The Use of BAL in Heavy Metal Poisoning, with Particular Reference to Antimonial Intoxication[1]

By D. SANTIAGO STEVENSON, RAMÓN M. SUÁREZ, JR., and ERNESTO J. MARCHAND

From the University Hospital, School of Tropical Medicine, San Juan, Puerto Rico

WAR is usually considered synonymous with chaos and destruction, yet no one can deny that under the stress and strain of war, medical science receives considerable impetus.

In previous wars surgery and its related branches gained most from battlefield experience; World War II brought about more advancement in the purely medical field. To mention only a few: (*a*) acceleration of the development and production of antibiotics (penicillin, streptomycin, and so forth); (*b*) new antimalarials; (*c*) DDT; (*d*) a new understanding of hepatitis; and (*e*) development and mass use of new immunizing substances. Among these last, British Anti-Lewisite, developed during this war, must be counted even though announcement of its discovery was withheld until the war was over, for reasons of security. An editorial in the New England *Journal of Medicine* has put it very nicely: "The ill wind that blew chlorine gas from the German lines across No Man's Land in World War I, and started a race for the development of more deadlier chemicals for use in warfare, has now blown in some good."[2]

During World War II extensive and highly secret work was undertaken in England in search of an antidote that would neutralize the vesicant and toxic action of arsenical poison gases, one of the most potent of which was Lewisite. This culminated in the successful development of a therapeutic agent, properly named British Anti-Lewisite, and known in the armed forces by its initials, BAL. This agent was found effective, not only in counteracting the local effects of arsenical vesicants in wartime, but also as a general antidote against arsenical compounds and, later on, against other metallic poisons, in peacetime civilian practice.

In 1939, during the first fortnight of World War II, a group of English investigators, headed by Dr. R. A. Peters, was commissioned by the government to work on an antidote to combat the

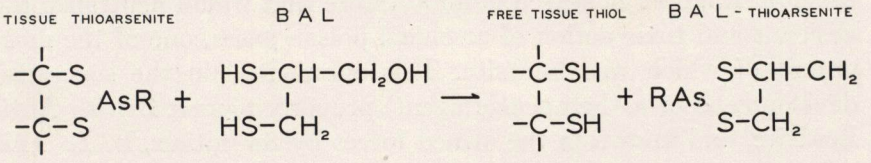
1. Received for publication December 28, 1947. Lecture delivered at the School of Tropical Medicine November 20, 1947.

2. Editorial. BAL, a cure for heavy metal poisoning. New England J.Med., **235**:695–697, 1946.

vesicant gases which it was feared the Germans might use. They based their research on the pioneer work of Ehrlich,[3] who, in 1909, had first suggested that the toxic effects of arsenic followed its combination with certain vital components of the cell, or, more precisely, that the toxic effect of arsenic was due to its attack on the sulfhydryl (–SH) group, a component of an enzyme system dealing, particularly, with carbohydrate and fat metabolism. The toxic action of this metal was thought to be mainly the result of a blocking of one or more enzyme actions, principally, the pyruvate-oxydase system, vital to cellular metabolism. Voegtlin, Dyer, and Leonard,[4] in subsequent work, demonstrated that the toxic action of arsenicals on trypanosomes and rats could be diminished, or even abolished, by cysteine or glutathione. The latter substances are monothiols containing one –SH, or sulfhydryl group, for which trivalent arsenicals have a marked affinity, so that they actually compete with the –SH group for the available arsenic in the tissue protein. They form a more stable compound which can be easily eliminated, thus leaving the tissue cells free of the noxious metal.

It was further found that dithiols (compounds containing two –SH groups) had an even greater affinity for arsenicals, and that they formed more stable and less toxic compounds than did the monothiols.[5] Of the numerous dithiolic compounds prepared and tested by Peters and his collaborators, one in particular—the 2, 3-dimercaptopropanol (BAL)—was found to be the best local decontaminant against arsenical blistering gases.[6]

The detoxification effect of BAL is shown in the following diagram:



At first, BAL was compounded as an ointment for use on the skin and eyes.[7] It soon became apparent that the drug, so applied, had a

3. P. Ehrlich, Über den Jetzigen Stand der Chemotherapie. Ber.d.deutsch.chem.Gesselsch., **1**:17, 1909.

4. C. Voegtlin, H. A. Dyer, and C. S. Leonard, On the mechanism of the action of arsenic upon protoplasm. U.S.Pub.Health Rep., **38**:1882–1912, 1923; On the specificity of the so-called arsenic receptors in the higher animals. J.Pharmacol. and Exper.Therap., **25**:297-307, 1925.

5. R. A. Peters, L. A. Stocken, and R. H. S. Thompson, British Anti-Lewisite (BAL). Nature, **156**:616–619, 1945.

6. *Ibid.*

7. W. F. Hughes, Jr., The treatment of lewisite burns of the eyes with BAL. J.Clin.Investigation, **25**:541–548, 1946.

systemic as well as a local action, since its external application to rats contaminated with Lewisite resulted in a pronounced increase in the urinary excretion of arsenic; this ointment was found to be effective even when applied to normal skin at a distance from the lesion. It was also observed that in cases of exfoliative arsenical dermatitis the urinary excretion of the poison increased after the application of the ointment.[8]

While the aqueous and propylene glycol solutions of BAL, injected into rats, proved successful in the treatment of arsenical poisoning, the use of these preparations was impractical because of their instability and insolubility.[9] BAL is a colorless liquid with a specific gravity of 1.21 and is soluble to the extent of only 6 percent. In common with other mercaptans it has a strong skunklike odor. Peanut oil proved to be a suitable vehicle, so that solutions of BAL in peanut oil, with benzyl-benzoate added as a solubilizing agent, were sterilized and made available in glass-sealed ampoules. Such solutions retained their activity for at least twenty-four months and were proved to be efficacious in the systemic treatment of arsenical poisoning. At present, the available BAL ampoules contain a 10 percent solution of BAL in peanut oil, with 20 percent benzyl-benzoate.

