THE WESTERN
Journal of Medicine

Refer to: Klock JC, Boerner U, Becker CE: Coma, hyperthermia and bleeding associated with massive LSD overdose—A report of eight cases. West J Med 120:183-188, Mar 1973

Eight patients were seen within 15 minutes of intranasal self-administration of large amounts of pure D-lysergic acid diethylamide (LSD) tartrate powder. Emesis and collapse occurred along with signs of sympathetic overactivity, hyperthermia, coma and respiratory arrest. Mild generalized bleeding occurred in several patients and evidence of platelet dysfunction was present in all. Serum and gastric concentrations of LSD tartrate ranged from 2.1 to 26 nanograms per ml and 1,000 to 7,000 μg per 100 ml, respectively. With supportive care, all patients recovered. Massive LSD overdose in man is life-threatening and produces striking and distinctive manifestations.

Coma, Hyperthermia and Bleeding Associated with Massive LSD Overdose

A Report of Eight Cases

JOHN C. KLOCK, MD
UDO BOERNER, MS
CHARLES E. BECKER, MD
San Francisco

ALTHOUGH THERE HAVE BEEN many reports of overdose with D-lysergic acid diethylamide (LSD) in man, little toxicologic data are available. The physiologic effects of LSD in doses greater than 1 mg have not been studied in man and the lethal dose must be interpolated from animal studies. We performed extensive toxicologic studies on eight people who took large doses of LSD; the results and clinical-toxicologic correlations are reported herein.

From the Division of Clinical Pharmacology, the Toxicology Laboratory, and the Medical Service, San Francisco General Hospital, and the Department of Medicine, University of California, San Francisco.

Presented by invitation at the American Academy of Clinical Toxicology Meeting, San Diego, California, August 2, 1973.

Submitted August 30, 1973.

Reprint requests to: J. C. Klock, MD, Department of Medicine, Division of Hematology, Room 506 M, University of California, San Francisco, San Francisco, CA 94143.

Reports of Cases

On 29 July 1972, four women and four men ranging in age from 19 to 39 years were admitted to the emergency room at San Francisco General Hospital for drug overdose. Following a dinner party, they had "snorted" (inhaled through a straw placed in one nostril) a small amount of cocaine and a quantity of white powder believed to be cocaine. All eight were reported to have snorted at least two "lines" (rows of powder measuring approximately $3 \times 4 \times 30$ mm) of the second substance. Within 5 minutes they experienced anxiety, restlessness, generalized parasthesias and muscle discomfort, vomiting and physical collapse. Ten minutes later they were admitted to the emergency room in varying degrees of intoxication (Table 1 and Appendix).

TABLE 1.—*Clinical Manifestations of Massive LSD Overdose in Eight Patients*

Patient No.	Age, Sex	Blood Pressure (mm Hg)	Respirations (breaths/min)	Pulse (beats/min)	Temperature (°F)	Pupils (mm)	Bleeding	Other
1	20♀	130/90	6	120	104.0	8	+	Coma, respiratory arrest
2	19♀	130/30	33	200	107.0	7	+	Coma, respiratory arrest, diarrhea
3	28♀	160/60	24	150	99.5	8	−	Writhing and dystonic movements, diarrhea
4	33♀	110/70	9	110	98.0	8	+	Coma, respiratory arrest, aspiration
5	39♂	130/80	20	120	100.8	7	−	Coma, aspiration
6	29♂	230/130	30	112	98.8	6	−	Coma, aspiration
7	28♂	130/80	20	170	98.6	6	−	Hyperactive, psychotic, hallucinating
8	28♂	190/95	20	120	102.4	7	+	Hyperactive, psychotic, hallucinating

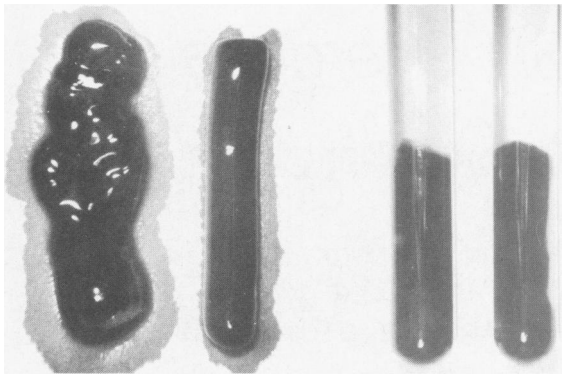

Figure 1.—Gross appearance of the blood clot from Patient 1 and a normal control clot (left) and results of autologous serum incubation at 37°C for 6 hours of clots from Patient 1 and a normal control clot (right). The normal control specimen is to the right in each picture.

