ARSINE POISONING

BY

D. BLAIR MACAULAY and D. AUSTEN STANLEY

From Bootle Hospital

(RECEIVED FOR PUBLICATION MARCH 26, 1956)

On June 20, 1952, at a tin smelting works in Bootle, six men were by mischance exposed to arsine gas of varying intensities. Two subsequently died. The following is an account of the nature of the accident, the clinical manifestations and the pathological findings, together with a review of the literature.

Nature of the Accident

Tin is manufactured on a very large scale in Bootle. It occurs naturally as pyrites, and arsenic is an invariable contaminant. The chemical composition of the ores varies considerably but arsenic is present in a concentration of up to 3%. The tin is liberated from its ores by heating with carbon. The arsenical impurities float to the surface of the molten tin and form a dross which has a high arsenical content. The dross is skimmed off and heated in another furnace in order to oxidize all the arsenic and in this form it is free of hazard. The tin is further purified by adding to it aluminium in the form of an aluminium-tin alloy. This causes the formation of aluminium arsenide, which has a higher melting point than that of tin and therefore floats to the surface as dross. It is a well recognized hazard of the tin smelting industry that this aluminium arsenide, when it comes into contact with water, generates arsine or arseniuretted hydrogen, which is highly toxic. Material which may contain aluminium arsenide is not, therefore, left lying about the factory.

On the day of the accident, a small amount of the dross from the aluminium-tin alloy melting was mixed with the roasted dross from the smelting furnace; the latter is known to be free from arsenide and the former is now known to contain it. This mixture was accidentally moistened. On this particular occasion, two men, J. E. and S. J., had been shovelling the dross mixture. A third man, A. B., was employed in bringing this dross by truck from another part of the factory. In error, he loaded

also into the same truck some moist material which consisted of gutter cleanings put there by men who were repairing the roof. Thus, in the truck were mixed three substances: roasted arsenical dross from the smelting furnace, which is safe, dross from the alloy furnace, which had become contaminated with arsenic, and waste material containing moisture. This mixture generated arsine which caused the accident.

When the men were taken ill the Works Manager immediately suspected arsine poisoning, because a similar accident had occurred at this factory 21 years previously. He immediately sent the severely affected men into hospital, and instructed other workmen to attend hospital if they felt ill. He then caused the affected area to be cleared, and had bleaching powder spread over all suspected material to oxidize arsenical compounds.

Clinical Manifestations

Six employees developed symptoms. Of these Cases 1 and 2 were actually shovelling the wet dross and came into close and sustained contact with the fumes. They developed symptoms within an hour or two and were admitted immediately to Bootle Hospital where they both subsequently died. Cases 3, 4, and 5 attended Bootle Hospital Casualty Department the following day, Case 3 being admitted and the others transferred to Walton Hospital. At the same time, Case 6 was admitted to Waterloo Hospital.

Case 1.—J. E., aged 23 years, while engaged between 1.40 and 2 p.m. in shovelling the dross mixture felt light-headed, reported sick, and was sent to hospital. On arrival, at 4.30 p.m., he was complaining of numbness and coldness of the hands, nausea, headache, pain in the loins, and severe colicky abdominal pains. Shortly after admission he vomited and passed dark greenish-black urine. His temperature was 100.5° F. A diagnosis of arsine poisoning was made and he was given 100 mg. "dimercaprol" (B.A.L.) and this was repeated four-hourly for five further doses. An intravenous dextrose

saline was administered with additional calcium gluconate.

