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Peripheral Neuropathy with Sympathetic Overactivity from Industrial Contact with Acrylamide

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This paper describes the experimental and clinical findings of acrylamide intoxication in a human being. It is believed that this is the first such case to be recorded in the medical literature.

Acrylamide is widely used as a "chemical grout". It is pumped into dirt, clay and stone walls of excavations in a liquid state together with a catalyst, and it then polymerizes to make a watertight shield.

This chemical is neurotoxic in its non-polymerized form and can be absorbed through the intact skin, mucous membranes and lungs. In spite of warnings with regard to its handling, this worker became careless, and developed a contact dermatitis and a polyneuropathy with bluish cold extremities which dripped perspiration.

In six months' time after his removal from contact with the chemical the patient made a complete clinical recovery. He was advised not to work with the chemical.

Cet article expose les constatations expérimentales et cliniques de l'intoxication par l'acrylamide chez l'homme. De l'avis des auteurs, il s'agit du premier cas qui ait été signalé dans la littérature médicale.

L'acrylamide est employé sur une grande échelle comme "ciment chimique". On le pompe à l'état liquide avec un catalyseur dans la boue, l'argile, et les murs de pierre des excavations, où il subit une polymérisation et forme un bouclier protecteur imperméable.

Ce produit chimique est cependant neurotoxique dans sa forme non polymérisée et peut être absorbé par la peau intacte, les muqueuses et les poumons. Malgré les avertissements répétés concernant sa manutention cet ouvrier est devenu négligent, et a présenté une dermatite de contact et une polyneuropathie, accompagnée d'une teinte bleuâtre des extrémités froides et qui présentaient une transpiration avec dégouttement.

Dans un délai de six mois après suppression du contact avec le chimique, le malade guérit complètement. Il fut conseillé de ne plus manipuler le produit en question.

PERIPHERAL neuropathy is well known to occur without recognized cause, and following infections or exposure to toxins. Sympathetic overactivity is uncommon with most varieties of peripheral neuropathy except in very severe cases.

This paper presents the findings in the first human case of acrylamide toxicity to be reported. This organic monomer is widely used in chemical grouts to prevent water seepage at construction, drilling and mining sites.

CASE REPORT

B.E.H., a 21-year-old white male, was perfectly well until early January 1965, when he went to work in a mine operated in Bathurst, New Brunswick. His job consisted of loading the hoppers with a 10% aqueous solution of acrylamide, and adding the catalyst B-dimethyl-amino-proprionitrile (DMAPN). He then aided in the wall drilling necessary to introduce the compound-plus-catalyst into the soil.

His actual working period was 35 hours per week. He returned to his home in Windsor, Nova Scotia, on week-ends.

He stated that neither he nor his colleague was particularly careful in handling the preparations because "no one ever got sick with it", and that many times he had the chemical on his face and forearms. In mid-January 1965 he noted a reddish "rash" on his forearms which he attributed to irritation from his rubber gloves and uniform.

In mid-February 1965, seven weeks after beginning to handle the material, he noted the onset of weakness of his legs, and by the end of February 1965 weakness of his hands. This became obvious to his friends as he stumbled when he walked, had difficulty climbing stairs (because of poor balance), and difficulty in writing and handling eating utensils.

In early March 1965 he noted blueness, coldness and profuse sweating of his arms, hands, fingers, lower legs, feet and toes. About this time, too, his hands and feet felt numb and "tender" when they were touched.

Also in early March 1965 his companion stopped work because of tiredness and a skin rash. This man was seen by a local physician and was considered to have only a contact dermatitis. He was able to return to work on March 15, 1965, with no complaints.

This patient became increasingly weak and ataxic and his peripheral sweating increased markedly. He was admitted to the Victoria General Hospital in Halifax on March 6, 1965, about 14 weeks after his exposure to acrylamide began.

He was not exposed to any other known chemicals. He drank beer occasionally but did not consume spirits. He was not diabetic and there was no family history of diabetes. His diet was adequate.

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He had no sore throat, "flu" or diarrhea before the onset of symptoms.

On examination in hospital he was a well-developed, well-nourished man with a blood pressure of 110/60 mm./Hg and a regular pulse of 84 beats per minute. On general examination there was a mild inflammation about his wrists. There was a bluish-red discolouration of his forearms and hands, his lower legs and feet. They dripped perspiration and were cold to touch. There was a slight impairment of temperature sensation and position, and vibration senses were slightly decreased. The tendon reflexes were absent and the plantar reflexes normal. There was weakness of the distal muscles of his arms and legs, particularly the legs. He was more unsteady on his feet than could be clearly related to the degree of weakness. The remainder of the general examination was normal.

Examination of the cerebrospinal fluid (CSF) showed no cells, protein 82 mg. % and normal sugar and chloride. The mastic curve was 2210000000, Two weeks later the protein was 70 mg. % and the mastic curve was 1000000000. All other studies remained normal. Exhaustive laboratory tests were all within normal limits.

With rest, gradual ambulation, and complete withdrawal from the exposure to acrylamide, he slowly made a complete recovery. By mid-April (six weeks after admission), his hands and feet had completely "peeled" and had normal colour, tactile sensation and temperature. The palms and soles were still somewhat moist. By mid-May the knee jerks had returned and by mid-June (14 weeks after admission to hospital), sensation, strength and reflexes had all returned to normal and he was able to go back to work.

He was strongly advised not to return to a job involving the handling of or possible exposure to acrylamide.[1] This meant a change in occupation.