Five were comatose when first seen and most were extremely hyperactive with severe visual and auditory hallucinations at some point during their course. Three required endotracheal intubation and assisted ventilation and three aspirated vomitus. All had sinus tachycardia, widely dilated and fixed pupils, emesis, flushing and sweating. Fever developed in four and diarrhea in two. Transient hypertension was present in three patients and no patient had convulsions. All had coagulopathy as manifested by the inability to form firm clots and absence of clot retraction in the blood specimen tubes. Seven had guaiac-positive vomitus and four showed exidence of mild generalized bleeding (microscopic hematuria in two, gross hematuria in two, oozing at venipuncture sites in three and small amounts of blood in the vomitus or stool in all four patients).

Laboratory data showed normal or negative values (see Appendix) for the following: blood glucose and serum sodium, potassium, and bicarbonate levels, hemoglobin (13.0 to 16.4 grams per deciliter), platelet count (186,000 to 458,000 per microliter), prothrombin time (11.0 to 12.5 seconds) and partial thromboplastin time (19.3 to 38.7 seconds), chest roentgenograms and electrocardiograms. Results of liver and renal function tests were within normal limits in the three patients studied. Direct examination of the blood clots and results of clot retraction tests on several patients showed friable clots that fell apart easily without dissection, and absence of clot retraction (Figure 1). Supportive care included respiratory assistance, use of hypothermic blankets, and administration of antibiotics and corticosteroids when indicated. Bleeding was mild and disappeared within 4 to 6 hours. Blood transfusions were unnecessary and all patients recovered completely within 12 hours. All were discharged or left the hospital within 48 hours of admission. No residua were observed in a year of direct follow-up of five patients.

Toxicologic Data

Specimens of blood, urine and gastric contents were obtained on admission from seven patients and analyses were performed as follows.

Gastric Content

Extraction of the gastric contents for toxicologic screening was performed according to the method of Sunshine[1] and analyzed by thin layer

TABLE 2.—*Toxicologic Data Obtained in Seven Patients with Massive LSD Overdose**

Patient No.	Blood			Urine	Gastric
	Ethanol (%)	*Cocaine† (μg/ml)*	*LSD (ng/ml)*	*Cocaine† (μg/ml)*	*LSD (mg/100 ml)*
1	0	0	NT	0	7.0
2	0.08	0	NT	1.3	NT
3	0	0	26.0	10.0	NT
4	NT	NT	NT	NT	1.2
5	0	0	6.6	0	<1 mg
6	4	0	11.6	0	NT
7	0.02	0	2.1	NT	3.1

*NT=not tested.
†Measured as benzoylecgonine.

chromatography according to a modified method of Mulé.[2] All basic gastric content extracts showed the presence of an ergot alkaloid. By the photodegradation method of Andersen[3] and using a combination of eight reference substances,* this substance was further characterized as D-lysergic acid diethylamide. The results, shown in Table 2, were confirmed by mass spectrography.† The mass peaks of the isolated material corresponded with those reported in the literature and those of authenticated LSD-25, which was used as a control sample.

Urine

Preliminary screening by Mulé's[2] method of thin layer chromatography showed possible traces of cocaine in some specimens. Therefore, specimens were rechecked by homogeneous enzyme immunoassay[4] for benzoylecgonine, the main cocaine metabolite in urine.[5] Two of the urine specimens contained small amounts of benzoylecgonine (Table 2).

Blood

Blood was analyzed for LSD by the back extraction method of Aghajanian and Bing[6] and the results were compared with standards of serum containing 5, 10, 20 and 40 nanograms (ng) LSD per ml. All specimens analyzed contained LSD (Table 2). Blood was analyzed for cocaine, using the same general method as for urine, and for ethanol and other volatile substances, using gas chromatography.[7] No specimen contained cocaine and two specimens contained small amounts of ethanol (Table 2).

