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Medical Memoranda

Trichloroethylene Neuropathy

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Trichloroethylene is a volatile, non-inflammable liquid, miscible with most organic liquids. It has a powerful solvent action on many organic solids, including rubber (Lloyd-Potter, 1958), and it is widely used in industry. Its toxicology is complex because standards of purity have varied in different countries at different times, and because breakdown products occur both in vitro (Browning, 1965) and in vivo (Mikiskova and Mikiska, 1966). Trichloroethylene has a narcotic effect (Lehmann, 1911), and Striker *et al.* (1935) proposed it as a safe anaesthetic, but the Council on Pharmacy and Chemistry of the American Medical Association (1936) restricted its use because some complications involving the cranial nerves had been reported. With the outbreak of the second world war, when renewed efforts were made to find an anaesthetic safer than chloroform, Hewer and Hadfield (1941) reported favourably on trichloroethylene, but later Hewer (1943) noted trigeminal analgesia, and then multiple cranial nerve lesions were encountered by Humphrey and McClelland (1944). The latter suggested that these complications, produced when trichloroethylene was used in closed circuit with soda lime, were due to the formation of dichloroacetylene. If contact with soda lime was avoided, trichloroethylene was regarded as a useful and safe anaesthetic harmless to the nervous system (Enderby, 1944; Ostlere, 1948), and it is now widely used.

Soon after trichloroethylene was introduced into German industry as a degreasing agent during the first world war, neurological sequels to exposure were described by Plessner (1915), and later by Baader (1927), Teleky (1931), and Isenschmid and Kunz (1935). Stüber (1931) described 284 cases of intoxication, of which 182 were chronic and had presented either with a functional neurosis or with cranial nerve involvement. Later reports stressed organic mental deterioration as the most serious complication (Grandjean *et al.*, 1955; Trense, 1965).

However, in Britain and America neurological complications have not been encountered in industry, except as a result of obvious acute overexposure. Opinion in these countries was summarized by Johnstone (1941), who stated: "Because trichloroethylene does not exercise any cumulative action, it is the belief of most authorities that organic disturbances do not take place following chronic exposure, although symptoms such as general malaise, lethargy, loss of appetite, etc., may be noted." Further doubts about chronic intoxication were published by the Department of National Health and Welfare, Canada (1949), Lloyd-Potter (1958), and Browning (1965). Hunter

(1962) stated that there was little evidence of cumulative action of trichloroethylene, though he did admit that it might have a special affinity for nervous tissue. Most convincing of all, Imperial Chemical Industries, sole manufacturers of trichloroethylene in Britain, have never encountered any suggestion of ill-health among their employees resulting from exposure to the chemical during its manufacture (K. P. Whitehead, personal communication, 1968).

In view of this we think it important to report the following case.

CASE HISTORY

A 33-year-old West Indian man from Grenada was first referred to Charing Cross Hospital on 27 April 1967 complaining of loss of taste of three weeks' duration. He had lost 14 lb. (6.4 kg.) in weight in this time. He was otherwise asymptomatic. His sense of smell was unimpaired, and no abnormal physical signs were detected apart from ageusia. His past history and family history were non-contributory. He was teetotal and a non-smoker.

He was not exposed to toxic preparations until March 1967, when he began work as a metal degreaser. His job was to lower a basket containing metal objects into an open bath of warm trichloroethylene. Some larger objects had to be put in by hand. The objects were later lifted and drained for three minutes. Despite the condenser coil at the rim of the bath the smell of trichloroethylene was always present, and the fumes occasionally escaped in sufficient quantities as to be visible. The extractor inlet was 10 ft. (3 m.) from the bath. He had noted no ill-effects at this work, but had become excessively sleepy in the evenings and his sexual desire had diminished.

The medical officer of health was informed, and the patient was taken off work as a degreaser.

At the end of June he noticed a "drawing, pulling" sensation on the right side of the face, and that that side felt different when shaving. His right eye began to feel odd, "uncomfortable, as if the eye is coming out." He had several attacks of vertigo, and was becoming depressed.

On 6 July he was found to have analgesia in all divisions of the right trigeminal nerve, and the complete loss of taste on the anterior two-thirds of both sides of the tongue persisted. Perimetry showed an enlargement of four degrees of the blind spot on the right compared with the left.

The following investigations showed nothing abnormal: X-ray examination of chest, skull, and hands, haemoglobin, white blood count, platelets, erythrocyte sedimentation rate, cerebrospinal fluid, electroencephalogram, gamma brain scan, electronystagmogram, Wassermann reaction, and serum calcium.

