Medical Memoranda

Treatment of Status Asthmaticus with Nitrogen Mustard

Professor C. Jiménez Díaz and his associates (1950, 1951) have reported encouraging results with nitrogen mustard in the treatment of status asthmaticus. The value of cortisone and A.C.T.H. in alleviation, temporarily at least, of severe and exhausting symptoms of the asthmatic state now seems to be definitely established (Bordley *et al.*, 1949; Randolph and Rollins, 1950; Friedlaender and Friedlaender, 1951). A certain relationship seems to exist between these hormones and nitrogen mustard. During the administration of nitrogen mustard there occurs progressive lymphopenia and eosinopenia. The same results can be obtained with A.C.T.H. and cortisone (Dougherty and White, 1943; Thorn *et al.*, 1949). Noting the close relationship that exists between A.C.T.H. and cortisone on the one hand, and nitrogen mustard on the other, Díaz and his associates decided to try nitrogen mustard in asthma. Their extremely encouraging results prompted the use of nitrogen mustard in the following case.

CASE REPORT

A girl aged 13 had been having attacks of bronchial asthma for the past two years. In the beginning these occurred at infrequent intervals and were quickly relieved by the administration of adrenaline. During the second year the frequency and severity of the attacks had gradually increased, but they could still be terminated by adrenaline. On February 1, 1951, the patient had another severe attack. She was given an injection of adrenaline, which brought only slight relief lasting for about one hour. Repeated injections of adrenaline and ephedrine failed to give her any further relief.

On the morning of February 2 she was given an intravenous injection of 0.25 g. of aminophylline. She had prompt relief of her symptoms, which, however, lasted for only about eight hours. In the evening she was given a further 0.25 g. The relief produced this time, however, was not so dramatic and lasted for a shorter time. During the next two days she had repeated injections of adrenaline, aminophylline, and khellin with minimal response. Her general condition during the past four days had deteriorated considerably. She was unable to lie down in bed and was completely exhausted. At this stage it was decided to administer nitrogen mustard intravenously. Her white blood cell count at this stage was 10,328 per c.mm. (polymorphs 45%, lymphocytes 39%, eosinophils 14%, monocytes 2%).

Nitrogen mustard, 2.5 mg. dissolved in 2.5 ml. of normal saline, was administered intravenously very slowly. No precautions were taken to prevent the vomiting which usually occurs a few hours after the intravenous administration of nitrogen mustard, since it was thought that by liquefying the tenacious bronchial secretions the vomiting might further benefit the patient. One hour after the injection the condition of the patient began to improve. Vomiting started two hours after the injection; anything by mouth provoked it. In the next six hours she vomited about 15 to 20 times. As anticipated, the bronchial secretions were to a great extent liquefied, and she was able to expectorate with great ease. Eight hours after the first injection her clinical condition was much improved. There was no more respiratory discomfort, and on examination her chest was much clearer. She was now able to lie down in bed without discomfort. Vomiting, however, was still occurring, and at this stage she was given phenobarbitone, 1½ gr. (0.1 g.), after which the vomiting gradually stopped and she slept an uneventful night. Next morning she had no asthmatic symptoms and no foreign sounds could be heard in the chest. All anti-asthmatic treatment was suspended. Her white blood cell count at this stage was 11,240 per c.mm. (polymorphs 66%, lymphocytes 29%, eosinophils 5%, monocytes 0%).

Further injections of 2.5 mg. of nitrogen mustard were given intravenously on alternate days to a total of four injections. She was given 1½ gr. (0.1 g.) of phenobarbitone immediately after the injections to diminish vomiting, the severity and frequency of which was much diminished by this procedure.

Since her last injection of nitrogen mustard the patient has been seen and examined repeatedly till the time of writing (about three and a half months), and she has remained completely symptom-free.