Confiscated Material

A white flaky material (208 mg) was confiscated by police and identified as the large quantity of powder used at the party. Analysis by thin layer chromatography, fluorescent analysis, mass spectrography and the melting point and mix melting point identified this substance as almost pure (80 to 90 percent) D-lysergic acid diethylamide tartrate.

Discussion

Intranasal administration of crushed LSD tablets is a common method of administration by LSD users when a rapid onset of action is desired. The active use of this route by our patients was corroborated by the onset of symptoms soon after administration of the white powder, the absence of LSD in screening samples of food and wine from the party and the absence of symptoms in members of the party who did not use the powder. The lethal dose of LSD for man is not known, but it ranges from 46 mg per kg in mice[8] to 0.3 mg per kg in rabbits[8] to 0.1 mg per kg in Asiatic elephants.[9] Interpolated for the body weight of man, this would result in a lethal dose of 0.2 mg per kg or an approximate lethal dose of 14,000 μg.[8] The toxicologic data and the purity of the powder used by our patients indicate that milligram amounts of the drug were administered, placing the patients at risk of having severe and possibly lethal reactions.

LSD is capable of many and varied physiologic, psychologic and biochemical effects.[8,10,11] Most of these effects are thought to be due to LSD's ability to affect 5-hydroxytryptamine receptors both centrally and peripherally[12-14] and to its generalized stimulation of the reticulocortical system.[8] The previously observed physiologic manifestations of psychosis, hyperexcitability, tachycardia, mydriasis[8,15,16] and hyperthermia[17] were prominent in our patients, but the degree of central nervous system depression and respiratory inhibition that occurred in these patients has only been demonstrated in animals given very large doses.[8] Furthermore, the generalized bleeding problem observed in four of our patients has not been described before with LSD. The clinical and laboratory data suggest that platelet function was abnormal. Little literature on LSD and platelet function is available. However, Michal[18] showed that LSD-25 in 1

*D-lysergic acid diethylamide tartrate (LSD-25®, Sandoz), ergotamine tartrate (Sandoz), methysergid(e) maleate (Sansert®, Sandoz), methylergonovine maleate (Methergine®, Sandoz), ergonovine maleate (Ergotrate® maleate, Lilly), dihydroergotamine (methanesulfonate) (DHE-45®, Sandoz), D-lysergamide tartrate (ergine), D-iso-lysergamide tartrate (iso-ergine tartrate).

†Varian NAT-GNOME quadropol mass spectrograph, Varian Associates, Palo Alto, California.

to 3 nanomolar concentrations could significantly inhibit 5-hydroxytryptamine-induced platelet aggregation *in vitro;* no effect on adenosine diphosphate-induced aggregation was noted. Cocaine also affects platelet function *in vitro* in much larger concentration.[19,20] Our analytical data do not indicate that cocaine played a significant role in these cases, making the possibility of cocaine-induced platelet dysfunction unlikely. However, more evidence is needed before LSD can be implicated as the cause of the bleeding in these patients.

Treatment of our patients was entirely supportive and recovery was relatively rapid. Some of them were able to converse after 4 to 5 hours and all were normal within 12 hours. Most did not remember being brought to the hospital; otherwise, no apparent psychologic or physical ill effects were noted in a year of follow-up examinations of five patients. Most of the patients continue to use LSD intermittently. Death from LSD overdose still has not been confirmed toxicologically; nevertheless, the rapid administration of large doses of LSD in man is associated with striking and distinctive clinical manifestations and is life-threatening.

