POLYNEURITIS AFTER EXPOSURE TO DINITRO-*ORTHO*-CRESOL

BY

HUGH STOTT, M.D., D.P.H., D.I.H.

*Specialist in Occupational Health, Labour Department,
Kenya*

Although polyneuritis is known to occur as the result of exposure to certain of the aromatic carbon compounds such as benzene, dinitrobenzene, dinitrotoluene, and trinitrotoluene there does not appear to be any record of its occurrence among persons exposed to dinitro-*ortho*-cresol (D.N.O.C.). Nadler (1935) has, however, recorded two cases of peripheral neuritis caused by dinitrophenol (D.N.P.) given therapeutically for the treatment of obesity. As D.N.P. and D.N.O.C. are not only chemically closely allied but exert a similar physiological action on the living cell, it is not unreasonable to suppose that D.N.O.C. also might cause similar neurological complications. Two cases of polyneuritis have been observed, and are described here, among staff who were servicing aircraft which were being used for spraying D.N.O.C. on locust swarms.

Case 1

A male native Mkamba, aged about 47, had been engaged continually for two months on checking and cleaning the jets on the spray booms of aircraft spraying a 20% solution of D.N.O.C. in oil. He was working in hot and arid areas of Kenya and Tanganyika, and, in spite of regulations to the contrary, he had been wearing no protective clothing of any sort. He stated that he washed his hands invariably before eating and drinking, and that he did not smoke. He strongly denied that he cleaned out blocked jets by blowing through them, and said that he had noticed that the maximal staining with D.N.O.C. was on his arms, hands, and feet.

He said that his symptoms started about one month after his first exposure to D.N.O.C., when he began to feel a sensation of pins-and-needles on the back of his hands and fingers. A little later his legs were similarly affected. He had no difficulty in walking or handling objects, but he had particularly noticed that he sweated excessively on his arms from the mid-forearm down to his fingers, and on the lower third of his legs. Apart from this localized sweating he had no excessive sweating from other parts of his body. He had no other complaints, but on being questioned carefully he thought that latterly he had become unduly thirsty. He denied that he had had any restlessness, insomnia, or upset in his appetite, and he was unable to say whether he had lost any weight.

He was admitted to hospital three days after his last exposure to D.N.O.C., and on examination his temperature was 99° F. (37.2° C.) and his pulse 80. There was marked yellow staining from D.N.O.C. both on the palms of his hands and on the soles of his feet. There was a loss of sensation to pinprick and cotton-wool on the back of all his fingers, and sweating was very marked on the lower parts of his arms and the backs of his hands. He also had loss of sensation to pinprick and cotton-wool on the dorsal aspect of the toes of both feet, and much sweating was observed over the lower legs and feet. There was no evidence of excessive sweating on any other part of his body. He showed no loss of motor function or co-ordination in his arms and legs. The arm-jerks were equal and normal, but the right knee-jerk was depressed. No other abnormality was found in the nervous or other systems. The serum D.N.O.C. level one week after his last exposure was 7.6 µg./ml., and his B.M.R. a fortnight after his last exposure was +6%.

His condition cleared rapidly, and after nine days in hospital, and 12 days after his last exposure, he had neither symptoms nor signs.

Case 2

A male Asian aged 24 was engaged by the same firm as the above patient. His job was to clean and reservice the engines and spraying system of aircraft which were spraying a 20% solution of D.N.O.C. in oil. He was doing this job in the field for 10 days, and after this he returned to base, where he was engaged for a further week overhauling and testing the engine and spraying-gear of an aircraft which had been used for spraying D.N.O.C. He was therefore exposed to contact with D.N.O.C. for a total of 17 days, and during this time the only protective clothing he wore was a white overall over his clothes. He stated that he frequently washed his hands, and always before eating and drinking. He was a non-smoker, and he denied that he "blew out" the jets of the spraying-boom in order to clean them. He was sure that neither he nor the other patient (Case 1) was exposed to D.N.O.C. spray from the aircraft.

