0	+	0	0	+	0	+
		5.0		0	0	0	0	0	0	0	0	0	0
Is Bl	5/5	5.0	2 hrs. 4 hrs. 4 hrs.	+	+	++	0	++	0	0	0	++	0
		5.0		+	+	++	++	0	0	0	++++	++	+
		5.0		+	+	++	0	0	0	0	++	++	0
		5.0		+	+	+	0	0	0	0	0	++	0

ended after the fourth 5.0 mgm. dose of BAL in 10 hours in the range of 138/70. There were no symptoms associated with this fall in the blood pressure.

There is some indication of the development of tolerance to BAL since, as may be seen in Table II, the fourth, and sometimes the third, dose of 5.0 mgm. produced less severe symptoms than the first.

Symptoms. The pattern of symptoms varied from case to case (see Table II). Vomiting was usually associated with the most severe reactions. In the course of the more severe reactions, the patients showed paresthesias (burning or tingling of the nose, eyes, mouth or skin), pain (involv-

ing the limbs, jaws, abdomen, chest and head), lacrimation, blépharospasm, and salivation. An indescribable sense of illness developed with extreme unrest and apprehension. Occasionally the patient perspired freely and complained of being very warm. As the symptoms subsided, most patients with the more severe reactions complained of weakness and fatigue. At 4 hours after the 5.0 mgm. doses they were free of systemic symptoms.

While most doses caused some pain during the injection, a moderately tender area in the region of the injection, still present some hours later, was encountered in 4 of the 9 cases.

The complete protocols of the experiments are appended.

Schedules. Single doses of BAL of from 5 to 8 mgm. per kgm. intramuscularly in man produced reactions which did not appear to be dangerous, so also for total doses of 20 mgm. per kgm. in fractions of 5 mgm. over a period of 8 hours.

A single dose of 5 mgm. per kgm. caused no symptoms in 50 per cent of the cases, negligible effects in 25 per cent, and slight and fleeting symptoms in the remaining 25 per cent. The course of the reaction is fairly brief, lasting approximately an hour. The indications are that a schedule of dosage involving 5 mgm. per kgm. for 4 doses at intervals of 3 hours is likely to show little cumulation. In such a schedule, the effects of the first dose are not likely to become greater as a result of its repetition. The effect of the third and fourth dose may actually be less. Shorter intervals with such doses, namely 2 hours or less, result in cumulation.

The review by Waters and Stock (1) indicates that others have obtained substantially similar results (2, 3).

SUMMARY AND CONCLUSIONS

1. The toxic effects of BAL by intramuscular injection were studied in 9 human subjects with secondary or tertiary lues.

2. The results are based on 28 injections of single doses of from 3 to 8 mgm. per kgm.

3. In man BAL produces paresthesias (burning or tingling of the nose, eyes, mouth, and skin), perspiration and sense of warmth, pain (limbs, jaws, abdomen, head), lacrimation, blepharospasm, salivation, vomiting, unrest, apprehension, weakness, and fatigue. The heart rate is accelerated and both systolic and diastolic blood pressure usually increased.

4. The minimal dose which produces toxic effects lies between 3 and 5 mgm. per kgm. A single dose of 8 mgm. produces marked symptoms.

5. The effects of doses up to 8 mgm. per kgm. are completely reversible, the reactions lasting only about an hour or two.

6. Doses of 5 mgm. per kgm. may be given at intervals of three hours during the course of one day without significant cumulation.

PROTOCOLS

Patient: Cl Wa; female; colored; age 18; wt. 59.1 kgm.

Lues; active treatment.

4/18/44

Time	Blood pressure	Heart rate	Respiration	Remarks-Symptoms
10:40	110/74	108	22	
10:48	110/76	104	22	
10:55	106/72	98	22	
10:57	BAL, 3 mgm. per kgm. (1.8 ml.), muscle, local pain lasting 1 min.			
11:05	108/78	104	24	
11:07	106/74	102	20	
11:18	108/76	100	21	
11:28	108/78	96	22	
11:42	104/72	92	24	No complaints offered at any time, "I feel fine except my hip is stiff from needle," fell asleep during observations.