Extensive clinical and experimental work[10] has definitely established that the optimal dose of BAL is from 2.5 to 3 mg. per kilogram of body weight, injected intramuscularly, at four-hour intervals. For milder cases, such as "arsenical fever," rash, mild arsenical dermatitis, 2.5 mg. per kilogram is recommended. This means that, for a man weighing 60 kilograms, the dose is 150 mg., or 1.5 cc. of the 10 percent solution. During the first two days the patient should receive from four to six daily injections, at intervals of four hours. Thereafter, the dosage may be reduced to one or two daily injections for ten days, or until complete recovery has taken place.[11] Severe cases, such as those with encephalopathy, blood dyscrasias, jaundice,

---

8. J. A. Luetscher, Jr., H. Eagle, and W. T. Longcope, The effect of BAL on excretion of arsenical intoxication. J.Clin.Investigation., **25**:534–540, 1946.

9. H. Eagle, H. J. Magnuson, and R. Fleischman, Clinical uses of BAL. The systemic treatment of experimental arsenic poisoning (Mapharsen, Lewisite, Phenyl arsenoxide) with BAL. J.Clin.Investigation, **25**:451–466, 1946.

10. J. A. Leutscher, Jr., H. Eagle, and W. T. Longcope, *op. cit.*

H. Eagle, H. J. Magnuson, and R. Fleischman, *op. cit.*

H. Eagle and H. J. Magnuson, The treatment of 227 cases of arsenical poisoning (encephalitis, dermatitis, blood dyscrasias, jaundice, fever) with BAL. Am.J.Syph., **30**:420–441, 1946.

W. T. Longcope, J. A. Luetscher, Jr., M. M. Wintrobe, and V. Jager, The treatment of arsenical dermatitis with preparations of BAL. J.Clin.Investigation, **25**:528–533, 1946.

H. L. Holley, The use of BAL in the treatment of agranulocytosis following intensive arsenotherapy for syphilis. Ann.Int.Med., **27**:231–238, 1947.

11. H. Eagle and H. J. Magnuson, *op. cit.*

exfoliative dermatitis, and so forth, should receive 3 mg. per kilogram. This is equivalent to 180 mg. of BAL, or 1.8 cc. of the 10 per cent solution for a man weighing 60 kilograms. As in the milder cases, injections should be given at four-hour intervals at the onset of treatment, reducing the number of injections according to the therapeutic response.

Eagle and his co-workers, in their various investigations,[12] pointed out that the cases of exfoliative dermatitis are apt to suffer relapses if the treatment is not extended sufficiently. These authors insisted on the fact that, for optimal results, BAL should be administered *as soon as possible* after exposure, or after the development of toxic manifestations in the course of arsenical chemotherapy. The shorter the time between exposure, or the development of toxic manifestations, and the time of therapy, the better the results.

If the recommended dosage is used, toxic manifestations to BAL are comparatively rare, although the following side effects may occasionally be observed: pain at the site of injection; nausea, vomiting, and headache; burning sensation of the lips, mouth, throat, and eyes; pain in the teeth, lacrimation and salivation; muscular aches, burning and tingling of the extremities; feeling of constriction of the throat and chest, and elevation of the systolic and diastolic blood pressure. These untoward reactions are temporary in nature and persist for only twenty to thirty minutes.[13] It has been recently reported that toxic reactions to BAL may be prevented by the previous administration of ephedrine in 25 mg. doses.[14]

There are numerous reports in recent literature regarding the use of BAL[15] in arsenical intoxication of all types, including (*a*) arsenical encephalitis, (*b*) dermatitis, (*c*) agranulocytosis, (*d*) fever, and (*e*) hepatitis. Striking results have been obtained in all but hepatitis and the blood dyscrasias. BAL has also been found effective in experimental animals poisoned with several other heavy metals, such as mercury, gold, cadmium, chromium, bismuth, nickel, and

---

12. *Ibid*; W. T. Longcope, J. A. Luetscher, Jr., M. M. Wintrobe, and V. Jager, *op. cit.*

13. W. Modell, H. Gold, and M. Catell, Clinical uses of BAL. Pharmacologic observations on BAL by intramuscular injection in man. J.Clin.Investigation, **25**:480–487, 1946.

M. Sulzberger, R. L. Baer, and A. Kanof, Studies on the toxicity of BAL on percutaneous and parenteral administration. J. Clin.Investigation, **25**:474–479, 1946.

14. M. Tye and J. M. Siegel, Prevention of reaction to BAL. J.A.M.A., **134**:1477, 1947.

15. H. Eagle, H. J. Magnuson, and R. Fleischman, *op. cit.*; H. Eagle and H. J. Magnuson, *op. cit.*; W. T. Longcope, J. A. Luetscher, Jr., M. M. Wintrobe, and V. Jager, *op. cit.*; H. L. Holley, *op. cit.*

A. Cohen, J. Golman, and A. W. Dubbs, The treatment of acute gold and arsenic poisoning. J.A.M.A., **133**:749–752, 1947.

antimony, but it has failed in lead, thallium, and selenium intoxication.[16]

Eagle[17] and his associates found that BAL had a definite protective action on rabbits given lethal doses of anthiomaline (antimony lithium thiomalate), Fuadin (sodium antimony tartrate), and tartar emetic (antimony potassium tartrate), and that this antidotal effect was always associated with a significantly increased urinary excretion of antimony. Braun *et al.*[18] reported similar results in their trials of BAL for antimonial intoxication of experimental animals. On the other hand, another group of investigators[19] found while working with rats that, although the acute lethal action of tartar emetic was reduced by BAL, mortality increased when fuadin, neostam, and neostibosan were the toxic agents. No effect was demonstrated in the case of rats receiving stibanose. The difference in results might probably be explained by the different doses and experimental animals utilized.