That evening the haemoglobin was 75% (11.1 g. %). By 10 a.m. next day the haemoglobin had fallen to 55% (8.1 g. %), R.B.C.s to 2.6 million, and the blood urea level was 88 mg. %. He was still vomiting but the pains in the loins and abdomen were less, probably as a result of the sedative effect of pethidine, 50 mg. The skin had become a dusky bronze colour and the conjunctivae were evenly suffused and red. He was anuric. An electrocardiogram showed normal complexes. Blood withdrawn from a vein and immediately centrifuged produced plasma the colour of a dark port wine. One pint (570 ml.) of matched blood and 1 pint (570 ml.) of dextrose saline were administered intravenously. At midday the blood urea level was 120 mg. %. By 11 p.m. the blood urea level had risen to 176 mg. %. In an attempt to improve renal circulation 2 ml. of heavy nupercaine was injected intrathecally to produce a high spinal anaesthesia. Two hours later he passed 8 oz. (235 ml.) of nearly black urine and seemed a little better. During the next 24 hours his condition steadily deteriorated. Fluid by mouth (Bull's régime) even in restricted quantities was poorly retained. One pint (570 ml.) of glucose saline was administered intravenously. A further 9 oz. (252 ml.) of dark urine was passed during the day and a blood-stained motion was evacuated. There were intervals of delirium. The spinal anaesthetic was repeated without any benefit and he died at 11 p.m., approximately 57 hours after exposure to the arsine.

At necropsy the whole of the skin was pigmented a reddish brown colour. The conjunctiva of both eyes was yellow. The tongue was stained green. Both kidneys were enlarged and congested. The right kidney weighed 7 oz. and the left kidney 7½ oz. The spleen was enlarged, weighing 10½ oz. The stomach contained a little mucus only and there were a few petechial haemorrhages in its mucous membrane. The lungs showed bilateral hypostatic pneumonia. The bladder contained about half an ounce of fluid with the appearance of blood. There were no haemorrhages in the bladder wall.

Estimates of arsenious oxide and arsine gave the following results.

TABLE 1
ANALYSIS OF ARSENIOS OXIDE AND ARSINE AT
NECROPSY

Substance	Arsenious Oxide (p.p.m.)	Arsine (p.p.m.)
Blood	Trace	Trace
Contents of bladder	8	6.3
Liver	15	11.8
Spleen	10	7.9
Kidney	4	3.2
Brain	0.8	0.6

Case 2.—S. J., aged 33 years, was working side by side with J. E. and felt ill simultaneously. He was admitted to hospital at 4.30 p.m. At work he had complained of feeling sick with burning lips and excessive sweating within an hour of the onset of exposure. On admission

he complained of numbness and coldness of the hands and feet, headache, severe pain in the loins, and abdominal colicky pains. Soon after admission he vomited dark brown fluid. He was ordered 100 mg. "dimercaprol" (B.A.L.) four-hourly, pethidine, 50 mg., for the pain, and a glucose saline with calcium gluconate added was given by intravenous drip. Five hours later the skin had become bronzed, the conjunctivae were evenly blood-stained, and a small amount of almost black urine was passed. The tongue was coated with brown fur, the pulse was 90 per minute with a poor volume, and he was sweating profusely with a normal temperature. The headache and backache were still distressing. Haemoglobin was 56% (8.3 g. %). Vomiting continued throughout the night and the temperature rose to 100° F. Next morning there was still total anuria but a loose, dark, reddish-brown stool was passed. Blood withdrawn from a vein and immediately centrifuged produced a dark serum similar to that of Case 1. The blood picture was: Hb 52% (7.7 g. %), R.B.C.s 2.56 m., blood urea level 88 mg. %.

Two pints (1,140 ml.) of matched blood were given but anuria persisted. At 11 p.m. high spinal anaesthesia was administered with no relief of the anuria or vomiting. The following morning the blood picture was, in spite of transfusion, Hb 50% (7.4 g. %), R.B.C.s 2.47 m., blood urea level 235 mg. %.

Before midday 10 oz. of dark urine was passed. Bull's régime was started but poorly tolerated. A further high spinal anaesthetic produced no urine. From this time the patient's condition gradually deteriorated. Haemolysis was still continuing, and on June 25 (five days after exposure) the blood picture was: Hb 38% (5.6 g. %), R.B.C.s 1.94 m., blood urea level 230 mg. %.