4/21/44

1:46	116/74	76		
1:57	120/68	74		
2:16	116/80	88		
2:25	BAL, 5 mgm. per kgm. (2.95 ml.), right gluteus, no local pain.			
2:38	110/74	88		
2:48	106/72	86		
2:55	BAL, second dose as above, left side, no local pain.			
2:56	118/78	84		
3:05	126/84	96		"Feel fine except for medicine in my mouth," "pepper in eyes and mouth."
3:10	152/98	96		About the same.
3:20	130/90	94		Seems weak, restless, says chest hurts, cries.
3:38	128/80	80		Better, can hardly keep eyes open because of smarting.
3:48	116/76	76		Better, eyes almost normal.

Patient: El De; female; colored; age 42; wt. 80 kgm.

Lues; no treatment.

4/20/44

Time	Blood pressure	Heart-rate	Respiration	Remarks-Symptoms
9:40	132/80	78	22	
9:50	124/82	78	22	
9:55	130/90	72	20	
9:59	138/88	70	24	
10:01	BAL, 5.0 mgm. per kgm. (4.0 ml.) muscle, buttock, local pain during injection only.			
10:10	130/90	76	20	
10:22	134/94	72	24	
10:30	128/86	68	24	"Little indigestion."
10:31	BAL, 3 mgm. per kgm. (2.4 ml.), muscle, buttock, immediate local pain.			
10:41	134/92	64	18	"Indigestion."
10:49	132/90	76		Salivation, "indigestion" worse, face and jaws "feel funny," burning in gums.
11:02	156/110	80		
11:06				Warmth in mouth and head.
11:10	164/104	80		Nausea, slightly restless, "I feel miserable."
11:20				Pain in left arm.
11:21	166/118	80		
11:30	130/100	72		Symptoms subsiding.
11:40	130/92	68		All symptoms still present but intensity much less.

4/21/44

1:55	142/96	66		Moderate soreness of right hip from previous inject. No swelling.
2:02	134/94	66		
2:32	134/90	64		
3:00	BAL, 8 mgm. per kgm. (6.4 ml.), muscle, left buttock.			
3:02	122/80	72		Soreness during injection.
3:08				"Feels it in mouth," spits.
3:10	126/88	72		No symptoms.
3:15	138/90	72		No symptoms.
3:21	148/88	76		Salivation, itching in jaw, pain in left elbow, extremely restless, nausea.
3:36	170/110	96		Strange sensations in limbs, sensation of stiffness in jaws, "feels miserable all over."
3:43				Still feels bad, insists on walking about, aches all over.
3:50	160/94	88		Pain in both arms and in neck, "would rather have a baby," no eye signs.
4:00	140/88	78		Distinctly improved, vomits.
4:05				Much better and insists on going home, gait normal, some nausea.

Patient: Et Wo; female; colored; age 26; wt. 49 kgm.

Lues; active treatment.

4/19/44

Time	Blood pressure	Heart-rate	Respiration	Remarks-Symptoms
9:40	100/64	72	22	Patient lies comfortably.
9:50	98/62	70	20	Patient lies comfortably.
9:58	96/60	70	20	Patient lies comfortably.
10:00	BAL, 5 mgm. per kgm. (2.5 ml.), muscle, left buttock, immediate pain.			
10:06	92/62	72	20	
10:17	92/60	80	18	Still some local pain in leg.
10:25				Nose stings, "head feels funny."
10:30	94/64	80	22	
10:32	BAL, 3 mgm. per kgm. (1.4 ml.), muscle, right buttock, immediate local pain lasting 1 minute.			
10:37	110/70	80	24	Pain in head, mouth burns, "I feel sick."
10:40				Profuse salivation, prefers to sit.
10:45	132/100	100		"Very sick," unrest, squirms, "I feel nervous," profuse salivation.
10:46				Improving.
10:47				"Lots better," "feel warm," "short of breath."
10:52	130/96	88		Very restless, complains of feeling "very sick," "throat very dry".
10:55		98		Shakes and shivers.
10:58				Less disturbed.
11:01		92	26	Feels cold, no lacrimation.
11:05				Improving.
11:10				Pain in shoulders, "most of misery gone."
11:11		76	26	"I feel worse again."
11:15	110/82			Improving, quieter.
11:20	120/76	68		Nervous, feels weak, premature beats, given phenobarbital gr. $\frac{3}{4}$.
11:25				"Feel stronger now."
11:30	110/68	66		"Feel strong enough to go home now," seems well.
11:36		64		Normal.