Reports have appeared in recent literature regarding the clinical use of BAL in the treatment of poisoning by heavy metals other than arsenic, including mercury and gold. To our knowledge, however, no observations have been published on the treatment of antimonial poisoning in man. Occasionally, toxic manifestations produced by antimony are encountered during the use of its compounds in the treatment of tropical diseases, such as granuloma venereum, schistosomiasis, filariasis, and leishmaniasis, with the following signs: (*a*) pain in the joints; (*b*) nausea, vomiting, and diarrhea; (*c*) cough while the drug is given; (*d*) general malaise and headache; (*e*) salivation; (*f*) skin eruptions; (*g*) cardiovascular envolvement, bradycardia, hypotension, shocklike syndrome; (*h*)

16. W. F. Riker, The treatment of experimental arsenic poisoning with the dithiols. J. Pharmacol.& Exper.Therap., Supp., **87**:66–71, 1946.

W. F. Riker and G. Rosefeld, The effect of 2, 3-dimercaptopropanol (BAL) on the whole blood and plasma concentration of arsenic after Mapharsen in cats. J.Pharmacol.and Exper. Therap., **87**:72–75, 1946.

A. Gilman, F. S. Philips, R. P. Allen, and E. S. Koelle, The treatment of acute cadmium intoxication in rabbits with 2, 3-dimercaptopropanol (BAL) and other mercaptans. J. Pharmacol. and Exper.Therap., Supp., **87**:85–101, 1946.

J. M. Tobias, C. C. Lushbaugh, H. M. Patt, S. Postel, M. N. Swift, and R. W. Gerard, The pathology and therapy with 2, 3-dimercaptopropanol (BAL) of experimental Cd. poisoning. J.Pharmacol.and Exper.Therap., Supp., **87**:102–118, 1946.

17. H. Eagle, G. G. Frederick, J. Magnuson, and R. Fleischman, The protective action of BAL in experimental antimony poisoning. J.Pharmacol.and Exper.Therap., **89**:196–204, 1947.

18. H. A. Braun, L. M. Lusky, and H. O. Calvery, The efficacy of 2, 3-dimercaptopropanol (BAL) in the therapy of poisoning by compounds of antimony, bismuth, chromium, mercury, and nickel. J.Pharmacol.and Exper.Therap., Supp., **87**:119-125, 1946.

19. J. F. Gammill, C. H. Shoutham, and H. B. Van Dyke, Effect of BAL on acute poisoning by tervalent and quinquevalent antimonial drugs. Proc.Soc.Exper.Biol. and Med., **64**:13–16, 1947.

hepatic and renal insufficiency; (*i*) bone-marrow depression; (*j*) retinitis, optic neuritis; (*k*) encephalopathy and neuritis. While most of these toxic manifestations have not been severe or more than transient, they may be very bothersome, with an occasional fatality resulting.[20]

The present report includes seven cases of heavy metal poisoning treated with BAL. There were two cases of arsenical intoxication: encephalitis and arsenical ingestion. The other five cases were toxic reactions encountered during the treatment of schistosomiasis or filariasis with antimonials. One of these cases (No. 3) was treated five months before reports appeared in the literature regarding the use of BAL in experimental animals poisoned with antimonials.

CASE REPORTS

CASE No. 1. R. R. E., 32-year-old Puerto Rican mulatto, foundry worker, was brought to the Outpatient Department at 9 A.M. of August 31, 1946, in deep coma.

The history obtained was meager, the patient's sister informing the physician that she did not live at home but had been notified by her mother of his illness only two hours before. Her mother had said that the patient arrived home around 8 P.M. of the previous evening, complaining of severe headache. Around 6:30 of that day, he had received an intravenous injection of arsenic at a Public Health Unit, where he was under anti-luetic treatment. A dull headache, which commenced about half an hour later, became progressively worse; the patient went to bed after taking aspirin. The headache became so severe that he screamed with pain. During the night the patient complained of faintness and dizziness and of spots before his eyes. Around 3 A.M. he vomited, the vomitus consisting of that evening's food. Then he became unconscious.

Physical examination. Temperature, 98.6°; respiration, 24; pulse, 76; blood pressure, 130/75.

A well-developed and well-nourished young mulatto lying flat in bed, with eyes closed and not responding to usual stimuli.

There was no evidence of external trauma; neck moderately rigid; pupils dilated and responding sluggishly to light; corneal reflex and eyegrounds normal. Chest clear and heart sounds also normal. Abdominal wall soft; no organs or masses felt. Moderate rigidity of all extremities, but reflexes normal; no pathological ones could be

20. F. Hernández Morales, J. Oliver González, and C. K. Pratt, The treatment of schistosomiasis mansoni with urea stibamine (Squibb). Am.J.Trop.Med., **26**:327–229, 1946.

elicited. During examination, when painful stimuli were applied, patient became excited, yelling incoherently and not responding to questions; totally uncoöperative. As he commenced to thrash about in bed, screaming all the time, he had to be restrained forcefully, at which time he bit one of the doctors in the leg. Following admission diagnoses were considered: (*a*) diabetic coma, (*b*) meningitis, (*c*) arsenical encephalitis, (*d*) cerebro-vascular accident, and (*e*) cerebral malaria.