Since then there has been no recovery of taste or trigeminal sensation, and no improvement in the right visual field. He regained his lost weight within a few months, and the episodes of vertigo subsided.

The results of psychometry performed in January and in March 1968 suggested the possibility of early organic mental deterioration, but were not conclusive. On Eysenck's personality inventory he was not found to be neurotic.

COMMENT

Metal degreasing is the occupation from which most chronic toxic effects have been reported. Our patient was exposed for only six weeks, an unusually short duration for the development of chronic poisoning, which has been claimed never to occur with exposure of less than a few months (Ahlmark and Forssman, 1951; Grandjean *et al.*, 1955). The effects of trichloroethylene must depend on the intensity as well as the duration of exposure. The trichloroethylene vapour density is higher if open vats are used, if the condenser coils are inefficient, if the articles are removed by hand, or if only a short time is allowed for them to drain before being removed from the vats (Grandjean *et al.*, 1955). All these conditions were fulfilled in this case.

Trigeminal analgesia is the commonest cranial nerve disturbance to be reported. Because the trigeminal analgesia was thought to be a specific effect of trichloroethylene, it was used in the treatment of trigeminal neuralgia with encouraging results (Plessner, 1916; Hildesheimer, 1921; Seelert, 1922), but later reports (Kramer, 1921; Blumenthal, 1924; Glaser, 1931) showed that the effect was due to general analgesia. Cases of trigeminal analgesia after industrial exposure were reported by Stüber (1931), Grandjean *et al.* (1955), Andersson (1957), Hill (1966), and Buxton and Hayward (1967), and after anaesthesia by Hewer (1943) and Humphrey and McClelland (1944). Bardoděj and Vyskočil (1956) studied workers in contact with trichloroethylene, and often found a neuropathy affecting the brachial plexus and first division of the fifth cranial nerve. Dillon (1956) described trigeminal analgesia in a woman after repeated inhalation of trichloroethylene for relief of pain due to malignant disease.

The second cranial nerve may be damaged (Plessner, 1915; Baader, 1927; Stüber, 1931; Teleky, 1931; Isenschmid and Kunz, 1935; Chief Inspector of Factories, 1954). Buxton and Hayward (1967) demonstrated an enlarged blind spot in one eye and a paracentral scotoma with constriction of the visual field in the other eye in one of their patients. Loss of taste was found by Plessner (1915), Cotter (1950), Yoshiya (1952), and Buxton and Hayward (1967).

Dizziness and unsteadiness have been attributed to the narcotic effect of trichloroethylene, though these symptoms often persist after the narcotic effect has worn off. Cotter (1950), Hill (1966), and Buxton and Hayward (1967) described cases after acute exposure. Bardoděj and Vyskočil (1956) found this in industrial workers, as did Grandjean *et al.* (1955), and Hickish *et al.* (1956) also reported a case.

Psychosomatic symptoms are the most commonly described complication of trichloroethylene exposure (Lachnit and Rankl, 1950; Trense, 1965). Bardoděj and Vyskočil (1956) showed that these symptoms became more frequent with increasing excretion of trichloroacetic acid, a metabolite of trichloroethylene, but Frant and Westendorp (1950) found no correlation between symptoms and trichloroacetic acid excretion, and Andersson (1957) thought the symptoms were neurasthenic and not necessarily connected with trichloroethylene.

Borbely (1956) described phases of chronic trichloroethylene intoxication with the eventual development of organic dementia. Grandjean *et al.* (1955), in their study of 50 metal degreasers, found evidence of slight or moderate "psycho-organic syndrome" in 34%. They noted that neither neurological nor psychotic syndromes occurred in workers exposed to trichloro-

ethylene for only a few months. Bardoděj and Vyskočil (1956) also found mental impairment in some of their workers. Trense (1965) examined 342 workmen and found 108 showing evidence of the "psycho-organic syndrome."

The electroencephalogram is usually unaffected. Andersson (1957) concluded that the six mild non-specific abnormalities seen in her patients were not significant. However, a high incidence of such abnormalities is reported in Czechoslovakia (Chalupa *et al.*, 1960).

Trichloroethylene as an anaesthetic no longer produces neurological complications, but when used in industry the nervous system may be damaged. This is unlikely to be due to trichloroethylene itself, but may be due to breakdown products formed before inhalation, to metabolites formed in the body, or to triethylamine, which is used as a stabilizer in the industrial fluid but not in the anaesthetic fluid (Trilene).

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