ACRYLAMIDE—PROPERTIES

Acrylamide is unique, because it is a water-soluble powder in its monomeric form (Fig. 1) and an inert gel, impermeable to water, in its polymerized form (Fig. 1). Polymerization results from the use of DMAPN and ammonium persulfate as catalysts.

When completely polymerized, acrylamide is considered to be non-toxic by most observers. Fassett,[2] however, refers to it as a primary skin irritant (it could have been the cause of the contact dermatitis in this patient and his co-worker).

The polymerization of acrylamide is not completely understood. Under heat (i.e. drilling) acrylamide can decompose to produce many products including hydrogen cyanide and dimethylamine (another skin irritant), but in this case the drilling was done before the compound was pumped into the ground.

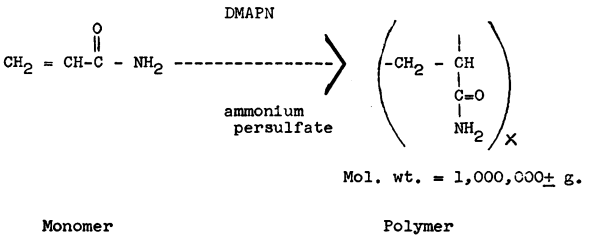

Fig. 1.

Acrylamide as a substance produces an interesting toxicological phenomenon which Stokinger[1] refers to as its "anamnestic effect"—meaning that following recovery from the effects of poisoning by it, the same syndrome can recur with lesser amounts of the drug on re-exposure. It was for this reason our patient was strongly advised not to return to his former job.

When used as a 10% solution, monomeric acrylamide is toxic. Its effects are cumulative and it is absorbed through the intact skin and mucous membranes, the lung and the gut. The oral LD_{50} in rodents is 150-180 mg./kg.

The catalysts are irritating to the skin. DMAPN (in animal experiments) is believed to be of low toxicity from acute (brief) exposure. The effects of chronic exposure are unknown. It is, however, an organic cyanide, but there was no evidence of cyanide poisoning in this patient.

DISCUSSION

Two points deserve discussion: (a) that acrylamide is neurotoxic with its main effect on peripheral nerves; and (b) that the clinical findings in this case are in keeping with chronic exposure to acrylamide (Am-9 Cyanamid).

Based on the findings of earlier German workers, Hamblin[3] in 1956 reported that various laboratory animals exhibited reproducible neurotoxicity. The picture was one of ataxia, incoordination and weakness of the extremities, the hind quarters being involved primarily. He also demonstrated the toxic effects to be dose-dependent and cumulative. He was unable to demonstrate any characteristic pathological changes of the central nervous system.

Kuperman[4] in 1958 and McCollister, Oyen and Rowe[5] in 1963 confirmed Hamblin's findings. They also were unable to demonstrate any pathological changes in the central nervous system.

Recently Fullerton and Barnes[6] have produced chronic paralysis in rats by oral feeding of acrylamide for several months. They demonstrated primary axonal degeneration of peri-

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pheral nerves, affecting the distal ends of longest fibres. The changes are similar to those seen in isoniazid poisoning.

No human cases have been reported in detail in the medical literature. Since 1955 a few cases in which acrylamide was implicated as a neurotoxin have been reported to the American Cyanamid Company. Typically, prolonged handling of the chemical without adequate safeguards was followed by initial lassitude and drowsiness with subsequent rather vague symptoms of numbness and tingling of the fingers and unsteadiness, particularly on ascending stairs. Physical signs were not striking. Complete but slow recovery occurred following withdrawal from the chemical.

Initially the possibility of cyanide poisoning was considered. It is recognized experimentally that chronic cyanide poisoning can lead to weakness and signs of neuropathy, but with the lack of evidence for acrylamide decomposition, and the minute amounts of catalyst used, it was felt that this was not significant in this problem.

In this patient the problem was one of differentiating between postinfectious polyneuritis (Landry-Guillain-Barré-Strohl syndrome) and neural toxicity from acrylamide. The lack of a preceding illness, the absence of infectious mononucleosis, and the low CSF protein reduced the probability of postinfectious polyneuritis. There was no contact with other known neurotoxins. In keeping with acrylamide toxicity were his previous good health, indifferent handling of and repeated exposure to monomeric acrylamide parallel with the clinical picture of generalized fatigue, ataxia, leg weakness and minimal sensory changes. We concluded therefore that this patient had a toxic polyneuropathy due to acrylamide.

With a peripheral neuropathy from any cause trophic and vasomotor disturbances are not infrequent, "but are seen more particularly in severe cases".[7]

This phenomenon was not reported in the animal experiments. We could not classify our patient's disability as "severe" and therefore suggest that this may be a feature of the human illness. We felt that the bluish mottling, coldness and sweating of the distal parts of he limbs were due to sympathetic overactivity.

SUMMARY

What is believed to be the first human case reported in the medical literature of peripheral neuropathy with sympathetic overactivity resulting from acrylamide toxicity has been presented. The toxic effects in animals of this commonly used industrial compound have been reviewed. In animals and man recovery is complete upon withdrawal from the chemical. The wide use of acrylamide makes it imperative for physicians to be aware of its dangers.

We would like to acknowledge the excellent co-operation and aid of our colleagues at the Victoria General Hospital, and of the Medical Department of the American Cyanamid Company in Wayne, New Jersey, who keep a complete file of the world literature and reports about this compound and who freely shared their experience.

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