Small quantities of urine were passed daily. A further blood transfusion of 1 pint (570 ml.) was given with little benefit. Electrocardiograms on June 21 and again on June 25 were normal. The patient died on June 29 (ninth day of illness). Fig. 1 gives the results of the investigation of blood cytology and biochemistry throughout most of his illness.

Necropsy showed that death was due to pulmonary oedema. The kidneys were swollen and congested, and microscopically showed extensive tubular necrosis and they were blocked by haemoglobin casts. The skin colour had faded considerably and there was no jaundice. The intestines showed a greyish black discoloration. There was blood-stained urine in the bladder.

Case 3.—J. H., aged 32 years, was working near the first two patients, but was not actually shovelling the dross. On the day of exposure he felt nothing beyond a slight headache. He went home at the usual time, had a few drinks in the course of the evening, and went to bed feeling well. Between 1 and 2 a.m. (12 hours after exposure) he woke feeling sick and vomited. In the morning he noticed that his urine was red. He went to work and was sent to Bootle Hospital where he was admitted from the Casualty Department.

On admission he had no symptoms. The conjunctivae were slightly reddened. The urine was very scanty and

FIG. 1.—Results of cytological and biochemical investigations in Case 2.

reddish brown. The temperature was 101° F. Centrifuged plasma was slightly stained with haemoglobin. Haemoglobin was 100% (14.8 g. %). The following morning the haemoglobin reading was 90% (13.3 g. %) and R.B.C.s 4.9 m. The blood urea level was 35 mg. % rising to 44 mg. % the following day.

A high spinal anaesthetic was given at 11 p.m. on June 21. By the following morning he was passing urine freely and by June 24 the colour of the urine was nearly normal. Apart from a feeling of general weakness he kept well and was discharged on June 30 (tenth day of illness). The blood urea level was by then maintaining a steady level of 35 mg. %. He remained under observation as an out-patient for some months and made a complete recovery.

Cases 4, 5, and 6 were admitted to other hospitals and through the courtesy of Dr. Summers we have seen

their case notes. They all exhibited haemoglobinaemia and some degree of anaemia, but all made a satisfactory recovery.

Discussion and Review

The nature of the exposure to arsine, while unusual, is not unique. Hamilton and Hardy (1949) state that the most frequent cause of industrial poisoning by arsine is in the cleaning out of tanks with a heavy acid (HCl or H_2SO_4), the acid acting on arsenic-bearing metals. Accidents in the tin industry, due to wetting of the dross, were described by Legge in 1924 who quotes six reports of a total of 30 cases with 12 deaths. Through the courtesy of Dr. Robert Coope we have had access to the records of two previously unreported cases in this

same Bootle smelting works who were admitted to Liverpool Royal Infirmary on November 16, 1931, five days after exposure under very similar circumstances. One patient was moribund and died within 24 hours. He was stated to be "bronzed, especially over the face, the nipples were black, and the conjunctivae were bloodshot. He had tenderness in both loins". The urine report was "dark red, a few R.B.C.s, oxyhaemoglobin and methaemoglobin in large amounts". The other patient had considerable haemolysis (R.B.C.s 3.5 m., Hb 35%), abdominal cramp, tenderness in the loins, and red urine, but this cleared rapidly and he was discharged in 10 days with a normal urea clearance test and a blood non-protein nitrogen level of 20 mg. %. A more recent outbreak in Indiana was fully reported by Spolyar and Harger (1950) and by Pinto, Petronella, Johns, and Arnold (1950). In this series 50 workmen (all negroes) were exposed to the fumes from storage drums of dross obtained during the manufacture of a lead-tin alloy. The drums had been exposed to rain, and arsine fumes thereby generated. Of the 50 men at risk, 13 developed toxic symptoms and four died. Locket, Grieve, and Phillips (1952) have described a recent fatal case of arsine poisoning in this country and have reviewed some of the literature. One of us has had the wartime experience of investigating suspected arsine poisoning in submarine personnel and observed that submarine commanders were well aware of the risk of arsine being generated during battery charging if the lead plates contained arsenic.

