Medical Memoranda

Disseminated Lupus Erythematosus, with Renal Involvement, Treated with Nitrogen Mustard

Nitrogen mustard was used by Chasis *et al.* (1949) in treating patients with glomerulonephritis. It was assumed that this disease was caused by an antigen-antibody reaction, and known that nitrogen mustard inhibited such reactions. Baldwin *et al.* (1953) found that, while the course of glomerulonephritis was not influenced by nitrogen mustard, temporary remissions might occur in some patients. Rohn and Bond (1953) treated five cases of disseminated lupus (without renal involvement) with nitrogen mustard. Three were benefited and remissions of 6–217 days were noted. Dubois (1954) treated 24 cases of disseminated lupus with cortisone (or corticotrophin) and nitrogen mustard : 15 had renal involvement with oedema and 13 were benefited ; 2 had renal involvement without oedema and were not benefited ; and 7 without renal involvement had no benefit. It was pointed out that the greater the oedema the more spectacular the result.

Nitrogen mustard may also be effective in oedematous nephroses due to other causes (Taylor *et al.*, 1950 ; Kelley and Panos, 1952).

The following case is recorded because no similar report has been seen in the British literature. There was a dramatic response to nitrogen mustard when cortisone could not be given.

Case Report

A married woman aged 31 was admitted to hospital in September, 1954, complaining of headaches and slight swelling of the feet. Two years previously, when seven months pregnant, she had been in hospital with toxaemia of pregnancy. Blood pressure was then recorded at 140/90. A healthy baby was born after the labour had been artificially terminated. For 18 months her feet had been swollen at the end of the day and for a few months she had been unduly dyspnoeic on exertion. Ten days before admission her headaches had become severe and albuminuria was discovered. At the age of 20 she had a " nervous breakdown " severe enough to require hospital admission. There were no abnormal physical signs beyond albuminuria and a slight fever (reaching 99° F. (37.2° C.) every day). Blood pressure was 140/85 and the blood urea 20 mg. per 100 ml. Two weeks later, however, she was readmitted because she had developed generalized oedema, joint pains, and vomiting.

On examination her temperature was 100° F. (37.8° C.) Her face was swollen and there was pitting oedema of the sacrum and legs. The pulse was 90 and regular ; B.P. 170/110 ; no cardiac enlargement. A loud systolic murmur was present over the praecordium. The fundi were normal. The right kidney was easily palpable and tender. There was no evidence of a peripheral neuritis or arthritis, and no rash was present.

Ten days later she developed a left-sided pleural effusion and a pericardial friction rub was heard, as was a presystolic triple rhythm. An intermittent fever, often reaching 101° F. (38.3° C.) every day, was present.

Investigations.—Urine : Albumin present (Esbach readings varied from 1 to 8 g. per litre) ; casts of all types were seen, while the specific gravity was often over 1020. Blood : Hb, 85% ; white cells, normal ; E.S.R., 59 mm. (Wintrobe, uncorrected) ; serum albumin, 2.4 g.% ; serum globulin, 2.1 g.% ; blood urea, 50 mg. per 100 ml. ; L.E. cells present in peripheral blood.

A diagnosis of disseminated lupus erythematosus with renal involvement was made.

Treatment.—Despite the history of a " nervous breakdown " and the presence of many neurotic symptoms, 200 mg. of cortisone was given daily. The fever lessened and she seemed to improve, but no diuresis occurred. After 12 days' treatment with cortisone she became depressed and there were marked mental disturbances. The dose of cortisone was reduced, but three days later it had to be discontinued because of her mental condition. Her general condition then rapidly deteriorated and the blood urea reached 140 mg. per 100 ml. Corticotrophin gel, 60 units a day, was then given, and she became afebrile ; but no diuresis was noted, and after 10 days she again became depressed and hallucinated, and the corticotrophin had to be discontinued. A small dose of cortisone, 12.5 mg. twice daily, was then tried, but after four days it had to be discontinued because of mental symptoms. Bilateral pleural effusions were aspirated. At this time the patient was grossly oedematous and febrile, and had a blood urea of 100 mg. per 100 ml. In view of her condition, and our inability to use cortisone, on December 26 we gave 10 mg. of nitrogen mustard in 500 ml. of 5% dextrose. Within two days there was a marked diuresis, and in eight days she had lost 6 lb. (2.7 kg.) in weight. Twelve days later a further 10 mg. was given, and again there was a marked diuresis. She was discharged soon after this, free from oedema and with a blood urea level of 45 mg. per 100 ml. A slight fever and albuminuria were still present.