Patient: Ma Jo; female; colored; age 25; wt. 44.5 kgm.

Lues; active treatment; rheumatic heart disease.

4/18/44

Time	Blood pressure	Heart-rate	Respiration	Remarks-Symptoms
9:34	124/84	76	19	Patient lies comfortably.
9:40	130/82	76	16	Patient lies comfortably.
9:48	126/84	76	16	Patient lies comfortably.
9:59	BAL, 3 mgm. per kgm. (1.3 ml.), muscle, buttock, no local pain.			
10:04	124/82	82	18	
10:11	130/86	88	17	
10:21	126/86	84	18	
10:28	130/84	78	18	
10:43	122/82	81	16	
11:00	122/82	78	16	No complaints at any time, "I feel excellent."

Patient: Id Vi; female; white; age 34; wt. 64.5 kgm.

Lues; no treatment.

4/29/44

Time	Blood pressure	Heart-rate	Remarks-Symptoms
3:55	106/74	80	
4:00	106/74	76	
4:05	BAL, 5 mgm. per kgm. (3.2 ml.), muscle, buttock.		
4:15	106/76	80	
4:25	106/78	84	
4:35	132/94	88	Nausea, "nose tickles, pressure in ears" (paresthesias), "feel funny."
4:36			Vomits, "chills."
4:40			Vomits.
4:45	120/82	94	Salivation, abdominal cramps, other symptoms begin to subside.
5:00	122/82	84	
5:15	108/76	88	
5:30	106/70	82	Nervous, headache, given phenobarbital 0.1 and aspirin 0.3.
5:45	98/74	76	Symptoms entirely gone.
6:00	98/62	76	No symptoms.
6:03	BAL, second dose as above. Local pain lasting one minute.		
6:20	124/96	84	Cramps, "pressure in ears," paresthesias, tingling in gums, marked salivation, nausea.
6:33	136/98	100	Intense cramps, "pressure in chest," restlessness, anxiety.
6:37			Vise-like squeezing in chest, "I can't stand it any more," vomits.
6:40	128/92	94	Lacrimination, diffuse erythematous rash over shoulders.
6:50	116/90	96	Symptoms subsiding, pentobarbital sodium 0.1.
7:00	118/86	88	Much better but very fatigued.
10:00	107/70	70	Tenderness in left buttock, otherwise no symptoms.
	BAL, third dose as above, pain during injection.		
10:15			Slight nausea, sneezing.
10:35			Copious vomiting.
10:37	128/90	91	
10:50	137/94	94	Marked headache, no other symptoms.

Patient: An Mo; female; colored; age 49; wt. 64.2 kgm.

Lues; no treatment.

5/1/44

Time	Blood pressure	Heart-rate	Remarks-Symptoms
10:43	170/88	92	Patient lies comfortably.
10:53	178/90	98	Patient lies comfortably.
10:58	180/90	96	Patient lies comfortably.
11:00	BAL, 5 mgm. per kgm. (3.2 ml.), muscle, right buttock, no pain.		
11:15	176/90	92	No effect.
11:30	174/88	88	No effect.
11:40	176/88	82	No effect.
12:45	166/88	88	No effect.
1:00	BAL, second dose as above, in left buttock, local pain during injection lasting 1 minute.		
1:12	188/110	104	"Strange feeling."
1:20			Tingling in mouth, salivation.
1:35	192/98	96	"Feel very sick."
1:40	142/72	82	Improving, profuse salivation.
1:55	148/84	76	Much improved.
1:58			Normal.
5:00	170/84	84	Normal.
5:03	BAL, third dose as above in left buttock.		
5:18	166/78	80	No effect.
5:33	164/74	80	"Tickling" in mouth.

5:44	174/90	84	Itching in mouth, salivation.
5:54			Normal.
8:46	158/78	78	Normal.
8:54	BAL, fourth dose as above in right buttock.		
9:20	152/74	76	No effect.
9:35	138/70	76	No effect.
9:45	136/72	72	No effect.