Laboratory Findings

Blood Count:

RBC 4,460,000
WBC 11,840
Hemoglobin . . . . . 12.6 g.
Differential polymorphonuclears:
Neutrophils . . . . . 88 percent { seg.—86 per per cent / stab—2 per cent
Lymphocytes . . . . . 12 percent

Blood sugar . . . . . 142.8 mg. per 100 cc.

Urinalysis (catherized specimen)

Color: amber, slightly turbid, and alkaline
Albumin: negative
Sugar: negative
Acetone: positive
Sediment: WBC–6–8 phpf; occasional red blood cells; few squamous epithelial cells; moderate crystals; numerous amorphous PO_4; few mucous cells

Malaria smear (thin and thick): negative

Spinal puncture: fluid under increased pressure, appearing slightly hazy WBC—728 per cmm.; polys.—46 percent; lymphos.—42 percent; eosinos.—8 percent; endothilial cells—4 percent; sugar—49.0 mg. per 100 cc.; total proteins—100 mg. per 100 cc.; chlorides—695 mg. per 100 cc.

Patient was admitted with diagnosis of arsenical encephalitis. Meningitis (type undetermined) had not as yet been entirely ruled out.

Course. At 2:00 P.M., 1.75 cc. of a 10 percent solution of BAL, in oil, was given intramuscularly, and penicillin therapy—100,000 units every three hours—was commenced. One hour after first dose of BAL, patient had regained consciousness but complained only of severe headache. After second dose of BAL he vomited; he still had a headache but complained of no other untoward reactions. Next morning patient was up and about and did not complain. He was able then to give further information regarding his illness, telling us that four months previous, he had developed an ulcerated lesion in

the genitalia which, after repeated examinations, had been found to contain spirochetes. Kahn test found positive, he was referred to local Health Unit for antiluetic treatment. On evening of the day of illness he had received the eighth injection of intravenous arsenical.

A total of four injections of BAL was given the patient. From the second day on, he had no further complaints, except for occasional mild headache. Since serology on admission was still positive, and it was thought inadvisable to resume arsenical medication, the patient was kept in hospital for twenty-seven days, or until a total dose of 9,000,000 units of penicillin had been administered.

Spinal tap on fourth hospital day revealed clear fluid under normal pressure:

WBC—272 per cmm.; polys.—32 percent; lymphos.—68 percent;
Sugar—38.81 mg. per 100 cc.; total proteins—30.0 mg. per 100 cc.;
Chlorides—680 mg. per 100 cc.
Pandy test: normal
Kolmer test: 4+ positive

On day of discharge another spinal tap was performed; fluid was under normal pressure and showed the following:

WBC—26 per cmm.; RBC—many; sugar: total proteins—20 mg. per 100 cc.
Pandy test: normal
Kolmer test: 4+ positive
Gold curve: insufficient

The patient has been followed up periodically in the OPD, having been last seen on March 7, 1947. He had no complaints except for occasional frontal headaches that lasted two or three days and then disappeared spontaneously. Spinal fluid obtained on that date revealed normal pressure; no cells, except for few erythrocytes; Pandy test, normal; Wassermann, negative; gold curve, 0000000000; blood Kahn, 000.

A case of arsenical encephalopathy following administration of mapharsen, admitted in coma and with convulsions, which responded almost miraculously even to the first injection of BAL. There was a rapid and complete recovery.

Case No. 2. A. R., white Puerto Rican male, 26 years old, hospital orderly, who was brought to University Hospital at 10:00 A.M. of January 10, 1947, complaining of severe abdominal pain and weakness.

His history, details of which were obtained later, was as follows: the patient worked as orderly in a private clinic, where he had suffered several attacks of hysteria; had once attempted suicide by ingesting insufficient number of sleeping tablets and had been generally emotionally unstable for some time. Around 8:00 A.M., on day of admission, patient had again attempted suicide by ingesting two large tablespoonfuls of Paris green; felt some burning in stomach immediately after taking it. About half an hour later he had severe abdominal pain which, by 9:30, was sharp enough for fellow workers to notice his condition and take him to the hospital. Patient vomited once before arrival.

Gastric lavage with sodium bicarbonate was performed. The patient was given sedatives, and five injections of BAL of 1.7 cc. each were administered at four-hour intervals without untoward reactions except for lacrimation. He failed to return after the last injection but was interviewed two months later, at which time he had developed no untoward symptoms following Paris green intoxication except for a diarrhea that lasted two days. When seen again in September, 1947, the patient was found in normal health.

An attempted suicide by arsenical ingestion in the form of Paris green. BAL was given prophylactically, and other measures usual in such cases were taken. The patient recovered without toxic sequalae. However, as there was no way of knowing whether the patient would have developed toxic symptoms had the drug not been given, the action of BAL is difficult to evaluate in this case.

CASE NO. 3. A. C. M., 17-year-old female student who was referred to the Outpatient Department on February 12, 1946, with a diagnosis of intestinal schistosomiasis.

Patient gave history of bathing in infected fresh-water streams and of having noticed a rash after such bathing. Stools had been found positive for *S. mansoni* eggs by referring physician; main complaint was occasional abdominal pain accompanied sometimes by diarrhea.

Physical examination in OPD entirely negative though last of six fecal examinations was positive for *S. mansoni* eggs. Rectal biopsy also showed four eggs, two of which were alive.