APPENDIX

PATIENT 1. A 20-year-old woman was comatose and unresponsive to pain with vomitus in the mouth and hypopharynx on arrival at San Francisco General Hospital. Breathing was shallow, irregular and ineffective; the pupils were dilated and unreactive. There were hyperactive bowel sounds, but no diarrhea. Bleeding at venipuncture sites persisted for more than 20 minutes. The hemoglobin was 13.9 grams per deciliter (dL), packed cell volume 43.2 percent, platelets 245,000 per microliter (μL), and white blood cell count 19,000 per μL with 35 percent segmented neutrophils, 2 percent eosinophils, 1 percent basophils, and 62 percent lymphocytes. On urinalysis there was a 2 plus reaction for blood. The blood urea nitrogen was 9 mg and creatinine 0.7 mg per dL, serum sodium was 140 mEq, potassium 4.4 mEq, chloride 108 mEq and bicarbonate 25 mEq per liter, glucose was 115 mg per dL, prothrombin time 12.4 seconds and partial thromboplastin time 24.5 seconds. Both the stool and vomitus were 3 plus reactive for blood.

The patient was supported by artificial ventilation via endotracheal tube and was placed on a hypothermic blanket and given intravenous fluids. She remained comatose and continued to bleed at the site of insertion of the endotracheal tube and in the urine. After 5 hours, the fever, coma and bleeding gradually resolved. The patient was fully awake by the 12th hour, was able to walk after removal of the tube and was discharged on the second hospital day.

PATIENT 2. A 19-year-old woman arrived at the hospital in an extremely lethargic state, responding only to very painful stimuli. Within 10 minutes she became severely agitated, spontaneously flailing her arms and legs and continuously screaming. The pupils were dilated and unresponsive to light. There was no nuchal rigidity. The bowel sounds were hyperactive, stools were formed and greenish, and the nasogastric aspirate contained small amounts of blood mixed with food. Blood oozed from venipuncture sites and large bruises formed at sites of trauma. Hemoglobin was 14 grams per dL, packed cell volume 40.8 percent, platelets 186,000 per μL, and leukocytes 21,500 per μL with 80 percent neutrophils, 19 percent lymphocytes and 1 percent monocytes. Prothrombin time was 12.5 seconds, partial thromboplastin time 27.3 seconds. Glucose was 180 mg, creatinine 1.5 mg and blood urea nitrogen 20 mg per dL. Serum sodium was 142 mEq, potassium 4.0 mEq, chloride 110 mEq, and bicarbonate 25 mEq per liter. There was a 4 plus reaction for blood in the urine, and the stool guaiac test reaction was 2 plus. An electrocardiogram showed sinus tachycardia.

Diazepam, 10 mg, was administered intravenously and the patient was packed in ice bags. She began to have many watery greenish stools. She was placed in a quiet dark room and became quieter. Over the next hour she became gradually less responsive and finally only responded to deep pain. The arterial blood pO_2 was 56 mm of mercury, pCO_2 46 mm of mercury, and pH 7.28. Respiratory arrest necessitated intubation and respiratory assistance for 4 hours at which time she began to regain consciousness. Within the next 8 hours the patient recovered fully and was discharged the following day.

PATIENT 3. A 28-year-old woman arrived at the hosiptal vomiting and unable to speak, had an expressionless stare and was unresponsive even to severe pain. The pupils were dilated and fixed and the reflexes were hyperactive. She did not have diarrhea. The hemoglobin was 14.5 grams per dL, packed cell volume 41.2 percent and leukocytes 23,200 per μL with 67 percent neutro-

phils, 1 percent basophils, 36 percent lymphocytes and 6 percent monocytes. The platelets were normal on a blood smear. The prothrombin time was 11.9 seconds, partial thromboplastin time 38.7 seconds and blood glucose 105 mg per dL. The vomitus was positive for blood.

Dextrose and saline solution were administered intravenously. The patient gradually became more responsive. Except for three episodes of brown watery diarrhea and transient writhing dystonic movements, the course of recovery was uneventful. The patient was completely normal after 12 hours and was discharged on the second hospital day.

PATIENT 4. A 33-year-old woman arrived at the hospital unconscious and unresponsive to painful stimuli. She had frothy sputum and vomitus in the mouth, nose and hypopharynx. The vomitus contained small flecks of blood. The pupils were dilated and unresponsive to light. The bowel sounds were hyperactive but there was no diarrhea. The hemoglobin was 13.0 grams per dL, packed cell volume 38.8 percent and white blood cell count 22,300 per μL with a normal differential. Urinalysis showed a 4 plus reaction for glucose and blood. Blood glucose was 204 mg, creatinine 0.7 mg and urea nitrogen 11 mg per dL. Serum sodium was 141 mEq, potassium 3.7 mEq, chloride 103 mEq and bicarbonate 28 mEq per liter. The plasma prothrombin time was 11.6 seconds and partial thromboplastin time 19.3 seconds. The platelets were normal on a blood smear.