Patient: Li Co; female; colored; age 43; wt. 60 kgm.

Lues, no treatment; diabetes; receives insulin.

5/3/44

Time	Blood pressure	Heart-rate	Remarks-Symptoms
6:40	144/80	64	
6:48	144/82	60	
6:58	138/80	60	
7:00	BAL, 5 mgm. per kgm. (3.0 ml.) muscle, buttock, local pain at site of injection.		
7:15	144/86	64	
7:30	158/102	76	"Ache all over."
7:45	152/90	72	Salivation.
8:50	138/68	60	No symptoms.
9:00	BAL, second dose as above.		
9:15	176/104		Restless, groaning.
9:28	196/120		Restless, writhing, groaning, crying, nausea, salivation, pain, "I can't stand it."
9:44	138/80	70	Tingling in hands, otherwise symptoms gone.
12:45	136/74	68	No symptoms.
1:00	BAL, third dose as above.		
1:15	128/68	68	No symptoms.
1:25	144/80	76	Slight pain in head and arms, "not bad."
1:40	144/80	72	Almost no symptoms, fatigued.
4:50	130/68	80	No symptoms.
5:00	BAL, fourth dose as above.		
5:14	128/68	88	Slight salivation.
5:28	134/76	80	No symptoms.
5:42	134/74	72	No symptoms.

Patient: An Ma; white male; age 41; wt. 56.8 kgm.

Lues; no treatment.

5/4/44

Time	Blood pressure	Heart-rate	Remarks-Symptoms
10:33	138/78	96	
10:43	136/80	100	
10:55	138/84	92	
10:58	BAL, 5 mgm. per kgm. (2.8 ml.), muscle, buttock.		
11:14	134/84	88	
11:29	146/98	84	
12:40	148/92	92	
12:55	148/96	88	No symptoms at any time.
12:57	BAL, second dose as above.		
1:15	148/98	82	
1:30	180/112	88	Slight paresthesias in hands, face, eyes, nose and mouth, "like somebody is touching me."
1:45	164/104	88	Practically no symptoms.
3:55	138/88	96	No symptoms.
3:58	BAL, third dose as above.		
4:15	174/110	94	Very slight paresthesias like those at 1:30.
4:30	166/100	100	Symptoms more intense, restless, pain, sweating.
4:45	154/94	96	Symptoms subsiding.
6:55	132/80	82	No symptoms.
6:58	BAL, fourth dose as above.		
7:15	128/74	78	
7:30	124/70	84	
7:40	124/76	92	No symptoms after this dose.

Patient; Is Bl; female; colored; age 41; wt. 58.6 kgm.

Lues; no treatment.

5/5/44

Time	Blood pressure	Heart-rate	Remarks-Symptoms
6:47	122/64	72	
6:52	122/70	68	
6:58	118/72	68	

6:59	BAL, 5 mgm. per kgm. (2.9 ml.), muscle, left buttock.		
7:16	132/80	74	"Feel funny and sick all over," salivating.
7:29	130/110	84	Headache, vomited, profuse salivation, pain in injected leg.
7:43	122/88	92	Better but still feeling sick.
8:53	132/84	96	No symptoms.
8:59	BAL, second dose as above in right buttock.		
9:06			"Funny feeling," salivation.
9:15	154/98	92	"Hot," symptoms more severe than after first dose.
9:30	162/100	96	Lacrimination, symptoms slightly less.
9:43	154/80	88	Vomited, but otherwise better.
12:53	118/70	88	Hungry, no symptoms except pain in both buttocks.
12:58	BAL, third dose as above in left buttock.		
1:14	116/70	86	"Funny feeling" starts, salivation.
1:30	120/86	88	Symptoms slightly more intense.
1:50	116/72	84	Nausea and vomiting, symptoms subsiding.
2:25			No symptoms, effects slightly less than from previous doses.
4:58	128/70	98	
5:02	BAL, fourth dose as above in right buttock.		
5:14	120/70	100	No effect.
5:28	124/72	96	"Feel something coming on," salivation.
5:38			Vomiting.
5:40	134/82	98	Feels better.
5:56	128/74	88	No symptoms other than pain at the site of injections, last dose caused least symptoms.

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