Laboratory Findings

Blood Count—

RBC	4,410,000
WBC	11,760
Hemoglobin	91% (13.0 g.)

Blood chemistry:

Non-protein nitrogen	26.16%
Urea	8.97%
Sugar	81 mg.
Serum globulin	2.9 mg.
Serum albumin	3.4 mg.
Total protein	6.3 mg.

Urinalysis:

Color: yellow, turbid, acid
Albumin: negative
Sugar: negative
Sediment: WBC—1–3 phpf; occasional blood, many squamous and red epithelial cells
Kahn test: 000
Hanger test: 1+ positive
Bromsulfthalein test: 2% retention 30 min. after injection of dye

Course. Treatment with 50 cc. fuadin prescribed, which patient received at local Health Unit. Immediately following first 5 cc. dose, she complained of chilly sensation and nausea followed by headache and fever that lasted one day. Second injection produced similar reaction. Despite fact that each injection was accompanied by similar toxic reactions, patient continued treatment until 5 injections had been given. Fifth injection also produced nausea and vomiting and, by following day, patient complained of headache and noted puffiness of face. On that day, July 5, 1947, she visited OPD of University Hospital.

Physical examination was essentially negative except for considerable palpebral edema. Blood pressure—100/70.

Laboratory Findings

Urinalysis:

Color: turbid appearance
Albumin: 2+ positive
Sediment: WBC—14–18 phpf; RBC—50–60 phpf; many amorphous urate crystals
Specific gravity: not performed because of insufficient quantity

Diagnosis of antimonial nephritis was made, the patient then given 2.5 cc. of BAL at OPD, two additional doses of 2 cc. each to be administered at home at four-hour intervals.

By the following day palpebral edema had disappeared entirely, and the patient felt well; urine was entirely normal on this day. The patient was admitted to the Hospital nine months later and given full course of anthiomaline (45 cc.) under strict clinical observation.

BAL was kept at hand in case toxic manifestations would appear but, surprisingly, none occurred.

A case of antimonial toxic nephritis which responded, both objectively and subjectively, to BAL administration rapidly and satisfactorily.

CASE No. 4. A. C. A., 23-year-old white male admitted to the Outpatient Department in December, 1946.

The patient gave history of bathing in fresh-water streams known to be infested with schistosomes and of having suffered bouts of bloody diarrhea; stools were positive for *S. mansoni*, rectal biopsy having showed 92 eggs, some of which were alive. Course of fuadin was ordered to be given in 5 cc. doses every other day at local Health Unit. By second injection, patient noticed burning sensation and lacrimation of eyes that persisted throughout treatment which continued until 45 cc. of fuadin had been administered. On March 17, 1947, when admitted to the Hospital, patient complained mainly of progressive blindness, particularly of right eye.

Physical examination essentially negative except that sclerae and conjunctivae were red and infected; there was pronounced photophobia. Patient was referred same day to the Ophthalmologic Institute, in San Juan, where an examination disclosed the following: "There is a bilateral peripapillary and central edema of both fundi, which is about two diopters high at the edge of the discs. The vessels are partially blurred by the edema of the disc, but their caliber is about normal. The visual acuity was O.D. 2/10; O.S. 3/10. The visual field of the right eye was taken, and it showed a large central scotoma with the 1 mm. target at 333 mm. distance. The peripheral field was normal." (Fig. 1) Diagnosis of optic neuritis and edema of central retina, due to antimony poisoning, was made.

Patient was given 1.4 cc. of BAL every four hours for two days. By the following day he voluntarily informed improvement of vision. He was again seen by ophtalmologists on March 20, three days after admission, who reported the following: "The scotoma is much reduced, but the edema of the nerve and retina is still present." (Fig. 2)

The patient was discharged on March 22, 1947, by which time there was no lacrimation or conjunctival irritation, and vision was very much improved. On April 11, patient went again to the Ophthalmologic Institute, and the report this time was: "The visual fields were found to be normal; the fundi looked perfectly normal, and the visual acuity was restored to 10/10 in both eyes." (Fig. 3)

Since then, patient has been seen at various times in OPD with no visual complaints. On last visit, September 11, 1947, fundoscopic examination and visual acuity were reported as normal.

This case, one of optic neuritis and retinitis, due to antimonial intoxication, showed objectively the rapid beneficial effects of BAL therapy. Usually such toxic optic neuritis follows a prolonged clinical course before recovery, if this is ever fully achieved.

Case No. 5. A. M. M., 34-year-old white, male furniture store clerk, who was admitted to the University Hospital on May 1, 1947, with progressive weakness and bleeding from gums.

History revealed that three years previous, the patient had had episodes of acute lymphangitis of left leg, accompanied by chills and fever, which a druggist had diagnosed as attacks of filariasis without having performed nocturnal blood tests. Fever subsided in four days and acute swelling disappeared in two weeks. Physician saw patient during acute phase of illness and diagnosed condition as filariasis but again without resorting to blood examination for microfilariae; he prescribed neostibosan injections which were given every other day. Up to the sixth injection, the patient experienced no untoward reaction, but this one produced painful swelling in left gluteal region, which finally had to be incised. He became progressively weaker and paler; fainting spells and bleeding from gums next occurred. Despite medication with folic acid, iron, and liver extract for about one month prior to admission, patient became progressively worse.

Physical examination revealed a very pale man, lying quietly in bed with pronounced pallor of the conjunctivae and evidences of recent and old bleeding from margin of gums; he had soft blowing apical systolic murmur. Liver edge was palpable 3 cm. below costal margin; spleen was not enlarged; left ankle showed 3+ pitting edema and dark brown discoloration over lower third of leg. There were no ecchymoses nor petechiae.