The patient vomited in the emergency room, aspirated vomitus and became apneic. Endotracheal intubation and artificial ventilation were instituted and hydrocortisone, 500 mg, and penicillin, 6 million units, were administered intravenously. Blood oozed at venipuncture sites and at the site of insertion of the endotracheal tube. Artificial ventilation was maintained for 2 hours and then terminated when the patient began thrashing about. Bleeding continued for several hours and the tube was removed approximately 8 hours after insertion. She made an uneventful recovery and left the hospital on the third hospital day.

PATIENT 5. A 39-year-old man arrived at the hospital unconscious and unresponsive to pain. He had no gag reflex while vomitus was being suctioned from his mouth and hypopharynx. He was diaphoretic with widely dilated pupils and hyperactive bowel sounds but there was no hemorrhage or diarrhea. The hemoglobin was 15.7 grams per dL, packed cell volume 46 percent, platelet count 294,000 per μL and leukocytes 17,500 per μL with 39 percent neutrophils, 54 percent lymphocytes, 1 percent eosinophils and 6 percent monocytes. Blood urea nitrogen was 22 mg and creatinine 1.4 mg per dL. Serum sodium was 141 mEq, potassium 3.5 mEq, chloride 109 mEq and bicarbonate 20 mEq per liter. Arterial blood pO_2 was 52 mm of mercury, pCO_2 46 mm of mercury, and pH 7.25. Urinalysis showed a 1 plus reaction for ketones and a 3 plus reaction for blood. The vomitus was positive for blood.

After 30 minutes it was easier to arouse the patient from coma. He was increasingly psychotic and had severe visual hallucinations. However, during the next 4 hours he became sleepy and less agitated. He gradually recovered and left the hospital against medical advice 12 hours after admission.

PATIENT 6. A 29-year-old man was unresponsive on arrival at the hospital. Except for blood pressure of 230/130 mm of mercury, dilated pupils and diaphoresis, the results of physical examination were within normal limits. There was no evidence of bleeding. The hemoglobin was 16.4 grams per dL, packed cell volume 46.7 vols percent and leukocytes 17,900 per μL with a normal differential count. The platelets were normal on smear and the prothrombin time was 12.5 seconds. Blood glucose was 142 mg, blood urea nitrogen 19 mg and creatinine 0.8 mg per dL. Arterial pO_2 was 104 mm of mercury, pCO_2 was 28 mm of mercury, and pH was 7.41. The vomitus was positive for blood.

After 40 minutes the patient had gradually become more responsive though he was grossly psychotic, screamed loudly and had severe visual hallucinations. The blood pressure gradually fell to 170/110 mm of mercury over an hour and was 130/70 3 hours after admission. The patient recovered without complication over the next 8 hours and left the hospital the following day.

PATIENT 7. A 28-year-old man walked into the emergency room stating that he thought he had been poisoned. He was belligerent and was having visual hallucinations. Physical examination showed no abnormalities with no evidence of diarrhea or bleeding; however, he subsequently vomited material containing blood. The hemoglobin was 16.3 grams per dL, packed cell volume 47.2 percent and white blood cell count 13,500 per μL with 66 percent neutrophils, 3 percent

basophils, 21 percent lymphocytes and 10 percent monocytes. The platelet count was 458,000 per μL, the prothrombin time was 11.0 seconds and partial thromboplastin time 34.6 seconds. Serum sodium was 140 mEq, potassium 4.3 mEq, chloride 101 mEq, bicarbonate 24 mEq and creatinine 1.4 mEq per liter. Protein was 7.6 grams, albumin 4.6 grams and bilirubin 0.3 mg per dL. Lactic dehydrogenase was 116 international units per liter, glutamic oxaloacetic transaminase 32 IU per liter, creatine phosphokinase 160 IU per liter, glucose 120 mg per dL and alkaline phosphatase 47 IU per liter. The patient refused admission to the hospital and left after 5 hours in the emergency room.