In comparing the above cases with those described in the recent literature some important facts emerge.

Mode of Onset.—The heavier the exposure to arsine gas, the sooner was the onset and the greater the gravity of the prognosis. Early symptoms in our cases were dizziness and nausea within two hours of exposure, followed by abdominal colic and pains in the loins. These loin pains were not observed in the Indiana series (Spolyar and Harger, 1950; Pinto and others, 1950), but were stressed by Jones (1907) in an earlier record.

Discoloration of urine appeared in four to 12 hours. In the milder cases it appeared later but was the first and only symptom of illness.

Within 12 hours the more seriously affected cases had developed conjunctival staining of a reddish colour probably due to haemoglobin and the skin had become dusky bronzed for a similar reason. The colour of the conjunctiva and skin produced by the presence of haemoglobin is quite unlike jaundice which is due to the presence of bilirubin. Glaister (1908) (quoting Maljean) wrote in 1908 that "the colour of these patients resembles jaundice

only at first sight". Most standard textbooks still erroneously describe this pigmentation as "jaundice". None of our patients reached high levels of bilirubinaemia, and Pinto in his series states that "in only one patient (out of 13) was there any suggestion of jaundice. The bilirubinaemia was found to be 3 mg. on the fourth day after being exposed to arsine".

Haemolysis was rapid and severe in all cases and was only temporarily checked by blood transfusions.

Dimercaprol (B.A.L.) was given to the three most seriously affected cases without any apparent benefit. This is in agreement with the findings of all workers and also with experimental work on animals (Kensler, Abels, and Rhoads, 1946). It was felt, however, that if patients recovered from the acute renal lesion, the use of B.A.L. might prevent later symptoms of arsine poisoning.

Course of the Disease.—The anuria which followed on the haemoglobinuria did not differ from the anuria of an incompatible transfusion or of blackwater fever. The danger of hyperpotassaemia has been stressed. Pinto regards the electrocardiographic evidence of this (exaggerated T waves) as one of the earliest and most sensitive signs for the diagnosis of arsine poisoning. None of our patients exhibited this electrocardiographic change and in none of them was the serum potassium level materially raised, except terminally. From the onset of the condition a very considerable amount of intracellular potassium must have been liberated and a further amount of potassium had been introduced into the circulation by blood transfusion. No appreciable potassium loss could have occurred by renal excretion. The fact that serum potassium levels remained normal for many days in spite of the above suggests that some regulating mechanism was operating until very shortly before death. With the danger of hyperpotassaemia in mind, transfusions were given sparingly—in the event probably too sparingly. The high spinal anaesthetic given in an attempt to improve renal circulation was a forlorn hope and met with no success. It was felt that the diuresis which followed it in Case 3 would have occurred in any case.

Summary

Arsine poisoning affecting six employees at a lead works is described.

The nature of the hazard is discussed.

Clinical and pathological findings are described and discussed.

Our thanks are due to Dr. G. B. Manning who carried out the necropsy on Case 1 (J. E.), to Dr. J. B. Firth

of the North Western Forensic Science Laboratory for the estimations of arsenious oxide and arsine, and to Professor Sheehan for his interest and advice.

REFERENCES

- Glaister, J. (1908). *Poisoning by Arseniuretted Hydrogen or Hydrogen Arsenide*. Livingstone, Edinburgh.
- Hamilton, A., and Hardy, H. L. (1949). *Industrial Toxicology*, 2nd ed. Hoeber, New York.
- Jones, N. W. (1907). *J. Amer. med. Ass.*, **48**, 1099.
- Kensler, C. J., Abels, J. C., and Rhoads, C. P. (1946). *J. Pharmacol.*, **88**, 99.
- Legge, T. M. (1924). Annual Report of the Chief Inspector of Factories and Workshops 1923, p. 64. H.M.S.O., London.
- Locket, S., Grieve, W. S. M., and Phillips, L. (1952). *Trans. Ass. industr. med. Offrs.*, **2**, 14.
- Pinto, S. S., Petronella, S. J., Johns, D. R., and Arnold, M. F. (1950). *Arch. industr. Hyg.*, **1**, 437.
- Spolyar, L. W., and Harger, R. N. (1950). *Ibid.*, **1**, 419.