Laboratory Findings

Blood Count:

RBC	660,000
WBC	3,450
Hemoglobin	25% (3.8 g.)
Differential polymorphonuclears:	
Neutrophils	21%
Basophils	1%
Eosinophils	2%
Segmented	18%
Lymphocytes	79%

Platelets..... 45,000
Bleeding time: 2′30″
Clotting time: 6′25″
Fragility test: hemolysis began at 0.42%; completed at 0.32%
Clot retraction: no retraction after 24 hours
Icterus index: 5.97

Upon admission sternal bone-marrow was of the aplastic type, as shown by the following figures:

Early erythroblasts	1.0%	7.5%
Late erythroblasts	1.0	
Normoblasts	5.5	
Neut. myelocytes	1.5	31.5%
Metamyelocytes	5.0	
Baso-myelocytes		
Non-segmented	4.0	
Poly-neutrophils	19.5	
Poly-eosinophils	1.5	
Lymphocytes	59.0	61.0%
Monocytes	1.5	
Plasma cells	.5	

Course. Six injections of BAL (2.5 mg. per kilo of body weight) were administered at intervals of four hours. The patient was also given a blood transfusion three days after admission, and seven others during hospital stay that lasted seventy-six days. Patient also received pentnucleotide, folic acid, liver extract, and iron. By eighth hospital day blood count was:

RBC	1,800,000
WBC	3,050
Hemoglobin	38% (5.4 g.)
Differential polymorphonuclears:	
Neutrophils	30%
Lymphocytes	69%
Eosinophils	1%

Patient continued to improve slowly and a month later showed:

RBC	3,360,000
WBC	6,300
Hemoglobin	70% (10.4 g.)
Differential polymorphonuclears:	
Eosinophils	14%
Segmented	32%
Lymphocytes	54%

This was the highest count reached. Upon discharge count was:

RBC	2,310,000
WBC	3,950
Hemoglobin	52% (7.6 g.)

Bone-marrow continued to show hypoplastic picture. The patient was followed up weekly in the OPD, but counts remained about same. On August 20, 1947, there was a blood count of:

RBC	2,090,000
WBC	3,900
Hemoglobin	58% (8.4 g.)
Differential polymorphonuclears:	
Neutrophils	13%
Lymphocytes	87%
Segmented	12%
Juveniles	1%
Platelets	215,000
Clotting time: 4′35″	
Bleeding time: 1′35″	

When the patient was seen last, he had been given sulfonamide by a physician elsewhere, following which he suffered bleeding from nose and gums. Bleeding time was 16′ and blood count as follows:

RBC	1,440,000
WBC	3,720
Hemoglobin	38% (5.6 g.)
Differential polymorphonuclears	22%
Platelets	20,000

He was given blood transfusion and sent home.

Evaluation of BAL therapy was very difficult in this case, for regardless of therapy, the bone-marrow has continued hypoplastic. This patient received BAL after one month, or more, of exposure to antimony; therefore, optimal results were not to be expected. Again, it must be recalled that the poorest results reported in arsenical poisoning have been in cases of hepatitis and blood discrasias, which apparently also holds good in the case of antimony.

Case No. 6. L. M. M., 21-year-old female admitted to hospital on July 15, 1947, because of a generalized petechial rash. Patient was first seen in the Outpatient Department on March 3, 1947, when she presented typical signs and symptoms of Banti's syndrome,

secondary to schistosomiasis. Stools were positive for *S. mansoni*, and so was rectal biopsy.

On admission, patient had a count of:

RBC	4,020,000
WBC	4,250
Hemoglobin	75% (10.9 g.)
Blood chemistry	Normal
Bromsulfthalein test	40% retention in 30 minutes
Hanger test	2+ positive

The patient had been started on a course of fuadin in the Outpatient Department and had already received twenty-two injections of 5 cc. each. She claimed that the last three or four had produced nausea accompanied by vomiting, which contained some specks of bright red blood; she also complained of profuse epistaxis that lasted one day. There was no bleeding from gums.

The physical examination was essentially negative, except for fact that entire body was covered with petechial rash ranging from pinpoint size to the size of a pinhead. The rash did not fade on pressure and was especially pronounced over both lower extremities. Liver edge palpable 2.5 cm. below costal margin; the spleen, 4.5 cm. Few petechiae in left lower tarsal conjunctiva and a small, shallow nonbleeding ulcer in the mucous membrane of left cheek. Patient was menstruating profusely at time.

Laboratory Findings

Blood Count:

RBC	3,700,000
WBC	8,700
Hemoglobin	87% (12.6 g.)
Differential polymorphonuclears	69%
Eosinophils	4%
Segmented	65%
Lymphocytes	31%
Platelets	70,000

Clotting time: 4′50″

Bleeding time: 1′50″

Blood chemistry: normal

Diagnosis was made for thrombocytopenic purpura hemorrhagica, secondary to fuadin intoxication.

Course. The patient was given course of five injections of BAL of 1.4 cc. each every four hours, feeling nausea and having vomited twice after the injections. By the following day the rash was fading,

and the mouth ulcer showed evidence of healing. No new petechiae appeared, and six days after hospitalization, the old one had completely disappeared. Fragility cuff test reported normal after treatment.

Menstruation, which had been present for eight days prior to admission, lasted for seven days while the patient was in the hospital; normally, periods lasted only four days.