He was seen 17 days after his first exposure to D.N.O.C., when he complained that he had felt tingling sensations on the backs of his fingers for the previous four days. These were restricted to his fingers and had not occurred on his feet, but recently his legs tended to become numb at night. He did not complain of excessive sweating or thirst, although he thought that he might have lost a little weight within the recent past. His appetite had been satisfactory and he had suffered from no restlessness or insomnia.

On examination his hands were stained a bright yellow, but there was no sign of staining on other parts of his body. There was no loss of sensation to pinprick or cotton-wool on his hands or his feet, and clinical examination of the neurological and other systems showed no abnormality. He had a localized petechial rash over the left shoulder-joint which he had first noticed the day before examination. Serum D.N.O.C. estimations were performed. The first, done after he had been exposed for a week, was found to be 16.8 µg./ml., and the second, done on the day of examination, and the last day of exposure, was found to be 11.5 µg./ml.

He was removed from exposure, and after a week all his symptoms had disappeared.

Discussion

Both these cases occurred in men who were particularly exposed to contamination of the skin by D.N.O.C. They wore no protective clothing in spite of constantly handling parts of the aircraft which were heavily contaminated with the chemical. The position was aggravated by the fact that the spraying-gear on the aircraft often needed attention owing to the blockage of nozzles on the spraying-boom, and this inevitably led to very heavy skin exposure.

Both men insisted that they had always washed their hands and arms thoroughly before drinking and eating, and as there was corroborative evidence to substantiate this it is unlikely that they ingested much D.N.O.C. As neither of them smoked this possibility is further reduced. Neither man was particularly exposed to inhalation of D.N.O.C., as they were not working anywhere near the field of spraying operations. The low serum D.N.O.C. levels in both cases confirm that the inhalation and ingestion of the chemical was not of a high order. It was well below the level of 20 µg./ml. of D.N.O.C. in whole blood, corresponding to a serum level of about 40 µg./ml., which was found by Harvey *et al.* (1951) to result in mild symptoms of poisoning in five volunteers who were given pure D.N.O.C. by mouth. In Case 1 the D.N.O.C. level was not estimated until the patient had ceased to be exposed for seven days, but, assuming that he was excreting D.N.O.C. at a normal rate, it is unlikely that he would have had a level of 20 µg./ml. of whole blood at the time exposure ceased.

The peripheral neuritis in each of these cases made its appearance before any general effects of D.N.O.C. poisoning were noted by the patient, and indeed before these would be expected as judged by the serum D.N.O.C. level. It is therefore tempting to speculate whether the symptoms were due to the action of D.N.O.C. locally following its absorption through the skin. D.N.O.C. stimulates the general metabolism of man by acting peripherally and directly on the cell, and it exerts its action independently of thyroxine. It is believed that the carbohydrate metabolism and breakdown is increased and that the resultant energy is converted to heat rather than muscular work. Where skin contamination is great, as in these two cases, the local concentration of D.N.O.C. at the site of absorption must be much greater than in the blood stream, and it is possible that under these circumstances a local effect might be exerted on the tissues before general symptoms would occur, and even without the necessity for their occurrence. The localized appearance of symptoms in these cases are suggestive. The hands, which were the most contaminated parts of both patients, were affected first and most severely, and in Case 2 the feet, which were unstained with D.N.O.C., were unaffected. The sweating which was noticed in Case 1, and which was strictly confined to those areas particularly exposed to D.N.O.C., certainly suggests a local action by the chemical.

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OCULAR NERVE PALSY ASSOCIATED WITH SEVERE HEADACHE

BY

A. P. B. WAIND, D.S.C., M.D., M.R.C.P.
*Consultant Physician, North Lonsdale Hospital,
Barrow-in-Furness*

In 1955 Jackson described four cases of ocular nerve palsy associated with severe headache occurring in diabetic patients. He pointed out that such an association of pain and ocular nerve palsy in diabetics has been only rarely mentioned in the literature (Groenouw, 1920; Herson, 1948; Larson and Auchincloss, 1950; Goodman *et al.*, 1954). Hirson *et al.* (1953) have also described a similar case. I have recently seen two cases of this syndrome in diabetics and an entirely similar case in a non-diabetic.