COMMENT

The management of status asthmaticus often becomes a serious medical problem. It taxes the skill, patience, and experience of all physicians. Rigorous methods of treatment may sometimes be justified in an occasional case. The advent of A.C.T.H. and cortisone in the field of therapeutics is a real advance in the management of severe intractable cases of status asthmaticus; indeed, their use may be a life-saving procedure in certain cases. But the prohibitive cost of these drugs often precludes their use in a really deserving case. Nitrogen mustard, which is a comparatively cheap drug, has given very encouraging results in the hands of Continental workers. The case reported above confirms its versatility. The benefit produced by it parallels the fall in the eosinophil count. But nitrogen mustard is a potentially toxic drug, and it is essential that blood counts be carried out at regular intervals to prevent a serious depression of the bone marrow.

As yet it is too early to draw any conclusions on the therapeutic efficacy of nitrogen mustard in asthma, but the response obtained in the above case and by Continental workers warrants further clinical trials.

ADDENDUM.—Since this case report was written three further cases of chronic bronchial asthma have been treated with nitrogen mustard with encouraging results.

B. P. ARYA, M.D.

Nairobi.

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Isolation of Bact. Coli O.26.B.6 from a Child with Recurrent Diarrhoea

Specific serological types of *Bact. coli* are now fairly widely recognized as a factor in the aetiology of infantile gastro-enteritis. So far, however, there are few reports of such organisms playing a pathogenic part in the later age groups.

CASE REPORT

In October, 1952, a mother brought her daughter, aged 12, to me suffering from diarrhoea. The girl had been quite well until eight days previously, when her stools became watery and yellow, and she had frequent bouts of abdominal colic. These symptoms lasted two days, and the girl was free from symptoms until the night before seeing me, when again she had abdominal pain followed by diarrhoea.

Asked whether anyone else in the family had had a similar illness, the mother said that her son, aged 1 year, had had stomach trouble for the previous three months. The baby seemed well, but about once a week had had frequent loose stools. She had attributed this to teething.

I requested a pathological examination of the faeces of both these children. A report on the infant stated that *Bact. coli* type O.26.B.6 was present and that no other intestinal pathogens or parasites were found.

I then asked for an examination of the older child's stool, with special reference to the presence of this type

of *Bact. coli*. The organism was found to be present. Both strains were found sensitive to sulphathiazole and chloramphenicol.

Treatment.—While investigations were being made, both patients were treated symptomatically with kaolin. This had no effect, for the condition recurred under my observation—that is, normal bowel action for five days was followed by pain and loose discoloured stools for two days.

I gave a seven-day course of sulphathiazole. During this treatment symptoms were absent, but at the end of treatment the specific strain of *Bact. coli* was still present, and a week later the condition relapsed. Chloramphenicol was then given, diarrhoea ceased at first but returned after five days' treatment (possibly due to the drug). I then instituted a combined course of chloramphenicol and sulphathiazole extending over ten days. Diarrhoea stopped and pains ceased. A week after the end of this treatment, specimens from both children were negative. Further specimens remained negative. After three months both children were well.

COMMENT

Two children, aged 2 years and 1 year respectively, suffered from recurrent diarrhoea and colic. Repeated faeces examinations revealed none of the usual intestinal parasites or pathogens, but a sero-specific strain of *Bact. coli*, Type O.26.B.6, known to be associated with infantile gastro-enteritis, was repeatedly isolated from the faeces of both children, and not until the organism had disappeared from the stools after a course of sulphathiazole and chloramphenicol did clinical recovery take place. Specimens examined from the unaffected members of the household were consistently negative for *Bact. coli* O.26.B.6.

It therefore seems worth while to consider such organisms when investigating cases of diarrhoea even after the age of infancy.

I am grateful to Dr. M. Thomas, of the Public Health Laboratory, Edmonton, for examining the faeces specimens from these cases.

R. L. MACQUEEN, M.R.C.S., L.R.C.P.,
General Practitioner, Edmonton.

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Acute Psychotic Reaction after Inhaling Methylamphetamine

The following case is reported because of its unusual psychiatric interest and also to indicate a possible danger in the indiscriminate use of the amphetamine group of drugs by inhalation of the vapours.