Clinical improvement paralleled improvement in hematologic picture as follows:

Day	*Platelets*	*Bleeding Time*	*Clotting Time*	*RBC*	*WBC*	*Hb. %*
Admission	70,000					
1	100,000					
3	195,000					
6	225,000			4,020,000	4,550	63.0
7	118,000	3′10″	4′5″	3,650,000	4,450	67.0
9				3,830,000	4,300	71.0
14				3,940,000	5,000	77.0
16	200,000	4′15″	3′5″	3,760,000	6,650	65.9

On the sixteenth hospital day, the patient was discharged, asymptomatic, to await future splenectomy.

This case, one of thrombocytopenic purpura secondary to fuadin intoxication, responded very rapidly to BAL treatment. As soon as the drug was administered, the patient showed a noticeable clinical improvement paralleled by changes in the hematologic picture.

Case No. 7. M. D. (A–10293), 20-year-old colored female, was admitted to Hospital on December 15, 1947, because of severe bleeding from gums, occurring one hour after third 5 cc.-injection of a second course of Fuadin. The patient was first seen in the Outpatient Department on April 8, 1947, when she was clinically diagnosed as suffering from Manson's schistosomiasis. Stools were negative for *S. mansoni*, but rectal biopsy was positive. On admission to OPD, she had the following blood count:

RBC 4,560,000
WBC 7,600
Hemoglobin ..... 88% (12.8 g.)
Blood chemistry ..... Normal
Bromsulfthalein test: No retention in 30 minutes
Hanger test: 2+ positive

The patient had received eighteen injections of fuadin in OPD four months previous without suffering any untoward reactions except for occasional mild nausea and pains in the joints. Rectal biopsy after treatment revealed living ova of *S. mansoni*, so that fuadin was commenced a week before admission to the hospital. A few hours after the second injection, the patient noticed a little bleeding from gums, which lasted a few minutes. One hour after the third injection, the patient commenced to bleed profusely from gums and was hospitalized immediately.

Physical examination essentially negative except for puffy eyes and congested conjunctivae; pinpoint petechiae were scattered over body. Rash did not fade on pressure and was most pronounced around eyes and over both lower extremities. There was profuse bleeding from gums which interfered with oral examination. No hepato-splenomegaly.

Laboratory Findings

RBC	4,390,000
WBC	11,150
Hemoglobin	80.1% (11.4 g.)
Differential polymorphonuclears	73% (Seg.—63%)
Eosinophils	10%
Lymphocytes	27%
Reticulocytes	2%
Platelets	80,000

Clotting time: 4′
Bleeding time: still bleeding after 45′
CSR: 15 mm.
MCV: 91
BM: 9

Capillary fragility test strongly positive; bone-marrow showed 3 percent megaloblasts and 6.5 percent megakariocytes.

Diagnosis was made of thrombocytopenic purpura hemorrhagica, secondary to fuadin intoxication.

Course. The patient was given course of six injections of BAL of 1.2 cc. each every four hours with no untoward manifestations. Within twenty-four hours the rash started to fade, and bleeding from gums disappeared. No new petechiae appeared, and after the fifth hospital day, old ones had almost disappeared. Capillary fragility test was reported as normal immediately after end of treatment; clot retracted after forty-five minutes.

Clinical improvement was paralleled by improvement in hematologic picture, as evidenced by the following:

Day	*Platelets*	*Bleeding Time*	*Clotting Time*	*RBC*	*WBC*	*Hb. %*
1	80,000	45.0′	4.0′	4,390,000	11,150	80.1
2	104,000	5.1′	3.4′	4,200,000	6,800	80.1
3	112,000	3.6′	3.08′			
4	130,000	3.8′	3.0′	3,990,000	7,000	77.9
5	124,000	3.5′	3.0′	4,100,000	8,000	80.1

Patient was discharged as recovered.

A second case of toxic purpura, secondary to fuadin intoxication, followed a rapid and spectacular recovery after BAL administration.

SUMMARY

BAL (British Anti-Lewisite), developed during World War II to combat the local vesicant action of arsenical blister gases, has been found to exert generalized antidotal properties in all types of arsenical intoxication. In experimental animals, these properties were found to apply to other heavy metal intoxicants, including mercury, gold, bismuth, and antimony. To the best of our knowledge, no reports of the use of BAL in clinical cases of antimony intoxication have appeared as yet in the medical literature.

A clinical report of the use of BAL in two cases of arsenical intoxication is given. Five cases of antimonial intoxication treated with BAL are also presented.

The results of therapy in these cases indicate that, clinically, antimonial poisoning is amenable to treatment with BAL. It would seem to us that BAL is thus a valuable addition to the medical armamentarium of physicians who practice in the tropics, where antimony compounds are frequently used.

ACKNOWLEDGMENT

We wish to acknowledge the coöperation of Dr. Ricardo Fernández and of Dr. Luis Morales, of the Ophthalmologic Institute, who kindly undertook the ophthalmological studies and follow-up of Case No. 4.

