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CLINICAL AND ELECTROPHYSIOLOGICAL STUDIES OF ACRYLAMIDE POISONING

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ABSTRACT

Five cases of poisoning from handling acrylamide monomer are described. The poisoning occurred after a short exposure during the process of polymerization and injection of the monomer in tunnelling operations. The main signs and symptoms were itching, erythema, peeling and increased sweating of the hands, numbness and tingling of the fingers, muscle weakness, muscle pain, excessive fatigue, absence of tendon reflexes in the legs and in the arms, nausea and vomiting. In all cases, even with no other clinical neurological symptoms, peripheral neuropathy was observed.

This study showed that the degree of pathological change was related to the duration and level of acrylamide exposure and that the nervous system damage developed insidiously. In the early stages of intoxication electrophysiological studies showed early abnormalities in conduction of distal and proximal parts of nerves. The recovery was slow. With time, conduction velocity improved, but marked dispersion of the muscle response to nerve stimulation as well as potentials with markedly prolonged distal latencies were found.

Our results suggest that the central nervous system is regenerated, even if very slowly.

Monomeric acrylamide has had a widespread application throughout the world. Potential occupational exposure to this compound may occur in acrylamide and textile manufacture, in chemical grouting, in soil stabilization, in flocculation operations and so on.

Acrylamide is known to be neurotoxic to many species[8]. The skin is the primary portal of entry[5,7]. Acrylamide is biologically very specific[6].

In this study we describe the results of neurological and electrophysiological examinations performed on five workers who had been handling acrylamide for the first time in Italy in tunnelling operations in order to render the soil waterproof.

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SUBJECTS AND METHODS

The workers used solutions of AM-9 which were catalyzed at the time they were injected into the soil. AM-9 is a mixture of two organic monomers: acrylamide and N,N'-methylenebisacrylamide in proportions which produce very stiff gels from dilute, aqueous solutions when properly catalyzed. It is white powder with a bulk density of 0.56 kg/dm^3. When stored dry in original containers at temperatures below 30 °C its stability is excellent. AM-9 is very soluble in water, methanol, ethanol, but it is insoluble in kerosene, gasoline and oils.

The process by which gelation occurs is polymerization-crosslinking reaction. The gel is formed by a two-step process: Step 1 – an aqueous solution of AM-9, containing additives for controlling the gel time and one component of the catalyst system (the activator) is prepared, and Step 2 – the remaining component of the catalyst system (the initiator) is added to the solution of AM-9 prepared in Step 1. Timing of the induction period (gel time) is started. Two reactions occur in sequence: catalyst → free radicals → free radicals + AM-9 → polymer.

The catalyst system is composed of DMAPN (beta-dimethyl-aminopropionitrile), AP (ammonium persulphate) and potassium ferricyanide. DMAPN is a caustic liquid, used as an activator for the reaction. AP is a granular material and a very strong oxidizing agent, used as an initiator for the reaction. Potassium ferricyanide is a granular material, used to control the reaction.

Neurological examination and routine electromyography were performed on all subjects. Motor nerve conduction velocity (maximum and minimum conduction velocity of peroneal, median and ulnar nerves) was measured with bifilar technique: muscle action potentials were recorded through Adrian and Bronck's coaxial needle electrodes. The latencies from the stimulus to the response were measured and MCV was calculated by dividing the distance between the stimulation points by the difference of the latencies. The responses were amplified with the electromyograph (Medelec, SDC 3). The patterns of maximal contraction, shape, duration and amplitude of single motor units, as well as possible spontaneous activity during muscular relaxation were noted. The MCV of the arm nerves ranged from 50 to 60 m/sec and those of the leg nerves from 45 to 55 m/sec.

An EEG examination was also performed on the subjects under study. The EEG apparatus had 19 channels. The recording of the electrical activity of the brain was amplified with a specific apparatus and was recorded on paper. According to the international 10–20 system, 19 electrodes were placed on anatomically-fixed regions of the scalp, and one electrode was attached to each ear lobe.

RESULTS

Signs and symptoms found in five workers poisoned with acrylamide as related to exposure are shown in Table 1.

TABLE 1

Main signs, symptoms and length of exposure in the five workers poisoned with acrylamide.