Follow-up.—One month later a goitre had developed, but with no evidence of toxicity. The B.P. was 180/100 ; no oedema ; blood urea, 25 mg. per 100 ml. ; a trace of albuminuria. Plasma proteins were normal quantitatively. Nine months later the goitre seemed larger and many psychoneurotic symptoms were present, but her general condition was good and she was able to do her own housework. The B.P. was 120/70 and the blood urea normal. Urine : trace of albumin ; no casts present. The E.S.R. was 52 mm. in one hour. The blood cholesterol was 550 mg. per 100 ml. Plasma protein electrophoresis showed an increase in the gamma globulins. No L.E. cells were found. On reassurance and sedation the patient improved, but there was still some evidence of activity and renal involvement.

Comment

The history, physical signs, and pathological investigations allowed a firm diagnosis of disseminated lupus erythematosus with renal involvement to be made. The peculiar urine—showing all types of casts with protein in the same specimen—is an unusual finding and has been described by Krupp (1943). Neither cortisone nor corticotrophin could be continued with because of severe mental disturbances, but they did seem to cause slight improvement, particularly in lessening fever. We had to look for alternative treatment, and Dubois's article was consulted. He recommended a dose of nitrogen mustard equivalent to 0.4 mg. per kg. body weight and gave 20 mg. to most of his cases as a single dose.

While the occurrence of spontaneous remissions in this condition are appreciated, the dramatic effect of nitrogen mustard, when cortisone could not be given, was impressive.

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Acute Dexamphetamine Sulphate Poisoning in a Child

In recent years dexamphetamine sulphate (" dexedrine ") has become widely used. The general public is familiar with its use, and it has rapidly gained popularity as a slimming agent. It is also sometimes employed in the management of depressive states, narcolepsy (Harper, 1945), epilepsy (Livingston *et al.*, 1948), and enuresis in children.

A review of the literature between 1939 and 1954 shows that there have been at least eight reported fatalities attributed to amphetamine sulphate or its dextro-rotatory form, dexamphetamine sulphate (Smith, 1939 ; Ivy and Krasno, 1941 ; Pontrelli, 1942 ; Hertzog *et al.*, 1943 ; Gericke, 1945 ; Harvey *et al.*, 1949 ; Mitchell and Denton, 1950). Other

reports describe accidental poisoning, with recovery (Freyre, 1946, 1948; Fletcher, 1953).

Its toxicity is claimed to be slight, but nevertheless it is a source of accidental poisoning which may prove fatal. Pretorius (1953) reports the fatal case of a boy aged 3 years, who took 320 mg. of dexamphetamine sulphate. Pontrelli (1942) describes the case of a soldier aged 25 who took about 100 mg. with a fatal outcome. The child in the case reported below, aged 2 years 8 months, took 115 mg. and survived. It would appear from these three instances that tolerance for the drug varies greatly.

CASE REPORT

A child aged 2 years 8 months, weighing 32 lb. (14.5 kg.), was taken to a casualty department, having swallowed some of his mother's reducing tablets. Between 7.30 and 8 a.m. his brother, aged 5, had climbed on to a chair and taken a medicine box, thought to be out of reach of the children, from the top of a cupboard. The box contained 54 5-mg. tablets of dexamphetamine sulphate. He took one, disliked the taste, and handed the rest to his younger brother, who crammed as many as he could into his mouth. The total estimated amount of dexamphetamine sulphate taken was at least 115 mg.

At 8.30 a.m. the patient said he did not feel well. His mother noticed that he was very restless and agitated. Realizing what had happened, she took him to a hospital casualty department. His stomach was washed out through a Ryle tube, but no remains of the tablets could be traced. As he was very restless, with a pulse rate of 200 a minute, 2 ml. of paraldehyde and 2 gr. (0.13 g.) of sodium phenobarbitone, both by intramuscular injection, were given during the next five hours, in divided doses.