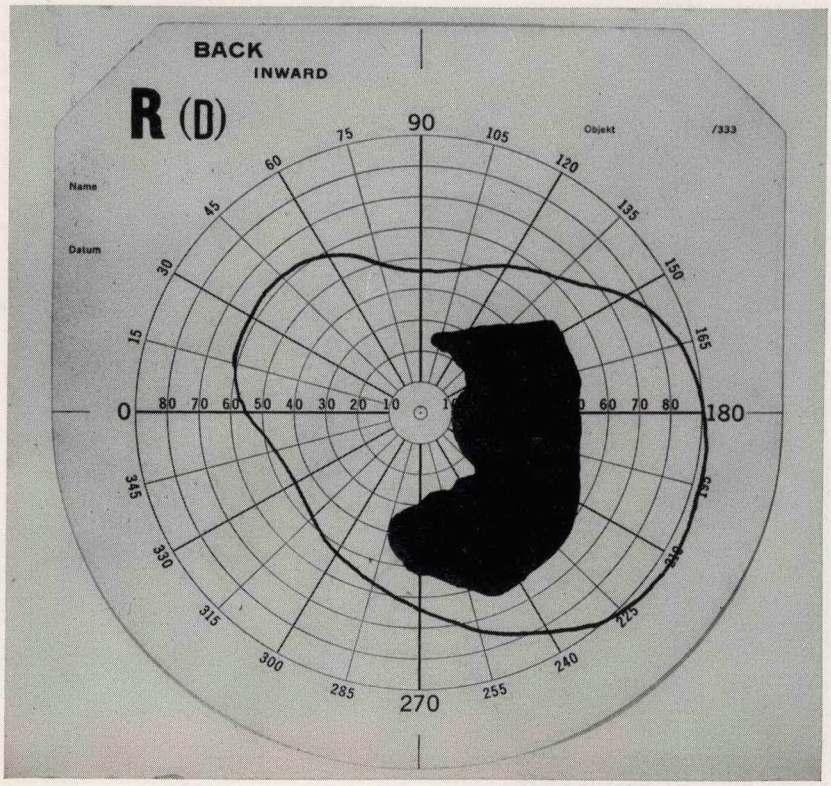


FIG. 1. Visual field O.D. showing large central scotoma

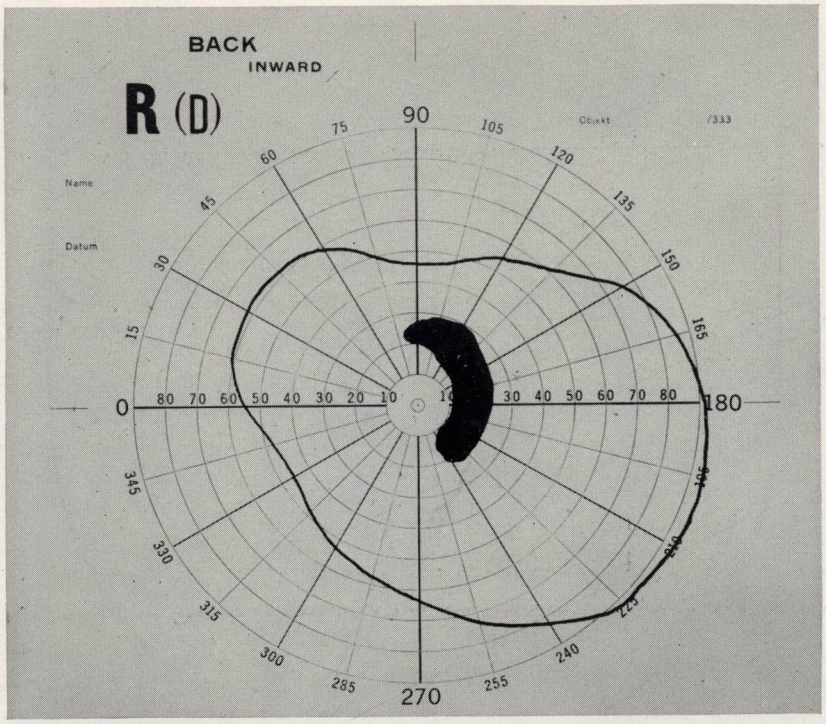


FIG. 2. Visual field O.D. showing marked reduction of scotoma, three days after treatment

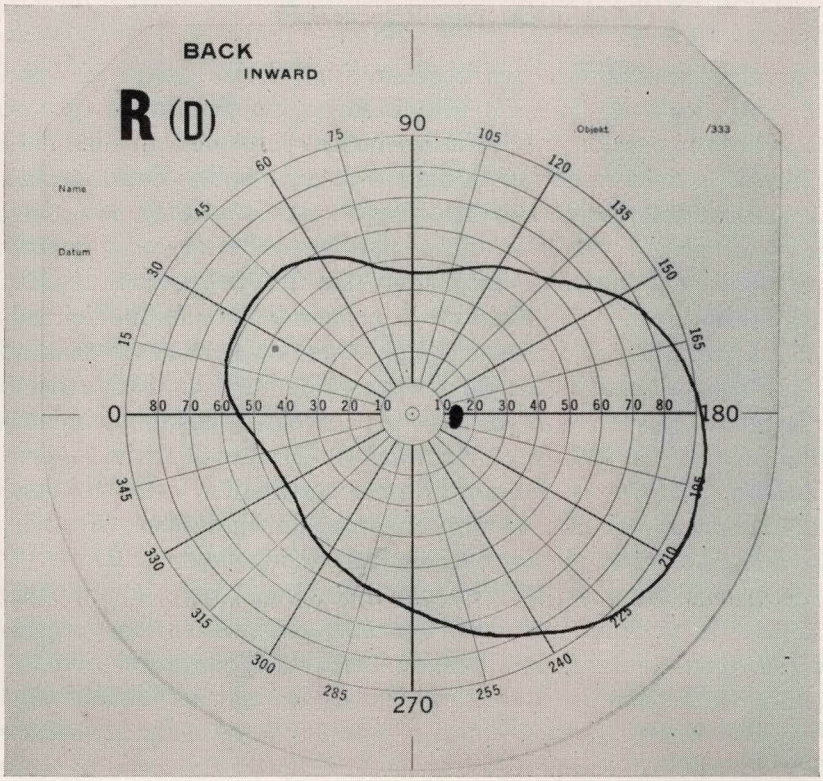


FIG. 3. Visual field O.D., 25 days after treatment appears normal