Finding	Worker				
	1	2	3	4	5
Exposure (weeks)	12	12	4	12	12
Itching	+	−	+	+	+
Sweating of hands	+	−	−	+	+
Hands peeling	+	+	+	+	+
Fatigue	−	+	−	+	+
Muscle weakness	−	−	−	+	+
Nausea, vomiting	−	+	+	−	−
Absent tendon reflexes	−	−	−	+	+
Ataxic gait	−	−	−	−	+
Romberg's sign	−	−	−	−	+
Cerebellar asynergia	−	−	−	−	+
Altered vibration sense	−	−	−	+	+
Altered position sense	−	−	−	+	+
EEG abnormalities	−	−	−	−	+
EMG changes	+	+	+	+	+
Altered visual fields	−	−	−	−	+
Altered vestibular function	−	−	−	−	+
Sexual impotence	−	−	−	−	+

Worker No. 1

Man, aged 23, worked with acrylamide for three months. He smoked 10 cigarettes per day. No relevant data from the family and past history were found. After handling acrylamide he experienced itching, excess sweating in the palms and then hands peeling.

Routine clinical laboratory tests, neurological examination, electroencephalography, vestibular function test, visual acuity test, chest X-rays and respiratory function tests were normal. The results of electromyography are shown in Table 2.

TABLE 2

Motor conduction velocity (MCV) and distal latencies (DL) in peroneal nerve of three workers.

Worker	MCV (m/sec)		DL (msec)	
	Right	Left	Right	Left
No. 1	45–43	42	8–20	5–20
No. 2	45–43	45–41	5–12	7–11
No. 3	41	41	7–16	7–18

Worker No. 2

Man, aged 38, was exposed to acrylamide for three months. He smoked 15 cigarettes per day. There were no remarkable findings from the family and past

history. After handling acrylamide for ten days he experienced nausea, vomiting, epigastralgia, asthenia, hands peeling.

Routine clinical laboratory tests, neurological examination, vestibular function test, visual acuity test, electroencephalography, chest X-rays and respiratory function tests were normal. The results of electromyography are shown in Table 2.

Worker No. 3

Man, aged 31, worked with acrylamide for one month. He smoked 10 cigarettes per day. No relevant data from the family and past history were found.

After handling acrylamide for one week he experienced nausea, epigastralgia, itching of hands. The skin of his hands peeled. The results of electromyography are shown in Table 2.

Worker No. 4

Man, aged 32, worked with acrylamide (during the process of polymerization and injection) for three months. He smoked 20 cigarettes per day. No relevant data from the family and past history were found.

After handling acrylamide for ten days he experienced pins and needles, coldness in the hands, increasing sweating and peeling of the hands. Fine movements of the hands became difficult. Also fatigue was present. Two months later he experienced dyspnoea, altered visual acuity, loss of power in the small muscles of hands, sensation was altered in the hands.

He was seen three months after the last contact with acrylamide. Neurological examination revealed absent tendon reflexes in the arms, sluggish reflexes in the legs, altered peripheral sensation, altered vibration and position sense in the arms. Routine clinical laboratory tests showed a high lymphocyte count. Vestibular function test, visual acuity test and electroencephalography were normal. The results of electromyography are shown in Table 3.

After six months the loss of power in the small muscles of the hands and altered vibration sense were still present. Fine movements of the hands were

TABLE 3

Motor nerve conduction velocity (MCV) and distal latencies (DL) in worker No. 4.

Nerve		3 months*	6 months	12 months	30 months
Right median	MCV (m/sec)	46–42	57–42	55–49	58
	DL (msec)	4–14	4–36	4–20	10–20
Right ulnar	MCV (m/sec)	54–49	54–45	48–44	61–51
	DL (msec)	4–20	4–30	3–13	4–10

*Time since last exposure to acrylamide.

difficult. Neurological examination revealed sluggish tendon reflexes in the arms and absent Achilles reflexes in the legs. After twelve months he experienced weakness in the arms. Tendon reflexes in the arms and Achilles reflexes in the legs were sluggish. After thirty months he experienced insomnia, asthenia, loss of power in the small muscles of the hands. Tendon reflexes in the arms were sluggish.

Worker No. 5

Man, aged 22, worked closely with acrylamide (in the process of polymerization and injection) for three months. He was a non-smoker. No relevant data from the family and past history were found.

After working with acrylamide he experienced asthenia, disturbance of sleep, lassitude, dizziness, then impotence, strong peeling of hands and feet, altered visual acuity. There was a strong slurring of speech. He was unable to drink from a cup and to walk without support.

Neurological examination revealed ataxic gait, Romberg's sign was strongly positive, all tendon reflexes were absent in the legs. Cerebellar impairment, dysarthria, hypertensive retinopathy were present. EEG examination showed widespread cerebral impairment. Vestibular impairment was also present. Ten days later the visual field was constricted for red and green. Sense of vibration was absent and sense of position was present.