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS: 21st ANNIVERSARY MEETING

The 21st Anniversary Meeting will be held in London from Monday, September 24, until Friday, September 28. All the scientific sessions (except the Mackenzie Industrial Health Lecture) will be held at The London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

The first day of the meeting will be devoted to registrations and to a reception at Canterbury Hall, Cartwright Gardens, W.C.1, when the London Group of the Association, the organizers of the Meeting, will be the hosts.

An exhibition illustrating the work of the Ministry of Supply Medical Service will be opened on the first day of the meeting between 2 and 6 p.m. in the Pillar Hall, Whitehall Gardens, S.W.1, and will be open each day of the meeting.

On Tuesday, September 25, at 10 a.m., the inaugural meeting will be opened by The Rt. Hon. Iain MacLeod, M.P., and will be followed by the Presidential Address by Dr. R. S. F. Schilling.

PROGRAMME OF SCIENTIFIC MEETINGS

Tuesday, September 25

11.15 a.m. "The Elderly Worker"

Chairman: Donald Stewart, M.D., F.R.C.P. (Ed.), Chief Medical Officer, Austin Motor Company, founder member of the Association.

Opening paper by Professor Sven Forssman, M.D., Medical Adviser to the Swedish Employers' Confederation, President of the Permanent International Committee on Industrial Medicine, Associate Professor of Occupational Health, Karolinska Institutet, Stockholm.

"The Health Problems of the Older Worker—A Study in Swedish Industry"

Discussion to be opened by A. Meiklejohn, M.D., M.R.C.P., Past President of the Association.

3.0 p.m. In the Great Hall, B.M.A. House, Tavistock Square, W.C.1.

The British Medical Association Mackenzie Industrial Health Lecture

Chairman: Alex H. Hall, O.B.E., M.D., President, British Medical Association.

Lecturer: R. S. F. Schilling, M.D., M.R.C.P., D.P.H., D.I.H., Reader, Nuffield Department of Occupational Health, University of Manchester; Editor, *British Journal of Industrial Medicine*.

"The Assessment of Health in Industry"

Wednesday, September 26

9.30 a.m. "Research in Occupational Health"

Chairman: M. W. Goldblatt, C.B.E., M.D., M.R.C.P., Ph.D., D.I.H., Director, Industrial Hygiene Laboratories, Imperial Chemical Industries Ltd., Past President and founder member of the Association

Speakers: The Earl of Verulam, M.A., F.I.I.A., Comp. I.E.E., J.P., Chairman, Enfield Rolling Mills Ltd.

Sir Harold Himsworth, K.C.B., M.D., F.R.C.P., F.R.S., Secretary, Medical Research Council.

Sir Alfred Roberts, C.B.E., M.A., J.P., Past President, Trades Union Congress.

11.30 a.m. A Discussion on "Research in Occupational Health" will be opened by J. N. Morris, M.A., M.R.C.P., D.P.H., J.P., Director, Social Medicine Research Unit, Medical Research Council.

Thursday, September 27

9.30 a.m. "The Impact on Medicine and Industry of the Use of Atomic Energy"

Chairman: W. Blood, O.B.E., M.R.C.S., L.R.C.P., D.I.H., Senior Medical Officer, J. Lyons & Co. Ltd., Past President of the Association.

Speaker: E. Katharine Williams, B.Sc., M.B., B.Ch., M.R.C.P., D.I.H., Research Group Medical Officer, Atomic Energy Research Establishment.