PATIENT 8. A 28-year-old man walked into the hospital complaining of being severely frightened and of having visual hallucinations and "nightmares." Physical examination revealed no abnormalities except for diaphoresis and dilated pupils unresponsive to light. The hemoglobin was 16 grams per dL, packed cell volume 48 vols percent and white blood cell count 23,200 per μL with 86 percent neutrophils, 11 percent lymphocytes and 3 percent monocytes. The prothrombin time was 10.0 seconds and partial thromboplastin time 22.4 seconds. Platelet count was within normal limits. There was a 3 plus reaction for blood in the urine and a 1 plus reaction for protein. The patient remained in the emergency room for several hours, said he felt better and was discharged.

REFERENCES

1. Sunshine I: Handbook of Analytical Toxicology. Cleveland, Chemical Rubber Co, 1969, pp 394-395
2. Mulé SJ: Identification of narcotics, barbiturates, amphetamines, tranquilizers and psychomimetics in human urine. J Chromatogr 39:302-311, 1969
3. Andersen DL: Identification of LSD and other indole alkaloids by ultraviolet degradation products. J Chromatogr 41:491-493, 1969
4. Rubenstein KE, Schneider RS, Ullman EF: "Homogenous" enzyme immunoassay—A new immunochemical technique. Biochem Biophys Res Commun 47:846-851, 1972
5. Fish F, Wilson WD: Excretion of cocaine and its metabolites in man. J Pharm Pharmacol 21 (suppl):135S-138S, 1969
6. Aghajanian GK, Bing OHL: Persistence of lysergic-acid diethylamide in the plasma of human subjects. Clin Pharmacol Ther 5:611-614, 1964
7. Parker KD, Fountan CR, Yee JL, et al: Gas chromatographic determination of ethyl alcohol in blood for medicolegal purposes: separation of other volatiles from blood or aqueous solutions. Anal Chem 34:1234-1236, 1962
8. Hoffer A: D-lysergic acid diethylamide (LSD): A review of its present status. Clin Pharmacol Ther 6:183-255, 1965
9. West LJ, Pierce CM, Thomas WD: Lysergic acid diethylamide: Its effects on a male asiatic elephant. Science 138:1100-1103, 1962
10. Louria DB: Lysergic acid diethylamide. N Engl J Med 278: 435-438, 1968
11. Brawley P, Duffield JC: The pharmacology of hallucinogens. Pharmacol Rev 24:31-66, 1972
12. Andén NE, Corrodi H, Fuxe K, et al: Evidence for a central 5-hydroxytryptamine receptor stimulation by lysergic acid diethylamide. Br J Pharmacol 34:1-7, 1968
13. Boakes RJ, Bradley PB, Briggs I, et al: Antagonism of 5-hydroxytryptamine by LSD 25 in the central nervous system—A possible neuronal basis for the actions of LSD 25. Br J Pharmacol 40:202-218, 1970
14. Martin WR, Sloan JW: Effects of infused tryptamine in man. Psychopharmacologica 18:231-237, 1970
15. Forrer GR, Goldner RD: Experimental physiological studies with lysergic acid diethylamide (LSD-25). Arch Neurol Psychiat 65:581-588, 1951
16. Rinkel M, Hyde RW, Soloman HC, et al: Experimental psychiatry II. Clinical and physio-chemical observations in experimental psychosis. Am J Psychiat 111:881-895, 1955
17. Friedman SA, Hirsch SE: Extreme hyperthermia after LSD ingestion. JAMA 217:1549-1550, 1971
18. Michal F: D-receptor for serotonin on blood platelets. Nature 221:1253-1254, 1969
19. Aledort LM, Niemetz J: Dissociation of platelet aggregation from clot retraction, potassium loss, and adenosine triphosphatase activity. Proc Soc Exp Biol Med 128:658-661, 1968
20. Behnke O: Effects of some chemicals on blood platelet microtubules, platelet shape and some platelet functions in vitro. Scand J Haemat 7:123-140, 1970