Case Reports

Case 1.—A man aged 60 was first seen in April, 1954, complaining of thirst, polyuria, and loss of weight. He was found to have diabetes and was well controlled on a mixed dose of 20 units of soluble and 20 units of zinc-protamine insulin. In June he developed diplopia due to a right external rectus palsy. This recovered spontaneously in August. Towards the end of March, 1955, he developed pain localized in the first and second divisions of the right fifth nerve. This increased in intensity and was followed by complete third-nerve palsy on that side at the beginning of April. There were no other abnormal physical signs; the Wassermann reaction was negative and radiographs of the skull and a right carotid angiogram were normal. In May complete recovery of paresis took place, with relief of the pain.

Case 2.—An elderly obese woman aged 72 was first seen in 1951 with thirst and pruritus vulvae. She was found to be a diabetic and was treated with a 1,500-calorie diet. She did not attend the diabetic clinic, and was lost sight of until October, 1955. A fortnight previously she had wakened with complete ptosis of the right eyelid, and a week later severe pain started in the area of the first division of the fifth right nerve. On physical examination she was found to have a complete third-nerve palsy on the right side. Her diabetic condition was somewhat better than might have been expected, inasmuch as her urine was clear of sugar most of the day. There was, however, diabetic retinopathy, with loss of knee- and ankle-jerks. Her blood pressure was 180/110. The W.R. was negative. Her condition gradually resolved, relief of pain preceding recovery of the paralysis, which had disappeared by the early part of December, 1955. The patient refused admission to hospital, and other investigations were not possible.

Case 3.—A man aged 51 was first seen on November 10, 1955, when he gave a history that seven weeks previously he had started to have severe pain in the distribution of the first division of the left fifth nerve. This was accompanied by drooping of the lid of the left eye and double vision. The pain abated after two weeks, and by the time he was seen in the out-patient department his ptosis and double vision had disappeared. On examination there were no abnormal physical signs, no sensory loss in the area of the left fifth nerve, and no diminution of the left corneal reflex. His blood pressure was 140/80, and the urine was clear. X-ray examination of the skull, the W.R., glucose-tolerance test, full blood count, and E.S.R. were all normal.

Discussion

The first two of these cases support Jackson's observations that a syndrome of ocular nerve palsy associated with headache occurs in diabetics. The third case is clinically identical, except that the patient is not a diabetic.

This syndrome of ocular nerve palsy associated with headache, presumably due to involvement of branches of the fifth nerve, has been recognized for a long time, and has been attributed to orbital periostitis affecting the sphenoidal fissure. Brain (1947) has pointed out that the prognosis of this disorder is good and recovery takes place within a few months.

In Jackson's cases, and in those reported here and in the literature referred to, such spontaneous recovery within three months was invariable. In my cases recovery took place independently of treatment. This property of complete recovery within a relatively short space of time is in my opinion the most noteworthy feature of this syndrome, and must always be borne in mind when speculating upon its aetiology. It suggests that the proximate aetiology of diabetic and non-diabetic cases is the same, and that therefore the syndrome is not specific to diabetes, although it may well be relatively common in that condition.

In recent years cases such as these have usually been ascribed to pressure upon nerves exerted by supraclinoid aneurysms of the internal carotid artery. There are reasons for believing, however, that such aneurysms may not be responsible for all of these cases. Firstly, the natural history of this disorder with its short course and spontaneous recovery does not accord well with that of aneurysm (Jefferson, 1938). Secondly, if these cases are due to aneurysm it is difficult to understand why recovery is not followed more often by occlusion of the internal carotid artery with the production of central signs. Finally, there is the evidence against aneurysm provided by those occasions when angiography has failed to demonstrate an aneurysm.

It seems, therefore, that this syndrome of ocular nerve palsy associated with headache is perhaps relatively common in diabetes but not specific to that disease, that recovery usually takes place within three months, and that some cases at least are not due to supraclinoid aneurysm of the internal carotid artery.