There appear to have been no similar cases reported in the literature or known to the manufacturers of these inhalers. There have, of course, been many cases of addiction and even of psychosis associated with ingestion of amphetamines, and in this connexion inhalers are often used as a ready source of the solid drug.

CASE REPORT

A man aged 41 was admitted on July 8, 1951, to a mental hospital on an urgency order. Physical examination revealed a robust healthy man. He was rather flushed and sweated readily; pulse 100; blood pressure 150/92. There were a few rhonchi in both lung fields. Further investigations showed him to have nasal polypi and chronic maxillary antritis. The urine contained traces of sugar and acetone. The Wassermann reaction and Kahn test were negative. Mentally he was well orientated, but acutely hallucinated both visually and aurally. He was anxious and had severe insomnia. His pockets contained five "methedrine" inhalers, which before use had each contained 250 mg. of methylamphetamine base.

On July 11, after rest and sedation, he was much improved and able to give the following history. He was an Irish unskilled worker who had been separated from

his wife and living alone in this country for many years. He denied alcoholism and any previous mental illness in himself or his relatives. On the evening before admission he had felt unwell and had used his inhalers to relieve his nasal congestion. He often used them three or four times an hour, and thought that on this occasion he may have inhaled as often as every five or ten minutes. He admitted that they gave him a pleasant feeling, described as a "lift" with something sexual about it. After a few hours he had noticed that he "saw" women and animals in the room, although he realized they were unreal.

These hallucinations were in bright colours and were rather diminutive. He also described an illusion in which a coat over a chair "turned into a woman." He had the feeling that these happenings were supernatural, and seeing some shadows at the window of a house opposite he got the idea that he was being hypnotized. He went over the road to investigate and called in the police. It was this that led to his admission to hospital.

By July 15 he had completely remitted, but voluntarily remained in hospital in order that certain tests could be carried out. He appeared intelligent and informative, if not garrulous, but gave the impression of being a rather unreliable witness. His affect was cheerful and congruous, but a little shallow. The hallucinations had gradually disappeared over four to five days.

A Rorschach test was carried out on July 26. With full co-operation the patient could produce only 13 responses. His intelligence was tested on a shortened Wechsler verbal scale; it gave an I.Q. of 120. It seemed likely that his meagre and constricted Rorschach record was due to an "accuracy compulsion" so powerful as to inhibit his ability to make anything of the ink-blots.

On July 27 he was given 30 mg. of methylamphetamine intravenously. He became flushed, his pulse rose to 120, and his blood pressure to 190/120. He expressed a feeling of well-being and a desire to "get up and do things." He stated that marks on the ceiling became more conspicuous and that when he looked up at a certain object he felt as if it looked back at him. Colours appeared to change and he had erotic sensations. He later remarked on the similarity of these feelings to those following methedrine inhalation.

In 30 minutes he appeared to have recovered and was subjected to a second Rorschach test. The number of responses had risen to 47, considerably more than is usual, in spite of the compulsiveness being still very marked. He left hospital the next day, but later claimed that the injection test had produced hallucinations lasting for several days, which he had kept quiet about.

Six weeks later he had a third acute hallucinatory episode following the further use of inhalers. He then underwent an operation for removal of his nasal polypi and has apparently remained well since.

COMMENT

There seems to have been established in this case a causal relationship between methylamphetamine absorbed by inhalation and an acute psychotic reaction. The drug was, of course, used in excess of the recommended dose. Also it appeared that the man's previous personality was such as to predispose to psychotic breakdown and possibly to addiction. The illness was at first thought to be an acute schizophrenic episode, but was subsequently diagnosed as an acute organic confusion, although confusion in the sense of severe disorientation was singularly lacking. However, the overactivity and the paranoid element were fairly typical of previously described amphetamine psychoses. It is thought possible, in view of the time lag of a few hours after injection before the occurrence of definite hallucinations, and their persistence for several days, that the psychotic reaction may not have been directly due to the action of the drug on the higher centres, but to a withdrawal or exhaustion phenomenon.

R. B. CARR, M.B., B.S., D.P.M.,
Late Senior Registrar, Friern Hospital, London, N.11.