The child's condition failed to improve. He became completely uncontrollable, and lay rolling about, swinging his arms and legs continually. He was becoming exhausted, and was therefore admitted to the paediatric department of King Edward VII Hospital, Windsor, arriving five hours after taking the tablets.

Physical examination showed a well-developed little boy, who appeared acutely ill. He was hyperactive, throwing himself about wildly, although fully conscious and able to talk. His face was flushed, but his limbs and body were cold and clammy. The rectal temperature was 100° F. (37.8° C.). The heart rate was approximately 220 a minute and the respiratory rate very rapid. His eyes were staring, with widely dilated pupils, which reacted normally to light. Clinical examination was difficult, as he could not be controlled. Each time he was forcibly restrained he became more violent. He had also started to vomit.

In cases of death following dexamphetamine sulphate poisoning one of the post-mortem findings is marked cerebral oedema and congestion (Pretorius, 1953). It was therefore decided to give the child hypertonic magnesium sulphate intramuscularly in addition to sedation with barbiturates.

The magnesium ion also has a depressant effect on the central nervous system, as well as a curare-like action peripherally. Intramuscular injections of 5 ml. of a 25% magnesium sulphate solution and 1 gr. (65 mg.) of amylobarbitone sodium were given at approximately two-hourly intervals.

It was noticed that every external stimulus, however small, increased his hyperactivity. He was therefore nursed in a darkened sound-proof cubicle, in a cot with padded sides. The nurses were instructed not to touch him unless to prevent him injuring himself.

Fourteen hours after taking the tablets he was quieter and having short periods of rest. But the slightest stimulus caused him to cry and thrash about in his cot. His pulse rate had fallen and his general condition was improving.

During the second twenty-four hours in hospital he gradually had longer periods of sleep and needed no further sedation or magnesium sulphate. Vomiting had stopped and he started to take fluids. Hyperactivity persisted, and he forcibly resented examination. He was also confused and hallucinated.

By the third day he was irritable and excitable, and screamed at the slightest provocation. With persuasion he took a full diet. By the fourth day he had greatly improved and was allowed out of his cot. Marked ataxia and euphoria were present. By the sixth day he was symptom-free and appeared to be a normal healthy little boy. Subsequent physical examination showed him to be perfectly well.

Investigations.—Examination showed his urine to be normal. A blood count on the day after admission showed: haemoglobin, 90% (13.3 g. per 100 ml.); white cells, 13,100 per c.mm. (polymorphs 52%, lymphocytes 39%, eosinophils 7%, basophils 1%, mononuclears 1%). Blood counts ten days and three months after taking the tablets showed no significant change. An electroencephalogram eight days after he had taken the tablets was normal.

Dexamphetamine sulphate has been reported to have caused a panhaemocytopenia and eventual death in a student nurse aged 21 who took large doses over a long period (Mitchell and Denton, 1950).

COMMENT

There is no specific antidote for dexamphetamine sulphate poisoning. Recovery in the present case is attributed to several factors: the high natural tolerance of the child, sedation with barbiturates, relief of cerebral oedema with hypertonic magnesium sulphate, and protection from all forms of external stimulation.

Restraint of and interference with the child was reduced to a minimum. Disturbing routine measures were deliberately omitted. This method of nursing was adopted following the conclusions of Chance (1947), reached as a result of his work on the effect of amphetamine on mice.

In 1946 Chance showed that the lethal dose of amphetamine for mice in solitary confinement was 117 mg. per kg. body weight. When the mice were 10 in a cage the lethal dose fell to 14 mg. per kg. body weight. Later he reported that the most striking feature shown by mice which have taken large amounts of amphetamine is the wide variety of factors to which the mouse becomes sensitive. He suggested that the drug acts by sensitizing the central nervous system to incoming stimuli. Hiebel *et al.* (1954) have also shown that amphetamine is effective because it increases the activity of the reticular cells of the brain stem. This increased activity secondarily leads to intensified and prolonged cortical responses to incoming sensory stimuli.

Dexamphetamine sulphate is to be found in the medicine chest of many families. The potential danger of this drug is not always appreciated; often it is not locked away, and may be within easy reach of children. Cases of accidental poisoning in childhood occur with disturbing frequency, and this drug is yet another hazard. Trauma and poisoning, so often preventable, seem to be playing an increasing part in the mortality and morbidity of children.

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