TABLE 4

Motor nerve conduction velocity (MCV) and distal latencies (DL) in worker No. 5.

Nerve		1 month*	6 months	13 months	27 months
Right peroneal	MCV (m/sec)	42–33	35	43	43
	DL (msec)	10–22	8–20	6–25	8–35
Left peroneal	MCV (m/sec)	37–34	37–35	39	43
	DL (msec)	7–22	6–22	7–15	5–12

*Time since last exposure to acrylamide.

Twenty days later both the sense of vibration and sense of position were absent, the gait was ataxic, Romberg's sign was positive and cerebellar asynergia was present. One month later tendon reflexes in the legs and arms were absent. Four months later ataxic gait was still present, Romberg's test showed a few oscillations, speech was normal and so was vestibular function but all tendon reflexes in the legs were absent. Six months later the gait and visual fields were normal but vibration sense was altered, and cerebellar symptoms were only mild. Ten months later tendon reflexes in the legs were sluggish, Achilles reflexes were absent. Vibration sense became intact. Recovery of the damage of the central

nervous system was observed. Twenty months later the subject experienced pins and needles and weakness in his hands and cramps in the legs. Tendon reflexes in the legs were present, Achilles reflexes were sluggish. Twenty-seven months later the subject experienced pins and needles in the hands, anaesthesia of the fingers, cramps in the legs. Tendon reflexes in the arms and Achilles reflexes were sluggish. The results of electromyography are shown in Table 4.

DISCUSSION AND CONCLUSIONS

Dying-back of the peripheral branches of axons is seen in a number of toxic neuropathies, including those due to acrylamide. Possible explanations include a decrease of axonal transport, a decrease in neuronal synthesis, an increase in catabolism of essential nutrients in the peripheral branches of the nerves or nicotinamide-antagonism.

A study of axonal transport in experimental acrylamide neuropathy in the rat[1] has shown a 50 per cent reduction in the rate of transport of acetylcholinesterase, though the amount of acetylcholinesterase transported was normal.

An experimental study[10] showed that acrylamide, at high concentrations, caused a total block of axonal transport in rabbits.

Studies of the pattern of nerve fibre damage in experimental animals demonstrated that distal regions of nerves were more affected than proximal regions[3]. Human intoxication in industry appears to result from dermal contact[2,7].

Acrylamide intoxication may first become evident in the form of excessive sweating, erythema and peeling of the hands, pins and needles, coldness and excessive fatigue. Fine movements of the hands become difficult. Weakness in the legs and in the hands, the loss of power of the small muscles of the hands and the loss of vibration and position sense appear more slowly. In addition to signs of peripheral neuropathy, signs of impairment of the central nervous system such as ataxic gait and slurring speech, or a mild organic mental syndrome may appear[11].

The symptoms we have summarized in Table 1 correspond to those described by other authors[5]. In the light of our cases we consider that acrylamide intoxication causes peripheral neuropathy and a central nervous system lesion. Removal from exposure was followed by complete recovery of the less severely poisoned workers. In more severely poisoned subjects, thirty months after the removal from acrylamide exposure, signs of nervous system damage and abnormalities in the motor conduction velocity were still present. It appears that the degree of pathological changes is related to the duration and level of acrylamide exposure. In the early stages of intoxication, electrophysiological studies showed early abnormalities in conduction of distal and proximal parts of nerves. The persistence of abnormalities in conduction (increased values for distal latencies) demonstrated that axonal changes were present.

Our results suggest that nerve fibres undergo a progressive retrograde degeneration. Similar results were found by other authors[9]. With time,

conduction velocity improves but marked dispersion of the muscle response to nerve stimulation as well as potentials with prolonged distal latencies may appear. This phenomenon is an indication of regeneration of the fibres[4]. Damages to the central nervous system are serious. However, our results suggest that the central nervous system is regenerated although the recovery is slow.

Itching, increased sweating, erythema and peeling of the hands were the first signs. It should be pointed out that an early diagnosis of the cause of neuropathy is very important and that clinical diagnostic tests like electromyography are useful in evaluating and following symptomatic subjects. Industrial hygiene measures and close supervision of workers (monitoring of workers by periodic examination of palmar sensibility) are more important in preventing clinically manifest intoxication. Since acrylamide is a contact poison, measures for prevention of skin exposure should be undertaken.

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